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Basel (Switzerland), 10.–12. Mai 2023 / 10–12 mai 2023

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7ème Congrès de printemps SSMIG

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FM1

Severity of Pulmonary Embolism and Quality of Life

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Introduction: Up to 50% of patients who survive acute pulmonary embolism (PE) suffer from a decreased quality of life (QoL), dyspnea, or exercise intolerance at 3-12 months, a condition referred to as the post-PE syndrome (PPES). While the PPES is a consequence of deconditioning or cardiopulmonary comorbidities in most instances, it remains unclear whether the severity of the initial PE event has an impact on later QoL. We therefore evaluated whether QoL up to 12 months differed by PE severity at the time of presentation.

Methods: We used data from SWITCO65+, a prospective multicenter cohort of patients aged ≥65 years with acute symptomatic PE. The outcome was QoL up to 12 months. Disease-specific and generic QoL was assessed using the Pulmonary Embolism Quality of Life (PEmb-QoL) and the Physical (PCS) and Mental Component Score (MCS) of the Short Form-36 (SF-36) questionnaires, respectively, with higher scores indicating a better QoL. To assess whether QoL differed by PE severity, we compared QoL scores between higher- (≥1 point) vs. low-risk patients (0 points) based on the simplified Pulmonary Embolism Severity Index (sPESI) in a repeated measures mixed effects model with random intercepts, adjusting for previously identified predictors of QoL after PE.

Results: We enrolled 551 patients. The median age was 74 years (IQR 69-80) and 296 (54%) were male. Overall, 327 (59%) patients were in the sPESI higher risk category (≥1 point). The mean PEmb-QoL summary score was 65 ± SD 20 points at baseline and increased to 76 ±20 points at 12 months. While the mean PCS improved from 39 ±10 points at baseline to 44 ±10 points at 12 months, the MCS remained stable over time (49 ±12 vs. 50 ±11 points). Mean PEmb-QoL summary scores and SF-36 PCS (but not MCS) were statistically significantly lower in sPESI higher- vs. low-risk patients at each time point (Table).

Conclusion: While QoL following acute PE improves over time, patients with more severe PE continue to have a lower QoL up to 12 months than those with less severe PE. Whether patients with more severe PE may benefit from early rehabilitation measures must be prospectively examined.

Table: Difference in QoL between sPESI higher- and low-risk patients over time

Outcome	Time point	Adjusted mean difference (95%-CI)*	p-value
PEmb-QoL Summary Score	Baseline	-6.30 (-9.82;-2.77)	<0.001
	3 months	-7.72 (-11.24;-4.20)	<0.001
	12 months	-6.39 (-10.00;-2.79)	0.001
SF-36 Physical Component Score	Baseline	-3.54 (-5.27;-1.81)	<0.001
	3 months	-4.48 (-6.20;-2.75)	<0.001
	12 months	-3.80 (-5.59;-2.01)	<0.001
SF-36 Mental Component Score	Baseline	-1.33 (-3.40;0.75)	0.210
	3 months	-0.80 (-2.88;1.27)	0.446
	12 months	-2.05 (-4.19;0.09)	0.061

*Adjusted for sex, BMI, prior venous thromboembolism, classification of PE (cancer-associated, un-/ provoked), stroke/transient ischemic attack, immobilization, vascular disease, diabetes mellitus, arthritis, and fracture.

FM2

"Do-not-resuscitate" preferences of the general Swiss population: results from a National Survey

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Introduction: The aim was to assess the do-not-resuscitate preferences of the general Swiss population and to identify potential predictors influencing decision-making.

Methods: A nationwide web-based survey was conducted in Switzerland on a representative sample of the general adult population (18 – 99 years of age). The primary endpoint was the preference for a "Do Not Resuscitate" order (DNR Code Status) vs. cardiopulmonary resuscitation (CPR Code Status) in a clinical case vignette of a 70-year-old patient suffering from an out-of-hospital cardiac arrest with a no-flow time of 10 minutes. Secondary endpoint was participants' own personal preferences for DNR.

Results: Of 1138 subjects asked to participate in the web-based survey, 1044 agreed and were included in the final analysis. Preference for DNR was found in 40.5% (n = 423) in the case vignette and in 20.3% (n = 209) when making a personal decision for themselves. Independent predictors for DNR Code Status for the case vignette were: personal preferences for their own DNR Status (adjusted OR 2.49, 95%CI 1.72 to 3.6; p < 0.001), intubation following respiratory failure (adjusted OR 2.25, 95%CI 1.41 to 3.59; p = 0.001), time-period after which resuscitation should not be attempted (adjusted OR 0.91, 95%CI 0.89 to 0.93); p < 0.001), and estimated chance of survival in case of a cardiac arrest (adjusted OR per decile 0.9, 95%CI 0.84 to 0.98, p=0.01; which was overestimated by all participants.

Conclusions: Within this Swiss nationwide survey, the main predictors of "for or against" DNR related to personal preferences and the estimation of survival rates after a cardiac arrest; which were often overly optimistic. Overestimation of positive outcomes after cardiac arrest strongly influences patient opinion and should thus be addressed adequately during the shared decision-making process.

FM3

Impact of the COVID-19 pandemic on CVD prevention in Switzerland

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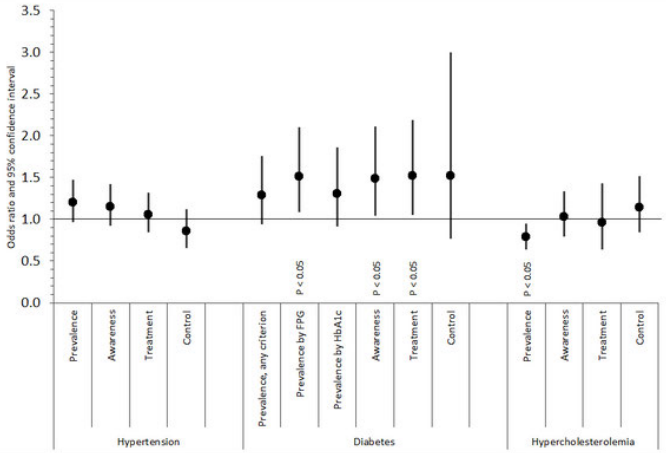
Introduction: The rapid spread of COVID-19 pandemic has disrupted nearly 75% of the health services worldwide, reducing in the number of patients admitted with CVD. Socioeconomic status (SES) is a major determinant of health. Whereas the COVID-19 pandemic increased the SES gap in CVD management is unknown. We aimed to compare management of CVD risk factors and the SES gap in CVD prevention before and during the pandemic.

Methods: Data from cross-sectional study conducted in Lausanne, Switzerland (CoLaus study), for the period between April 2018 (n=2883, 55.4% women, 65.7±10.0 years) and May 2021 (N=868, 56.0% women, 64.0±9.2 years) was used. For the CVD risk factors management, the management of three cardiovascular risk factors (hypertension, dyslipidaemia and diabetes) was considered. SES was defined by education and categorized as low (compulsory or apprenticeship), middle (high school) and high (university)-

Results: After multivariable analysis, no differences were found before and during the pandemic regarding prevalence, awareness, treatment and control rates for hypertension. For dyslipidaemia, prevalence decreased during the pandemic, while awareness increased and no differences were found regarding treatment and control. For diabetes, no differences were found regarding prevalence and control rates while awareness and treatment rates were higher during the pandemic (**Figure**). Regarding the association between SES and management of CVD risk factors, control of hypertension decreased during the pandemic among low and middle

SES categories (p for interaction<0.05), while no changes were found for prevalence, awareness and control. Also, no changes in the association between SES and dyslipidaemia prevalence, awareness, treatment and control were found during the pandemic. Prevalence of diabetes increased during the pandemic among low and middle SES categories (p for interaction<0.05), while no changes were found for awareness, treatment and control (**table**).

Conclusions: prevalence and management of CVD risk factors changed little during the pandemic. The SES gap tended to increase regarding hypertension control and the prevalence of diabetes.



Results are expressed as OR and 95%CI relative to the period before the pandemic.

	Before			P for	During			P for	P for interaction	
	High	Middle	Low	trend	High	Middle	Low	trend	Middle	Low
Hypertension										
Prevalence	1 (ref.)	1.05 (0.79 - 1.40)	1.19 (0.91 - 1.55)	0.200	1 (ref.)	1.54 (0.92 - 2.58)	1.68 (1.05 - 2.68)	**0.031**	0.246	0.271
Awareness	1 (ref.)	0.90 (0.66 - 1.23)	1.05 (0.79 - 1.39)	0.745	1 (ref.)	0.91 (0.52 - 1.59)	1.37 (0.84 - 2.22)	0.204	0.995	0.396
Treatment	1 (ref.)	1.19 (0.87 - 1.63)	1.26 (0.95 - 1.69)	0.112	1 (ref.)	0.84 (0.47 - 1.49)	1.35 (0.82 - 2.23)	0.233	0.277	0.932
Control	1 (ref.)	1.12 (0.76 - 1.64)	1.02 (0.72 - 1.45)	0.916	1 (ref.)	0.28 (0.14 - 0.59)	0.41 (0.22 - 0.78)	**0.006**	**0.001**	**0.015**
Diabetes										
Prevalence, any criterion	1 (ref.)	0.78 (0.47 - 1.28)	1.30 (0.84 - 2.01)	0.232	1 (ref.)	2.49 (0.91 - 6.82)	3.00 (1.18 - 7.62)	**0.021**	**0.029**	0.052
Prevalence by FPG	1 (ref.)	0.93 (0.54 - 1.62)	1.27 (0.78 - 2.07)	0.335	1 (ref.)	2.23 (0.81 - 6.19)	2.53 (0.99 - 6.48)	0.054	0.105	0.127
Prevalence by HbA1c	1 (ref.)	0.97 (0.54 - 1.75)	1.41 (0.84 - 2.38)	0.197	1 (ref.)	2.61 (0.79 - 8.68)	3.4 (1.12 - 10.32)	**0.031**	0.149	0.130
Awareness	1 (ref.)	1.36 (0.71 - 2.60)	2.06 (1.14 - 3.69)	**0.016**	1 (ref.)	2.10 (0.69 - 6.41)	2.76 (1.00 - 7.65)	**0.050**	0.476	0.498
Treatment	1 (ref.)	1.19 (0.62 - 2.25)	1.42 (0.79 - 2.55)	0.237	1 (ref.)	2.68 (0.81 - 8.89)	3.19 (1.04 - 9.76)	**0.042**	0.262	0.216
Control	1 (ref.)	0.37 (0.12 - 1.14)	0.74 (0.26 - 2.06)	0.560	1 (ref.)	0.88 (0.06 – 12.0)	0.84 (0.07 - 10.2)	0.893	0.766	0.737
Hypercholesterolemia										
Prevalence	1 (ref.)	1.08 (0.83 - 1.41)	1.50 (1.17 - 1.92)	**0.001**	1 (ref.)	1.03 (0.64 - 1.66)	0.93 (0.61 - 1.44)	0.759	0.868	0.074
Awareness	1 (ref.)	0.84 (0.58 - 1.22)	0.97 (0.69 - 1.37)	0.862	1 (ref.)	0.57 (0.29 - 1.14)	0.97 (0.53 - 1.80)	0.931	0.387	0.980
Treatment	1 (ref.)	0.87 (0.49 - 1.55)	1.04 (0.62 - 1.72)	0.892	1 (ref.)	0.47 (0.15 - 1.52)	1.4 (0.50 - 3.88)	0.519	0.578	0.404
Control	1 (ref.)	0.84 (0.55 - 1.27)	0.92 (0.63 - 1.33)	0.648	1 (ref.)	0.84 (0.38 - 1.84)	1.34 (0.67 - 2.68)	0.415	0.922	0.351

Multivariable analyses using logistic regression, and results were expressed as odds ratio and (95% CI). Analyses were adjusted on gender, age, marital status, smoking, and body mass index categories (normal, overweight, obese)

FM4

Is hyponatremia at hospital admission associated with higher risk of death within 1 year in multimorbid older adults?

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Introduction: Hyponatremia is the most common electrolyte disorder in older hospitalized patients. An association between hyponatremia and adverse outcomes such as mortality and hospital readmission in adults has been documented in observational data. Even though multimorbid older patients are most commonly affected, there are no large prospective studies focusing on them. Our aim was to assess the association between hyponatremia and mortality and readmission in multimorbid older patients.

Methods: This study used longitudinal data from a European multicenter, cluster randomized trial among hospitalized patients aged ≥70 years with ≥3 chronic medical conditions and taking ≥5 long-term medications followed for 1 year. We included participants with available sodium values at admission and excluded participants with hypernatremia. Hyponatremia was defined as serum sodium values <135mmol/l. Primary outcome was all-cause 1-year mortality, secondary outcomes were 30-day mortality, readmission at 1 year and 30 days. We tested the association between hyponatremia and mortality in comparison to normonatremia using a mixed-effects survival model, with adjustment for age, sex, comorbidities, study intervention, study site and cluster; and the association between hyponatremia and readmission using competing risk models with death as the competing risk. Subgroup analyses were performed across sodium categories (mild 134-130mmol/l, moderate 129-125mmol/l, profound <125 mmol/l).

Results: Of 2008 OPERAM participants, 1968 had a sodium value at admission, 33 were excluded due to hypernatremia (>145mmol/l). In 1935 participants, mean age was 79.4 years (standard deviation[SD] 6.3), 866 (44.8%) were female, median number of comorbidities was 11 (IQR 8-16), mean number of drugs 10 (IQR 7-13), 401 (20.7%) had hyponatremia at admission. The adjusted hazard ratio (HR) for 1-year mortality compared to normonatremia was 1.43 (95% confidence interval [CI] 1.13-1.81, p=0.003, 364 deaths), and the adjusted HR at 30 days was 1.16 (95% CI 0.72-1.87, p=0.55, 89 deaths). Adjusted sub-HR for 1-year readmission was 0.93 (95% CI 0.78-1.10, p=0.39), and at 30 days 1.11 (95% CI 0.78-1.59, p=0.55). There was statistically significant linear increase of 1-year mortality across hyponatremia categories (p=0.002).

Conclusion: Among hospitalized multimorbid older patients, hyponatremia at admission is associated with mortality at 1 year, with increasing risk for lower sodium values. Identification of the cause and treatment of hyponatremia are needed to potentially decrease this risk.

Table 1: Mortality and readmission in older multimorbid adults with hyponatremia vs. normonatremia in sodium categories

	n†	No. of events (%) †	Hazard Ratio*	95% CI	P
1-year mortality	**1935**	**364 (18.8)**			
Normal sodium°	1534	266 (17.3)	Ref.		
Hyponatremia	401	98 (24.4)	**1.41**	**1.11-1.78**	**0.005**
- mild°	283	66 (23.3)	1.31	1.00-1.73	
- moderate°	82	19 (23.1)	1.33	0.83-2.13	0.001¤
- severe°	36	13 (36.1)	2.64	1.50-4.67	
30-day mortality	**1935**	**89 (4.6)**			
Normal sodium	1534	66 (4.3)	Ref.		
Hyponatremia	401	23 (5.7)	**1.20**	**0.74-1.94**	**0.46**
- mild°	283	14 (4.9)	1.04	0.58-1.86	
- moderate°	82	4 (4.9)	0.97	0.35-2.68	0.02 ¤
- severe°	36	5 (13.9)	3.36	1.31-8.62	
1-year readmission	**1935**	**943 (48.7)**			
Normal sodium	1534	756 (49.3)	Ref.		
Hyponatremia	401	187 (46.6)	**0.94**	**0.79-1.11**	**0.46**
- mild°	283	135 (47.7)	0.94	0.77-1.15	
- moderate°	82	35 (42.7)	0.87	0.60-1.27	0.98 ¤
- severe°	36	17 (47.2)	1.03	0.64-1.69	
30-day readmission	**1935**	**210 (10.9)**			
Normal sodium	1534	163 (10.6)	Ref.		
Hyponatremia	401	47 (11.7)	**1.11**	**0.78-1.59**	**0.55**
- mild°	283	31 (11.0)	1.04	0.69-1.56	
- moderate°	82	11 (13.4)	1.27	0.70-2.31	0.40 ¤
- severe°	36	5 (13.9)	1.36	0.56-3.28	

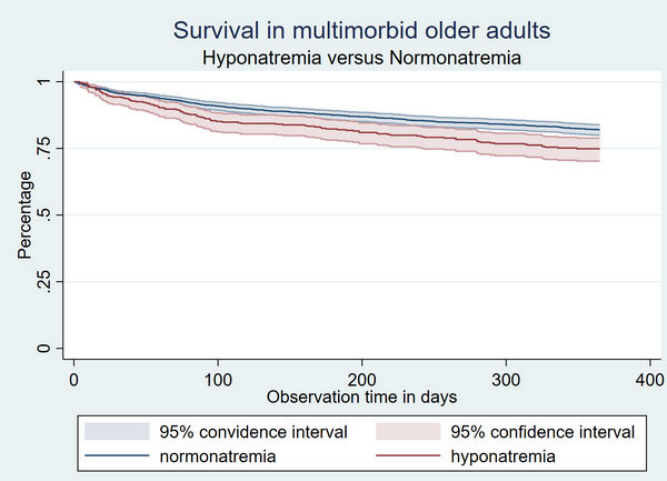
Abbreviations: No.: number, Ref.: reference, CI: confidence interval

*Hazard ratio comparing participants with hyponatremia (<135mmol/l) with participants with normal serum sodium levels. Higher numbers indicate higher likelihood of outcome for participants with hyponatremia. The results for mortality were obtained using a mixed effects survival model with adjustment for age, sex, intervention, weighted Charlson comorbidity index, and site. Cluster was added as a random effect. Readmission was obtained using a competing risk model with death as the competing risk, with otherwise the same adjustment variables.

†n/No. of events: number of participants overall, in hyponatremia and in hyponatremia categories, and the number of events (death or at least one readmission) in the corresponding participants.

°Sodium categories used were mild (134-130mmol/l), moderate (129-125mmol/l) and severe (<125mmol/l) hyponatremia in comparison to normal sodium values (135-145mmol/l).

¤Linear trend across sodium categories.



FM5

Prospective head-to-head comparison of risk assessment models to predict venous thromboembolism in medical inpatients: room for improvement

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Introduction: Provision of thromboprophylaxis is recommended in hospitalized medical patients at increased risk of venous thromboembolism (VTE). To simplify VTE risk stratification, risk assessment models (RAMs) have been developed. We aimed to prospectively validate a novel and easy to use RAM, the simplified Geneva score, and compare its prognostic performance with previously validated RAMs.

Methods: We conducted a prospective cohort study of acutely ill patients admitted to general internal medicine of 3 Swiss university hospitals. At admission, we collected items of 4 RAMs, i.e. the simplified and original Geneva score, the Padua score, and the IMPROVE score, and stratified patients into high and low VTE risk groups according to each RAM. Patients were followed for the occurrence of VTE within 90 days. We calculated sensitivity, specificity, and positive and negative likelihood ratios. Further, we assessed the predictive performance of all 4 RAMs by calculating sub-hazard ratios (sHRs) adjusted for pharmacological thromboprophylaxis use and the area under the receiver operating characteristic (AUC) curves.

Results: Of 1353 medical inpatients (median age 67 years, 44% women), 29 (2.1%) had a VTE event within 90 days. Based on the simplified Geneva score, 855 (63.2%) were classified as high and 498 (36.8%) as low risk, with a 90-day VTE risk of 2.7% and 1.2%, respectively. Sensitivity and specificity of the simplified Geneva score were 79.3% and 37.2%, respectively; positive and negative likelihood ratios were 1.26 and 0.56. Sensitivity was the highest for the original Geneva score (82.8%), while specificity was the highest for the IMPROVE score (67.7%). VTE risk adjusted for thromboprophylaxis use did not significantly differ in high and low risk groups based on the simplified Geneva score (sHR 2.07, 95% confidence interval [CI] 0.82-5.24, p=0.12) and other RAMs (**Table**). Discriminative performance was poor for all RAMs ranging from an AUC of 55.3% (95% CI 52.6-58.0%) for the original Geneva score to an AUC of 59.4% (95% CI 56.8-62.1%) for the simplified Geneva score.

Conclusion: This study provides the first prospective head-to-head comparison of validated RAMs. The accuracy and prognostic performance of the simplified Geneva score and other RAMs to predict hospital-acquired VTE in medical inpatients is limited, and their clinical usefulness is questionable. More accurate strategies to predict VTE risk in medical inpatients are needed.

Table. Risks of hospital-acquired VTE and their association with RAMs

RAM	High risk	Low risk	SHR (95% CI)*	p-value
	90-day VTE risk (%)			
Simplified Geneva score	2.7	1.2	2.07 (0.82-5.24)	0.12
Original Geneva score	2.7	1.1	2.27 (0.85-6.06)	0.10
Padua score	3.0	1.4	1.97 (0.90-4.29)	0.09
IMPROVE score	3.0	1.8	1.57 (0.75-3.29)	0.24

Abbreviations: CI, confidence interval; SHR, sub-hazard ratio; RAM, risk assessment model, VTE, venous thromboembolism.

*adjusted for thromboprophylaxis use as a time-varying covariate

FM6

A model to predict future exacerbation in the general practitioners based Swiss Chronic Obstructive Pulmonary Disease (COPD) cohort

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Background: Chronic obstructive pulmonary disease (COPD) is a widely spread chronic disease, characterized by an irreversible airway obstruction. COPD exacerbations are correlated with higher mortality. Our objective was to develop and validate a model to predict recurrent exacerbation.

Methods: The data of questionnaire-based general practitioners based Swiss COPD cohort, COPD patients from 23 Swiss cantons were screened and enrolled and observed over 2 years. The COPD patients were seen by their GPs at least twice a year. Data was split into training (75%) and validation (25%) dataset. Negative binomial regression model was developed using the training dataset to predict the exacerbation rate within 1 year. Based on Akaike's information criterion, an exacerbation prediction model was developed, and the overall performance was externally validated in the validation dataset. A prediction nomogram was created to facilitate clinical use of the model.

Results: 229 COPD patients (35% Female, mean age 67yrs) were analyzed. 77% of patients had no exacerbation during the follow-up, we observed 73 exacerbations in total. The best subset in the training dataset found that lower forced expiratory volume, high scores on MRC dyspnoea scale, exacerbation history, not being on combination therapy of LABA+ICS or LAMA+LABA at baseline were associated with higher rate of exacerbation. When validated, the area-under-curve (AUC) was 0.75 for one or more exacerbations as well as 0.75 for two or more exacerbations. Calibration was accurate.

Conclusion: Current severe symptoms and previous exacerbations were good predictors for future exacerbation in our primary care based COPD Cohort. A prediction model was built from these models to assist clinicians and patients in the shared decision-making process of their care.

FM7

The differential impact of a 6- versus 12-month pharmacist-led interprofessional medication adherence program on medication adherence in patients with diabetic kidney disease: the randomized and controlled PANDIA-IRIS study

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Introduction: Patients with diabetic kidney disease (DKD) may have had a history of nonadherence to medications, i.e., when patients do not take their medications as prescribed. We aimed at evaluating the differential impact of a 6- vs. 12-month pharmacist-led interprofessional medication adherence program (IMAP) on components of adherence (i.e., implementation and discontinuation) in patients with DKD, during and after the intervention.

Methods: All included patients benefited from the IMAP, which consists in face-to-face motivational interviews between the patient and the pharmacist based on the adherence feedback from electronic monitors (EM), in which the medications were delivered. Patients were randomized 1:1 into two parallel arms: 12-month IMAP intervention in group A, vs. 6-month intervention in group B. Adherence was monitored continuously during 24 months post-inclusion. In the follow-up phase post-intervention, EM data were blinded. The repeated measures of daily implementation outcomes (1/0) to antidiabetics, antihypertensive drugs and statins were modelled longitudinally by generalized estimated equations in both groups, and in both the intervention and the follow-up phases.

Results: EM data of 34 patients in group A and 38 in group B were analyzed. Implementation to antidiabetics and antihypertensive drugs increased during the IMAP intervention phase and decreased progressively during the follow-up period. At 12 months, implementation to antidiabetics in group A vs. B was resp. of 93.8% and 86.8%, Δ7.0% (CI95% 5.7%; 8.3%); implementation to antihypertensive drugs was resp. of 97.9% and 92.1%, Δ5.8% (CI95% 4.8%; 6.7%). At 24 months, implementation to antidiabetic drugs in group A vs. B was resp. of 88.6% and 85.6%, Δ3.0% (CI95% 1.7%; 4.4%); implementation to antihypertensive drugs was resp. of 94.4% and 85.9%, Δ 8.5% (CI95% 6.6%; 10.7%). Implementation to statins was comparable at each time point between groups. All the three patients who discontinued at least one medication were in group B.

Conclusions: The IMAP supports the implementation of chronic medications in patients with DKD. The longer the patients benefit from the intervention, the more implementation increases over time and the more the effect lasts after the end of the intervention. A 12-month rather than a 6-month program should be embedded in the standard of care to support medication adherence in this population. The impact on clinical outcomes needs to be investigated.

FM8

Trends in the burden of cirrhosis in patients hospitalized in Switzerland between 1998 and 2020

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Introduction: Liver cirrhosis is an increasing cause of morbidity and mortality worldwide with a heavy load on healthcare systems. Multiple data show a shift in aetiologies of cirrhosis from viral hepatitis to alcoholic liver disease (ALD) and non-alcoholic fatty liver disease (NAFLD) in Western Europe and the USA. We aimed to analyse the trends in hospitalized patients with cirrhosis in Switzerland from 1998 to 2020.

Methods: Using data from the Swiss hospital statistics from 1998 to 2020, we identified patients with 1) a primary diagnosis of cirrhosis or 2) a primary diagnosis of a cirrhosis-related disease plus a secondary diagnosis of cirrhosis. We assessed demographic characteristics, length of hospital stay and mortality. Causes of cirrhosis were established according to registered diagnosis and NAFLD was determined after excluding other causes. Total hospital costs were available for years 2012 to 2020.

Results: Cirrhosis-related hospitalizations in Switzerland increased from 1'631 in 1998 to 4'052 in 2020, with 44% increase in the proportion of total hospitalizations (257 per 100'000 to 369 per 100'000, respectively). The overall proportion of male patients was 68.7% and 77.1% were Swiss. Age at hospitalization increased over the study period, the 65-84-years category representing 28.3% (95% CI, 26.1-30.5) in 1998 and 43.9% (95% CI, 42.3-45.4) in 2020. ALD was the leading and increasing cause of cirrhosis, representing 27.9% (95% CI, 25.7-30.1) in 1998 and 47.9% (95% CI, 46.4-49.5) in 2020. NAFLD-related cirrhosis could not be assessed effectively before 2012 due to reporting issues, but remained thereafter the second cause of cirrhosis in hospitalized patients with a stable proportion at 42.7% (95% CI, 41.2-44.3) in 2020. Hepatitis C virus was the third cause of cirrhosis and showed a steady decrease starting in 2011 from 13.6% (95% CI, 12.5-14.9) to only 3.2% (95% CI, 2.7-3.8) in 2020. In-hospital mortality decreased from 12.1% (95% CI, 10.5-13.8) in 1998 to 9.7% (95% CI, 8.8-10.7) in 2020. From 2012 to 2020, annual costs for cirrhosis-related hospitalizations increased from ~50 to ~85 million CHF.

Conclusion: In 2020, ALD and NAFLD were the two most frequent causes of cirrhosis in patients hospitalized in Switzerland. Cirrhosis-related hospitalizations and related costs increased from 1998 to 2020, but in-hospital mortality decreased during the same period.

FM9

Use of complementary medicine and association with SARS-CoV-2 vaccination during the COVID-19 pandemic

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Introduction: Complementary and alternative medicine (CAM) were used during to COVID-19 pandemic (1), sometimes directly linked to COVID-19 (prevention or treatment), and sometimes for other conditions or wellbeing (1). While the benefits or potential risks have not been clearly demonstrated, individuals have usually reported subjective improvement (2). Vaccine hesitancy increased recently, and specifically against the COVID-19 vaccine. In this study we examine the use and initiation of CAM and their associations with vaccination during the COVID-19 pandemic.

Methods: Between April and December 2021, all outpatients tested at the Geneva University Hospitals 12 months prior (SARS-CoV-2 positive and negative), were invited for an online follow-up. The use of CAM was evaluated. Results were stratified for each therapy by age, sex, education, profession and SARS-CoV-2 infection. Logistic regression models were used to evaluate associations between vaccination and the overall use of CAM, as well as the use of specific therapies such as zinc, vitamin D, or vitamin C.

Results: Overall, n=12,246 individuals participated, with a mean age of 42.8 years, 59.4% were women, and 26.2% had at least one positive SARS-CoV-2 test. Overall, 63.7% of individuals used some type of CAM. Of note, 31.6% of CAM users and 21.1% of non-CAM users had insurance covering complementary medicine. The use of CAM was higher in women, 40-60 years old, professional-managers and individuals with a higher education level. Almost a third of individuals started CAM therapy in relation to COVID-19 (most for prevention, and a smaller proportion for treatment). Participants had rarely discussed the use of CAM with ther primary care physician. Not being vaccinated was independently associated with the use of CAM (adjusted odds ratio aOR 1.22 [1.09-1.37]), the use of zinc (aOR 2.25 [1.98-2.55]); the use of vitamin D (aOR 1.45 [1.30-1.62]), and the use of vitamin C (aOR 1.59 [1.42-1.78]).

Conclusion: The prevalence of CAM use during the COVID-19 pandemic was high, even though communication about CAM approaches with the primary care physician was lacking. Individuals using CAM were less likely to be vaccinated against COVID-19. The role of physicians in advising and helping patients make their choices is important and the use of CAM should potentially move towards shared decision making.

Fig 1. COVID-19 related use of CAM

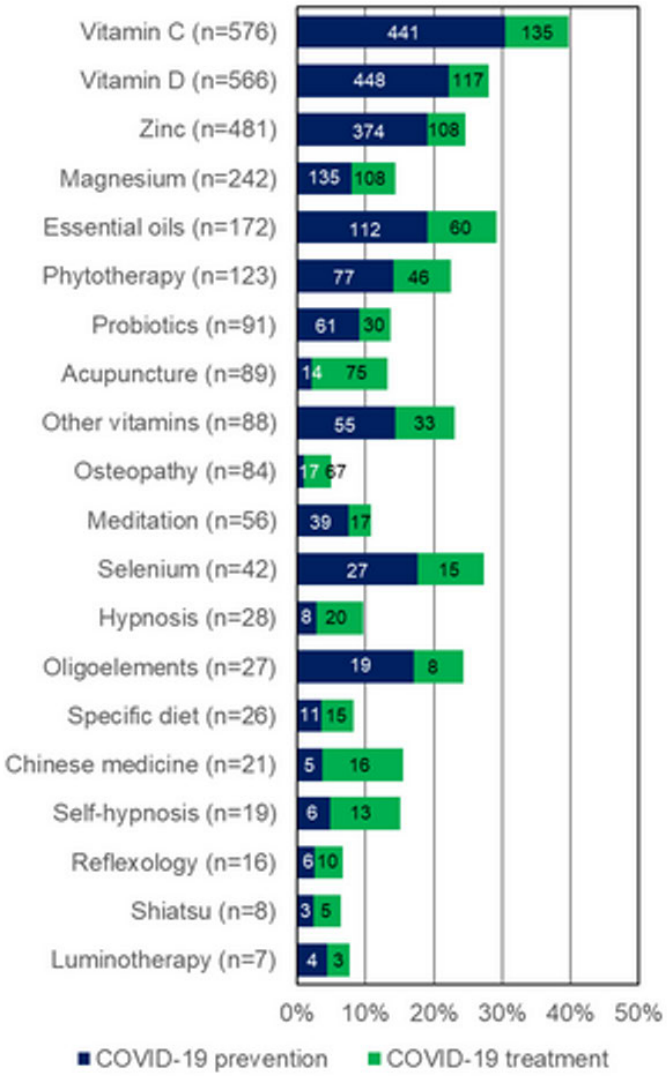
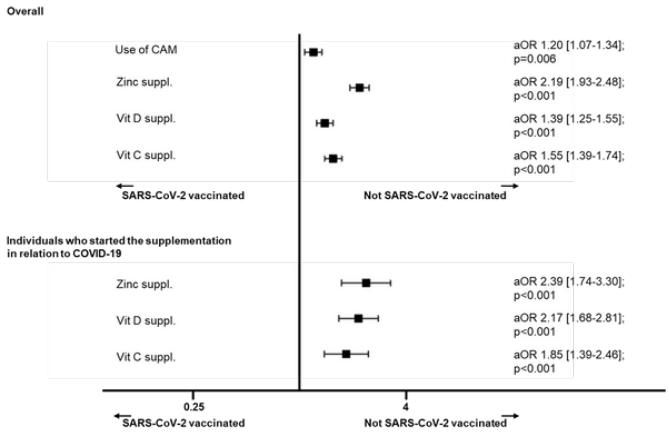


Fig 2. Associations between vaccination status and the use of CAM



FM10

What is the association between central nervous system-active medications and risk of hospital admission in older multimorbid adults?

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Introduction: Central nervous system (CNS) active medications are amongst the most prescribed medications in older patients and are highly affected by age-related pharmacodynamic changes. We lack data on the outcomes associated with the use of multiple CNS-active medications in multimorbid older adults. Our aim was to assess the association between the number of CNS-active medications at discharge and the risk of 1-year all-cause hospital admission, drug-related hospital admission (DRA), death, quality of life (QoL) and functional status in this high-risk population.

Methods: We used data from the OPERAM trial, which assessed optimizing prescribing to prevent DRAs in 2,008 inpatients aged ≥70 years with ≥3 chronic conditions and ≥5 chronic medications from 4 European centers. We assessed the association between the number of CNS-active medications and 1-year all-cause hospital admission, DRA and death by Cox proportional hazard models adjusted for age, sex, discharge location, Charlson Comorbidity Index, presence of depression/anxiety and randomization arm. We assessed the association of number of CNS-active medications with QoL (measured with the EQ-5D-VAS; 0-100 points, higher scores indicating higher QoL) and functional status (measured with the Barthel Index; 0-100 points, higher scores indicating higher functional independence) using linear regression models adjusting for the same covariates.

Results: Of the 2,008 patients, 1141 (56.8%) were prescribed ≥1 CNS-active medication (median 1, IQR 0-2) at discharge. Within 1 year, 963 (48%) participants experienced ≥1 all-cause hospital admission, 444 (22.1%) participants ≥1 DRA and 375 (18.7%) died. The risk for all-cause hospital admission and DRA was increased by 7% by each additional CNS-active medication (multivariate adjusted hazard ratio (HR) 1.07 [95% confidence interval 1.03 to 1.12] for all-cause hospital admission and 1.07 [1.03 to 1.12] for DRA). Risk of death did not differ significantly (HR 1.04 [0.97 to 1.12]). The adjusted mean difference of QoL after 1 year was -2.1 (-2.8 to -1.4; minimal important difference [MID]=8) and of functional status -2.5 (-3.2 to -1.8; MID=9.8) for each additional CNS-active medication.

Conclusion: The number of CNS-active medications at discharge was associated with a higher risk for 1-year all-cause hospital admission and DRA in older adults. A careful risk-benefit assessment when prescribing CNS-active medications in this vulnerable population is essential.

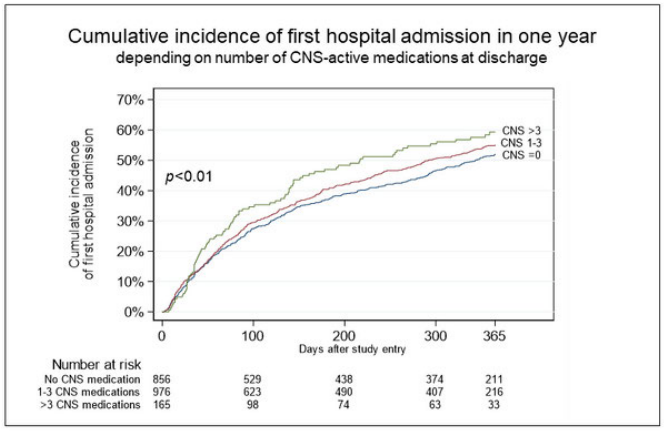

Figure 1 Cumulative incidence of first all cause hospital admission displayed by strata of patients with no CNS-active medication, with 1 - 3 CNS-active medications and with >3 CNS-active medications. Curve truncated at 365 days. P-value from Wald statistic.

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FM11

Hyponatremia and aging-related diseases: key player or innocent bystander? A systematic review

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Introduction: Hyponatremia, defined as a serum sodium concentration lower than 135 mEq/l, is the most common electrolytic disorder amongst adults aged 65 years and older. Increasing evidences suggested that hyponatremia may be associated with poor clinical outcomes in older subjects including falls (1), osteoporosis (2), fractures (3), neurocognitive disorders (4).

Objectives: Investigate whether hyponatremia may be considered a key player, a surrogate marker, or an innocent bystander in the occurrence of falls, fractures, and cognitive impairment.

Methods: Systematic review performed according to the Preferred Reporting Items for Systematic Reviews and Meta-Analysis (PRISMA). The protocol of this study is available on the International prospective register of systematic reviews (PROSPERO). MEDLINE, EMBASE and PsycINFO database were searched. Three reviewers identified studies meeting inclusion criteria and check decisions. Each study was independently evaluated by two reviewers, discrepancies between the two reviewers were solved by the third. Two hundred and fifteen articles were retrieved. Thirty-two were included in the review. The Hill's criteria (strength, consistency, specificity, temporality, biological gradient, plausibility, coherence, experiment, and analogy) for causality were used to verify the existence of a causal relationship between hyponatremia and outcomes.

Results: The majority of the studies found a significant association between hyponatremia and falls even after correction for confounding factors. Some studies suggested an association between persistent hyponatremia and increased osteoporosis and fracture risk. On the contrary, the evidence of an association between hyponatremia and cognitive impairment is lacking.

Conclusions: Our results show that falls, osteoporosis and fractures are multifactorial, and that hyponatremia is not clearly temporally related with those outcomes; hence, we suggest that hyponatremia may be regarded rather as a marker of unhealthy aging and a confounder than a causal factor or an innocent bystander for falls and fractures. As regards cognitive impairment, the evidence provided until now, are not sufficient to support a real role of hyponatremia that may be regarded as an innocent bystander in neurodegeneration.

FM12

"I live my own little life": Opinion of nursing home residents concerning interventions to improve their will to live

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Introduction: The will to live (WTL) is a valuable indicator of subjective well-being in older people, and the study of this indicator may enable a deeper understanding of older nursing home residents. Previous results indicate that nursing home residents express a rather strong WTL. However, no study has explored if residents want to improve their WTL and which interventions they suggest.
This study investigated residents' wish for support to improve their WTL and interventions they suggest to achieve this goal.

Method: This study used a qualitative approach with interviews conducted among nursing home residents (N = 88), aged 70+, who have been living in a nursing home for ≥ 1 month with preserved decision-making capacity. Openness towards interventions supporting their WTL has been explored with a yes-no question, along with an open question about which interventions residents suggested.

Results: Overall, 45 residents (53%) expressed that they wouldn't want interventions aiming to support their WTL either because they were satisfied with their situation or because they no longer wanted to improve their WTL at this stage of their life.
Whether or not they wanted interventions to improve their WTL, when asked what could improve their WTL, 78 residents (89%) were able to give an answer. Most of the time, residents needed probing before answering. In the responses given by residents about what would improve their WTL, we observed that the needs were different from one person to another and specific to each person's interests.
One of the needs expressed was more social contact, e.g., spending more quality time with their loved ones and having in-depth discussions with someone. Another need revolved around health, e.g., reducing pain and improving functional autonomy, although many residents considered themselves lucky in comparison to their peers' health status. Regarding activities, there was a desire to act more independently and conduct varied activities adapted to their abilities and interests, also outside of the nursing home. In addition, the residents expressed that they felt the lack of staff and would appreciate more availability from them. Finally, they mentioned the wish for more flexibility by the institutions and more financial support for the elderly.

Conclusion: Overall, this study allows a concrete perception of the subjective needs and concerns of older nursing home residents, indicating ways how to improve their care and ultimately their WTL.

FM13

Intensive diabetes treatment in cognitively impaired older patients: where is the damage?

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Introduction: A too strict control of diabetes is often applied in cognitively impaired older patients with a consequent risk of hypoglycemia[1,2], but little is known about brain pattern injury in overtreated diabetic older patients.

Methods: Retrospective case series of patients aged 60+ years with type 2 diabetes and cognitive impairment. Based on target glycated hemoglobin (HbA1c) values defined according to geriatric health profile (i.e., HbA1c between 7% to 8% and 7.6% to 8.5% for *vulnerable* and *dependent* patients, respectively), patients were classified as over-treated (HbA1c below target values) or not. Under-treated were excluded.
Grey matter volume in defined brain regions was compared in patients over-treated or not, using voxel-based morphometry from T1-weighted volumetric MRI scans (1.5 or 3T). Multivariable logistic regression models adjusting for age and gender, and then also for clinical cognitive impairment severity (MOCA score) were performed.

Results: Among N=71 patients, 46 (65%) were defined as over-treated. Over-treatment was associated with grey matter loss in left caudate (βcoeff:-.23, 95%CI : [-.44 to -.02] , p=.03), right thalamus (βcoeff:-.26, 95%CI : [-.53 to -.00] , p=.05), left orbital part of the inferior frontal gyrus (βcoeff:-.13, 95%CI : [-.23 to -.03] , p=.01), right and left precentral gyrus (βcoeff:-.92, 95%CI : [-1.67 to -.18] , p=.02 ; resp.βcoeff:-.96, 95%CI : [-1.72 to -.21] , p=.01), left superior frontal gyrus (βcoeff:-.94, 95%CI : [-1.80 to -.09] , p=.03), left calcarine cortex (βcoeff:-.22, 95%CI : [-.41 to -.02] , p=.03), left cuneus (βcoeff:-.31, 95%CI : [-.58 to -.03] , p=.03), and left superior occipital gyrus (βcoeff:-.31, 95%CI : [-.52 to -.10] , p=.01).
When adjusting for MOCA score, associations remained in left orbital part of the inferior frontal gyrus (βcoeff:-.11, 95%CI : [-.21 to -.00] , p=.05), right and left precentral gyrus (βcoeff:-.91, 95%CI : [-1.70 to -.11] , p=.03; resp. βcoeff:-.87, 95%CI : [-1.68 to -.06] , p=.04), and left superior occipital gyrus (βcoeff:-.26, 95%CI : [-.47 to -.05] , p=.01).

Conclusions: Results suggest several associations between over-treatment and damage in specific brain regions. As in the newborn, the occipital region could be particularly sensitive to hypoglycemia [3]. Future studies should investigate in larger sample the cerebral damages caused by repeated hypoglycemia to add further support deprescription in over-treated older patients with diabetes.

FM14

Interdisciplinary home-based rehabilitation following inpatient rehabilitation: utilization rate and patients characteristics

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Introduction: Designed as an alternative to inpatient rehabilitation, home-based interdisciplinary programs are increasingly offered to older patients to complete their rehabilitation in their usual environment. Our study has the objective to determine the utilization rate of home based rehabilitation and to investigate the profile of users from the home-based rehabilitation program.METHODS:Patients who benefited from home-based rehabilitation after an inpatient rehabilitation stay between june 2018 and may 2021 were identified from the hospital database (N=1623).Socio-demographic, health and functional status characteristics were retrieved from electronic medical records.Bivariable and multivariable analysis was performed.

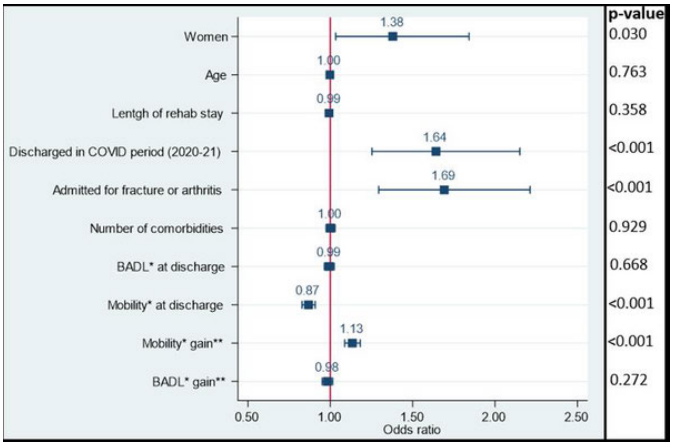
Results: Over the study period 15.5% (253/1623) patients benefited from home-based rehabilitation. Compared to the others, they were more frequently women (69.6% vs 61.5%, p=0.008), suffering of multiple comorbidities (57.8% vs 52.2% with > 14 conditions, p= 0.077), admitted for orthopaedic problems (64.2% vs 49.1%, p< 0.001) with poorer functional performance at admission (mean MIF score:80.1+/-15.7% vs 88.3 +/-14.7, p<0.001) and at discharge(95.7+/-13.4 vs 101.3 +/- 13.2, p< 0.001), but greater functional gain during their inpatient stay (14.9+/-10.1 vs 13.1+/-9.5, p=0.002).In multivariable analysis, being a woman (adjOR 1.38, 95%CI 1.03-1.84,p=0.03),admission for orthopaedic problems (adjOR 1.69,95%CI:1.3-2.20, p<0.001) and greater gain in mobility (adjOR 1.13,95%CI:1.08-1.18,p<0.001) remained predictors of orientation towards home-based rehabilitation.

Conclusions: One in six patients benefited from home-based rehabilitation after their inpatient stay. Althoug these patients had poorer functional performance at admission and discharge, they showed greater functional improvement over their inpatient stay, strongly suggesting that their good recovery potential was a key determinant of their orientation toward home-based rehabilitation.

Title of the table: Characteristics of the patients discharged with home-based rehabilitation (multivariable analysis)

* from FIM

** difference between admission and discharge



FM15

Risk factors for early hospital readmission in geriatric patients: a systematic review

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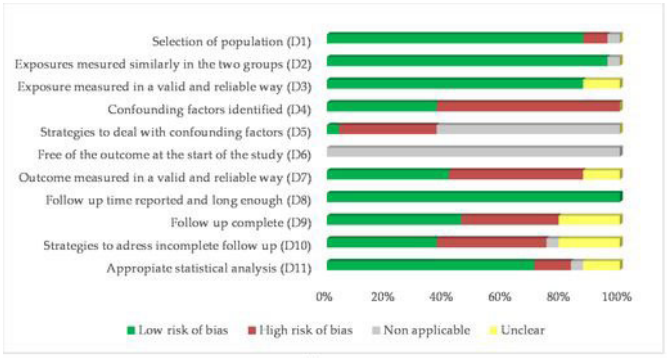
Introduction: The number of older patients is constantly growing, and early hospital readmissions in this population represent a major problem from a health, social and economic point of view [1]. Furthermore, the early readmission rate is often used as an indicator of the quality of care [2].
According to the literature [3;4], the readmission rate varies depending on the population studied, the geographical area and the wards examined. The role of frailty and, in particular, sarcopenia in early readmission rates is currently unclear. The aim of this systematic review is to update the existing evidence on this topic identifying the risk factors for early readmissions (30 and 90 days) in geriatric patients hospitalized in medical units.

Methods: The search was carried out on the MEDLINE, EMBASE and PsycINFO databases. Only studies published in the past decade were included.
Three independent reviewers assessed the potential inclusion of the studies, and then each study was independently assessed by two reviewers using Joanna Briggs Institute critical appraisal tools; any discrepancies were resolved by the third reviewer. Studies that included inpatients in surgical wards were excluded. Twenty-nine studies were included in the review.

Results: Risk factors of early readmission can be classified into socio-economic factors, factors relating to the patient's health characteristics, factors related to the use of the healthcare system and clinical factors. Among these risk factors, those linked to patient frailty play an important role, in particular malnutrition, reduced mobility, risk of falls, fatigue and functional dependence.

Conclusions: The early identification of patients at higher risk of early readmission may allow for targeted interventions in view of discharge.
Amongst the risk factors highlighted by different studies, those associated with frailty syndrome play an important role. This result is of paramount importance as these conditions are modifiable and must be taken into account in patients' evaluation and treatment.
Careful nutritional management and early mobilization during hospitalization are, therefore, low-cost measures that can lead to a reduction in the readmission rate with significant improvement in patients' quality of life and reduction of health costs.



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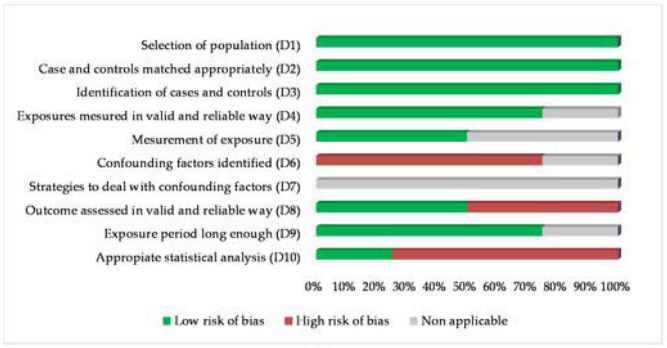

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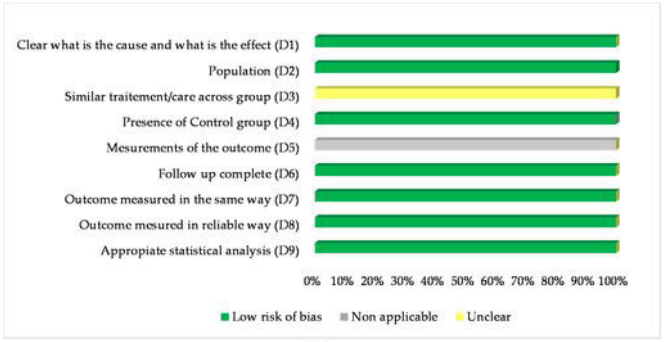

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FM16

Structural and procedural predictors of hospitalization of nursing home residents

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Introduction: Hospitalizations of nursing home (NH) residents are a major challenge for healthcare systems and a burden for residents. While a large body of data is available regarding residents' characteristics associated with hospitalizations, data on facilities' structural and procedural characteristics are scarce.

Objectives: To investigate the relationship between NH structural and procedural characteristics and their residents' hospitalization rates.

Methods: This study used the Swiss NHs Human Resources Project (SHURP 2018) database, a cross-sectional study of 118 NH in Switzerland that investigated national quality indicators and their relationship with NH characteristics. In the present study, we investigated in a subsample of 70 NHs the bivariable and multivariable association between structural (e.g., number of beds, nurse-to-resident ratio) and procedural (e.g., policy about advanced directives, about antibiotic treatments) characteristics with their hospitalization rates (per 1'000 NH residents-days). Analyses were adjusted for several indicators of NH case-mix.

Results: Median hospitalization rate was 1.04 per 1'000 NH residents-days. In multivariable analysis, hospitalization rate was inversely associated with facility care load and with institutional policy to discuss resident's wish regarding hospitalization (all $p<.05$), whereas no association was observed with any structural characteristics.

Conclusions: These results challenge popular beliefs in showing that NH tend to avoid hospitalization for residents requiring a higher care level, a proxy for worse functional and cognitive status. These results highlight the importance of institutional policy to discuss residents' wishes about hospitalization and strongly suggest that such policy might contribute to avoiding some undesired and therefore inappropriate hospitalizations.

Beste Poster SGAIM / Meilleurs posters SSMIG

P1

A paediatric case of methotrexate induced acute liver and kidney failure

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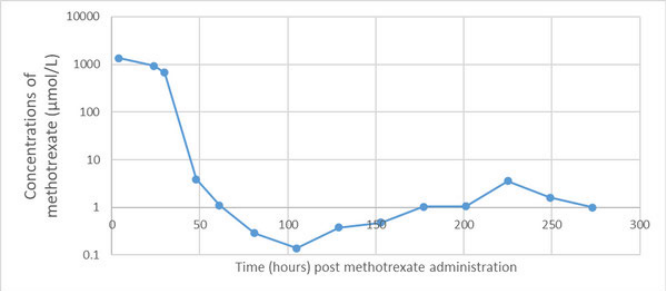
Learning objectives: The importance of the inter-individual pharmacokinetic differences between patients can justify the pre-therapy pharmacogenetic testing for drugs with a low therapeutic index.

Case: Methotrexate, a competitive inhibitor of dihydrofolate reductase, is used for the treatment of a range of auto-immune disorders and cancers. It enters the cells through different transporters, notably OATP1B1, an organo-anion transporter in hepatocytes. Methotrexate also interacts with intracellular enzymes particularly 5,10-methylenetetrahydrofolate reductase (MTHFR). Methotrexate is eliminated through ABC transporters, most importantly the Breast Cancer Resistance Protein (BCRP) and the P-glycoprotein (P-gp). (1-3) We report the case of a 14-year-old female patient with a high-grade osteosarcoma of the right tibia was treated according to the EURASMOS protocol. At day 23 of the protocol, a first dose of intravenous methotrexate (12g/m2) was administered. The plasma methotrexate level measured at H4 and H24 were 1'356 and 937 µmol/L respectively (expected methotrexate plasma levels at H24 : < 10 µmol/L). At 24 hours, the patient started to present with an altered state of consciousness and hemodynamic instability. The laboratory showed severe renal failure and severe hepatic impairment, two less commonly observed side effects with the use of methotrexate. The patient received different treatments to help eliminate the accumulated methotrexate (leucovorin, glucarpidase 4000E, cholestyramine, N-acetylcysteine). Nevertheless, presenting with a refractory severe metabolic acidosis and hyperkalaemia, haemodialysis was initiated and a transfer to the intensive care of the University Hospital of Geneva was organised for hepatic organ support and hepatic dialysis . Pharmacogenetic testing revealed a reduced activity of the P-gp, BCRP and OATP1B1 transporters as well as the MTHFR enzyme, predisposing the patient to develop toxicities related to a reduced methotrexate clearance. Our patient had a >10x higher plasma level of methotrexate 24h after the infusion, explained by the genetic polymorphisms present. The rescue

therapy provided had quickly corrected it. The use of pharmacogenomics pre-therapy could improve the security/efficacy profile of highly toxic drug therapies such as methotrexate.

Discussion: In summary, our patient had polymorphisms that put her at an increased risk of methotrexate toxicity. By identifying these genetic abnormalities prior to the first dose of methotrexate, it would have been possible to either to change the chemotherapy regimen or perform an unguided dose reduction of methotrexate in the absence of alternatives. Precision medicine, including pharmacogenomics, makes it possible to individualize the treatment of each patient to balance its therapeutic/toxic profile in the benefit of the patient. A prospective randomized study with methotrexate dose adjustements based on the patients' polymorphisms would allow us to better anticipate the dose-dependent complications of methotrexate toxicity, and minimise the mortality-morbidity burden.

Graph 1: Evolution of the concentrations of methotrexate over 11 days



Results of the genotyping of the germline DNA:

Gene	Variants detected	Genotype*	Interpretation/predicted phenotype
ABCB1 (P-gp)	c.3435C>T c.1236T>C c.2677G>T c.210A>G	T/T T/C G/T A/G	**Reduced** activity
MTHFR	c.1298A>C c.677C>T	A/C C/T	**Reduced** activity
ABCG2	c.421C>A	C/A	**Reduced** activity
SLCO1B1	c.388A>G c.521T>C	G/G T/C (*1/*15 or *1/*17)	**Reduced** activity

P2

Atrial fibrillation detected before or after stroke: role of anticoagulation

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Figure 1. Kaplan-Meier and cumulative incidence curves for recurrent ischemic stroke according to (A) AF category and (B) anticoagulation before stroke.

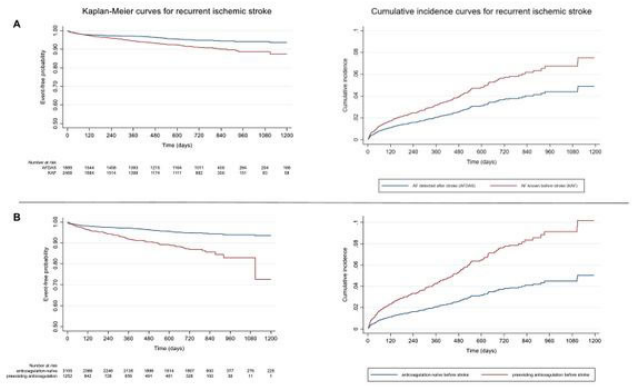
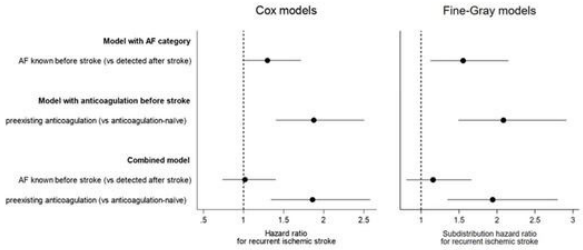


Figure 2. Adjusted hazard ratio estimates for the effect of AF category and anticoagulation before stroke on ischemic stroke recurrence from Cox and Fine-Gray models. When modelled separately, AF category shows a weaker association with ischemic stroke recurrence than anticoagulation before stroke. In the combined model, only anticoagulation before stroke but not AF category retains a strong association with ischemic stroke recurrence.



Background: Atrial fibrillation (AF) known before ischemic stroke (KAF) has been postulated to be an independent category with a recurrence risk higher than that of AF detected after stroke (AFDAS). However, it is unknown whether this risk difference is confounded by pre-existing anticoagulation, which is most common in KAF and also indicates a high ischemic stroke recurrence risk.

Methods: Individual patient data analysis from 5 prospective cohorts of anticoagulated patients following AF-associated ischemic stroke. We compared the primary (ischemic stroke recurrence) and secondary outcome (all-cause death) among patients with AFDAS versus KAF and among anticoagulation-naïve versus previously anticoagulated patients using multivariable Cox, Fine-Gray models and goodness-of-fit statistics to investigate the relative independent prognostic importance of AF-category and pre-existing anticoagulation.

Results: Of 4,357 patients, 1,889(43%) had AFDAS and 2,468(57%) had KAF, while 3,105(71%) were anticoagulation-naïve before stroke and 1,252(29%) were previously anticoagulated. During 6,071 patient-years of follow-up we observed 244 recurrent strokes and 661 deaths. Only pre-existing anticoagulation (but not KAF) was independently associated with a higher hazard for stroke recurrence in both Cox and Fine-Gray models. Models incorporating pre-existing anticoagulation showed better fit than those with AF-category; adding AF-category did not result in better model fit. Neither pre-existing anticoagulation nor KAF were independently associated with death.

Conclusion: Our findings challenge the notion that KAF and AFDAS are clinically relevant and distinct prognostic entities. Instead of attributing an independently high stroke recurrence risk to KAF, future research should focus on the causes of stroke despite anticoagulation to develop improved preventive treatments.

P3

Between the duty of care to patients and the duty to protect oneself and one's family during a pandemic: a cross-sectional observational study of healthcare providers' opinions in the emergency department

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Introduction: Healthcare workers (HCW) in the Emergency Department (ED) play a key role in the care of infected patients during a pandemic. Based on social contract theories, society expects that HCW provide care to patients even in the face of personal health risks. This contract also entails a reciprocal obligation to provide HCW adequate working conditions and personal protective equipment (PPE), so that they can protect themselves and their families from contamination. The COVID-19 pandemic was the first event in over 100 years to challenge this contract, as many ED HCW died or lacked PPE during the first COVID wave. The ED HCWs' opinion on this contract has not been studied recently. The goal of our study was to seek ED HCWs' opinions.

Methods: Survey conducted at the end of the first wave, from June to November 2020 in 8 Swiss (3 in French-, 4 in Italian- and 1 in German-speaking parts of Switzerland) and 2 Belgian EDs; 558 doctors (MD) and 667 nurses (RN) were invited to respond anonymously to an online questionnaire querying their demographics, COVID-related health risks, their family and their perceptions about work-related duties and institutional obligations.

Results: response rates were 52% for MD and 60% for RN.

Respondents' characteristics:	RN (n=399)	MD (n=292)	P
Female, n (%)	259 (65)	291 (51)	<0.001
Mean age, (SD)	39 (10)	36 (9)	<0.001
Median ED experience, years (interquartile range)	8 (4;15)	3 (1;9)	<0.001
Couple/married/partnered, n (%)	274 (69)	189 (65)	0.27
With child(ren), n (%)	160 (40)	115 (39)	0.85
At risk for severe COVID, n (%)	28 (7.4)	8 (2.8)	0.009
Infected by COVID , n (%)	35 (9.3)	22 (7.6)	0.49
Relatives at risk for severe COVID, n (%)	102 (27)	46 (16)	0.001

Agreed with the following statements: n (%)	RN (n=399)	MD (n=292)	P
Main duty to one's own family	125 (38)	81 (31)	0.09
Had to work to make a living	115 (35)	84 (32)	0.51
Had a duty of care for the infected patients despite the risks	136 (41)	131 (50)	0.03
Had the choice to refuse caring for infected patients	90 (27)	54 (21)	0.07
Punishment for those refusing to work	152 (46)	124 (48)	0.70
Had to «stick together» during a pandemic	192 (58)	160 (61)	0.42
Had to be rewarded in some ways	207 (63)	74 (28)	<0.001
Professional bodies and unions had a duty to provide guidance	86 (26)	62 (24)	0.57
Employers had responsibility to provide PPE	290 (88)	224 (86)	0.52

Conclusion: RN' and MD's opinions on their respective duties and expectations sometimes diverged, but less than half respondents agreed with the duty of care statement, and a third considered their family as their main duty. This may represent a "breach" of the social contract and may point to a greater priority given to one›s own or family›s protection. As the literature has reported great solidarity between HCW and society during the pandemic, these opinions may not equate to a failure to one›s duty. However, given the current high resignation rates among ED HCW following COVID successive waves, our results should prompt additional studies, as an insufficient number of ED staff may jeopardize ED capacity to meet increased workload during a pandemic.

P4

Definitions of fatal bleeding in clinical studies evaluating anticoagulant treatment for venous thromboembolism: a scoping review

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Introduction: Fatal bleeding is a component of the primary safety outcome in most studies evaluating anticoagulation for venous thromboembolism (VTE), but a standardized definition for fatal bleeding is lacking. We aimed to summarize definitions of fatal bleeding, and to describe the range of case-fatality rates of major bleeding in VTE studies.

Methods: MEDLINE, Embase, and CENTRAL were searched from 01/2008-07/2021, for prospective studies that enrolled patients with VTE and evaluated the efficacy/safety of anticoagulation for VTE treatment or included fatal or major bleeding as primary outcome. Two authors independently performed study selection and data extraction. The primary outcome was the definition of fatal bleeding. The key secondary outcome was the case-fatality rate of major bleeding, defined as the proportion of fatal bleeding events relative to the total number of major bleeding events. Data were analyzed using descriptive statistics.

Results: Of 4,911 records identified, we included 132 articles representing 89 distinct studies. Twenty-seven (20%) articles and 7 of 89 (8%) studies reported a definition of fatal bleeding. Overall, we identified three different types of definitions that were either based on a specific time interval between bleeding and death, bleeding location (intracranial) or clinical presentation (hemodynamic deterioration), or mainly relied on the judgment of the adjudication committee to determine the cause of death (Table). The case-fatality rate of major bleeding ranged from 0 to 60% (median, 9.1%; interquartile range, 2.8-18%).

Conclusion: Less than 10% of studies assessing anticoagulant treatment for VTE reported a definition for fatal bleeding. The lack of a (standardized) definition for fatal bleeding may lead to inaccurate estimates of the risk of fatal bleeding, particularly when comparing across studies. A standardized definition of fatal bleeding in VTE studies is needed.

Table. Summary of definitions for fatal bleeding reported in the included studies

Study	Definition of fatal bleeding
RIETE	Any death occurring within 7 or 10 days of a major bleeding episode, in the absence of an alternative cause of death.
COMMAND VTE, SWITCO65+	Death that followed an intracranial hemorrhage or a bleeding episode leading to hemodynamic deterioration.
AMPLIFY, AMPLIFY-EXT, Caravaggio, Hokusai-VTE Cancer	A bleeding event that the independent adjudication committee determined was the primary cause of death or contributed directly to death.

P5

Electricity needs of neuromuscular and respiratory insufficient patients in times of potential power cuts

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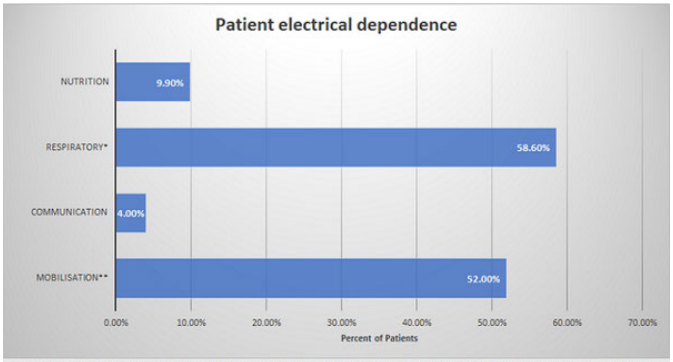
Introduction: Due to international political tensions, electricity cuts are possible in the future and the price of electricity has increased significantly in Western Europe. Many comorbid patients use medical (oxygen, non-invasive ventilation (NIV), invasive ventilation (IV), nutrition pump) and non-medical (communication, lift, wheel chair) devices, all requiring electrical power. Here, we describe the electricity needs of patients with mechanical home ventilation and/or neuromuscular pathologies followed in the division of pulmonary medicine of the Lausanne University Hospital (CHUV) and their resulting costs.

Methods: We collected the use of any electric respiratory and non-respiratory device. We used the average price of electricity in the canton of Vaud in January 2023 and the wattage consumption declared by the manufacturers to estimate the costs.

Results: We included 205 patients (44.4% female). Mean age was 53.9 years (min 18 – max 89), Thirty-five percent had a neurological slowly progressive disease, 11% a obstructive lung disease, 10% an obesity hypoventilation syndrome and 7% amyotrophic lateral sclerosis. For 31 patients (15%) dependence on electrical aids is due to multiple co-occurring illnesses. Fifty-eight percent (n= 119) used an electricity-consuming device for respiratory dependence (Figure 1). The mean electrical device per patient was 2.95 (SD +/- 2.28) (Figure 2). Fifty-five percent (n=113) used NIV, including 20% (n=23) with life-support NIV (24h/24). The average electricity price was 0.3226chf/kWatt. The estimated cost per year is 94 CHF for a NIV using 8h/day, 424 CHF for a life support NIV and 989 CHF for a stationary concentrator of O2.

Conclusion: Neuromuscular and respiratory insufficient patients are dependent on electricity not only for respiratory problems, but also for mobilization, nutrition and communication. The electrical and financial burden is high in these complex comorbid patients. We need national coordinated strategies focused on electricity politics taking in consideration the care of these patients.



* Including 55.1% NIV, 31.2% home O2 therapy, 21.8% mechanical insufflator-exsufflator, 4.4% intrapulmonary percussive ventilator, 2.4% IV

** Including 48.5% electric bed, 42.7% lift, 34.8% electric wheelchair, 17.0% patient lift system, 4.1% sit-to-stand lift, 2.1% stair-lift

Figure 1

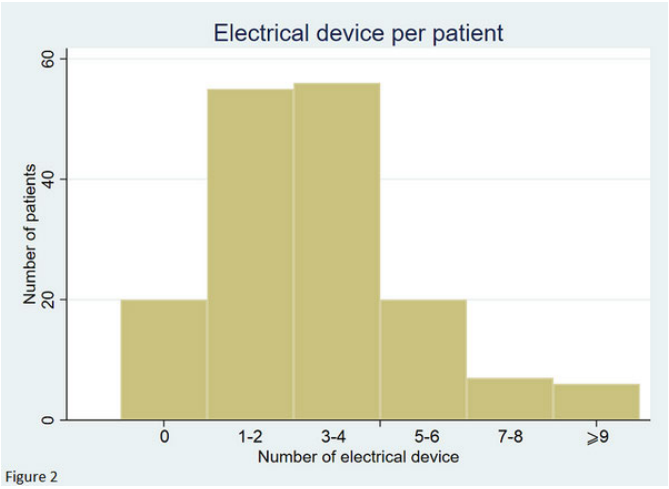


Figure 2

P6

Prediction of in-hospital bleeding in acutely ill medical patients: external validation of the IMPROVE bleeding risk score

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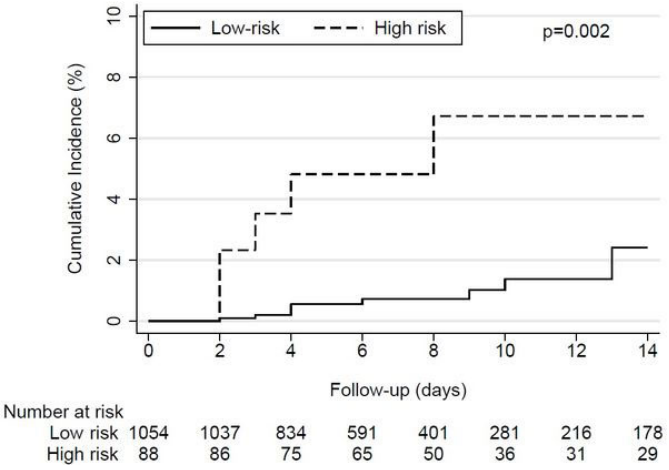
Introduction: Hospital acquired venous thromboembolism (VTE) is one of the leading preventable causes of death in hospitalized patients. Therefore, pharmacological thromboprophylaxis is recommended in medically ill inpatients at high risk of VTE, which leads to a small increase in bleeding risk. The only risk assessment model to predict bleeding in medical inpatients, the IMPROVE bleeding risk score, has never been validated using prospectively collected outcome data.

Methods: We validated the IMPROVE bleeding risk score in a prospective Swiss multicenter cohort of acutely-ill medical inpatients without therapeutic anticoagulation. We classified patients into high-risk (≥7 points) and low-risk (<7 points) of bleeding according to the IMPROVE bleeding risk score. Primary outcome was in-hospital clinically relevant bleeding (CRB) within 14 days after admission. The secondary outcome was in-hospital major bleeding (MB) within 14 days after admission. We evaluated outcome incidences according to risk groups, and assessed the score's predictive performance by calculating subhazard ratios (sHRs) adjusted for pharmacological thromboprophylaxis use and the area under the receiver operating characteristic (AUROC) curves.

Results: Of 1155 patients, 89 (8%) patients were classified as high bleeding risk. In-hospital CRB within 14 days and in-hospital MB within 14 days occurred in 15 (1.3%) and 8 (0.7%) patients, respectively. The cumulative incidence of CRB within 14 days was significantly higher in the high-risk (6.72%, 95% confidence interval [CI] 2.79-15.72%) compared to the low-risk group (2.41%, 95% CI 1.15-5.02; p-value 0.002; Figure). Adjusted for thromboprophylaxis, classification in the high-risk group was associated with an increased risk of 14-day CRB (sHR 4.7, 95% CI 1.5-14.5) and MB (sHR 4.9, 95% CI 1.0-23.4). AUROC curve ranged from 0.68 (95% CI 0.66-0.71) for 14 days in-hospital CRB to 0.73 (95% CI 0.71-0.76) for 14 days in-hospital MB.

Conclusion: The IMPROVE bleeding risk score showed moderate to good discriminatory power to predict bleeding in these Swiss medical inpatients. The score may help identify patients at high risk of in-hospital bleeding, in whom careful assessment of the risk-benefit ratio of pharmacological thromboprophylaxis is warranted.

Figure. Cumulative incidence of in-hospital CRB within 14 days after hospital admission according to the IMPROVE bleeding risk score



P7

Rates of cardiovascular events up to 8 years after uncomplicated myocarditis: *a population-based cohort study*

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Introduction: Acute myocarditis is a challenge for many clinicians due to the large spectrum of etiologies, heterogenous clinical presentation and broad range of clinical courses. While prognosis of acute myocarditis with uncomplicated presentation is perceived as benign, data on long-term outcomes is scarce. We evaluated rates of myocarditis-associated cardiovascular events after a first-time hospitalization with uncomplicated acute myocarditis in patients without known heart disease.

Methods: In this retrospective nationwide population-based cohort study from 2013 to 2020, hospitalized patients with uncomplicated acute myocarditis but without known heart disease were 1:1 propensity score-matched with controls after appendectomy. As assessed in time-to-event analyses, the primary outcome was a composite of re-hospitalization for myocarditis, pericardial disease, heart failure and its complications, arrhythmias, implantation of cardiac devices and heart transplant. The main subgroup analysis explored differences between those patients with and without an immediate diagnostic work-up.

Results: After matching, we identified 1,443 patients who had a first-time hospitalization with uncomplicated acute myocarditis (median age of 35 years, 74.0% male, median length of hospital stay 3 days) and 1,443 surgical controls (median age of 35 years, 74.8% male, median length of hospital stay 2 days). Over a median follow-up of 39 months, compared with surgical controls, the hazard ratio (HR) for the primary composite outcome was 42.03 (95% confidence interval [CI], 17.31 to 102.08), corresponding to an incidence rate (IR) of 43.24 vs. 0.94 per 1'000 person-years and an incidence rate difference (IRD) of 42.30 (95% CI, 36.28 to 48.32) per 1'000 person-years. Patients with uncomplicated acute myocarditis who did not undergo myocarditis-related diagnostic work-up during index hospitalization had higher rates of the cardiovascular composite outcome as compared with those who received immediate cardiac diagnostics (IRD 61.89 [no immediate diagnostic work-up vs. surgical controls] vs. 28.95 [immediate diagnostic work-up vs. surgical controls] per 1'000 person-years, HR 57.24 vs. 11.97; p for homogeneity <0.0001 [IRD] and 0.03 [HR], respectively).

Conclusion: Over a 8-year follow-up, patients hospitalized with uncomplicated acute myocarditis without known heart disease had higher rates of cardiovascular events as compared with surgical controls after appendectomy.

P8

Regulation of new puff-like disposable e-cigarettes: expert consensus using a *fast-track Delphi* process

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Introduction: New disposable electronic cigarettes (*puffs*) have arrived on the Swiss market since 2020. Their appearance raises many public health issues.

Methods: Our study, conducted in 18 days according to the three steps of the *fast-track Delphi* process developed at Unisanté (one meeting following an adapted version of the nominal group technique and two rounds by e-questionnaire), aimed at reaching consensual agreements among Swiss experts on the regulation of these products. Consensual agreement was reached when the median of responses for a given statement was 7+ out of 9 (*agreement*) and the interquartile range did not exceed 3 scale points (*consensus*).

Results: Thirteen experts from the French-speaking part of Switzerland took part in the 1st stage. Ten additional experts took part in the 2nd stage (n = 23), and 21 of them in the 3rd stage. At the end of the process, 21 out of 26 statements (80.1%) reached consensual agreement. Experts agree that *puffs* represent a public health problem, especially for young people. The problem also extends to the ecological dimension, which is essential to take into account in political decisions: given the existence of reusable e-cigarettes, experts agree on the lack of added value of *puffs*. Ideally, the panel of experts recommends a ban on the sale of the product. If this is not possible, certain aspects must be strictly regulated: taxation, product composition and marketing, sales and consumption restrictions. These regulations should go further than the current European directive and the future Swiss law.

Conclusions: The findings will be useful to support and guide political decision making from a public health and environmental perspective, as well as to provide guidance for the development of clinical recommendations and patient counselling.

P9

SPEARHEAD: tackling antimicrobial resistance with federated machine learning

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Introduction: Antimicrobial resistance (AMR) occurs when microorganisms, such as bacteria, viruses, and parasites, become resistant to antimicrobial treatments, such as antibiotics, antivirals, and antimalarials. This makes it difficult to treat infections that were once easily manageable, leading to what is often referred to as the «other pandemic» or the «silent pandemic». The impact of AMR on health and the economy is significant and continues to grow as the problem spreads.

Methods: SPEARHEAD has formed a partnership of 8 public research institutes and 4 industry partners from Switzerland, with the aim of tackling antibiotic resistance using a machine learning-based solution. The primary focus is on urinary tract infections, as they are common, widespread, and lead to excessive antibiotic usage.
SPEARHEAD uses a machine learning framework called federated learning. This is a technique that allows multiple institutions to collaboratively train a common machine learning model without transferring their data (but only sharing some model parameters). This approach ensures greater data privacy and security as it eliminates the need for central collection or storage of data. For this reason, its popularity is growing in the healthcare sector.
The ultimate result of SPEARHEAD will be the creation of a user-friendly UTI-specific digital platform that utilizes machine learning models to assist clinicians in making data-informed decisions for optimal antibiotic prescription.

Results: SPEARHEAD started in January 2022 and is currently gaining momentum in its activities. The federated learning infrastructure is under development, with the first test of a toy configuration being successful. A stable version of the framework is expected to be achieved in the near future.
The project team is now focused on locating existing relevant data within the databases of three different hospitals (USB and UKBB in Basel, CHUV in Lausanne). Additionally, new data will be collected by means of a clinical study at HUG hospital, in Geneva. These four different data sources (and possibly others) will be used to train machine learning models.

Conclusions: The project SPEARHEAD is creating a pioneering, globally adaptable, machine learning-powered, modular digital platform for urinary tract infections (UTIs). The platform will be accessible through a web interface and will have the ultimate role of supporting clinicians in making a responsible use of antibiotics.

P10

Trends in diabetes prevalence, awareness, treatment and control in French-speaking Switzerland

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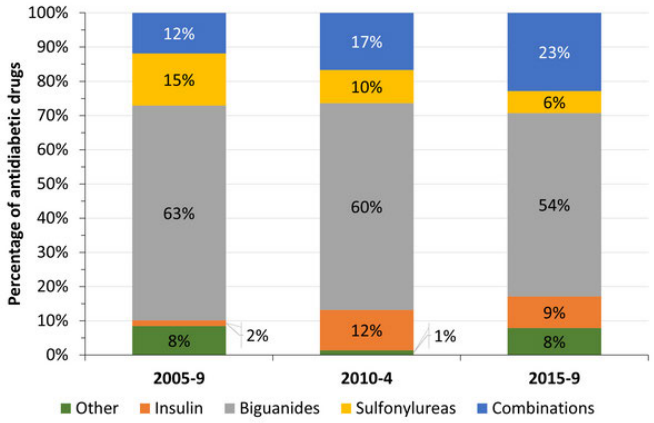
Introduction: diabetes is increasing in Switzerland, but whether its management has improved is unknown. We aimed at assessing diabetes prevalence, diagnosis, treatment and control in French-speaking Switzerland.

Methods: cross-sectional data for 2005-2019 from a population-based study in Geneva, Switzerland. Overall prevalence (defined reported diagnosis and/or fasting plasma glucose level ≥7 mmol/L), diagnosed, treated (among participants diagnosed) and controlled diabetes (defined as a FPG <6.7 mmol/L among participants treated for diabetes) were calculated for periods 2005-9, 2010-4 and 2015-9.

Results: data from 12,348 participants (mean age±standard deviation: 48.6±13.5 years, 51.7% women) was used. Between 2005-9 and 2015-9, overall prevalence and frequency of diagnosed diabetes decreased (from 8.7% to 6.2% and from 7.0% to 5.2%, respectively). Among participants diagnosed with diabetes, treatment and control rates did not change: from 44.1% to 51.9%, p=0.251 and from 30.2% to 34.0%, p=0.830, respectively. A trend towards higher treatment of participants with diabetes was found after multivariable adjustment, while no changes were found for overall prevalence, diagnosis or control. Among antidiabetic drugs, percentage of combinations increased (from 12% to 23%); percentage of sulfonylureas and biguanides decreased (15% to 6% and 63% to 54%, respectively), while no trend was found for insulin. After multivariable analysis, women with diabetes were less likely to be treated but more likely to be controlled, the opposite trend being found for obesity.

Conclusions: only about half of participants diagnosed with diabetes receive antidiabetic treatment, and glycaemic control remains poor. Trends in drug prescription are changing, with combination therapy gaining importance.

Keywords: diabetes; antidiabetic treatment; glycaemic control; Switzerland.



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P11

BabelDr vs. Google Translate: translation in a pharmacy setting

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Introduction: Refugees seeking medical help in busy emergency rooms face language barriers when interacting with doctors. One possibility to lower the burden of emergency rooms is performing triage for minor health disorders in community pharmacies. So far, no specialized machine translation system has been developed to help pharmacists and their team with the language barrier. Recent research shows that Google Translate (GT) is used in healthcare, although it is not trained for a medical setting. The research presented here aims to evaluate whether BabelDr (BD), a flexible speech-enabled phraselator developed for the medical domain, is better suited to perform triage in a pharmacy setting than GT with Arabic-speaking patients.

Methods: We adopted an experimental design inviting 8 pharmacists to orally perform triage in French with both systems on three scenarios (cystitis, headache, and sore throat) with two standardized Arabic patients. We collected system usage (time, interactions, diagnoses) and user satisfaction. In addition, both standard Arabic and Arabic dialects speakers evaluated the adequacy of the translations on a scale: correct, mistranslation, and nonsense. Translations were considered incorrect if rated as mistranslation or nonsense.

Results: Concerning diagnoses, all pharmacists reached a correct diagnosis with both systems. The time taken to complete the scenarios was similar across systems, with more total interactions and fewer unsuccessful interactions in GT. For satisfaction, pharmacists preferred BD to GT. For the standard Arabic speakers, 95% of BD›s translations were rated as correct compared to 90% of correct translations with GT. For the Arabic dialect speakers, 92% of BD›s translations were evaluated as correct as opposed to 85% of correct translations with GT.

Conclusions: Our pilot study suggests that BD is better suited than GT to perform triage in pharmacies for user satisfaction. For adequacy, BD's translations are slightly better for speakers of standard Arabic and Arabic dialects. For successful interactions, GT is the most usable system. Nonetheless, pharmacists reached a correct diagnosis with both systems.

P12

Change in e-liquids flavor use and nicotine concentration over 6-months in participants of a smoking cessation trial with electronic nicotine delivery systems (ENDS): the ESTxENDS trial

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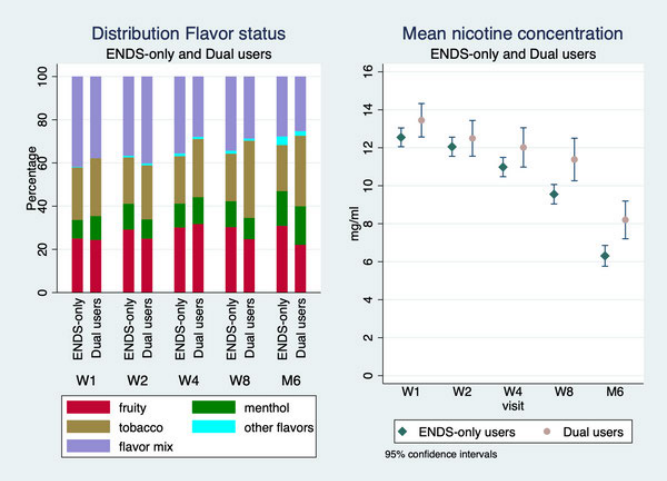
Introduction: Electronic nicotine delivery systems (ENDS) are increasingly used for smoking cessation. The broad choice of flavors and nicotine concentrations among ENDS e-liquids may help in smoking cessation. We aimed to describe the pattern of flavor choice and nicotine concentrations in e-liquids among ENDS-only and dual using participants of a smoking cessation RCT.

Methods: This is a subgroup analysis from the Efficacy, Safety, and Toxicology of ENDS for smoking cessation trial, an RCT on 1243 adult smokers willing to quit smoking with the help of ENDS. We described the pattern of used e-liquids over 6 months among participants from the intervention group (n=620). We offered ENDS and six different e-liquid flavors (two tobacco flavors, menthol, green apple, raspberry, and red fruits) in four different nicotine concentrations (0, 6, 11, and 19.6 mg/ml) that could be mixed. We assessed the use of flavors and nicotine concentrations at 1 week and 6 months after target quit date, comparing participants who only vaped (ENDS-only users) to those who vaped and smoked (dual users) in the previous 7 days. We applied multivariate logistic regression models to compute risk ratios of use of flavors and multivariate linear regression models for nicotine concentration. We used inverse probability weighting to account for attrition.

Results: Among 620 participants, median age was 38 years (IQR 29-52), and 53% identified as men. 409 ENDS-only and 129 dual users provided information on e-liquids at week 1. At month 6 there were 266 ENDS-only and 102 dual users. Other participants were quitters, smokers, or missing.
At week 1, flavor choices were similar between ENDS-only and dual users. At month 6, ENDS-only users reported fewer tobacco flavors (21% vs. 33%, RR 0.49, p<0.001) and more fruity flavors (31% vs. 22%, RR 2.10, p=0.007) than dual users. Other flavor choices among the two groups were similar.
The mean nicotine concentration used at week 1 was similar between ENDS-only and dual users (12.4 vs. 13.3 mg/ml, p=.51). At month 6, ENDS-only users used a lower mean nicotine concentration than dual users (6.2 vs. 8.3 mg/ml, p=0.02).

Conclusion: ENDS-only users used more fruity and less tobacco-flavored ENDS, and a lower nicotine concentration than dual users at 6 months. These data can help smokers and health care professionals to better understand the transition process from smoking to ENDS use.

Figure) Flavor choice and mean nicotine concentration



P13

Effects of Electronic Nicotine Delivery Systems (ENDS) for smoking cessation on systolic blood pressure - secondary analyses of the ESTxENDS trial

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Introduction: The existing evidence on the effect of electronic nicotine delivery systems (ENDS) for smoking cessation on blood pressure is conflicting. In a secondary analysis of a smoking cessation randomized controlled trial (RCT) we aimed to assess the differences in systolic blood pressure (SBP) at 6-months follow-up between participants who received ENDS and standards of care smoking cessation counselling (SOC) (intervention group[IG]) versus SOC alone (control group[CG]).

Methods: We analyzed data from participants of the ESTxENDS RCT. We assessed differences in SBP at 6-month follow-up and between baseline and 6-month follow-up in an intention to treat analysis (ITT). We also performed a per-exposure analysis in the IG where we compared changes in SBP among different user groups (quitters, continuing smokers, dual users [ENDS and tobacco], ENDS-only users with or without nicotine) based on self-reported use within 7 days before the 6-month follow-up. Data were analyzed using linear regression models adjusting for baseline covariates and using inverse probability censoring weights to account for attrition.

Results: Blood pressure measurements were available for 1239 participants at baseline (99.7%; n=617 in the IG, n=622 in the CG) and for 776 participants (62%; n=439 in the IG, n=337 in the CG) at 6-month follow-up. Participants' median age was 40 years, and 45% identified as women.
The mean (SD) SBP at baseline was 122.1 (14.5) mmHg in the IG and 123.3 (15.3) mmHg in the CG (p=.30). Mean change in the SBP after 6 months was -1.3mmHg (95%CI:-2.26 to -0.27) in the IG and -1.5mmHg (95%CI:-2.71 to -0.38) in the CG (p=.72). In the IG at the 6-month follow-up were 46 (10.5%) quitters, 86 (19.6%) continuing smokers, 85 (19.4%) dual users, 180 (41.1%) ENDS-only users with nicotine, and 41(9.4%) ENDS-only users without nicotine. In ITT analyses we found no evidence for an effect of the intervention on the mean SBP at 6-months follow-up (coeff -0.15; 95%CI:-1.51 to 1.22; p=.83) or on change of SBP from baseline to 6-months follow-up (coeff -0.10; 95%CI:-1.46 to 1.27; p=.89). In per-exposure analyses in the IG, we did not find significant differences (p≥.15) in the mean SBP at 6 months or in the change from baseline to 6-month follow-up between user groups.

Conclusion: Among smo kers participating in the ESTxENDS RCT, ENDS added to SOC did not affect blood pressure compared to SOC alone. ENDS for smoking cessation does not lead to changes in blood pressure.

P14

Genetic risk scores are not important for diabetes management

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Introduction: Several genetic risk scores (GRS) for type 2 diabetes (T2DM) have been published, but not replicated. We assessed the effect of different GRS on prevalence and management of T2DM in a sample of community-dwelling people from Switzerland.

Methods: Four waves from a prospective study conducted in Lausanne. Seven GRS related to T2DM were selected, and compared between participants with and without T2DM, and between controlled and uncontrolled participants treated for T2DM.

Results: data from 5426, 4017, 2873 and 2170 participants from the baseline, first, second and third follow-ups, respectively, was used. In all study periods, participants with T2DM scored higher than participants without T2DM in six out of seven GRS. Data from 367, 437, 285 and 207 participants with T2DM was used. In all study periods, approximately half of participants treated for T2DM did not achieve adequate fasting blood glucose or HbA1c levels, and no difference between controlled and uncontrolled participants was found for all seven GRS (see figure and table). Power analyses showed that most GRS needed a sample size above 1000 to consider the difference between controlled and uncontrolled participants as statistically significant at p=0.05.

Conclusion: In this study, we confirmed the association between most GRS and diabetes. Conversely, no consistent association between GRS and diabetes control was found. Use of GRS to manage patients with T2DM in clinical practice is not justified.

Figure: distribution of the genetic risk scores according to presence or absence of diabetes. Panel A) Andersson score; B) Liu score; C) Martono score; D) Pechlivanis score; E) Szczerbinski score; F) Wang score; G) Werissa score; H) Full score; I) Short score.

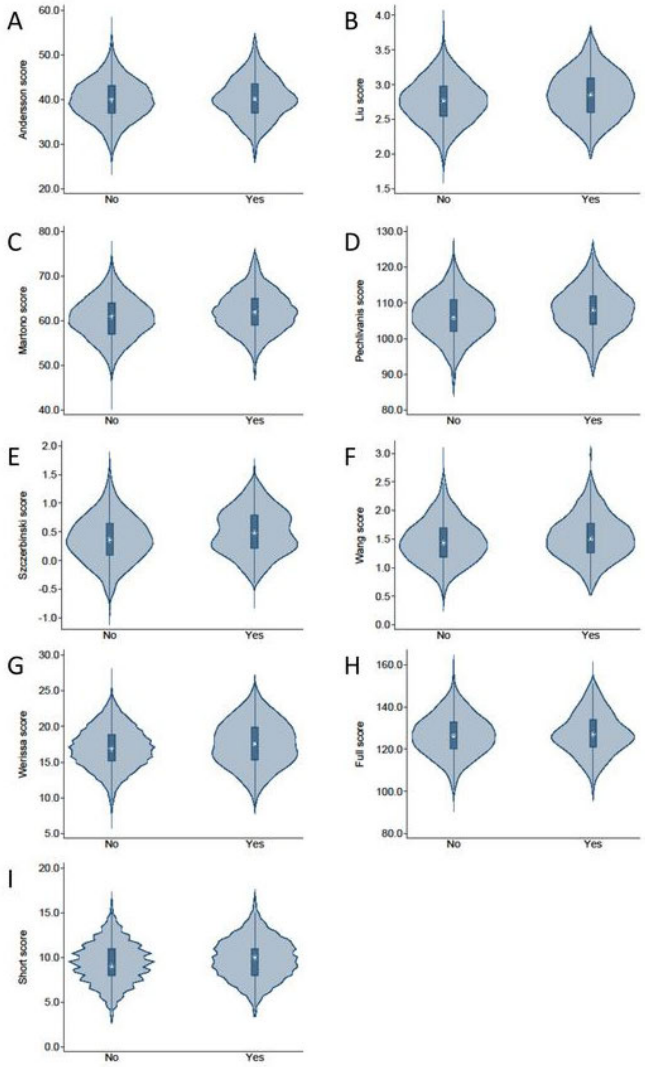

Table: multivariate analysis of diabetes genetic risk scores according to diabetes control as defined by HbA1c levels, by survey period, CoLaus study, Lausanne, Switzerland.

		Second follow-up (2014-2017)			Third follow-up (2019-2021)	
	Not controlled (n=132)	Controlled (n=92)	P-value	Not controlled (n=95)	Controlled (n=62)	P-value
Andersson	40.0 ± 0.4	40.6 ± 0.5	0.423	39.2 ± 0.5	41.0 ± 0.6	0.023
Martono	62.2 ± 0.4	61.1 ± 0.5	0.105	61.7 ± 0.5	62.3 ± 0.6	0.509
Szcerbinski	0.54 ± 0.04	0.50 ± 0.05	0.524	0.48 ± 0.04	0.58 ± 0.05	0.149
Werissa	17.6 ± 0.3	17.5 ± 0.4	0.759	17.1 ± 0.3	17.9 ± 0.4	0.188
Liu	2.89 ± 0.03	2.80 ± 0.04	0.067	2.83 ± 0.04	2.86 ± 0.05	0.671
Pechlivanis	109 ± 1	107 ± 1	0.129	109 ± 1	109 ± 1	0.582
Wang	1.50 ± 0.03	1.47 ± 0.04	0.542	1.52 ± 0.04	1.43 ± 0.05	0.172
Large score	126 ± 1	128 ± 1	0.070	125 ± 1	127 ± 1	0.351
Short score	9.8 ± 0.2	9.7 ± 0.3	0.840	9.4 ± 0.2	10.0 ± 0.3	0.123

Statistical analysis by ANOVA adjusting for age (continuous), gender, marital status (yes, no), educational level (high, medium, low), smoking categories (never, former, current), alcohol consumption (yes, no) and body mass index categories (normal, overweight, obese).

P15

Job stress and job satisfaction among general practitioners: evolution between 2012 and 2019 in 11 Western countries

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Introduction: General practitioners (GPs) occupy a crucial place in the health systems that are increasingly moving towards strengthening primary care. This situation is part of a context of an ageing population, a shortage of GPs and the feminisation of the profession. It is therefore essential to describe and to study the evolution of stress and job satisfaction among GPs so that policy makers can take the most appropriate decisions about the organization of health systems. Our study aimed to describe the change over time of frequency of job stress and job satisfaction of GPs in 11 Western countries between 2012 and 2019.

Methods: The data of this international cross-sectional study came from the Commonwealth Fund International Health Survey of Primary Care Physicians conducted in 2012, 2015 and 2019. 11 Western countries participated in these surveys. Random samples of primary care physicians practicing were drawn from government or private lists in each country. The question on job satisfaction as a GP is reported in 3 surveys (2012, 2015 and 2019) and the question on GPs' job stress is reported in 2 surveys (2015 and 2019). These two indicators were measured by using the questions: "How stressful, if at all, is your job as a GP?" (5-point Likert scale) and "Overall, how satisfied are you with practicing medicine?" (4-point Likert scale in 2012 and 2015; 5-point Likert scale in 2019). Sociodemographic characteristics of GPs, such as sex and age, completed the set of variables.

Results: In 2019, the prevalence of GPs' job stress varied from 29% to 65% according to country. Between 2015 and 2019, there was a significant increase ($p<0.01$) in job stress among GPs in 9 countries, among female and male GPs but with a consistently higher level of stress among female GPs and also in all age groups. In 2019, the prevalence of GPs' job satisfaction varied from 32% to almost 70% according to country. Between 2012 and 2015, the job satisfaction of GPs in different countries evolves in a distinct way, with an increase in some countries, a decrease in others and even stagnation. Finally, no significant differences ($p>0.05$) were found for the evolution of job satisfaction between 2012 and 2015 among female and male GPs and in all age groups.

Conclusion: It is worrying that job satisfaction among GPs is globally stagnating while there is a significant increase in perceived stress in the opposite. It is therefore essential to continue to monitor these parameters in order to make links with organisational factors and to move health systems in a satisfactory direction, particularly in the current context of resilient healthcare systems.

P16

Near-peer education, a powerful tool for clinical skills development

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Introduction: Formative objective structured clinical examinations (OSCE) are used to acquire clinical skill during undergraduate medical education. Involvement of senior students as tutors has been shown to be beneficial for the learning process. The aim of the study was to create a new near peer led formative OSCE and assess its feasibility, usefulness as well as its impact on students' performance during summative OSCE.

Method: The formative OSCE consisted of a 2 hour session during which 3rd year students (junior) could practice clinical skills on 3 clinical situations focused on systems often poorly mastered at the end of the bachelor years under the supervision of a tutor (4th-6th year medical student). The tutor facilitated a group of 3 students playing successively the roles of the clinician, the observer or the patient for musculoskeletal, neurological, gynaecological, emergency or haematological complaints. Both groups of students were asked to respond to an online survey evaluating their self-perceptions regarding the usefulness of the OSCE for clinical skills training, and the tutor's teaching skills (Likert scale 1-5). Students' scores at the summative 3rd year OSCE scores were collected.

Results: Out of 159, 115 3rd year medical students and 26 tutors participated. Response rates to the online survey were 33% and 61%. Junior students considered that attending the near peer formative OSCE improved their clinical history taking (mean 4.55 SD 0.64), physical exam (mean 4.60 SD=0.63) and clinical reasoning skills (mean 4.60 SD 0.69). Junior students highly valued tutors' feedback (mean 4.81;SD=0.82) and facilitation skills (mean 4.42 SD 1.02). They considered the formative OSCE to be useful (mean 4.77 SD=0.52). Junior students who attended the near peer formative OSCE had higher global scores (mean 79.0±7.2 vs 75.5±6.1 at the summative OSCE (p=0.015) after adjustment by gender and type of stations attended during the exam. Tutors perceived that they improved their clinical skills (mean 3.98 SD 0.94) and learned teaching skills during this OSCE (mean 4.80 SD 0.41).

Conclusion: Near peer OSCE are not only perceived a valuable way to improve junior students' clinical skills but they improve their performance at summative OSCEs. It also allows senior students to improve their own clinical skills and develop teaching skills. Near peer teaching should be more constantly used during undergraduate medical training.

P17

Recurrent episodes of febrile dyspnoea: hypersensitivity pneumonitis caused by a household ultrasonic humidifier

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Learning points: Hypersensitivity pneumonitis is an immune-mediated interstitial lung disease that presents with respiratory symptoms, with or without other constitutional symptoms, following exposure to an identified or unidentified external factor. It must be considered in patients with any newly identified interstitial lung disease. Diagnosis is achieved by combining clinical, radiological and histopathological patterns, with an interesting role for household investigations.

Case: A 50-year-old man presented with three repeated episodes of febrile dyspnoea within a period of 2 months. The first episode was accompanied by fever, loss of appetite and fatigue. Investigations showed an inflammatory syndrome with high c-reactive protein levels and leucocytosis. High-resolution computed tomography (HRCT) of the chest showed micronodular infiltrates with ground-glass opacities predominant in the upper lobes. The patient was hospitalised three times but no infectious, autoimmune, or neoplastic aetiology was identified. He recovered each time and went home, but was hospitalised again within 48 hours. His family members had no symptoms. The patient underwent a transbronchial biopsy with results showing a predominance of lymphocytes with increased mast cells and eosinophils. Finally, to search for the origin of the antigen exposure in the patient's environment, a household investigation was undertaken, and an ultrasonic humidifier was found. A positive reaction test to immunoglobulin precipitins specific to microorganisms found in humidifiers confirmed the diagnosis. Treatment consisted of eviction of the humidifier and a course of oral corticosteroids. The patient had no recurrence of symptoms and showed complete functional and radiological recovery.

Discussion: Hypersensitivity pneumonitis can be tiggered by various extrinsic factors, including household items like ultrasonic humidifiers. The clinical presentation of hypersensitivity pneumonitis can be dramatic, and the differential diagnosis is broad. An efficient diagnostic process lies in identifying the clinical syndrome of hypersensitivity pneumonitis, consistent chest HRCT scan results, bronchoscopy, and environmental evaluation.

Figure 1: Chest HRCT at admission with red arrows indicating interstitial micronodular infiltrates (left) and at 3 months follow-up (right).

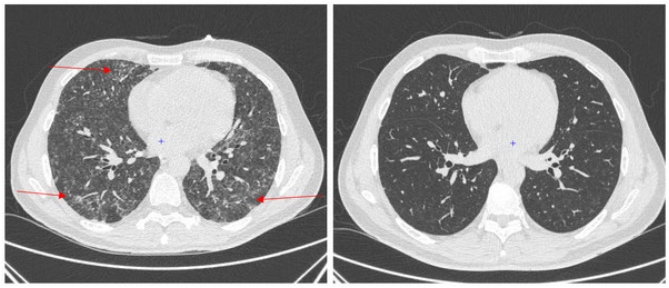

Figure 2: The ultrasonic humidifier used by the patient: (a) body (b) inside of tank. (c-d) small removable tray to infuse essential oils.

P18

Red cell Omega-3 fatty acid levels positively correlate with cognitive performance in atrial fibrillation

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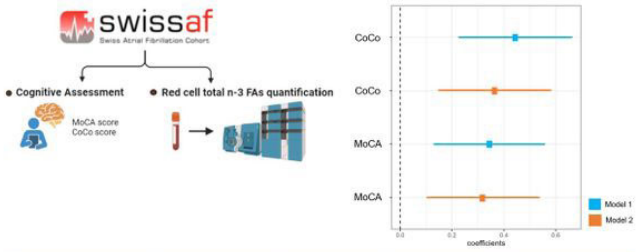
Introduction: Atrial fibrillation (AF) is associated with cognitive impairment and dementia. The neuroprotective effects of omega-3 Fatty Acids (n-3 FAs) against cognitive decline are controversial. We, therefore, aimed to determine the correlation of n-3 FAs with cognitive function in AF patients.

Methods: Red cell n-3 FAs levels were determined by gas chromatography and mass spectrometry in 2359 patients from the multicenter Swiss Atrial Fibrillation study (Swiss-AF). To assess the overall cognitive performance of patients, we used the cognitive construct (CoCo) to summarise all validated neurocognitive assessments. One of these assessments was the well-established Montreal Cognitive Assessment (MoCA). We performed mixed-effect linear regression analyses. Two adjustment models were applied; model 1 (adjusted for age, sex, and educational level) and model 2 (adjusted for age, sex, educational level, history of stroke, AF type, heart rate, arterial hypertension, diabetes, coronary artery disease, BMI, chronic kidney disease, smoking status, alcohol consumption, geriatric depression scale, use of oral anticoagulation and antiplatelet medication). We also included a random intercept to control for center-effect in both models.

Results: The mean age of our study population is 73 (standard deviation [SD] 8.4). 662 patients are females (28%). 318 and 716 patients had a history of stroke (13%) and coronary artery disease (30%), respectively. We observed a statistically relevant positive association of n-3 FAs levels with better cognitive performance as assessed by both the CoCo score (Model 1: coefficient 0.444, 95% CI [0.225, 0.664], p=0.001; Model 2: coefficient 0.363, 95% CI [0.15, 0.576], p=0.001) and the MoCA score (Model 1: coefficient 0.345, 95% CI [0.133, 0.559], p=0.002; Model 2: coefficient 0.317, 95% CI [0.105, 0.527], p=0.003)

Conclusions: Red cell n-3 FAs levels are associated with better cognitive performance in AF patients who are at risk for the development of dementia. However, the biological relevance remains to be determined.



	Model 1			Model 2		
Correlation of Total n-3 FAs levels and	Coefficient	95% CI	P value	Coefficient	95% CI	P value
MoCA score	0.345	0.133-0.559	0.002	0.317	0.105-0.527	0.003
CoCo score	0.444	0.225-0.664	0.001	0.363	0.15-0.576	0.001

P19

Social issues in general practice – an interprofessional perspective of general practitioners and social workers on frequency, challenges and needs

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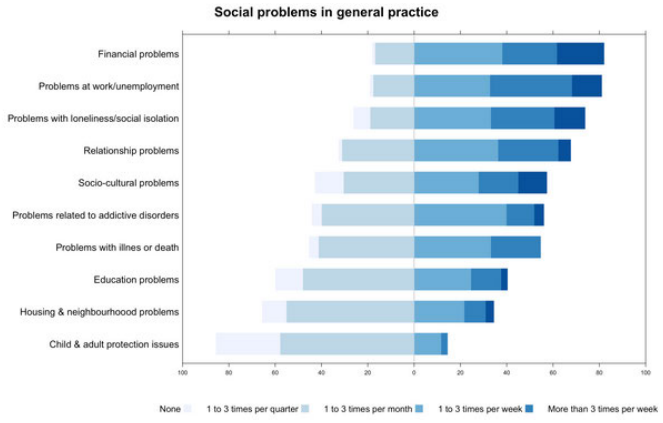
Introduction: Health or illness and social issues cannot be viewed in isolation. Social problems can influence well-being and disease. General Practitioners (GPs) are requested to offer counselling opportunities to adequately respond to the social issues of their patients. Counselling on non-medical issues in general practice increases GPs' workload. This study aimed to identify the strengths and weaknesses of current working arrangements between social services and general practice in the care of patients in a primary care setting and to explore views, attitudes, obstacles, and needs of the components of good practice in joint working.

Method: The cross-sectio nal online survey was carried out between December 2022 and January 2023 among a stratified random sample (sex, care region) of Swiss GPs from the Sentinella-Network[1], the uniham-bb-Network[2], and social workers from the SAGES-Network[3]. The questionnaire assessed the nature and frequency of social problems, and the challenges and needs, in terms of the current collaboration between GPs and social workers.

Results: Preliminary findings come from a sample of 89 GPs (mean age 55 years, 32.6% female), and 42 social workers (mean age 40 years, 77.8% female). The most common social issues mentioned by GPs were "Financial problems" (82% min. 1-3 per month), "Problems at work and unemployment" (81% min. 1-3 per month), and "Problems with loneliness and social isolation" (73.8% min. 1-3 per month) (see graph). Social issues often took up more than 50% of the consultation time (in 46.7% of all cases). More than half of GPs (n=41, 54.7%) reported having contact with social workers less than once a month, while social workers reported having contact with GPs one to three times a month on average (n=15, 44.1%). GPs (n=52, 69.3%) and social workers (n=24, 72.7%) would like to have more contact in the future. The most frequently mentioned benefits of an increased collaboration were "improved quality of care (more time for medical issues)" (n=54, 60.7%) and "improved mental health of patients" (n=49, 55.1%).

Conclusion: Preliminary results indicate that social problems in general practice are common and time-consuming. Currently, working arrangements between social services and general practice are still rare. For a majority of GPs and social workers, there is a desire for increased collaboration. To improve the quality of care as well as the mental health of patients, joint work should be promoted in the future.



P20

Vitamin and dietary supplements are not associated with total or cardiovascular mortality in Switzerland: the CoLaus|PsyCoLaus prospective study

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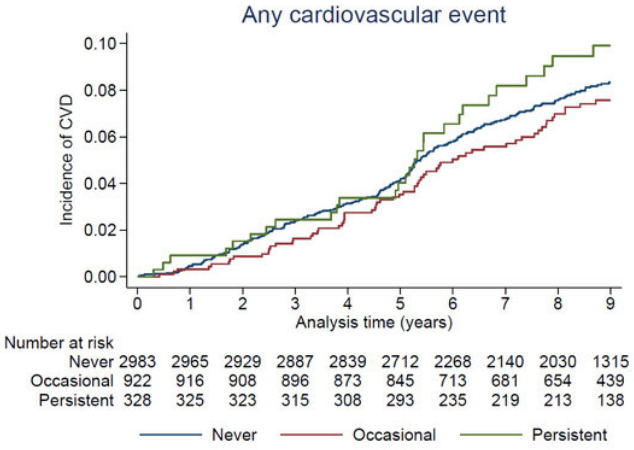
Introduction: Vitamin and dietary supplements are taken by a large fraction of the population, based on the belief of their beneficial effects on health. Whether taking vitamin or dietary supplements impacts mortality and CVD has seldom been studied.

Methods: Prospective study using data from the CoLaus study, a population-based cohort from Lausanne, Switzerland. Participants were categorized as non-users (no consumption at baseline and first follow-up), persistent users (consumption at baseline and follow-up), and occasional users (consumption either at baseline or follow-up). Incidence of cardiovascular events and of total mortality was assessed using the period between the first and the third follow-ups.

Results: Data from 4273 participants (57.4±10.4 years, 55% women) followed for a median of 9 years (interquartile range: 7-9) was used. The total mortality rate was 9.5 (8.3-10.9), 9.4 (7.5-11.7) and 11.5 (8.2-16.1) per 10,000 person-years for never, occasional, and persistent consumers, respectively (p=NS). The CVD mortality rate was 1.5 (1.1-2.1), 1.5 (0.9-2.7) and 2.4 (1.1-5.0) per 10,000 person-years for never, occasional, and persistent consumers respectively (p=NS). Incidence of CVD events was 9.1 (7.9-10.4), 8.2 (6.5-10.4) and 11.1 (7.9-15.7) per 10,000 person-years for never, occasional, and persistent consumers respectively (p=NS) (Figure). On multivariable analysis, no association was found between vitamin and supplement use and total or CVD mortality, or CVD events (Table).

Conclusion: In this prospective study, we found no association between vitamin and dietary supplement use and total or CVD mortality, or CVD events.

Figure: Incidence of cardiovascular disease according to vitamin/dietary supplement use, CoLaus|PsyCoLaus study, Lausanne, Switzerland"



	Bivariate	P-value	Multivariate	P-value
Mortality				
Never	1 (ref)		1 (ref)	
Occasional	0.98 (0.76 - 1.27)	0.874	0.96 (0.73 - 1.26)	0.778
Persistent	1.25 (0.87 - 1.79)	0.230	0.80 (0.55 - 1.18)	0.264
CVD mortality				
Never	1 (ref)		1 (ref)	
Occasional	1.04 (0.55 - 1.98)	0.894	0.97 (0.49 - 1.93)	0.926
Persistent	1.68 (0.74 - 3.79)	0.215	1.12 (0.48 - 2.63)	0.799
CVD events				
Never	1 (ref)		1 (ref)	
Occasional	0.91 (0.70 - 1.19)	0.498	0.95 (0.72 - 1.25)	0.704
Persistent	1.17 (0.81 - 1.69)	0.414	0.95 (0.64 - 1.40)	0.788

Poster SGAIM / Posters SSMIG

P21

A multimodal intervention to reduce the proportion of misused inhalers by COPD patients at hospital discharge – a monocentric quasi-experimental study

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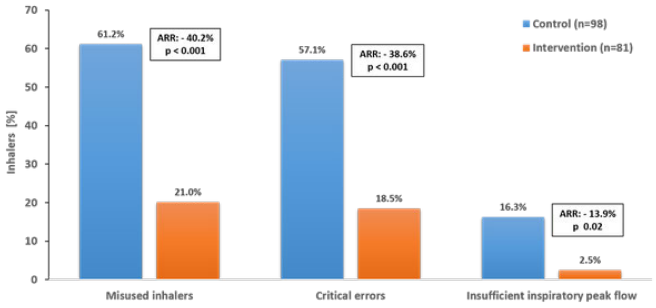
Introduction: Chronic obstructive pulmonary disease (COPD) is a common disease responsible for high symptoms burden and a significant number of hospitalization. The effectiveness of drug treatment is limited by the sub-optimal use of inhalers. Misused inhalers (MI) are common and associated with poor disease control. MI may result from errors in the inhalation technique or insufficient peak inspiratory flow (PIF). The proportion of MI at hospital discharge is poorly studied, but hospitalization could be a good opportunity to improve the use of inhalers.

Methods: We conducted a monocentric quasi-experimental study between April 2022 and December 2022 in the internal medicine department of the HFR Fribourg, Switzerland. The study aimed to compare the proportion of MI in a control group and in a group benefiting from a multimodal intervention. The intervention consisted of (1) an evaluation of the inhalation technique and of the PIF at admission, (2) the supply of a prescription guide to assist in the selection of an optimal inhaler, and (3) therapeutic education when prescribing a new inhaler or identifying errors in inhalation technique. The primary outcome was the proportion of MI at hospital discharge. MI is defined as an inhaler used with a critical error (CE) and/or insufficient PIF. CE is defined as an act or omission that impairs the delivery of the drug to the distal airways.

Results: The study included 93 patients, 46 in the control group and 47 in the intervention group. The mean age of the participants was 70.5 years, 56 (60.2%) were men and 57 (61%) were hospitalized for an exacerbation of COPD. The patients used an average of 1.92 inhalers at hospital discharge; therefore, 98 inhalers were analyzed in the control group and 81 in the intervention group. The proportion of MI at discharge was 61.2% in the control group and 21.0% in the intervention group (Absolute risk reduction 40.2%, 95% CI 23.4 - 57.0, p< 0.01). The proportion of inhalers used with at least one CE decreased from 57.1% to 18.5% (p< 0.01) and the proportion of inhalers used with insufficient PIF from 16.3% to 2.5% (p = 0.02) (Figure 1).

Conclusion: Misused inhalers are frequent at hospital discharge. An intervention including an assessment of inhalation technique and peak inspiratory flow, combined with a prescription guide and therapeutic education significantly reduced inhaler misuse. This intervention should become a standard of care for hospitalized COPD patients.

Figure 1: Reduction of misused inhaler, inhalers used with critical errors or insufficient peak inspiratory flow at hospital discharge
ARR: absolute risk reduction



P22

A unique paraneoplastic occurrence of Sweet syndrome with peripheral neuropathy in a patient with metastatic clear-cell renal carcinoma

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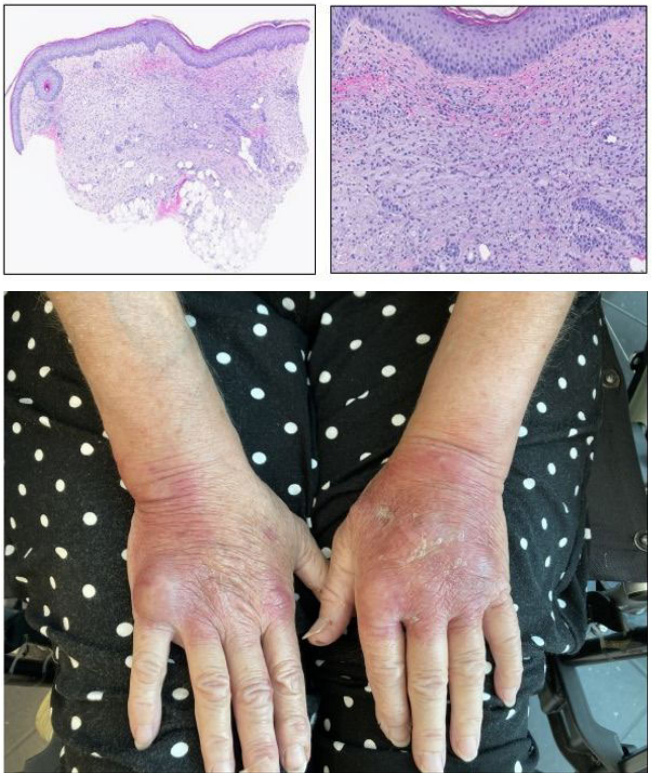
Learning Objectives: The pathogenesis of paraneoplastic Sweet Syndrome remains unclear. Sweet Syndrome belongs to a broad histologically diagnosed umbrella of neutrophil dermatosis. If suspecting Sweet Syndrome, guidelines are important to avoid misdiagnosis. The synergistic presentations of both Sweet Syndrome and sensorimotor axonal peripheral neuropathy (SMAPN) as a paraneoplastic manifestation in renal cell carcinoma (RCC) has not been documented in the literature so far.

Case Report: A 70-year-old female patient with a newly diagnosed clear-cell RCC with osseous metastasis presented with sudden onset fever with erythematous painful blistering lesions on both hands dorsally. Blood tests showed markedly elevated inflammatory levels (C-reactive protein (CRP) 257.8 mg/l, leukocytes 17.79 x10^6/L, with 94% neutrophils). Histologically, there was predominately-neutrophil dermal infiltrate without leucocytoclastic vasculitis. The diagnostic criterion of Sweet Syndrome were fulfilled. A week later, the patient developed abrupt left hand palsy, characterised as a paraneoplastic medial and ulnar SMAPN. Treatment with oral high-dose steroids significantly improved the skin lesions. The peripheral nerve palsy improved after 3 months.

Discussion: Sweet Syndrome, also known as acute febrile neutrophilic dermatosis, is characterised by the abrupt appearance of painful oedematous, erythematous skin papules, nodules or plaques. Classified as an inflammatory condition, it is associated with fever with raised inflammatory markers. Malignancy Sweet Syndrome is seen in approximately 21% of cases (15% haematological malignancy, 6% solid tumours). There has only been one recorded case of Sweet Syndrome seen in a patient with RCC so far. Paraneoplastic neurologic symptoms occur in only 0.5-1% of patients with RCC. As with Sweet Syndrome, neuropathy is very rarely associated with RCC. The clinical and laboratory presentation, along with good steroid response, were compatible with the modified diagnostic Sweet Syndrome criteria. In 2017 a new diagnostic criteria, incorporating a more histological diagnostic approach of neutrophilic dermatosis was suggested. The exact pathophysiology of paraneoplastic Sweet Syndrome is unknown. This case may allow further clues into the mechanisms similar to that seen in paraneoplastic SMAPN in solid tumor malignancies, which may improve the molecular understanding of Sweet Syndrome.



A: Neutrophilic dermatosis **B:** Leukocytoclasia formation

P23

Agreement and changes between emergency department diagnoses and hospital discharge diagnoses. A retrospective case study in a Swiss tertiary referral hospital (Cantonal Hospital of Lucerne) [Master's Thesis]

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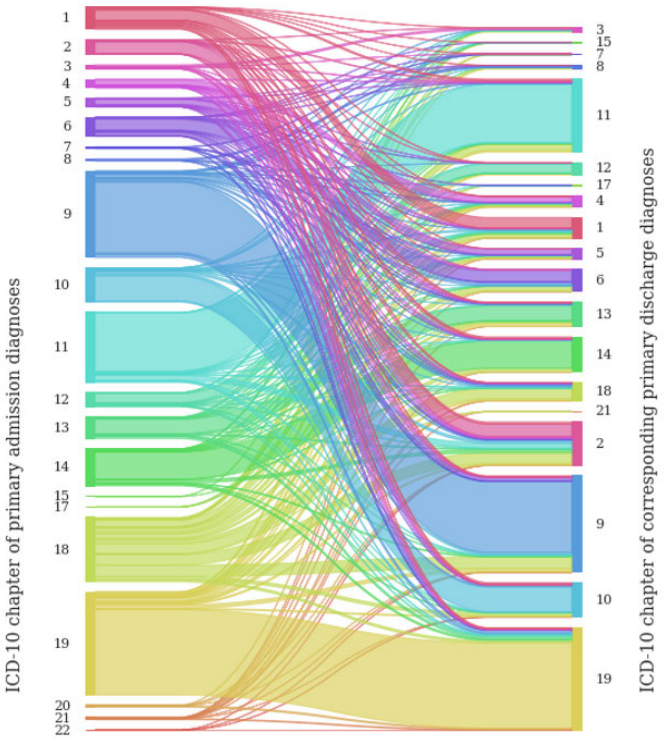
Introduction: Emergency departments are important access point to the care system and one of their challenging core task is diagnostics. This study examined the extent to which primary diagnoses made by emergency physicians agree with hospitals' primary discharge diagnoses. The aim was to gain data-based insight.

Methods: In this retrospective and descriptive study primary admission diagnoses of 7'317 inpatients of Lucerne Cantonal Hospital were analyzed over a two-year period (2020 to 2021). Main methods were machine learning and exploratory data analysis, including visual representation and descriptive statistics. To find patterns in disagreeing admission diagnoses a tree-based classification model was used. To quantify agreement, relative frequency within a diagnosis group was calculated, formed by highest level of monohierarchic ICD-10-GM classification.

Results: 68% of primary admission diagnoses agreed with primary discharge diagnoses and 21% became secondary discharge diagnoses. The extent of agreement between diagnosis groups varies, but gender does not affect it. 35% of inpatients over 60 have disagreeing primary admission diagnoses. By inpatients under 40 the extent of agreeing diagnoses is higher than that of disagreeing diagnoses. 28% of inpatients with disagreeing diagnoses has a leading symptom of abdominal pain (9.2%), general weakness (8.2%), shortness of breath (6.2%) or fever (4.4%).

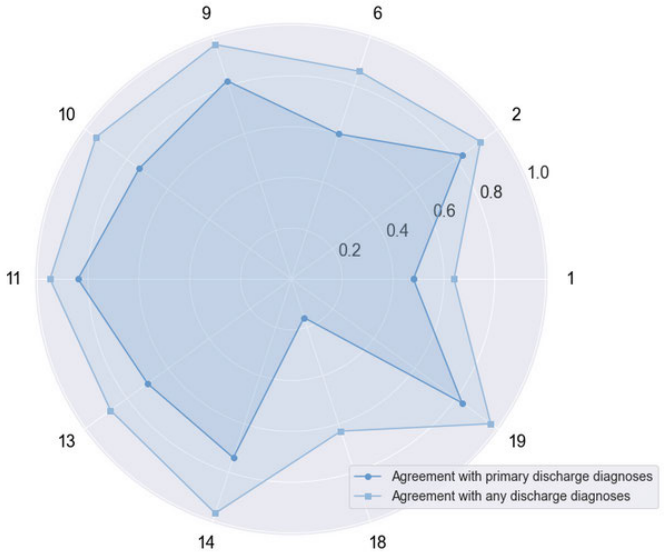
Conclusion: The extent of agreement depends on how the diagnoses are compared. Agreement of primary diagnoses decreases among older inpatients and inpatients with non-specific symptoms. A positive correlation was observed between these two patient groups.

Figure 1. Evolution of Primary Admission Diagnoses



ICD-10 chapters. Diseases of 1 infection, 2 neoplasms, 3 blood, 4 metabolism, 5 mental disorders, 6 nervous system, 7 eye, 8 ear, 9 circulatory, 10 respiratory and 11 digestive system, 12 skin, 13 musculoskeletal and 14 genitourinary system, 15 pregnancy, 17 congenital malformations, 18 abnormal clinical/laboratory findings, 19 injury and poisoning, 20 external causes of mortality, 21 factors influencing health status, 22 codes special purposes

Figure 2. Agreement Between Primary Admission and Discharge Diagnoses



ICD-10 chapters. 1 infectious diseases, 2 neoplasms, diseases of 6 nervous, 9 circulatory, 10 respiratory, 11 digestive, 13 musculoskeletal and 14 genitourinary system, 18 abnormal clinical/laboratory findings, 19 injury and poisoning

P24

Association of vaccination status with reported discrimination in patients with COVID-19

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Introducion: During the COVID-19 pandemic the debate regarding vaccination has become increasingly polarized within the general population. First studies show that vaccinated individuals feel moral reproach and antipathy towards people who are not vaccinated. However, there is no scientific evidence on the experience of non-vaccinated patients being treated at hospital due to Covid-19. Our aim was to investigate perceived healthcare-associated discrimination based on vaccination status in patients with Covid-19 receiving hospital treatment.

Methods: This exploratory observational study included adult patients presenting to the emergency department or hospitalized in two Swiss tertiary-care hospitals for Covid-19 between June 1 to December 31, 2021. The primary endpoint was patients perceived healthcare-associated discrimination, which we measured with the Discrimination in Medical Settings (DMS) scale. Secondary endpoints included different aspects of perceived quality of care.

Results: Patients that were not vaccinated (n=113) felt significantly more discriminated against by the healthcare team (mean, 9.54 points [SD, 4.84] vs. 7.79 points [SD, 1.85]; adjusted difference, 1.18 [95% CI, 0.04 to 2.33 points], p=0.04) and felt treated with less respect by the nursing team (mean, 8.39 points [SD, 2.39] vs. 9.30 points [SD,1.09], adjusted difference, -0.6 [95% CI, -1.18 to -0.02 points], p=0.04) compared to patients who were vaccinated (n=80).

Conclusion: Our findings suggest that unvaccinated patients treated for Covid-19 may have experienced healthcare-associated discrimination due to their vaccination status. Awareness of bias against unvaccinated patients and patient-centered communication trainings might buffer negative hospital experience.

P25

Case report: Invasive Group A Streptococcus (GAS) infection with rapid progression to Streptococcal Toxic Shock Syndrome

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Learning Objectives: Streptococcal Toxic Shock Syndrome (STSS) evaluation/therapy.

Case: A 66-year old woman with history of asthma and hypertension presented with flu-like symptoms, progressive weakness for 7 days and new dyspnea at rest. Her blood pressure was 90/60mmHg, pulse 102/min; peripheral oxygen saturation 89%; respiratory rate 24/min, examination revealed bilateral basal rales. Laboratory tests showed leukocytosis and elevated CRP 490 mg/l, creatinine (244µmol/l), D-Dimers (6.24 µg) and INR (1.4). Chest CT revealed a 4 cm necrotizing structure and focal infiltrates in the left lower lobe, with surrounding pleural exudative effusion.The patient became rapidly hemodynamically unstable with progressive respiratory distress (SOFA 6 to 10 points), even though antibiotic therapy (Tazobactam/Piperacillin) was started immediately. Despite supportive therapy with vasopressors, volume resuscitation and mechanical ventilation, the patient developed multi-organ failure with coma, shock, respiratory failure, and severe combined acidosis within hours. The patient failed to stabilize on maximal therapy and died 14 hours after admission.Two of two blood cultures showed *Streptococcus pyogenes* (time to positivity 24h). Autopsy revealed a large pulmonary abscess in the left lower lobe and a segmental pulmonary embolism (not seen in the initial angiography).

Discussion: In 2022/23, a rising incidence of invasive GAS infections was described among children,[1] reflected by 6 pneumonias by GAS in adults in our hospital in the last 2 months.

The patient presented with GAS-sepsis with rapidly developing STSS, associated with high mortality rates. The inflammatory response to toxins with superantigen activity leads to rapid progression (Fig.1/2), here shown by multi-organ failure (circulatory/respiratory/renal failure, coagulopathy). Pulmonary GAS-infections have the highest mortality. Suspicion of STSS did not arise immediately, as it might have in the presence of skin lesions. Although Clindamycin seems to have a positive effect by inhibiting exotoxin production[2], it is often underused in these cases. Moreover, there is evidence for rising resistance in streptococci and replacement with Linezolid was advocated.[3] IVIG-therapy to reduce the toxin effect is controversial regarding its effectiveness.[2]
In conclusion, early clinical suspicion, immediate appropriate antibiotic and supportive therapy are essential for early diagnosis and successful management of STSS.

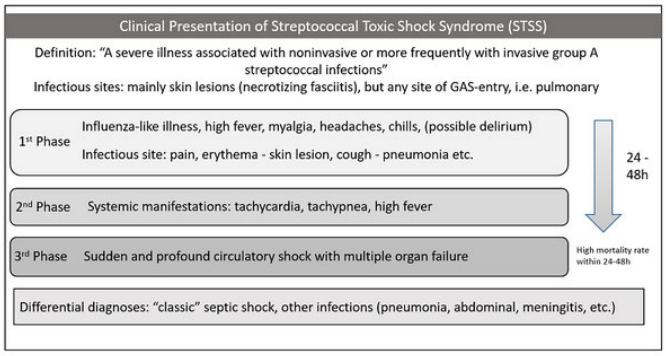

Figure 1

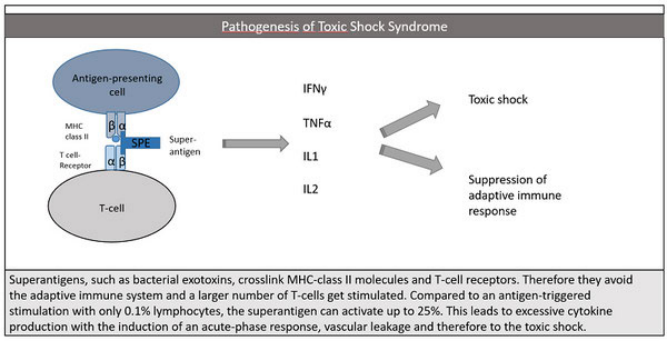

Figure 2

P26

Cutaneous adverse events due to Checkpoint Inhibitors – A single, retrospective analysis at the Lucerne Cantonal Hospital

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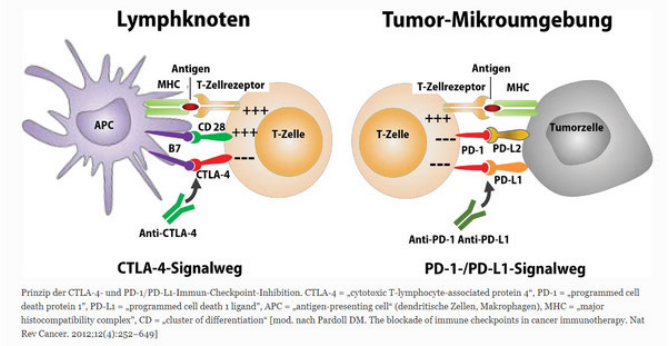
Introduction: Immunotherapy with Checkpoint-Inhibitors (CPI) revolutionized cancer treatment over the last years. They inhibit immune-checkpoints through small monoclonal antibodies by binding to the CTLA-4 (cytotoxic T-cell-lymphocyte-associated antigen-4) receptor, PD1-receptor (programmed cell death protein 1), or PD1-ligand (programmed cell death ligand 1), leading to an activation of the body's immune response against tumour cells. Beside the large benefit regarding cancer treatment, many adverse events are documented [1-3]. One of the most common and earliest adverse events are immune-related cutaneous adverse events (ir-CAE). In our study we analyse the role and basic characteristics of the ir-CAE and the impact on the further treatment.

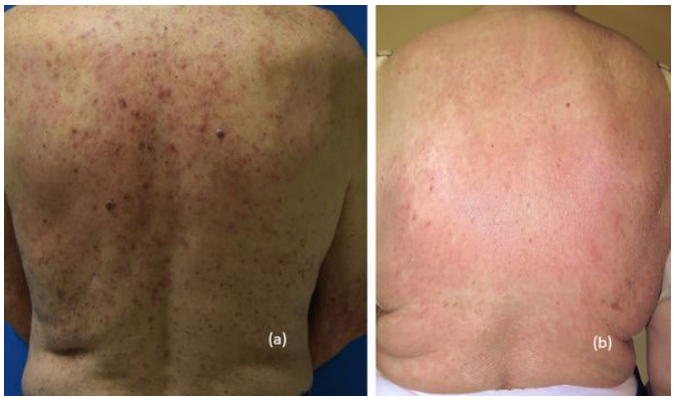


Prinzip der CTLA-4- und PD-1/PD-L1-Immun-Checkpoint-Inhibition. CTLA-4 = „cytotoxic T-lymphocyte-associated protein 4", PD-1 = „programmed cell death protein 1", PD-L1 = „programmed cell death 1 ligand", APC = „antigen-presenting cell" (dendritische Zellen, Makrophagen), MHC = „major histocompatibility complex", CD = „cluster of differentiation" [mod. nach Pardoll DM. The blockade of immune checkpoints in cancer immunotherapy. Nat Rev Cancer. 2012;12(4):252–649]

Methods: We performed a retrospective, monocentric descriptive study with data of the electronic health record data system from 09/2019 to 09/2022 at the Lucerne Cantonal Hospital. 380 patients (> 18 years old, with agreed general consent and immunotherapy with Pembrolizumab, Nivolumab, Ipilimumab, Avelumab, Durvalumab or Atezolizumab). We analysed the number of patients developing an ir-CAE, clinical presentation, the time to occurrence and how the ir-CAE were treated.

Preliminary Results: We demonstrate the preliminary data of our ongoing study. From what we have observed so far, following propositions can be done:

- 380 patients received a therapy with CPI.
- The most frequent tumours treated with CPI were squamous cell carcinoma (e.g. lung (n=126), nasopharyngeal (n=47)) and Melanoma (n=81).
- 26 % with Ir-CAE (n=97). 84% (n=83) of these patients suffered of pruritus, 53% (n=51) with maculopapular rash.
- 60% of Ir-CAE were managed with topical steroids and moisturizing externa
- 23 patients (24% with ir-CAE) were examined by a dermatologist.
- The therapy had to be stopped due to ir-CAE in 2% of all patients.
- 66% (n=251) of the therapies were interrupted. The interruption was mainly due to tumour progression (55%), death (13%) or not cutaneous immune related adverse events (20%).



Discussion: Immune-related cutaneous adverse events are often but mostly mild. In general the immunotherapy does not have to be stopped due to the cutaneous adverse events and can be managed with topical therapy. It is important to have a detailed clinical and histopathological report to correctly classify the skin reactions for a guideline-compliant treatment and possible improvement of the management for the future.

P27

Diagnostic workup and outcome in patients with profound hyponatremia

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Introduction: Hyponatremia is the most common disorder of electrolyte and water balance, affecting up to 35% of hospitalized patients.[1] We audited the management of hospitalized patients with profound hyponatremia (P-Na < 125 mmol/l) at KSBL (Kantonsspital Baselland).

Methods: In this retrospective, observational study, we included adult, hospitalized patients with a serum sodium < 125 mmol/l between October 2019 and March 2021. First, we audited the medical records for the diagnostic workup and its adherence to clinical practice guidelines[2], presence of a formulated treatment plan, treatment and outcome with regards to rehospitalisation within one year, in hospital mortality and one year mortality. Second, we compared patients with minimum diagnostic workup (measurement of sodium and osmolality in serum and urine, together with clinical volume status) and patients without, regarding outcome.

Results: Out of 263 identified patients 172 (67.3%) had complete minimum diagnostic workup (D-group). The other 91 patients (32.7%) did not get minimum diagnostic workup (N-group). Figure 1 shows the Kaplan Meier curves for 12-month survival for D- and N-group. Cox proportional hazards regression, corrected for polypharmacy and Charlson comorbidity index, did not show statistically significant differences in 12-month survival (HR 1.1, 95%-CI: 0.554 - 1.999). Regarding rehospitalization rate, 12-month mortality, and inpatient mortality there were no significant differences between the two groups (see Table 1).

Figure 1: Kaplan Meier curves for overall 12-month survival by group.

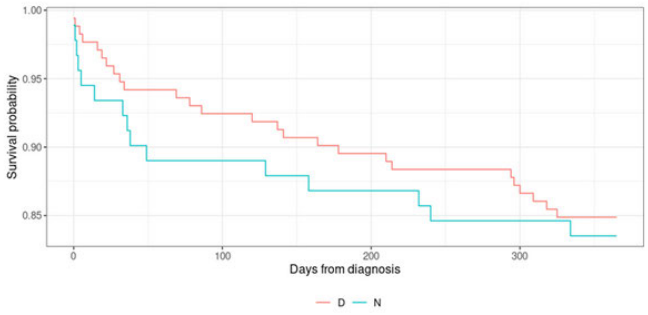

Table 1: Baseline characteristics and outcome in total and by group.

	Total	D-Group	N-Group	p-value
n (%)	**263 (100)**	**172 (67.3)**	**91 (32.7)**	
Age (years), median, IQR	77, 67 - 85	77, 68 - 85	77, 66.5 - 85	0.782
Sex female, n (%)	172 (65.4)	106 (61.6)	66 (72.5)	0.077
BMI (kg/m²), median, IQR	24.4, 21.8 - 28.1	25.1, 21.8 - 28.2	24.0, 21.8 - 27.6	0.429
P-Na at diagnosis (mmol/l), median, IQR	122, 119 - 124	121, 118 - 123	123, 121 - 124	0
Hyponatremia as main diagnosis, n (%)	43 (16.3)	37 (14.1)	6 (2.3)	0.007
Hyponatremia not mentioned in discharge report, n (%)	24 (9.1)	8 (3.0)	16 (6.1)	0.001
Rehospitalisation within 12 months[b], n (%)	**106 (42.1)**	**71 (42.5)**	**35 (41.2)**	**0.839**
Death as inpatient, n (%)	**11 (4.2)**	**5 (2.9)**	**6 (6.6)**	**0.155**
Death within 12 months, n (%)	**41 (15.6)**	**26 (12.8)**	**15 (16.5)**	**0.876**

Conclusions: There is need for improvement in initial laboratory testing and clinical workup of profound hyponatremia. Survival shows a trend for better outcome in patients with better adherence to clinical practice guidelines. Large prospective, randomized studies are needed to confirm theese findings.

P28

Factors that influence quality of life after attending a childhood cancer follow-up care program

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Background: Adult childhood cancer survivors (ACCS) are at risk for late effects due to their cancer and its treatment. Also, comorbidities occur earlier in life in ACCS compared to the general population. Therefore, follow-up care is needed to screen, treat, and potentially prevent late effects and comorbidities in ACCS. To date, the impact of follow-up care on the quality of life of ACCS is unclear.

Aim: We assessed the impact of the first clinical visit within a structured follow-up care program on the health-related quality of life (HRQoL) in ACCS and analyzed factors associated with a decreased HRQoL after the clinical visit.

Methods: Data of ACCS attending their first visit within a structured follow-up care program was derived from a prospective cohort study. ACCS completed a baseline and 3-months follow-up questionnaire on HRQoL (SF-36) and a baseline assessment on psychological distress (Global Severity Index (GSI), Mean=50, SD=10). We compared characteristics of ACCS with a clinically relevant decrease (MCID of ≥5 points) in the mental and/or physical component summary score of the SF-36 (MCS/PCS, Mean=50, SD=10) after three months to ACCS with unchanged or improved MCS/PCS.

Results: We analyzed 47 ACCS (median age 25.7 years [IQR 21.3; 38.9], 66% female, 79.6% employed). The table summarizes cancer-related information, late effects, and comorbidities. A clinically relevant decrease in the MCS and/or PCS after the consultation was reported in 14 (29.8%) ACCS (median decrease MCS -6.4 [IQR -11.4; 0.6], PCS -7.3 [IQR -10.7; -0.5]). ACCS, whose HRQoL decreased after the clinical visit, reported a lower PCS score at baseline (45.2 vs 55.6, p=0.007) but not a significantly different MCS. At baseline, ACCS with a decreased HRQoL reported more often low physical health (PCS<48) (71.4% vs. 27.3%, p=0.009) and high psychological distress (GSI≥63, 50% vs. 18.8%, p=0.03). In ACCS with decreased HRQoL, the proportion who reported more worries (53.9% vs 21.7%, p=0.05) and more fear (38.5% vs 16.0%, p=0.23) after the consultation was higher.

Conclusion: We observed a decrease in HRQoL in one-third of ACCS after attending a clinical follow-up care visit. Low baseline physical health and high psychological distress were associated with a decrease in HRQoL. Individualized care should also address potential distress, anxiety, and fear resulting from a clinical visit.

Table: Baseline characteristics of all included ACCS

Characteristics	Total	No decrease in HRQoL	Decrease in HRQoL	p-value[1]
	N (%) or median [IQR]			
Total	47 (100)	33 (70.2)	14 (29.8)	
Age, years	25.7 [21.3, 38.9]	24.8 [21.2, 36.3]	33.5 [23.5, 41.9]	0,08
Female sex	31 (66.0)	20 (60.6)	11 (78.6)	0,32
Current employment	35 (79.6)	22 (73.3)	13 (92.9)	0,30
Age at diagnosis	9.0 [4.2, 13.2]	5.9 [4.2, 12.4]	11.7 [4.2, 14.7]	0,58
Diagnosis				0,43
CNS Tumor	9 (19.2)	7 (21.2)	2 (14.3)	
Leukemia	15 (31.9)	11 (33.3)	4 (28.6)	
Lymphoma	11 (23.4)	5 (15.2)	6 (42.9)	
Sarcoma	6 (12.8)	5 (15.2)	1 (7.1)	
Others	6 (12.8)	5 (15.2)	1 (7.1)	
Treatment				
Surgery	35 (74.5)	24 (72.7)	11 (78.6)	1,00
Chemotherapy	45 (95.7)	32 (97.0)	13 (92.9)	0,51
Radiotherapy	28 (59.6)	20 (60.6)	8 (57.1)	0,83
Biologicals	18 (38.3)	14 (42.2)	4 (28.6)	0,37
Cisplatin	11 (23.4)	9 (27.3)	2 (14.3)	0,46
Years since treatment	18.5 [10, 27]	15.5 [9.5, 26]	25 [15, 28]	0,15
Relapse	4 (9.1)	3 (10.0)	1 (7.2)	1,00
Nr of patients suffering from a specific comorbidity				
cardiovascular	16 (34.0)	14 (42.2)	2 (14.3)	0.09
endocrinological	29 (61.7)	22 (66.7)	7 (50.0)	0,28
musculosceletal	29 (61.7)	20 (60.6)	9 (64.3)	0,81
neurological	22 (46.8)	14 (42.2)	8 (57.1)	0,36
pulmonal	18 (38.3)	15 (45.5)	3 (21.4)	0,19
renal	9 (19.2)	8 (24.2)	1 (7.1)	0,24
psychosocial	11 (23.4)	5 (15.2)	6 (42.9)	**0,040**
chronic pain	10 (21.3)	7 (21.2)	3 (21.4)	1,00
Low Physical Health	19 (40.4)	9 (27.3)	10 (71.4)	**0,009**
Low Mental Health	4 (8.51)	1 (3.0)	3 (21.4)	0,07

[1] Baseline characteristics were compared between the ACCS with a decrease in their HRQoL and the ACCS without a decrease using Wilcoxon rank sum test for continuous and chi-square or Fisher's exact test for categorical variables as appropriate

P29

Feasibility of monitoring of hospital aquired urinary tract infections using electronic health records

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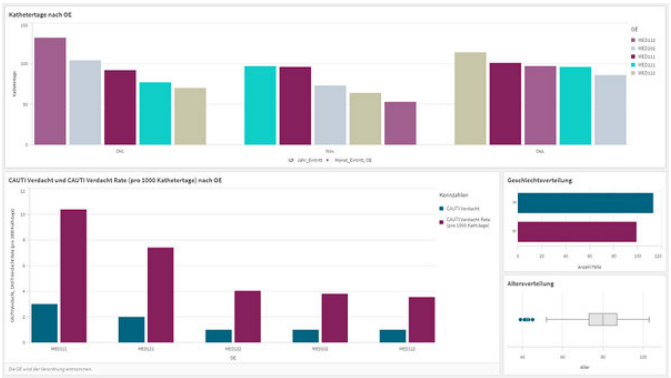
Introduction: Catheter-associated urinary tract infections (CAUTIs) contribute to morbidity and mortality as well as longer hospital stay and additional health care costs. Problems with surveillance of catheter use and associated complications arise mainly from data collection. Manual data collection requires a lot of personnel resources and manual data transmission is prone to error and thus, reduced data quality. Effective in-hospital surveillance therefore requires solutions that automatically monitor CAUTI by using existing data with low cost and high accuracy.

Methods: In this feasibility study, we used a business intelligence tool (QlikSense) to extract and analyze catheter data and temperature measures from the Hospital Information System (HIS) KISIM and laboratory values from the Laboratory Information System (LIS) DGlab between November and December 2022. Suspected CAUTI was defined as catheter in place for ≥ 2 days, urine-culture result was present, and the laboratory order was ≥ 2 days after catheter insertion or ≤ 1 day after catheter removal. CAUTI was defined as suspected CAUTI and body temperature > 38°C. The automated algorithm was valildated manually.

Results: Overall, 1'678 patients were discharged from the acute care medical wards of the cantonal hospital in Baden. The algorithm identified in total 256 patients with indwelling urinary catheter (15.2%) in the acute internal medicine ward. The patients with a urinary catheter were in 48% female, the median age was 80 years (interquartile range 73 years to 87 years), and the total number of catheter days was 1424 days. The monthly number of patients with indwelling catheters were 87 in October (16%, 486 catheter days), 75 in November (14%, 397 catheter days), and 94 in December (17%, 541 catheter days). The algorithm identified 8 suspected CAUTIs with one confirmed CAUTI.

Conclusions: Monitoring of hospital acquired urinary tract infections using electronic health records is feasible and may be used for quality improvement projects.



P30

High dose vitamin D substitution in hospitalized patients with Covid-19 in Switzerland: a randomized, placebo-controlled, double-blind, multicenter trial

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Introduction: Vitamin D and its role in the Covid-19 pandemic has been controversially discussed and the evidence is inconclusive. According to current knowledge, vitamin D plays an important role when it comes to the initiation and adaptation of the immune system. Therefore, vitamin D deficiency is an easily modifiable risk factor and vitamin D supplementation might influence disease severity in vitamin D deficient Covid-19 patients. The aim of this trial is to determine if patients with vitamin D deficiency and a Covid-19 infection profit from a single high dose of vitamin D in addition to a standard daily vitamin D dose.

Methods: This was a multicenter, randomized, placebo-controlled double-blind trial, that aimed to compare the effect on the length of hospital stay of a single high dose of vitamin D (140'000 IU) followed by treatment as usual (TAU) of daily 800 IU vitamin D until discharge versus placebo plus TAU in hospitalized patients with Covid-19 and vitamin D deficiency.

Results: 80 patients were included (40 per group) in this trial. Due to screening failures, 78 patients were included in the analysis (38 per group). No significant difference was found in the median length of hospital stay between the intervention and the control group (time from symptom onset to discharge: 16 days vs. 15 days, p = 0.193; time from hospital admission to discharge: 8 days vs. 8 days, p= 0.924 and time from randomization to discharge: 6 days vs. 6 days, p = 0.920). We adjusted the length of stay for Covid-19 risk factors, and 25(OH) D value at randomization (β = 0.03, 95 % CI: -2.17 – 2.22) and did not observe significant differences between the groups. 25(OH)-vitamin D level increased significantly in the intervention group compared to the control group (X̄ change of 25(OH) D level: + 26.35 [± 8.88] vs. control: - 2.73 [± 10.23], p < 0.001).

Conclusion: The intervention with a single high dose of vitamin D in addition to TAU did not significantly shorten the length of hospital stay in patients with vitamin D deficiency and Covid-19 but was effective for the elevation of serum 25(OH)-vitamin D levels without an increased occurrence of adverse or serious adverse events related to the intervention.

P31

How can we explain patient and clinician behaviours regarding mobility of older hospitalised patients?

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Background: Low mobility is frequent among older acutely hospitalised medical patients and associated with adverse outcomes. While there has been research on barriers and facilitators to mobility during an acute hospitalisation, we lack data on patient and clinician intentions and behaviours related to mobility in this setting, which could inform the development and implementation of behaviour-change interventions. We aimed to explain patient- and clinician-reported behaviours related to mobility of older patients hospitalised on an acute medical ward, based on health behaviour theory and on known barriers and facilitators to mobility.

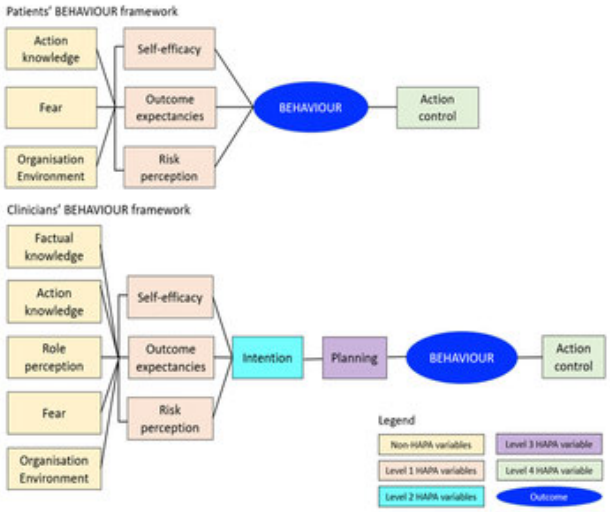
Methods: We conducted a cross-sectional survey of 200 patients aged ≥60 years recently hospitalised on an acute medical ward in 1 of 3 Swiss hospitals and of 142 clinicians (physicians, nursing staff, physiotherapists) working on those wards. The questionnaire was based on 1) the Health Action Process Approach (HAPA model), which assesses the mechanisms leading to behaviour, and 2) known barriers and facilitators to hospital mobility (i.e., factual/action knowledge, role perception, fear, organization/environment). The target behaviour was defined as "to move as much as possible at hospital" for patients, and "to ensure that patients move as much as possible" for clinicians. The frameworks, that we analysed using hierarchical linear regression, were different for patients and clinicians, because patient (but not clinician) behaviour was finished, since it happened during a past hospitalisation (Figure 1).

Results: Patient behaviour was associated with action knowledge (beta-coefficient, 0.37, 95%CI 0.19; 0.55) and action control (0.42, 0.27; 0.57) while clinician behaviour was associated with role perception (0.28, 0.14;0.42), planning (0.20, 0.06;0.34) and action control (0.47, 0.33;0.61).

Conclusion: This theory-based study identified potential drivers of patient and clinician behaviour related to mobility of older patients hospitalised on an acute medical ward in 3 Swiss hospitals. These

findings can inform the development of interventions in order to implement practice changes to improve older patient mobility in hospitals.

Figure 1. Framework for patient and clinician behaviour models. In the hierarchical regression models, the variables were added consecutively based on theory. Not all variables could be included in all frameworks, due to the nature of the assessment.



P32

Influence of vaccination status on the course of hospitalization in elderly COVID-19 patients: single center experience of a tertiary COVID-19-hospital

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Introduction: COVID-19 continues to be a major burden on the health care system and vaccines may be a modulating parameter. This study investigates the effects of COVID-19 vaccination on the course of hospitalization. Data from patients over 65 years of age, who were the primary target population for vaccination, are presented.

Methods: A retrospective data analysis of patients over 65 years of age (COVPat) hospitalized at Kantonsspital Winterthur (KSW) with respiratory symptoms due to COVID-19 between 10/2021 and 03/2022 was performed. COVPat who had not been hospitalized the entire time at KSW were excluded. COVPat were divided into 2 groups based on their vaccination status, regardless of the number or type of administered vaccine doses. The following parameters were collected: age, sex, 4C-mortalitiy score (4C-MS), number of relevant diagnoses (according to the 4C-MS), hospitalization duration, need for highflow oxygen treatment (HFOT) on the COVID-unit, stay on ICU, mortality and case mix index (CMI). Differences were analyzed using Chi-Squared-Tests as well as Mann-Whitney-Test for independent samples testing.

Results: Between 10/2021 and 3/2022 a total of 274 Patient were hospitalized due to COVID-19. 38% were younger than 65 years.

Results of the 171 analyzed COVPat are summarized in the table:

Factors	vaccinated	non-vaccinated	All	p
N (%)	99 (57.9)	72 (42.1)	171	
Sex [female, male; n,%]	38/61 (38/61)	30/42 (42/58)	68/103 (40/60)	ns
Age [years; mean±SD]	80.1±8.0	76.9±7.9	78.8±8	<0.01
4C-MS[mean±SD]	12.0±2.8	11.3±3.0	11.7±2.9	ns
Relevant Diagnoses [mean±SD]	2.9±1.7	2.1±1.5	2.6±1.6	<0.01
HFOT [N;%]	17 (17.2)	18 (25.0)	35 (20.5)	ns
ICU stay [N;%]	6 (6.1)	6 (8.3)	12 (7.0)	ns
Hospitalisation duration [days; mean±SD]	9.7±13.5	11.3±11.6	10.4±12.7	0.02
Mortality [N;%]	15 (15.2)	9 (12.5)	24 (14.0)	ns
Case Mix Index [mean±SD]	2.4±6.4	2.8±5.2	2.6±5.9	0.03

Conclusion: Despite the older age of the patients in the vaccinated group, their average length of hospital stay was shorter. Since age is one of the main factors for a higher 4C-MS and elderly people have more comorbidities, it can be speculated that the younger ones were more affected by COVID at the time of hospitalization. The trend toward more frequent use of cPAP (data not shown) and HFOT (delivered on the medical ward with specialized staff), as well as the trend toward greater need for intensive care and significantly longer hospital length of stay, suggest a higher likelihood of respiratory complications in unvaccinated patients. As a cost-relevant factor, the case-mix index of the vaccinated group was significantly lower.

P33

Inhospital Detection of Elevated Blood Pressure (INDEBP): preliminary results of a retrospective analysis

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Introduction: Elevated blood pressure (BP) values are commonly reported in hospitalized patients. Previous retrospective studies have shown that adaptions of BP medication are associated with a worse outcome (1, 2). Objective of this study was to analyze the prevalence of elevated BP values in medical non-cardiac inpatients and to assess the proportion of patients with treatment modifications in response to elevated BP values during the hospital stay.

Methods: Retrospective analysis of randomly selected non-cardiac medical inpatients in a tertiary hospital in 2019 and 2021. Exclusion criteria were cardio-vascular hospitalization, missing general consent or age <18 years. Routine BP measurements from clinical checks were recorded, elevated BP defined as ≥140 and/or ≥90 mmHg. Antihypertensive treatment at admission was compared to that at discharge. Complications during hospitalization were a compound of myocardial injury, intracerebral bleedings, ischemic stroke/TIA, acute kidney injury, falls/syncope and death. Data were extracted from electronic health records. Categorical data was analyzed with a Fisher's exact test, continuous data with a Mann-Whitney-U-test.

Results: 301 patients were included, 100 (33.6%) in 2019, and 200 (66.4%) in 2021, 130 (43.2%) were female, median age was 66 years (IQR 55.5 – 76). 152 (50.5%) had a history of hypertension. 47 patients (15.6%) had exclusively normal BP values during a median of 10 days (IQR 5 – 21) of hospitalization. Of those 254 patients (84.4%) with elevated BP during the hospitalization, 105 (41.3%) had their antihypertensive treatment adapted: 54/254 patients (21.3%) had ≥ 1 new antihypertensive, 18/254 patients (7.1%) had the antihypertensive dose increased, 11/254 (4.3%) had the antihypertensive agent exchanged, 47/254 (18.5%) had an antihypertensive stopped, and 22 (8.7%) had the dose decreased (multiple answers possible). Patients with treatment modifications had significantly more complications (22.9 vs 10.3%), p-value 0.012. Differences between patients with and without treatment adaptions are shown in the Table.

Conclusion: Elevated BP is a frequent and significant clinical problem during hospitalization. Nearly half of the patients with elevated BP had their medications adapted during hospitalization. Modification of antihypertensive therapy was associated with more complications, whereby no statement can be made about causality.

Parameter	Adapted medication	No adapted medication	p-value
Baseline characteristics:			
Age (years), median (IQR)	69 (62 – 79)	65 (54 – 75)	0.005
Female gender, n (%)	58 (55.2)	76 (55.9)	1.000
Body mass index (kg/m2), median (IQR)	26.4 (22.2 – 29.9)	24.3 (21.1 – 27.4)	0.033
History of hypertension, n (%)	73 (70.2)	60 (44.1)	<0.001
History of coronary artery disease, n (%)	24 (22.9)	21 (15.6)	0.183
History of stroke, n (%)	13 (12.5)	10 (7.4)	0.192
History of peripheral artery disease, n (%)	6 (5.8)	10 (7.4)	0.795
History of aortic aneurysm, n (%)	2 (1.9)	6 (4.4)	0.471
History of atrial fibrillation, n (%)	17 (16.7)	16 (11.9)	0.345
History of heart failure, n (%)	12 (11.7)	7 (5.3)	0.092
History of chronic kidney disease, n (%)	24 (23.1)	19 (14.2)	0.090
History of diabetes, n (%)	35 (33.3)	18 (13.5)	<0.001
History of dyslipidemia, n (%)	32 (30.5)	28 (20.7)	0.099
Hospitalization:			
Length of hospitalization (days), median (IQR)	16 (9 – 29)	7 (4 – 16)	<0.001
N elevated BP values, median (IQR)	19 (9 – 53)	6 (2 – 19)	<0.001
Percent elevated BP values, median (IQR)	29.6 (14.2 – 54.0)	24.4 (9.2 – 56.2)	0.351
N days with elevated BP values, , median (IQR)	7 (5 – 14)	3 (1 – 6)	<0.001
Max. systolic BP (mmHg), median (IQR)	168 (159 – 183)	157 (147 – 170)	<0.001
Max. diastolic BP (mmHg), median (IQR)	101 (90 – 121)	94 (87 – 104)	<0.001
Complications during hospitalization:			
Any complications during hospitalization, n (%)	24 (22.9)	14 (10.3)	0.012
Acute kidney injury during hospitalization, n (%)	18 (17.1)	12 (8.8)	0.075
Fall/Syncope during hospitalization, n (%)	5 (4.8)	5 (3.7)	0.751

Table: Baseline characteristics, duration of hospital stay, occurrence of elevated blood pressure (BP) values and complications during hospitalization. IQR = inter quartile range.

P34

Just an acute urinary retention? A case of infection-related nonhepatic hyperammonemic encephalopathy

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Learning objective: Ammonium is constantly produced by amino acids catabolism, muscle activity and kidney function, as well as from bacterial degradation of proteins within the intestine. This molecule passes the blood-brain barrier and has a selective neurotoxicity. In the liver, the urea cycle prevents ammonium accumulation. We present a case of hyperammonemia due to urinary tract infection with urinary retention in a middle-aged adult admitted for an acute confusional state.

Case: A 44-year-old man, known for chronic alcohol consumption (30g/day), was referred by a secondary care hospital for an acute confusional state. The last alcohol consumption was 48h before. Neurologic status reveals somnolence and disorientation. Routine blood work-up showed normal liver function. Contrast- enhanced computer tomography scan of the head was normal as well as the cerebrospinal fluid analysis. Urinalysis revealed elevated pH (9.0), presence of nitrites, leucocytes and non-glomerular erythrocytes with polymicrobial growth in urine culture. An electroencephalography showed a diffuse generalized rhythmic delta activity suggesting a toxic or metabolic encephalopathy. Ammonium was measured at 98µmol/l (N 11-35µmol/l). A bladder ultrasound revealed a urinary retention (2000ml). After insertion of Foley catheter the patient was hospitalized with endovenous ceftriaxone. The clinical course showed complete neurological recovery and normalization of the ammonium levels (31µmol/l). The patient returns home with planned transurethral resection of the prostate and had no relapse at two-month follow-up.

Discussion: We describe the case of a hyperammonemic non-hepatic encephalopathy. Several etiologies are described ranging from medications interfering with the urea cycle (valproic acid) to surgical treatments, such as portosystemic shunts, hyperalimentation through parenteral nutrition or increased catabolism (intense exercise, seizure, starvation) and late-onset errors of metabolism. Urinary tract infection can lead to hyperammonemia through the presence of urease-producing bacteria. Urease hydrolyzes urea to ammonium. In presence of acute urinary retention, ammonium ions cumulate and pass through the vesical venous plexus into the systemic circulation, bypassing the periportal hepatic detoxification system. This case highlights the importance of including ammonium in the diagnostic work-up of undifferentiated acute confusional state, even in the absence of hepatic dysfunction.

P35

Legionnaires` disease as a first manifestation of a neoplastic disease of the lymphoreticular cells

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Learning objectives: Severe Legionella pneumonia in young patients without risk factors is rare and needs further investigation to detect an underlying disease. Predisposing factors, such as immunocompromised states or immunodeficiency disorders, should be identified to start early treatment and prevent further harmful infections.

Case: A 40-year-old man was referred to the emergency room with persistent fever. He suffered from pneumonia with coughing and dyspnea for 5 days. He had no medical history. Clinical examination revealed subfebrile temperatures, tachypnea, tachycardia and hypotension. Crackles were present on auscultation over the left lung. Laboratory findings showed high CRP and a hypoosmolar hyponatremia. Because of the diagnostic findings and severe pneumonia (Fig.1) urinary antigen test for Legionella pneumophila was done and resulted positive as well as pleural fluid PCR. The diagnosis of Legionnaires` disease was confirmed, empiric therapy with amoxicillin-clavulanate and azithromycin was changed to levofloxacin consequently. A peripheral blood smear showed remarkable findings: hyporegenerative anemia, neutro- and monocytopenia with hairy appearance of lymphocytes. Together with the clinical findings of an enlarged spleen and cervical lymph nodes, we suspected the diagnosis of hairy cell leukemia (HCL). Immunophenotyping of the B-lymphocytes was typical for HCL (Fig.2). A marked elevated serum soluble IL2-receptor and bone marrow infiltration of hairy cells of 50-80% was present. Genetic analysis showed a *BRAF.V600E* mutation. Because of persistent neutro- and thrombocytopenia after antibiotic treatment, we initiated a cytostatic treatment with cladribine and achieved complete remission.

Discussion: Hairy cell leukemia, a rare variant of chronic lymphoid malignancies, is characterized by a monocyte dysfunction and a predisposition for bacterial infections who multiply in monocytes, such as Legionella pneumophila. It is recommended to search for underlying hematologic diseases in patients with abnormal hemogram and Legionnaires disease, as severe disorders of cell-mediated immunity can be present. HCL is a slow progressive disease and does not always require treatment directly, though at a given time, it needs therapy to prevent harmful infections.

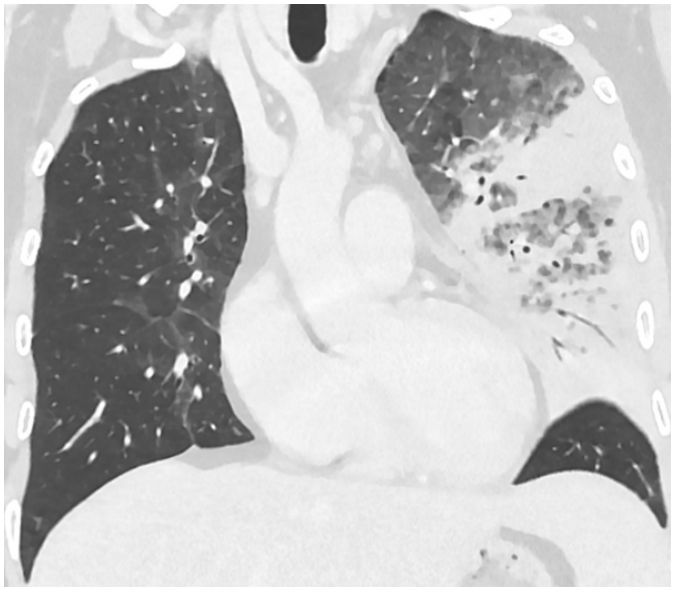

Fig. 1 Legionella pneumonia

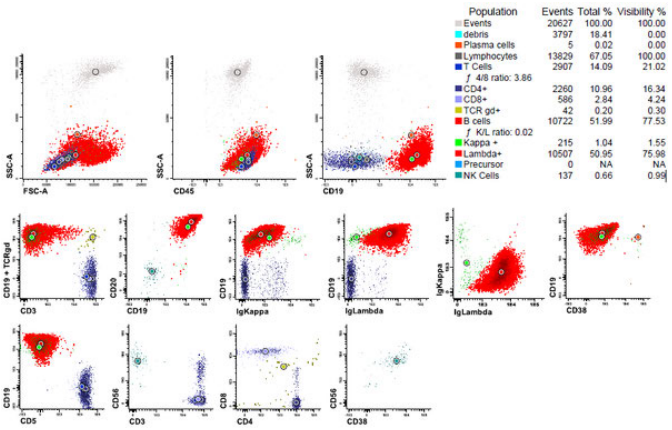

Fig. 2 Immunophanotyping of lymphocytes in HCL: monotypic for surface light chain lambda, expression of CD20, (not shown on panel) CD11c, CD22, CD25 and CD103.

P36

Levels of physical activity measured using accelerometers and hospital-acquired venous thromboembolism: the RISE study

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Introduction: Immobilization during hospitalization contributes to the occurrence of hospital-acquired venous thromboembolism (Ha-VTE). Existing Ha-VTE scores include an item of physical activity (PA), however with uneven and subjective definitions.We therefore aimed to 1) compare subjective and objective measures of PA levels using accelerometers; 2) assess whether objective measures of PA levels are associated with the occurrence of Ha-VTE.

Methods: We used data from a prospective cohort study on Ha-VTE prevention in 3 Swiss hospitals.
Adults medical patients with objective PA measurement for ≥24 hours, obtained by a wrist-worn accelerometer, were included. Subjective PA was based on clinical estimation of caregivers, using the Braden scale; physicians fulfilled the immobilization criteria as defined in the Padua score.
Patients were followed for the occurrence of symptomatic Ha-VTE during 90 days.
PA data were analyzed using an existing algorithm (GGIR) and described in mili-G, G is acceleration due to Earth gravity, (mG) and time. PA levels were defined using existing thresholds: no PA (< 30mG), light PA (30-99mG) moderate PA (100-399mG) and vigorous PA (≥400mG). Patients were considered physically active if they spent >20 min per day in moderate or vigorous PA.
We compared patients subjectively and objectively considered as inactive, as well as the overall incidence of Ha-VTE between active and inactive patients.

Results: In 963 patients (mean age 65), 279 (29%) were considered as physically active. Active patients were younger, healthier, leaner and had a shorter hospital stay (Table 1). Only 5% (n=44) of patients were able to perform ≥1 minute per day in vigorous PA.
Overall, 37% of patients had a reduced mobility, based on physicians' subjective evaluation, thereof 22% were classified as active by accelerometers.
Of patients considered unable to walk by nurses (n=158), 10% were classified as active by accelerometers.
Two third, mostly inactive, patients, received thromboprophylaxis.
Overall, Ha-VTE was uncommon (2.4%) and somewhat more frequent in inactive than in active patients (2.8% vs 1.4%; p-value 0.22).

Conclusion: In medical hospitalized patients, one in three patients are classified as physically inactive (less than 20 min per day) based on objective measures. Subjective mobility assessment performed by nurses or physicians correspond most of the time to objective measurements. Ha-VTE is somewhat more frequent in inactive than in active patients.

Table 1. Patient characteristics according to their objective physical activity.

	Total (n=963)	Inactive (n=684)	Active (n=279)	*p*-value
	n (%) or median (interquartile range)			
Demographic				
Age in years	68 [55 – 78]	71 [59 – 80]	59 [45 - 71]	<0.001
Women	401 (42)	282 (41)	119 (43)	<0.001
Comorbidities				
Charlson Comorbidity Index	4 [2 – 6]	5 [3 – 6]	3 [1 – 5]	<0.001
Active cancer	198 (21)	156 (23)	42 (15)	0.007
Cardiac failure	104 (11)	84 (12)	20 (7.2)	0.020
Respiratory failure	177 (18)	143 (21)	34 (12)	0.002
Renal failure	269 (28)	210 (31)	59 (21)	0.003
BMI	25 [22-29]	25 [22-29]	24 [21-28]	0.015
Mobility assessment				
Reduced mobility assessed **by physicians** [b]	354 (37)	292 (43)	62 (22)	<0.001
Patient subjectively considered unable to walk **by caregivers** [a]	158 (16)	130 (19)	28 (10)	<0.001
Physical therapy prescribed [a]	328 (34)	266 (39)	62 (22)	<0.001
VTE risk and hospitalization				
High risk for hospital-acquired venous thromboembolism [c]	629 (65)	497 (73)	132 (47)	<0.001
Thromboprophylaxis prescribed during stay	639 (66)	482 (70)	157 (56)	<0.001
Length of stay in days	8 [6 – 12]	9 [6 – 13]	7 [6 – 10]	<0.001
Any occurrence of symptomatic Ha-VTE	23 (2.4)	19 (2.8)	4 (1.4)	0.22

[a] on study inclusion; [b] bed rest with bathroom privileges for ≥ 3days, assessed by physician in charge of patient;
[c] as determined by a simplified Geneva score ≥3 points;
VTE: venous thromboembolism

P37

Management of hospitalized COVID-19 patients at a Swiss Cantonal Hospital, a retrospective analysis and medical audit

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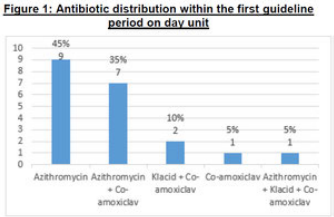
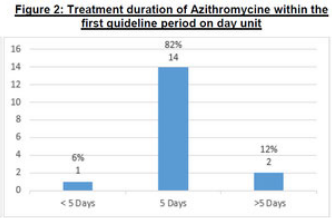
Introduction: When the Covid-19 pandemic reached Switzerland in February 2020, various Swiss hospitals had to adjust to a new and uncertain situation. From a medical point of view, an extremely high number of hospitalizations had to be expected within a very short time. Moreover, no meaningful therapeutic evidence existed for this new type of coronavirus. In order to successfully manage the pandemic, the Cantonal Hospital Baselland Liestal (KSBL) published eight in-house guidelines in the course of 2020. These guidelines were designed based on the latest evidence from the WHO. The aim of this retrospective study was to ultimately assess the treatment adherence regarding the usage of antibiotics, antiviral drugs, immunomodulators and systemic steroids to these internal guidelines over the period of two Covid-19 waves in 2020.

Methods: In this retrospective observational study in Switzerland at the Cantonal Hospital "Baselland" we analyzed 338 confirmed COVID-19 patients who were hospitalized for at least three days over the year 2020. The eight in-house guidelines were analysed in terms of recommended medication and compared on the basis of routine clinical data in the day unit and intensive care unit.

Results: Data of 338 patients (mean age 68.4 years, 61%male) with confirmed COVID-19 disease were included in the analysis. As an example, the application of antibiotics in day unit was analysed on basis of the first internal guidelines: data of 21 patients was compared. Antibiotics were apllied in 95% of the cases. The recommended antibiotics for this period were azithromycin with a treatment duration of five days and clarithromycin with a treatment duration of three days. Figure 1 shows the antibiotic distribution within the first guideline period on day unit. In 95% of the cases, at least one recommended antibiotic was used. The treatment duration of five days for azithromycin (figure 2) was adhered to 82% of cases (12% overtreatment, 6% undertreatment). The treatment duration of three days for clarithromycin was adhered to 33% of cases (33% overtreatment, 33% undertreatment). As this is an ongoing study, further results are not available yet. These will be completed in the near future and will be presented at the congress.

Conclusion: Future results will offer more evidence on the implementation of the in-house guidelines. This can make a significant contribution to medical quality assessment and will help to be better prepared for future events.





P38

Paralytic ileus as a first symptom of Guillain-Barré syndrome - a case report

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Learning objectives: Awareness for the diversity of clinical presentations of Guillain-Barré syndrome (GBS) is substantial in successful management of affected patients. Very few cases with paralytic ileus as a possible early symptom of GBS were reported so far.

Case: A 50-year old man presented with strong pain in the upper abdomen after having had an episode of watery diarrhea a few days ago. On admission, vital signs were normal, he had no fever and the diarrhea had improved. Clinical examination revealed tenderness and muscular defense on palpation of the upper abdomen with normal peristaltic sounds. Blood analysis showed minimally elevated CRP and stool samples were taken for analysis.
The next day he developed nausea and emesis and decreased bowel sounds were noticed. Ultrasound of the abdomen revealed dilated bowel loops of the small intestine, a CT scan confirmed a paralytic ileus. As the pain was not controlled with conventional analgetics including opiates, an epidural catheter was placed for pain management. Fluid replacement and prokinetic therapy with i.v. metoclopramide and neostigmine were initiated but showed no improvement of pain or ileus symptoms within the next 48 h. Meanwhile, *Campylobacter jejuni* was detected in the stool sample.
On the fifth day after admission, the patient developed numbness and paresthesia in both hands and feet. A progressive muscle weakness and areflexia on both forearms and legs appeared, leading to the inability to walk within hours. After exclusion of increased intracranial pressure in the cerebral CT scan a lumbar puncture was performed showing cytoalbuminic dissociation and a GBS was diagnosed. Despite immediate therapy with human immunoglobins the muscular weakness was increasing, the patient developed tachycardia and hypertension as well as a rapid decline of the respiratory capacity and was transferred to an intensive care unit where he got intubated the day after. After reduction of the sedative agents a tetraplegia remained. The patient got a tracheotomy and was transferred to a paraplegic rehabilitation center two weeks later.

Discussion: GBS is a rare complication of gastrointestinal infections such as with *Campylobacter jejuni*, typically presenting with symmetric weakness and paraesthesia of the extremities. A paralytic ileus preceeding the first neurologic symptoms is an extremely rare presentation and may delay rapid treatment of GBS.

P39

Physicians experienced frequent regrets during night shift work and displayed limited coping strategies: results from the Nightshift Ecological Study

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Introduction: Swiss hospital-based internists report a high level of turnover intention.[1] The experience of care-related regret – an emotion felt when people think that an outcome could have been better if they had acted differently – is associated with job dissatisfaction and resignation, especially among individuals with poorer coping abilities.[2] During night shifts, clinical work is particularly demanding with limited supervision. Little is known on the impact of regrets during night shifts, as well as the coping strategies used by young internists, both factors that could influence their satisfaction with work.

Methods: We conducted an ecological study of night shifts in the Division of Internal Medicine at the University Hospitals of Geneva, between October 2019 and March 2020. Before and after their 4 weeks rotation of night shifts, residents completed the Care-related Regret Coping Scale for Health-care Professionals (RCS-HCP)[3], a validated measure of their coping abilities. It assesses the use of 3 strategies to deal with one's regrets: problem-focused strategies (aiming to rectify the situation or avoid its reoccurrence by identifying solutions), emotion-focused adaptive strategies (aiming to cope with the emotions without modifying the situation, leading to reappraisal, acceptance or distanciation) and emotion-focused maladaptive strategies (aiming to cope with the emotions, yet without success, leading to rumination or self-attacking). We also measured the number and intensity of regrets by the RIS-10 instrument.[4]

Results: Among the 41 included residents – 27 (65.9%) women – 10 (24.4%) experienced regret during their shift, all of them were women. They showed overall limited coping abilities: 40 (97.6%) displayed mixed style including frequent use of maladaptive strategies, 1 (2.4%) used mostly maladaptive approaches, and none displayed only positive strategies (problem-focused and emotion-focused adaptive).

Conclusions: Exposition to clinical situations inducing care-related regret is frequent during night shift work. Our respondents showed poor coping abilities, with frequent use of maladaptive strategies, which are known to be associated with poor sleep, low job satisfaction and resignation.[2,3] Beside highlighting the need to include off-hours periods and fostering a safe culture of error, our findings suggest that programs promoting problem-focused and adaptive coping, while minimizing the use of maladaptive strategies, could prove useful.

P40

Physicians' perceptions and experiences regarding leadership: still a gap

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Introduction: Effective leadership skills are essential to the success of health care organizations. Despite the development of training programs in leadership, junior and more senior medical leaders often find themselves ill-prepared to take on these new responsibilities. The aim of our study was to explore perceptions, beliefs, self-efficacy regarding leadership among physicians with different hierarchical positions.

Methods: We conducted a qualitative study at the Geneva University Hospitals. A purposive sample of residents (R), chief residents (CR), attending physicians (AP) and chief physicians (CP) were invited to participate in focus groups (or semi-structured interviews) between April and June 2021. The interview guide included questions on their understanding of leadership, how they perceived themselves as leaders, what difficulties they experienced or observed in their work setting, and what helped or would help them to improve their leadership skills. Focus groups were transcribed ad verbatim and analysed both inductively and deductively using Fishbein's model of behaviour prediction and Irby's professional identity formation framework.

Results: We conducted 9 focus groups (R=3; CR=4, AP=2 and CP=1) and one semi-structured interview with a CP. Most physicians had an intuitive and idealised representation of leadership with a focus on personal characteristics rather than skills or processes. They described implicit and occult institutional norms and expectations, with a lack of clarification regarding their roles as leaders. This lead to several areas of dissonance that negatively impacted on their self-efficacy at all levels: feeling of insecurity and confusion among residents, frustration at CR and AP levels in managing inter-professional teams due to silo functioning of various health professionals, and CP feeling stuck between their division and the institutional governance. They reported having learned how to become a leader through trial and error, observation of role models, and using personal resources rather than through formal training.

Conclusion: Our results show that physicians' leadership skills are still mainly acquired on the job, and that institutional norms and practices do not encourage clarification of leadership roles and processes. Physicians' training in leadership skills, associated with more explicit and clear institutional processes, could help improve physicians' self-efficacy and develop their identity as leaders.

P41

Prediction of very early major bleeding risk in acute pulmonary embolism: an independent external validation of the PE-SARD Bleeding Score

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Introduction: The PE-SARD Bleeding Score, an easy-to-use clinical score to predict very early major bleeding (MB) in patients with acute pulmonary embolism (PE), has been recently derived. The discriminative power for MB was fair, with a C-index of 0.74 in the derivation and internal validation sample. Clinical scores require repeated external validations in different populations before adoption into practice.

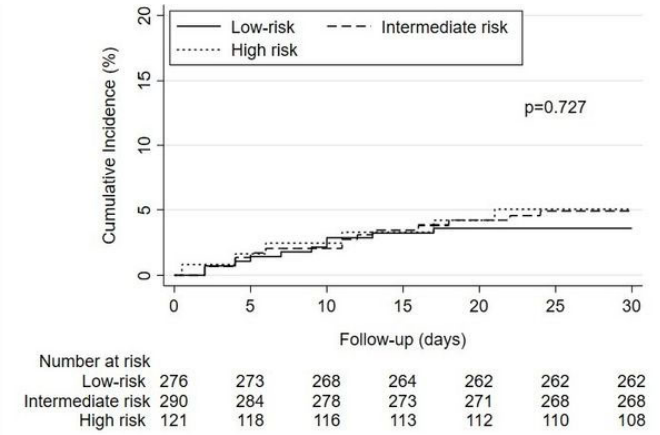
Methods: We independently validated the PE-SARD Bleeding Score in a prospective multicenter Swiss cohort of 687 patients aged ≥65 years with acute PE. The PE-SARD comprises 3 variables (syncope, anemia, renal dysfunction) to classify patients into 3 categories of increasing risk of MB (low, intermediate, high). The outcome was MB at 7 days and later points in time over the entire follow-up period. We calculated the proportion of patients classified as low, intermediate, and high risk based on the PE-SARD and the observed frequency of MB per risk category. To assess discrimination and calibration, we determined the area under the receiver operating characteristic (ROC) curve and the Hosmer-Lemeshow goodness-of-fit test, respectively.

Results: The prevalence of MB was 2.0% (14/687) at 7 days and 14.0% (96/687) at the end of follow-up (median duration: 30 months). The PE-SARD classified 40.2%, 42.2%, and 17.6% of patients as low, intermediate, and high risk for MB, respectively. The frequency of observed MB at 7 days was 1.8% in low-, 2.1% in intermediate-, and 2.5% in high-risk patients. The cumulative incidence of MB within 30 days did not differ significantly by risk categories (Figure). The area under the ROC curve for MB was 0.52 (95%CI 0.48-0.56) at 7 days and slightly increased to 0.60 (95%CI 0.56-0.64) at the end of follow-up. Score calibration for MB was adequate (P>0.05) over the entire follow-up.

Conclusion: In our independent validation, the PE-SARD did not accurately predict very early or late MB, and thus, may not be transportable to older patients with PE.

Figure. 30-day cumulative incidence of major bleeding by PE-SARD risk category

The cumulative incidence was 3.6% (95% confidence interval [CI] 2.0-6.7) for low-risk, 4.9% (95% CI 2.9-8.2) for intermediate-risk, and 5.0% (95% CI 2.3-10.9) for high-risk patients (P=0.73 by the log-rank test).



P42

Recurrent pneumonia: think cryptogen organizing pneumonia

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Learning objective: In cases of recurrent (atypical) pneumonia with fluctuating radiological infiltrates within a few weeks, cryptogenic organizing pneumonia (COP) should be considered.

Case: A 53-year old otherwise healthy male presented with fever, sore throat, unilateral conjunctivitis and cough at the emergency department. A month earlier, he presented with the same symptoms and bilateral patchy infiltrates on computer tomography (CT). Tests for SARS-CoV-2 and streptococcal infections were negative then and the initially elevated inflammation markers normalized under antibiotic therapy (penicillin and macrolid).
The patient's medical history included follicular lymphoma in remission after autologous stem cell transplantation in 2018.
On admission, laboratory results showed elevated inflammatory markers, serology for HIV, EBV, HSV, VZV, Streptococcus A and blood cultures were negative. A repeated CT showed new, changing infiltrates. To rule out other infectious causes of recurrent/relapsing atypical pneumonia, bronchoalveolar lavage (BAL) was performed and no pathogen was detected. Differential cytology showed high cell count (547cells/µl) with a lymphocytic predominance of 35.5% without atypical cells. In a multidisciplinary board, the diagnosis of cryptogenic organizing pneumonia (COP) was considered most likely. Due to a challenging sedation in the previous bronchoscopy, no additional biopsy was performed. The diagnosis of COP was supported by the COP-typical fluctuating infiltrates over time, the clinical picture with fever and dry cough, and the elevated inflammatory markers with corresponding lymphocytosis in the BAL. Infectious agents could not be detected. After initiation of oral steroid therapy with 0.5mg/kg/body weight, fever disappeared rapidly, and inflammatory markers decreased. A CT scan after 3 months showed resolving infiltrates and oral steroid tapering was continued.

Discussion: In patients with suspected atypical pneumonia who do not respond to antimicrobial therapy or relapse, COP should be considered as a differential diagnosis. In such cases, pneumological examination with bronchoscopy (BAL and usually transbronchial (cryo) biopsy) is indicated. Transient improvement with macrolides can be explained by their immunomodulatory effect.

P43

Red blood cell distribution width (RDW) – a new nutritional biomarker to assess nutritional risk and response to nutritional therapy?

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Introduction: Previous studies found red cell distribution width (RDW) to be a marker for chronic disease, nutritional deficits and adverse clinical outcome. We assessed the prognostic value of RDW regarding clinical outcomes and nutritional treatment response among medical patients at nutritional risk.

Methods: We conducted a post hoc analysis of EFFORT, a randomized, controlled trial investigating the effects of nutritional support in patients at nutritional risk in eight Swiss hospitals between April 2014 and February 2018. We stratified patients based on RDW admission levels. Using logistic regressions, we examined both the association between various predictors and high RDW, and the association between RDW and clinical outcome.

Results: From 1244 included patients (median age 75 years, 46.6% female) 473 (38.0%) had increased RDW (≥15%) and 771 (62.0%) normal RDW (<15%) levels. Patients with high RDW had an almost threefold increased risk for mortality at 180-days [adjusted OR 2.77 (95%CI 2.05 to 3.73); p < 0.001] and 5-years [adjusted OR 2.66 (95%CI 1.99 to 3.55); p < 0.001]. High RDW was also associated with longer hospital stays [8.0 versus 7.0 days, adjusted OR 1.22 (95%CI 0.43 to 2.01); p = 0.003] and with higher risk of rehospitalization [adjusted OR 1.59 (95%CI 1.04 to 2.44); p = 0.033]. Effects of nutritional support was similar among patients with low and high RDW levels.

Conclusion: Among medical patients at nutritional risk, RDW is a strong prognostic marker for clinical outcomes and may serve as a nutritional biomarker to identify vulnerable patients at high clinical risk.

P44

Respiratory syncytial virus infections in hospitalized adults: clinical observations in a local experience from 2016 to 2022

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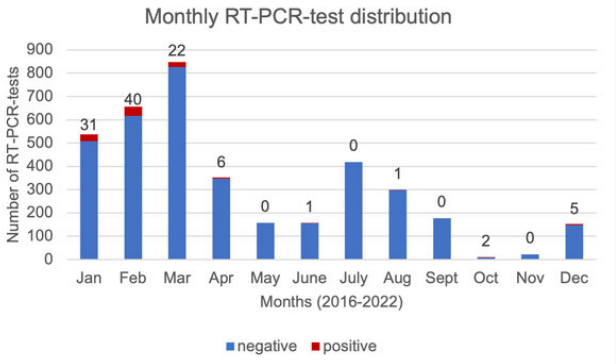
Introduction: Respiratory syncytial virus (RSV) infections are well known infections in children. In recent years, with the introduction of routine RT-PCR testing for RSV in emergency wards, these infections have been increasingly diagnosed in adults. The aim of the present study is to analyse clinical and epidemiological data of all hospitalized patients between 2016 and 2022 at our institution, with the focus on predisposing factors, patient groups, treatment and outcome.

Methods: In this retrospective, non-selected cohort study of the Regionalspital Emmental, all patients with respiratory symptoms tested by RT-PCR on a nasopharyngeal swab were evaluated from 26.12.2016 to 16.09.2022. Trivalent RT-PCR testing (Influenza A/B and RSV) was performed until 08.03.2022, followed by the quadrivalent test Xpert Xpress (SARS-CoV-2/Flu/RSV). Symptoms at the time of testing, age and sex, comorbidities, the necessity and duration of hospitalization, therapy, complications and outcome were recorded.

Results: A total of 3792 PCR tests were performed, and RSV was detected in 108 patients (figure). The mean age of patients with RSV infection was 76 years. Both male and female were equally affected. At the time of testing, main symptoms were cough or sore throat in 86%, fever in 44% and dyspnea in 54% of patients. Radiological evidence of an infiltrate was found in 41% of cases. Hospitalization was necessary in 71% of patients, and outpatient treatment was possible in 19%; in 10%, a positive test was obtained during hospitalization. The mean duration of hospitalization was 7 days (SE: ± 6.58). Forty-five percent of the hospitalized patients were treated with steroids because of obstructive pulmonal findings, and 60% received antibiotics because of suspected bacterial superinfection. Regarding possible predisposing comorbidities, 55% had a history of pulmonary disease and 52% had a cardiopathy. In 10 cases (9.6%) a treatment in the intensive or intermediate care unit was needed. Mortality was 5%.

Conclusion: In the elderly, RSV infections carry a significant burden of morbidity and mortality. Hospitalization and antibiotic therapy are frequently needed, and intensive treatment and mortality are not negligible. Similar to influenza, protective vaccination could be a desirable goal.

Fig. 1: Monthly distribution of positive and negative RT-PCR tests for RSV.



P45

Sensitive topics in medical ward rounds are frequent and associated with low satisfaction: ancillary analysis of the BEDSIDE-OUTSIDE Trial

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Introduction: Discussing sensitive topics (e.g., medical ambiguity, social issues, non-adherence) during the ward round is challenging and may negatively impact patient satisfaction with health care. Within the previous multicenter randomized BEDSIDE-OUTSIDE trial focusing on communication during the ward rounds, we investigated risk factors for satisfaction with care.

Methods: We analyzed predefined sensitive health topics and specific communication elements from audiotapes recorded during ward rounds. The primary endpoint was patients' overall satisfaction with care measured on a visual analogue scale from 0 to 100.

Results: From 919 included patients, 474 patients had at least one sensitive topic including medical ambiguity (n=251), psychiatric comorbidities (n=137), tumor diagnosis (n=137) and social issues (n= 125). Patients with sensitive topics reported lower satisfaction with care compared to patients without sensitive topics (mean (SD) [S1] , 90.2 [±12.1] vs. 87.7 [±14.6], adjusted difference -2.5 [95%CI -4.28 to -0.72], p=0.006. Among patients with sensitive topics, risk factors for low satisfaction included disagreements between physicians and patients (mean (SD)[S2], 14/212 [6.6%] vs. 41/254 [16.1%], adjusted OR 2.78 [95%CI 1.47 to 5.27], p=0.002).

Conclusion: A large proportion of medical inpatients have sensitive health topics, which was associated with lower satisfaction with care. Education of physicians on communication techniques may help to improve the care of these patients.

P46

Sporadic Creuztfeld-Jakob disease (sCJD): an important differential diagnosis in rapid progressive neurological disorders

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Introduction: Sporadic Creutzfeld-Jakob disease (sCJD) is a neurodegenerative disorder caused by structural abnormalities of prion proteins with a fatality rate of 100% and no known cure. The combination of rapid progressive dementia with either myocloni, visual or cerebellar symptoms, pyramidal and extrapyramidal signs or akinetic mutism are the leading symptoms. The world-wide incidence is estimated at about 1-2:1'000'000 persons per year.

Methods: From 2014 to 2021, we diagnosed 4 cases of sporadic Creutzfeld-Jakob disease. We report symptoms, diagnostic challenges and disease duration of these patients.

Cases: Four male patients aged 56 to 85 years presented with rapid progressive neurocognitive and neuropsychiatric symptoms of unknown etiology. One patient presented with depression. Agressivity, disorientation, and cerebellar symptoms such as walking instability and ataxia were common. Radiologic investigations including computed tomography and magnetic resonance imaging of the brain showed generalised brain atrophy, vascular changes and diffusion restrictions in in the cerebral grey matter. Spinal fluid was tested for the presence of a positive protein 14-3-3 and a positive Real-Time Quaking-Induced Conversion (RT-QuIC) for abnormal prion-aggregation. Pathological EEG showed general slowing with rhythmic delta activity and triphasic potentials as a sign of severe encephalopathy. The combination of clinical signs, findings of a typical EEG, a positive 14-3-3 or RT-QuIC assay in liquor or a high signal on MRI brain scan with no other explanation led to the probable diagnosis of sCJD. Autoptic findings confirmed the diagnosis. Time from beginning of symptoms to death ranged from 6 weeks to 1.5 years.

Conclusion: In our region, incidence from 2014-2021 was about 1:300'000. Clinicians should be aware of the diagnosis of sCJD and perform the diagnostic tests in suspected cases. Autoptic findings remain the gold standard. Giving a probable diagnosis of sCJD is important because of counselling, avoiding unnecessary tests, avoiding iatrogenic transmission and asking for an autopsy and informing the pathology teams because of special hygienic requirements.

P47

Transition cAre inteRvention tarGeted to high-risk patiEnts To Reduce rEADmission (TARGET-READ)

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Introduction: Hospital readmissions are frequent, costly, and sometimes preventable.

Methods: We evaluated the effects of a transitional care intervention targeting higher-risk medical patients using a composite outcome of 30-day unplanned readmission or death in a multicenter RCT. Patients with a HOSPITAL score ≥ 4 points, discharged from the internal general medical division of four Swiss hospitals, were randomized to receive either usual discharge care or a standardized multimodal transition intervention by the study team. The intervention included a systematic medication reconciliation, a fifteen minutes' patient education with teach-back, a planned first visit to the primary care physician, and post-discharge follow-up phone calls at 3 and 14 days. Post-discharge, 30-days mortality and unplanned readmission were recorded.

Results: The composite outcome of unplanned readmissions and death at 30 days was not statistically different between the intervention (145 out of 692; 21%, 18 to 24%) and the control group (134 out of 694; 19%, 17 to 22%) (1.7% Risk difference (95%CI: -2.5 to 5.9%, p=0.44)). There was also no evidence for an effect of the intervention on the time to unplanned readmission or death, the post-discharge health care utilization, patient satisfaction with the quality of transition of care, or the cost of readmission.

Conclusions: In this mutlicenter study, a standardized transition care intervention targeted to higher risk patients and composed of pre-discharge and post-discharge components did not decrease the risk for unplanned readmission or death within 30 days after discharge.

P48

Ultrasonography tutoring program in internal medicine: a randomized controlled trial

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In last decades, POCUS is gaining particular importance in internal medicine wards. Value of POCUS depends on the experience and skills of the operator. Indiscriminate use and lack of supervision can lead to incorrect diagnosis and increased number of additional tests. In 2018 the *Swiss Institute for Postgraduate and* Continuing *Medical* Education and the Swiss Society of Ultrasound in Medicine have established the minimal requirements for obtaining a POCUS certification. It is composed by 14 modules, 1 or 2 modules are needed for the certification, along with a total of 200 POCUS exams, half of them under the supervision of a certified POCUS tutor. In Geneva University Hospitals(HUG), since 2019 a post-graduate POCUS course composed by an eLearning course and a one-day supervised practice is offered to internal medicine doctors at the beginning of their residency without any experience in US.The aim of the *UltraSonography for Internal Medicine*(USIM) tutoring program is to investigate if a structured learning process including scheduled time slots of direct supervision will enhance the number of POCUS examinations and resident competences.The USIM tutoring program is a single center randomized open-label superiority trial and takes place in the general internal medicine service of HUG. Residents who successful passed a POCUS eLearning course and a one-day hands-on practice course were included. Participants were randomized in 2 groups with à 1:1 ratio. After randomization, residents included in the intervention arm were allocated to a POCUS tutor, with large experience in heart and lung ultrasonography. Participants underwent POCUS examinations under direct supervision. Participants included in control arm were encouraged to practice POCUS under supervision on a voluntary basis as usual so far in our service. In both arms, web-based indirect supervision(i.e. encoded video loops sent to a tutor for remote validation) was offered via an electronical logbook. The primary outcome was the proportion of residents who successfully completed 25 POCUS examination including at least 20 under direct supervision, 6 months after inclusion. Secondary outcomes included mean number of POCUS exams, US technical competences, self-estimated confidence and satisfaction. Between January and May 2022, 23 residents were included.Outcomes measurement ended the 26th of January 2023. Detailed participants characteristics and results are being presented in SSGIM spring congress 2023.

P49

What do patients and clinicians think about mobility of older hospitalised patients?

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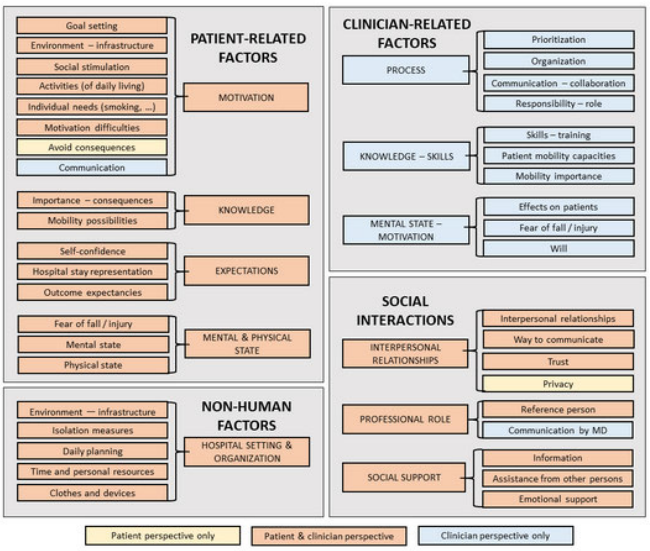
Introduction: Low patient mobility in hospitals is a widespread problem and has been associated with cascading effects such as falls, pulmonary compromise, delirium, prolonged length of stay, institutionalization and death. One study reported that almost 80% of patients were able to ambulate independently during an acute hospitalization, but that only about 3% of it was spent ambulating or standing. To improve patient mobility efficiently, we first need to better understand its barriers and facilitators. The goal of this study was thus to assess perspectives on hospital mobility of older recently hospitalised patients and clinicians, including nursing staff, physicians and physiotherapists.

Methods: In April-May 2022, we conducted a qualitative study with 5 focus groups (FGs) with 24 patients 60 years old and above recently hospitalised on an internal medicine ward of one of three Swiss hospitals (Inselspital Bern, Spital Tiefenau Bern, HFR-Fribourg), as well as 8 FGs with a total of 34 clinicians (15 physicians, 9 nurses or nursing assistants and 10 physiotherapists) working on those wards. The FG discussion included open-ended questions exploring mobility experiences, expectations, barriers and facilitators to mobility, consequences of low mobility and knowledge on mobility. We applied an inductive thematic analysis.

Results: Patient and clinician perspectives were categorized into four themes (Figure):
1) Patient-related factors,
2) clinician-related factors,
3) social interactions, and
4) non-human factors.
Clinician-related factors were only mentioned by clinicians. Otherwise, themes and subthemes identified from patient and clinician FGs were similar and codes broadly overlapped.
Subthemes included motivation, knowledge, expectations, mental and physical state (theme 1);
process, knowledge/skills, mental state/motivation (theme 2);
interpersonal relationships, support (theme 3);
hospital setting/organization (theme 4).

Conclusion: Within patient and clinician perspectives, a large spectrum of human and structural factors influences hospital patient mobility, many of which are actionable without requiring additional staff resources. This study is a first step in participatory research to improve mobility of older medical inpatients.

Figure 1. Thematic analysis according to mobility themes (patient-related factors, clinician-related factors, interactions, non-human factors) and origin of subthemes / codes (patient and clinician FGs).



P50

Breaking the silence: a content analysis of medical students' perceptions of failure in medicine

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Introduction: Failure is a powerful teacher, but an emotionally stressful experience. Before entering residency where failure is inevitable, medical students should ideally learn how to talk about and cope with failure in a productive manner. However, educational interventions to support learners to regulate fear of failure and its consequences are rare. Therefore, a four-day workshop entitled "How Physicians deal with Failure in Medicine" was offered to medical students at an academic institution to open the conversation about failure in medicine.

Methods: Two surgeons and a life coach developed and tutored the curriculum to provide insights into the ubiquity of failure in medicine. 30 participants wrote reflective essays about their perceptions on failure as a pre-curriculum task. Tutors then facilitated presentations, group discussions, journal clubs about failure, fear of failure and described potential coping strategies. As a post-curriculum activity, participants wrote another reflective essay to assess for knowledge transfer.

Results: The content analysis of all 60 reflective essays showed various self-experienced and observed failures in the clinical context by most students. Experiencing and witnessing failure was emotionally draining and often in conflict with self-expectations of being a physician. Perceived clinical supervision often protected medical students from failure and its potential consequences. However, open communication about failure by supervisors rarely occurred. The post-interventional essays revealed that fear of failure was omnipresent, while students realized and accepted that failure in medicine is human and inevitable. Gaining insights into failure stories of the tutors, helped students internalize this aspect.

Conclusion: Failure in medicine is inevitable. Therefore, medical students need to be prepared and supported regarding these challenges. Before entering residency, medical students wish to discuss failure in a safe environment. Without open discourse about failure, medical students feel left alone with their experiences, triggering fear. Medical schools should integrate curricula around failure and supervisors should support medical students entering clinical training by being more transparent about their own failures and sharing their coping strategies which will ultimately help them to make sense about failure experiences and learn from it.

P51

How to discuss, reflect and learn from a national survey of a medical society in a short multi-professional online conference: "Speed date your tool/idea"

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Background: Surveys are an important tool for assessing institutional practices/strategies. Moreover, a post-survey discussion is important to share, reflect on, and discuss the results. Because a survey normally takes a substantial amount of time to conduct, post-survey discussion needs to be time efficient. Online conferences have recently become popular, their efficacy varies. It remains uncertain how to structure a post-survey conference to discuss the results efficiently. The objective of this work is to share the structure of a successful conference.

Method: Description of the structure of a multi-professional online conference analyzing the results of a survey about a specific strategy (tools to identify palliative care needs) of the member-institutions of the Swiss Society of Palliative Care

Result(s): The healthcare professionals/institutions initially invited to participate in the survey were invited to a 90 min online conference using Zoom®. Local experts of the five tools identified by the survey, attended the conference. They presented their tool in a "speed dating" technique. First, a 3 min presentation (max. 3 slides) the key elements, strength and limitations of the tool were presented. Second, in a 3 min question and answer round participants raised their "virtual hand" with the videoconference tool and, when prompted by the moderator, asked their question. The presenter responded yes/maybe/no (no other responses were allowed). The other participants lowered their hands silently whenever their question had already been answered.
In the plenary, four groups (breakout sessions, 15min) were created to discuss the topic addressed by the tools (i.e., Identification of palliative care needs) on national, institutional, individual, and research levels. Followed by a plenary discussion initiated by a short presentation of the discussion's content by the group speaker. A written transcript was validated by all participants and provided (anonymized) further stakeholder information.The oral feedback of the participants was positive.

Conclusion: Consolidation of the results of a survey addressing institutional practices/strategies in a 90 min online conference is possible. Using a short, precise question for each practice/strategy followed by a group/plenary session to discuss the results on overarching national topics seems feasible.

P52

Population assessed sources to educate about health and disease prevention in Switzerland. A survey study

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Introduction: Health information is accessible through a growing number of media and interpersonal sources. Understanding where patients search for it and trust each source is crucial to educate the population.

Method: The Link Institute conducted an online survey representative of the adult Swiss population in November 2022. Participants reported the sources they used in the previous 12 months to educate themselves on health and disease prevention and the degree of trust for each one (with a 4-point Likert scale). Additionally, they reported the health topics they searched during this time.

Results: The data from 2020 participants were analysed: 49% were female, the mean age was 47 years old, 72% spoke German, 24% French, and 4% Italian.
Participants used the following media sources: websites of the Swiss federal government (ex. BAG, n=1004, 49.7%), TV (n=776, 38.4%), magazines and newspapers (n=575, 28.5%), media news sites (n= 523, 25.9%), radio (n=450, 22.3%), social media (n= 436, 21.6%), scientific journals (n= 292, 14.4%), books (n= 290, 14.4%), and websites of foreign authorities (n= 230, 11.4%).

Regarding interpersonal sources, survey participants consulted: general practitioner (n= 1144, 56.6%), family and friends (n=972, 48.1%), pharmacy (n= 782, 38.8%), specialized physicians (n= 564, 27.9%), health insurance advice by phone (n= 178, 8.8%), other health care providers (n=116, 5.8%), and community organisations (n=45, 2.2%).
The top most trusted media sources were websites of the Swiss federal government (42.4%), scientific journals (36.7%),TV (19.6%), books (17%), and media news sites (12.3%). The top most trusted interpersonal sources were specialized physicians (62.5%), general practitioners (55%), pharmacies (26.6%), family and friends (13.8%), and health insurance advice by phone (11.3%).
The most commonly searched health topics were: lifestyle (14%), diseases of bones, muscles, and joints (13%), infections (12%), pain (10%), and gender-specific issues (9%).

Conclusion: The most popular sources to find health information were the general practitioner followed by websites of the Swiss federal government, family and friends, and pharmacies. Generally, the most trusted sources of information were specialized physicians, general practitioners, pharmacies, and websites of the Swiss federal government. This information is key for the health system to develop effective education campaigns through the most used and trusted sources of information.

P53

Standard setting in assessment for case-based-simulations at the HSG school of medicine using the Hofstee method

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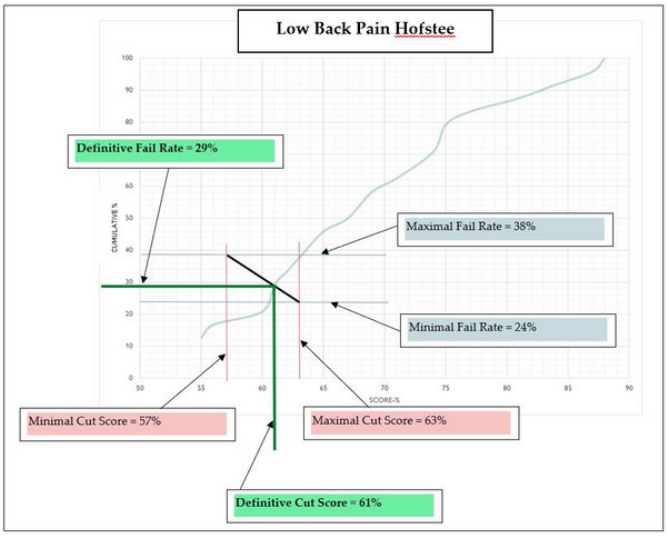
Learning objective: To introduce the Hofstee method as a resource-saving online variant (Zoom session) for standard setting in case-based-simulations (CBS) assessment.

Case: After a formative CBS – for example on low back pain – has been carried out, resulting data is processed. The score for each student is calculated as a percentage, taking into account the weighting of history taking, physical examination, management and communication. This data serves as the basis for the creation of a Hofstee diagram.
The task of the subject experts (examiners) is now to imagine the borderline student, i.e. a student who barely passes the examinations. Each expert now uses the chart to give his assessment of the following benchmarks:

1. Where do I set the **minimum cut score** below which the borderline student fails the exam? In our example: 57% (anything below is an unsatisfactory performance).
2. Where do I set the **maximum cut score** above which the borderline student passes the exam? In our example: 63% (anything above is a sufficient performance).
3. Where do I set the **minimum fail rate**? In our example: 24% (all students below have not passed)
4. Where do I set the **maximum fail rate**? In our example: 38% (all students above have passed)

These four values are now averaged and entered into the diagram. This results in a rectangle in the lower part of the curve. Now a diagonal line is drawn from the point at the top left (min. cut score/max. fail rate) to the bottom right (max. cut score/min. fail rate). **The intersection of this diagonal with the curve finally gives the definitive cut score and the definitive fail rate.** In our example these are:



Application of the Hofstee method for standard setting in assessment. X-axis: Point score as a percentage. Y-axis: Cumulative relative scores of all candidates.

Definitive cut score = 61% (anything below this is an unsatisfactory performance)
Definitive fail rate = 29% (all candidates below failed)
Discussion: There is extensive literature on the use of the Hofstee method in various examination situations in medical education. Since there is no gold standard for the standard setting in medical education, the Hofstee method is suitable according to Downing et al. as a defensible standard setting in connection with credible judges and a systematic approach to collect the judgements. This standard setting allows us to identify weak performers in our cohort and to address them directly in the sense of assurance of learning.

P54

What do chief residents address during feedback?

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Introduction: How to give feedback has been widely taught and assessed during Faculty Development programs. As part of a Faculty development program at the Geneva University Hospitals, chief residents attend objective structured teaching sessions (OSTEs), during which they are asked to give feedback to simulated residents on different tasks. The study aimed to analyse the feedback content provided during these OSTEs; to evaluate whether it changed according to the training phase, the medical discipline, or the type of task observed; to assess the alignment between feedback content addressed by the chief residents and content identified as key by experts.

Method: We conducted a multimethod study as part of this faculty development program. Chief residents from five departments were trained to supervise and give feedback to residents on several clinical topics in a six-month training program. Before and after the training, 91 of them completed four OSTE stations. OSTE stations focused on four tasks involving communication, interprofessional, physical or procedural skills. The feedback content was analysed descriptively according to the following categories: targeted (to the skills related to the task), other clinical content, learning strategies, and self-management. ANOVA test was applied to evaluate what factors influenced the feedback content. For each OSTE, we analysed the percentage of items identified as key by 3 experts (2-4 items per station) that were addressed by chief residents during the feedback.

Results: 317 feedback sessions were analysed, and 5388 occurrences coded. Feedback content distribution was: targeted feedback (73%), other clinical content (20%), learning strategies (4%), and self-management/other (3%). Feedback was more often negative than positive (73%). The phase of the training did not influence the content addressed. However, the topic of the observed task and

the clinical teachers' medical field somewhat influenced the feedback content. The percentage of alignment between content identified as key by experts and addressed by chief residents during OSTEs was low for all tasks (3-38%).

Conclusion: Chief residents give mostly negative and targeted feedback according to the task. There is little alignment in selecting the key content to be addressed. Reasons for choosing the feedback content may be multiple and should be further explored.

P55

Appropriateness of inpatient intravenous iron therapy in a Swiss tertiary care hospital – a quality control study

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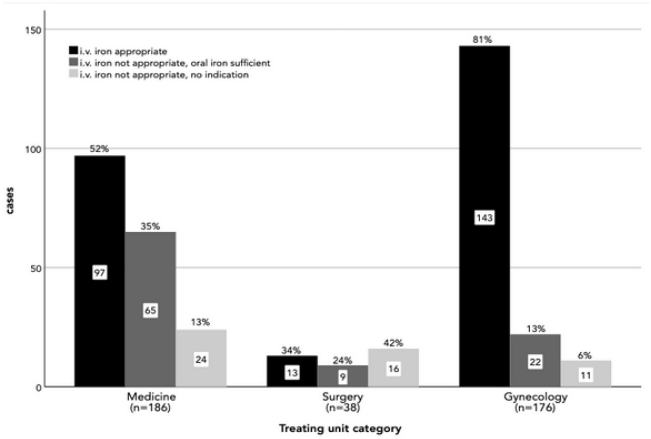
Introduction: Intravenous (IV) iron replacement is an accepted treatment for iron deficiency and is recommended in various medical guidelines, but evidence for its superiority compared to easy-to-administer and cheaper oral iron formulations is controversial. Data on adherence to current prescription standards are missing in Switzerland.

Methods: We performed a retrospective single center quality control study on the prescription quality of IV iron (ferric carboxymaltose) in 400 inpatient cases during 2019 and 2021 at the University Hospital Basel. Appropriateness of IV iron was assessed by expert chart review according to national and international guidelines.

Results: 147 (37%) of all IV iron prescriptions were judged to be inappropriate (indication for oral iron replacement in 24%, no indication in 13%). Inappropriate prescribing was more common ($p < 0.001$) on surgical wards (66%) compared to medical units (48%) and the gynecologic ward (19%). Iron studies were lacking in 29% of the inappropriate IV administrations. Amongst the cases with an appropriate indication for IV iron, an insufficient replacement dosage was chosen in 38% of patients. Baseline patient characteristics are median age of 49 years, 71% female sex; median length of stay was 6 days. Frequent comorbidities include chronic heart failure (23%), chronic kidney disease (21%), and active infection (18%), especially on the medical and surgery units. Active bleeding was documented in 55%, with overall median hemoglobin 89 (IQR 81 – 97) g/L before IV iron administration. An analysis of total IV iron use per patient showed an increase of 67% from 2012-2021 at the University Hospital Basel.

Conclusion:A concerning amount of IV iron has been prescribed without a clear indication based on current guidelines. Considerable differences exist between hospital units, which is consistent with diverging recommendations of the different medical societies. Despite the lack of robust evidence for its superiority, IV iron replacement was chosen in a significant number of patients. We recommend increased attention (educational tools, stewardship initiatives) towards the prescription quality to avoid an unnecessary, expensive and potentially harmful use of IV iron.



P56

Impact of food intake on oral SARS-CoV-2 RNA load

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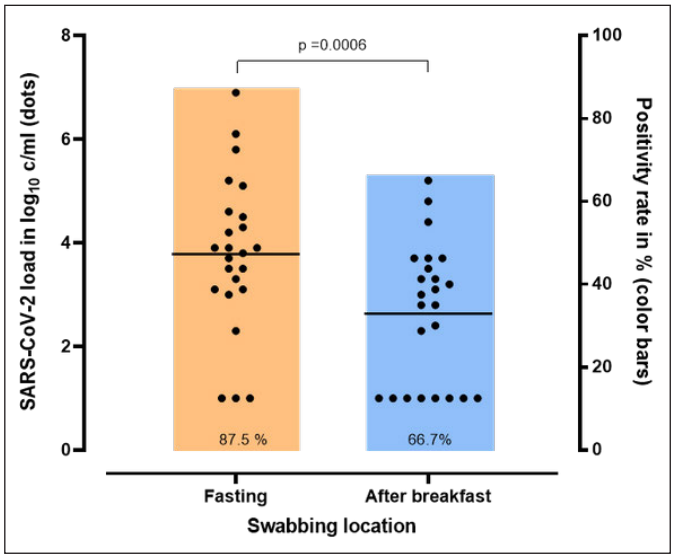
Introduction: During the course of the severe acute respiratory syndrome coronavirus type 2 (SARS-CoV-2) pandemic, oral specimens were increasingly used to detect SARS-CoV-2 infection despite their limited sensitivity. Furthermore, knowledge of the impact of food intake or oral hygiene procedures on oral SARS-CoV-2 RNA load is limited. The aim of the study was to assess the impact of food intake or oral hygiene on SARS-CoV-2 RNA load in self-collected buccal swabs.

Methods: COVID-19 patients were prospectively enrolled in a Swiss tertiary hospital between January and May 2022. Patients were instructed to fast in the morning. Written and visual instructions were provided and patients performed two self-collected buccal swabs: one before and a second one after breakfast. SARS-CoV-2 RNA loads were determined by RT-QNAT targeting the S-gene of SARS-CoV-2.

Results: 24 COVID-19 patients were included. 54.2% of the patients were male and the median age was 59 years [(interquartile range (IQR) 50 – 75)]. The median SARS-CoV-2 RNA load was 3.9 log10 c/mL [(interquartile range (IQR) 3.1 – 4.6 log10 c/mL) before, and 2.9 log10 c/mL (IQR 1.0 – 3.7 log10 c/mL) after breakfast. Accordingly, agreement with the professionally collected gold standard combined pharyngeal/nasopharyngeal PCR was demonstrated significantly more often before food compared after food intake. The positivity rate differed significantly before and after food intake (positivity rate 87.5% vs. 66.7%, p=0.0006) (Figure 1) compared to the professionally collected gold standard combined pharyngeal/nasopharyngeal swabs.

Conclusion: Food intake and oral hygiene impacts significantly on the oral SARS-CoV-2 RNA load. Therefore, if buccal swabbing or other oral specimens are used, they should be collected while fasting in the morning to improve sensitivity.

Figure 1. Impact of food intake on the SARS-CoV-2 RNA load and the positivity rate. Abbreviations: SARS-CoV-2: severe acute respiratory syndrome coronavirus. SARS-CoV-2 loads below the limit of detection were set to 1 log10 c/mL.



P57

Knowledge and training help: a toolbox for a trauma-focused integrated psychosomatic care in gynecology

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Introduction: Psychological and psychosomatic health disorders are common in somatic medicine. However, in everyday medical practice mental suffering often goes unrecognized or at least untreated, if only because of the still widespread distinction between somatic and mental medicine. In addition, patients may have difficulty sharing their suffering and/or present subclinical psychological or functional somatic symptoms that are not recognizable without further ado. Left unattended, such health issues can (co-)shape the somatic complaints and lead to unsatisfactory courses of treatment, to an increased somatic morbidity and even mortality. Thus, providing psychosomatically appropriate care within one›s own clinical activity is a major challenge for somatic physicians. However, instructions for action adapted to the requirements of the respective medical specialty are largely lacking.

Methods: A key objective of the research project «Psychotraumatology in somatic medicine» (Research Commission KSSG No. 20/19) is to provide a ***Toolbox*** including psychosomatic knowledge and clinical interventions tailored to the clinical requirements of the various medical disciplines. With focus on the care of patients with traumatic life experiences and trauma sequelae, a first practical step was made in gynecology. Starting point was a specific training course additionally used to survey the knowledge, concerns and wishes of the medical team. A study of outpatient consultations derived from this experience was able to confirm, among other things, that trauma-specific training of the physician improves the therapeutic relationship.

Results: Directly applicable, disorder-sensitive communicative skills are crucial, especially with regard to diagnostic attention - and the ability to address difficult topics that are stressful for patients, but also for the physician himself. The toolbox includes knowledge of gynecological symptoms, which may indicate trauma; of potentially traumatizing medical measures; of trauma-sensitive diagnostic and therapeutic standards; of the creation of an adequate setting and basic, relieving and supportive therapeutic interventions; of conversational techniques, appropriate terms and metaphors; of psychoeducational means; of specific treatment options and the targeted use of collegial intervision and Balint groups.

Conclusion: Psychosomatic knowledge and training improves medical care in a gynecological context, and relieves the physician as well.

P58

Post-COVID consultation at Winterthur Cantonal Hospital - follow-up over six months

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Introduction: Post-COVID is still incompletely understood and disease management is therefore partially untargeted. Our study investigated how main symptoms changed, what elements helped to cope with the condition and the satisfaction with the consultation and therapeutic interventions.

Methods: Data were collected at the time of consultation (t1), after 2 (t2) and 6 (t3) months. The survey included questions on sociodemographic characteristics; severity of symptoms using a visual analogue scale (VAS) from 0 (lowest) to 10 (highest); general health, on a VAS from 0 (worst) to 100 (best); ability to work; and standardized questionnaires: Post-COVID Function Scale (PCFS), from 0 (best) to 4 (worst); Chalder Fatigue Scale (CFS), from 0 (best) to 11 (worst). Statistical significances for the changes between the time points were calculated. Interviews were conducted with 10 patients at t1 and t3.

Results: 49 patients were included (67% women, age 44.1±12.5 years). Subjects were referred to: physical reconditioning (n=2, 4%), fatigue management (n=20, 41%), psychosomatic therapy (n=3, 6%) a combination (n=16, 33%) or no therapy (8,16%). For 10 (20%) further diagnostics was prescribed.

Main results:

	t1	t2	t3	p
n	49	43	33	
General health VAS	53.2	54.4	65.2	<0.01
PCFS	2.6	2.2	1.8	<0.001
CFS	9.2	8.8	7.5	<0.005
Remained sick leave (n, %)	15, 56	12, 44	10, 37	ns
Symptoms:				
Chronic fatigue n, %	46, 94	39, 91	31, 94	ns
VAS	7	7	7	
Decreased physical performance				
n, %	40, 82	36, 82	23, 70	<0.05
VAS	7	6.5	5	
Pain				
n, %	16, 33	18, 44	9, 27	ns
VAS	7	2	2	

In the interviews, patients indicated that they felt well cared for and that the consultation met their expectations. Helpful in the doctor-patient interaction were being taken seriously, appreciative attitude, no false hopes, and enough time to talk. Regarding disease management, early psychological support and guided fatigue management were perceived as helpful.

Conclusions: Most referrals to the post-COVID consultation were targeted and only few additional diagnostic measures had to be initiated. General health (measured with VAS), PCFS and CFS were mostly impaired, with a significant improvement over time. Interestingly, chronic fatigue measured with the CFS showed moderate improvement, this was not confirmed when measured with VAS. Over time, there was only a slightly improvement in physical performance. Currently, patients can best be supported by attentive interprofessional coaching in disease management.

P59

Wellbeing and absenteeism of healthcare workers during the COVID-19 pandemic: a longitudinal study

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Introduction: The COVID-19 pandemic is a crisis situation that became chronic potentially leading to long-term consequences for years to come. While experts have warned against the pandemic burden on healthcare workers early on (1), little is known on the evolution of this burden with time and with successive waves, additionally to the long-term effects of post-COVID symptoms in healthcare workers. After a first study showing the burden of COVID-19 on healthcare workers (2), we now conducted a longitudinal follow-up on this same cohort to evaluate the evolution of symptoms, functional capacity and quality of life.

Methods: Healthcare workers at the Geneva University Hospitals had an online follow-up in July and December 2021, collecting data on their physical and mental health, quality of life and functional capacity using validated scales. Descriptive analyses compared the prevalence of symptoms, functional impairment and quality of life in SARS-CoV-2 positive and negative individuals at baseline and at follow-up.

Results: Out of the initial n=3,083 participants that had answered at baseline, n=900 completed the follow-up. Participants had a mean age of 46.4 years, 70.1% were women, and 46.7% had no pre-existing comorbidities. Overall, n=489 (54.3%) of participants reported at least one symptom at baseline compared to n=616 (68.4%) at follow-up with an overall higher prevalence of symptoms in SARS-CoV-2 positive individuals. At follow-up, more individuals reported

fatigue (+9.4%), headache (+9.0%), insomnia (+2.3%), cognitive impairment (+1.4%), stress/burnout (+8.8%), pain (+8.3%), digestive symptoms (+3.6%), dyspnea (+1.0%), and cough (+7.7%) compared to baseline, with a differentially larger increase in symptoms in the SARS-CoV-2 negative group. Individuals had more functional impairment (12.7 % at baseline and 23.9% at follow-up), with more absenteeism and worsening quality of life.

Conclusion: Healthcare workers have an increased prevalence of symptoms related to the pandemic in general and post-COVID. Symptoms are manifested by fatigue, headache, insomnia, cognitive impairment and stress/burnout, and are associated with an increased functional impairment, absenteeism and worsening quality of life. This calls for an urgent look into the overall state and well-being of healthcare workers, along with potential solutions.

Fig 1. Symptoms evolution between baseline and follow-up

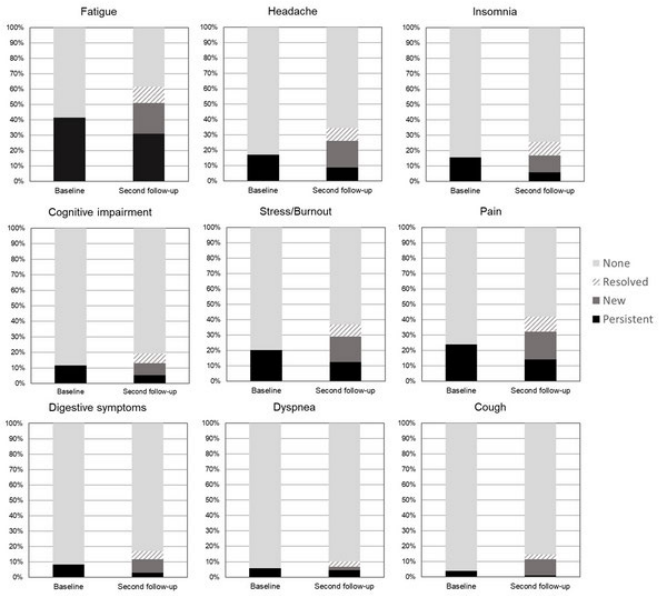
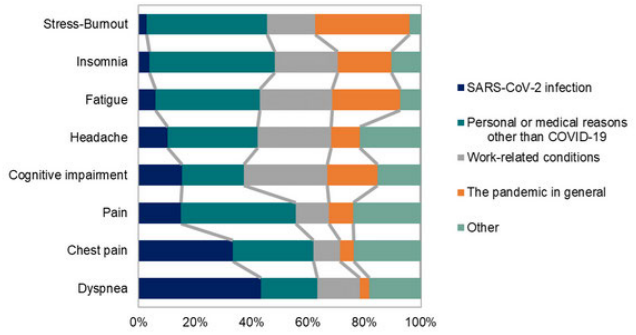


Fig 2. Self-reported reasons for symptoms by participants



P60

Diagnostic and prognostic role of Mannose-Binding Lectin in patients with suspected Functionally Relevant Coronary Artery Disease

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Introduction: Experimental studies have suggested a pathogenic role of Mannose-Binding Lectin (MBL) in the development of atherosclerosis. However, prospective data concerning diagnostic or prognostic values of MBL have been inconclusive. The present study aims to evaluate the clinical significance of MBL for detecting functionally relevant coronary artery disease (fCAD) and its prognostic value regarding long-term cardiovascular risk.

Methods: A total of 1,567 consecutive patients with suspected fCAD were included in a prospective cohort study. Single-photon emission tomography/computer tomography was used to adjudicate fCAD. We used an MBL lectin assay, an in-house time-resolved immunofluorometric assay, to measure MBL levels in non-fasting venous blood at baseline. Incident all-cause mortality, cardiovascular death, and nonfatal myocardial infarction were assessed over a five-year follow-up.

Results: In 462 patients, fCAD was diagnosed at baseline. The patients with confirmed fCAD were older and had more comorbidities. During follow-up, 106 patients suffered a myocardial infarction (MI) and 98 died. MBL did not demonstrate any diagnostic ability to distinguish patients with and without fCAD; AUC was 0.56 (95% CI 0.48–0.65, p = 0.102). In Kaplan-Meier analysis, higher MBL levels demonstrated the ability to predict MI in the whole group (p=0.032, Log-rank test). However, after adjustment for age, gender, history of cardiovascular disease, myocardial infarction, stroke, and diabetes, MBL did not prove any prognostic abilities concerning the development of MI (HR=1.01, 95% CI 0.99-1.1001, p=0.23) or death (HR=0.99, 95% CI 0.99-1.1011, p=0.23). Interestingly, we observed increased LDL cholesterol levels in patients with higher MBL levels (comparison of LDL levels in groups according to MBL quartiles: first 2.34 (1.77-3.00) mmol/l; second: 2.35 (1.72-3.01) mmol/l; third: 2.40 (1.82-3.15) mmol/l and fourth: 2.49(1.84-3.03) mmol/l, p=0.039, Kruskal-Wallis test). There were no significant differences between these groups in age, blood pressure and other blood lipids and creatinine levels.

Conclusion: Although we found an association between MBL and LDL cholesterol levels, MBL doesn't have any diagnostic and prognostic abilities in patients with suspected functionally relevant coronary heart disease.

P61

Direct diagnostic and prognostic comparison of carotid plaques (Total Plaque Area) with coronary calcifications (Agatston Score)

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Introduction: There are few studies comparing diagnostic and prognostic meaning of carotid plaques and coronary calcified plaques.

Methods: Patients were assessed between 2002-2022 comparing carotid total plaque area (TPA) and coronary calcifications (CAC). Follow-up was obtained by recall of patients, questionnaires or external clinical records. Comparison was made for SCORE2, TPA, and CAC using ROC, logistic regression, and Cox proportional hazards (Cox).

Results: In 942 patients, average age 59 (range 22-89) years, TPA > 21 mm^2 was found in 20%, of which none had coronary calcifications and CAC score >0 without carotid plaque was found in 14% of patients, and 15% had no plaques. 436 patients with a complete follow-up over 10 (range 1-20) years. Cox predictors of 50 events during follow-up (14 stents or CABG, 10 AMI, 5 strokes, 21 deaths of any cause) were TPA (p=0.048), DMII (p=0.002) and age (p=001), but not CAC. Area under the curve (AUC) was 0,618 (95%CI: 0,571 to 0,664) for TPA and was 0,686 (95%CI: 0,640 to 0,729, p for difference NS). In 302 patients, complete follow-up 31 events occurred (9 Stents/CABG, 7 AMI, 2 Strokes and 13 deaths of any cause during a follow-up time of 11 (range 1-20 years). Significant predictors of events were DMII (p=0.013), SCORE2 TPA risk category (p=0.011) and SCORE2 CAC risk category (p=0.013), but not sex, age, family history of ASCVD, medication, systolic blood pressure, cholesterol, HDL, LDL, and SCORE2 (p=0.502). Using ROC analysis, SCORE2 risk category AUC was 0,589 (95%CI: 0,531 to 0,645), for SCORE2 TPA risk category was 0,647 (95%CI: 0,590 to 0,700) and for SCORE2 CAC risk category was 0,662 (95%CI: 0,605 to 0,715, for all p=NS).

Conclusion: TPA was non-inferior to CAC regarding presence of significant atherosclerosis and ASCVD outcome in practice-based patients.

P62

Evaluation of health care utilization and mortality in multimorbid medical inpatients with and without kidney disease: a nationwide cohort study

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Introduction: The association of impaired kidney function and healthcare use among medical inpatients is incompletely understood. This study aimed to assess the prevalence of acute kidney injury (AKI) and chronic kidney disease (CKD), respectively, among multimorbid patients hospitalized in Switzerland for medical reasons and explore the associations of kidney disease with healthcare use across different frailty strata.

Methods: This observational study analyzed nationwide hospital discharge records from January 1, 2012 through December 31, 2020, provided by the Federal Statistical Office. We included adult patients (age ≥18 years) hospitalized on a medical ward with underlying multimorbidity. We compared hospitalizations of patients with no kidney disease (control group) and patients with AKI and CKD. Main outcomes were in-hospital mortality, intensive care unit (ICU) treatment, length of stay and 30-day readmission. We estimated multivariable adjusted odds ratios (aOR) and changes in percentage of log-transformed continuous outcomes with 95% confidence intervals (CI). Estimates for patients with AKI were calculated using data from 2017-2020 only due to coding issues.

Results: Among 2,651,501 multimorbid medical hospitalizations, 1,999,641 (75.4%) patients had no kidney disease, 198,870 had a diagnosis of AKI (7.5%) and 452,990 had CKD (17.1%). We found significantly increased risks among AKI and CKD patients in regard to mortality (4.4% in controls vs. 14.4% in AKI (aOR 2.56 [95% CI, 2.52, 2.61]) vs. 5.9% in CKD (aOR 0.98 [95% CI, 0.96, 0.99]), ICU admission (10.5% in controls vs. 21.8% in AKI (aOR 2.39 [95% CI, 2.36, 2.43]) vs. 9.3% in CKD (aOR 1.01 [95% CI, 1.00, 1.02]) and 30-day readmission (13.3% in controls vs. 13.7% in AKI (aOR 1.21 [95% CI, 1.19, 1.23]) vs. 14.8% in CKD (aOR 1.26 [95% CI, 1.25, 1.28]). Length of hospital stay (LOS) was also significantly higher in AKI and CKD patients (5 days vs. 9 days vs.7 days).

Conclusion: Acute and chronic kidney disease was associated with a significant higher inpatient healthcare utilization. This information is of importance for cost estimates and could drive future reimbursement strategies.

P63

Gender differences in direct diagnostic and prognostic comparison of carotid plaques (Total Plaque Area) with coronary calcifications (Agatston Score)

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Introduction: Gender studies comparing diagnostic and prognostic meaning of carotid plaques and coronary calcified plaques are currently missing.

Methods: Carotid total plaque area (TPA) and coronary calcifications (CAC) were compared using follow-up events, with area under the curve (AUC), logistic regression, and Cox proportional hazards (Cox).

Results: In 942 patients (age 59 years, 22-89), 22% women had TPA<22mm^2 and CAC=0, 36% had TPA>21mm^2 and CAC=0 and 11% had TPA<22mm^2 but CAC>0; 12% men had TPA<22mm^2 and CAC=0, 22% had TPA>21mm^2 with CAC=0 and 15% had TPA21mm^2 and CAC>0. Women had more frequently TPA>21mm^2 and CAC=0 than men (p=0.003).
In 578 patients SCORE2code was low/intermediate (N=239, 41%), high (N=295, 51%) and very high (N=44, 8%). SCORE2TPAcode "very high-risk" (cases) was present in 64 (35%) women and 238 (60%) men. AUC of SCORE2CACcode was 0,612 (95%CI: 0,537 to 0,603) in women and 0,640 (95%CI: 0,592 to 0,689) in men (p=NS). Predictors of cases in women were age (p=0.005), smoking (p=0.010), systolic blood pressure (p=0.001), SCORE2code (p=0.006), but not CAC or SCORE2CACcode. in men, significant predictors were age (p=0.0001), smoking (p=0.004), medication code (p=0.040), total cholesterol (p=0.017), SCORE2code (p=0.007) and SCORE2CACcode (p=0.027).
In 436 patients (132 women) with a complete follow-up of 10 (mean, range 1-20) years with 50 events during follow-up (14 stents/CABG, 10 AMI, 5 strokes, 21 deaths of any cause), Cox significant predictor of 13 events in women was DMII (p=0.031), but not TPA or CAC. In men, significant predictors of 37 events were TPA (p=0.018), DMII (p=0.011) and age (p=0.021), but not CAC.

Conclusion: In women with carotid plaque, 36% had significantly more frequently no CAC than men (22%). Preliminary outcome results suggest that TPA is at least non-inferior to CAC in men, but inconclusive in women (due to limited number of observations).

P64

Pharmacokinetics of SSRI/SNRI after bariatric surgery and the effects on depressive symptoms

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Introduction: Mental disorders and treatment with antidepressants SSRI/SNRI are common in people with morbid obesity who are candidates for bariatric surgery. There is few and inconsistent data about the postoperative pharmacokinetics of SSRI/SNRI. The aims of our study were to provide comprehensive data about the postoperative bioavailability of SSRI/SNRI, and the clinical effects on depressive symptoms.

Methods: Prospective multicenter study including 63 patients with morbid obesity and therapy with SSRI/SNRI: participants filled the Beck Depression Inventory (BDI) questionnaire, and plasma levels of SSRI/SNRI were measured by HPLC, preoperatively (T0), and 4 weeks (T1) and 6 months (T2) postoperatively.

Results: The plasma concentrations of SSRI/SNRI dropped significantly in the bariatric surgery group from T0 to T2 by 24.7% (95% confidence interval [CI], -36.8 to -16.6, p=0.0027): from T0 to T1 by 10.5% (95% CI, -22.7 to -2.3; p=0.016), and from T1 to T2 by 12.8% (95% CI, -29.3 to 3.5; p=0.123), respectively. There was no significant change in the BDI score during follow-up (-2.9, 95% CI, -7.4 to 1.0; p=0.13). The clinical outcome with respect to SSRI/SNRI plasma concentrations, weight change, and change of BDI score were similar in the subgroups undergoing gastric bypass surgery and sleeve gastrectomy, respectively. In the conservative group the plasma concentrations of SSRI/SNRI, and the BDI score remained unchanged throughout the six months follow-up (-14.7%, 95% CI, -32.6 to 1.7; p=0.076).

Conclusions: In patients undergoing bariatric surgery plasma concentrations of SSRI/SNRI decrease significantly by about 25% with wide individual variation, but without correlation to the severity of depression or weight loss.

P65

A case-series analysis of tuberculosis in patients treated in a Swiss tertiary-level hospital

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Introduction: In 2021, tuberculosis (TB) was the second leading cause of death from an infectious disease worldwide, after COVID-19. (1)
In Switzerland, TB has become rare (annual incidence: 5.1 per 100.000 people). (2) Nevertheless, the disease may make a come-

back owing to increasing migratory movements, which are triggered by climate change and conflicts. However, its diagnosis may be missed if not considered. [3]

Therefore, in order to create awareness and assist physicians in identifying affected individuals, the main aim of this study is to present TB patients' demography, affected sites of disease, and clinical presentation.

	Demography			Site of disease						Clinical presentation		
	Sex	Age	Nationality	Pulmonary	Extra-Pulmonary (60%)					Symptoms at first diagnosis		
	70% Male 30% Female	Median = 50.5 Mean = 47.3	100% Non-Swiss	(100%)	Lymphatic (40%)	Gastrointestinal (30%)	Musculoskeletal (20%)	Ocular (10%)	Pleural (10%)	Constitutional (100%)	Respiratory (70%)	Other (70%)
1	Female	22	Eritrea	X	X				X	Fatigue	Dry cough Shortness of breath	Pain: chest, abdomen and pereneus tendon
2	Male	22	Somalia	X						Fever Fatigue	Cough	None
3	Male	40	Togo	X	X	X	X	X		Weight loss	None	Pain: eye and head Visual disturbance
4	Male	45	Austria	X	X	X				Fever Fatigue Weight loss	Productive cough	Pain: abdomen Hematochezia Diarrhoe
5	Male	48	Dominican Republic	X						Fever Night sweats Weight loss	Haemoptysis	None
6	Male	53	Portugal	X	X					Weight loss Night sweats	None	Pain: chest and abdomen Regurgitation
7	Male	54	Portugal	X		X				Fatigue Night sweats Weight loss	None	Pain: chest and abdomen Odynophagie Regurgitation
8	Female	55	Ethiopia	X			X			Fatigue Night sweats Weight loss	Dry cough Shortness of breath	Pain: chest and back
9	Female	66	China (Tibet)	X						Increased sweating Appetite reduction	Productive cough	None
10	Male	68	Kosovo	X						Fever Night sweats Weight loss	Cough Haemoptysis Dyspnoea	Hematochezia

Methods: The study design was retrospective and observational. Data were collected from the electronic healthcare records of Lucerne Cantonal Hospital (LUKS) and statistically evaluated in a descriptive and anonymized form.
Included were patients who had provided written consent and had a culture-confirmed infection with mycobacterium tuberculosis registered at LUKS from January 1st, 2020, to December 31st, 2022. A total of 10 cases were included.
Investigating variables were the demography (age, sex, nationality), the affected site of disease, and the clinical presentation (symptoms at first diagnosis) of the patients included.

Results: Of 10 patients, 7 were male, and 3 were female. Their ages ranged from 22 to 68 years. The median age was 50.5 years, and the mean 47.3 age. All patients were non-Swiss citizens and came from 9 different countries.
Pulmonary manifestation was found in all 10 patients, and extrapulmonary manifestations in 6 patients. The distribution pattern of extrapulmonary manifestations in relation to all the cases was as follows: 40% lymphatic, 30% gastrointestinal, 20% musculoskeletal, 10% ocular, and 10% pleural.
Regarding the distribuition of symptoms at first diagnosis we found that 100% had constitutional symptoms (B-symptoms/systemic symptoms), 70% had respiratory symptoms, and 70% had other symptoms.

Conclusion: The results show that TB prevalence is strongly associated with migration and pulmonary affection and should therefore be specially considered in patients with a migratory background as well as constitutional and pulmonary symptoms.

P66

Adult survivors of childhood cancer: characteristics of a cohort from two long-term follow-up clinics in Switzerland

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Introduction: Since 2017, the interdisciplinary follow-up clinics at the Cantonal Hospital Baselland Liestal and the University Hospital Inselspital Bern offer the first structured follow-up care for adult childhood cancer survivors (ACCS) led by general internists in Switzerland. The „Passport for Care®"-Application (PfC) is used to plan the clinic visits. The PfC individualizes the Children's Oncology Group Long-Term Follow Up (LTFU)-guidelines based on the oncological treatment the ACCS had received. We aimed to char-

acterize the ACCS evaluating the burden of health problems and their health related quality of life (HRQOL).

Methods: A characterisation of ACCS attending the LTFU clinics and enrolled in the study cohort until January 2022 was performed. ACCS's clinical history, cancer diagnosis, treatment, comorbidities and their current health status were assessed. Questionnaires filled in before the first clinic visit included the Short Form-36 version 2 (SF-36v2) measuring HRQOL. Two summary measures of the SF-36v2 for physical and mental HRQOL were used. We compared the SF-36v2 summary measures to normative data in the Swiss general population (SGP; mean=50, SD=10).

Results: 103 ACCS were enrolled (Bern 53% and Liestal 47%). 68% were female, mean age 31.5 years (17.1-61.8 years). 43 of these ACCS had not visited regular LTFU before (36 ACCS >28 years, 7 ACCS ≤28 years). On average ACCS had 5.7 different health problems (range: 0-15, SD=3.6). All organ systems were affected. In total, 24 (23.3%) CCS had secondary malignancies (SMNs). Multivariable regression modelling showed an association of the number of health problems with age (β=0.1, $p < 0.001$) and cancer treatment intensity (maximal irradiation dose and cumulative Cyclophosphamide equivalent dose in grams/m^2; β=0.03, $p = 0.022$).
Before the first visit, physical (47.6, p=0.037) and mental (47.5, p=0.040) HRQOL were significantly lower in ACCS compared to the Swiss general population. ACCS >28 years of age reported lower physical and mental HRQOL compared to younger ACCS: 44.8 vs. 50.2, p=0.017 and 44.4 vs. 50.5, p=0.009.

Conclusion: ACCS visiting LTFU clinics suffer already at an early age from diverse health problems. They have a worse HRQOL than the SGP. These findings indicate a need for LTFU in specialised settings. Since all organ systems can be affected and secondary malignancies are not the main health problems of ACCS, involvement of general internists is necessary to optimize follow-up care.

P67

Are physician trainees a valid alternative to expert adjudicators? Validation of the ISTH definition of pulmonary embolism-related death in an autopsy cohort

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Introduction: Central adjudication committees (CACs) are often composed of experts in the corresponding medical field. Involving physician trainees in CACs would allow investigators to divide the workload and foster trainees' research experience. The aim of this study was to evaluate the accuracy of the International Society on Thrombosis and Haemostasis (ISTH) definition of pulmonary embolism (PE)-related death for autopsy-confirmed PE- versus non-PE-related death among physician trainees.

Methods: In this retrospective analysis of consecutive autopsies performed at the NewYork-Presbyterian Hospital, we included all patients with PE-related death between 01/2010 and 07/2019 and patients who died in 2018 from a cause other than PE. Two physician trainees, blinded to autopsy results, reviewed premortem clinical summaries, and independently adjudicated the cause of death in each patient using the ISTH definition of PE-related death. We calculated the sensitivity and specificity of the ISTH definition for autopsy-confirmed PE-related death, and its interrater agreement.

Results: Overall, 126 death events were adjudicated (median age 68 years; 60 [48%] women), of which 29 (23%) were due to PE, as confirmed by autopsy (Table). Sensitivity and specificity of the ISTH definition for autopsy-confirmed PE-related death was 48% (95% CI, 29-67) and 100% (95% CI, 96-100), respectively. Interrater agreement for PE-related death was substantial (percentage agreement, 93%; 95% CI, 87-96; Cohen's Kappa, 0.67; 95% CI, 44-85).

Conclusion: Our findings were very similar to those of a previous validation study in which thrombosis experts adjudicated the same death events (reference: PMID 34255928). They support the use of the ISTH definition of PE-related death in clinical venous thromboembolism studies and revealed high agreement between adjudicators with varied clinical and adjudication experience.

Table. Final classification of adjudicators by autopsy result

Adjudicators' classification*	All deaths (N=126)	Autopsy-confirmed PE-related death (n=29)	Autopsy-confirmed non-PE-related death (n=97)
A2. Objectively confirmed PE before death	11	11	0
A3. PE not objectively confirmed, but most likely the main cause of death	3	3	0
B1. Undetermined cause of death	41	10	31
B2. Insufficient clinical information available to determine the cause of death	0	0	0
C. Cause of death other than PE	71	5	66

* Deaths could not be classified as subcategory A1 (i.e., autopsy-confirmed PE) due to the study design.

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Cannabis use and risk of atherosclerosis cardiovascular disease: a two-sample Mendelian randomization study

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Introduction: Whether cannabis use causally associates with atherosclerotic cardiovascular disease, (ASCVD) remains unknown. A genetic approach, using Mendelian randomization principles, can help make inferences on the association between a risk factor and a disease outcome when a clinical trial is impracticable for ethical reasons.

Aims: To estimate the effect of genetically determined cannabis use on risk of ASCVD, including coronary artery disease (CAD) and ischemic stroke (IS).

Methods: Using two-sample Mendelian Randomization (MR), 65 independent (R^2<0.2) genetic markers associating with "ever use of cannabis" in 184'765 European individuals were employed to estimate the causal association between cannabis use and risk of ASCVD. The genetic instruments were first used to test the causal association between cannabis use and CAD in 60'801 cases and 123'504 controls. Second, we explored the causal association between cannabis use and IS in 34'217 cases and 406'111 controls. Genetic data for both outcomes predominantly comprised individuals from Caucasian origin. To triangulate genetic findings, we conducted a meta-analysis of observational studies reporting a link between cannabis use and ASCVD, CAD or AIS.

Results: Based on the genetic analysis, there was no evidence for a causal effect of cannabis use on the risk of CAD (OR=0.97, 95%CI 0.92-1.02, p-value=0.19) or AIS (OR=1.03, 95%CI 0.98-1.09, p-value=0.41). Sensitivity analyses, including MR-Egger, weighted median MR, Steiger filtering and multivariate MR analysis, yielded similar results, and no heterogeneity and directional pleiotropy were observed. Based on the meta-analysis of 6 observational studies for each outcome, ever use of cannabis was not associated with CAD (pooled OR=1.23, 95% CI, 0.78-1.69), nor AIS (pooled OR=1.22, 95%CI 0.95-1.50).

Conclusion: Using a genetic approach recapitulating a clinical trial, we found no evidence in support of a causal effect between cannabis use and CAD or AIS.

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Characteristics of hypertensive subjects not reaching target blood pressure: the CoLaus|PsyCoLaus study

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Objective: We prospectively assessed factors associated with uncontrolled hypertension by comparing treated subjects not reaching blood targets with treated subjects with controlled hypertension in the CoLaus|PsyCoLaus study.

Methods: 1'202 participants were eligible for analysis. Uncontrolled hypertension was defined as systolic blood pressure value >= 140 mm Hg and diastolic blood pressure >= 90 mm Hg. Baseline participants' characteristics were stratified by hypertension status (uncontrolled versus (vs) controlled hypertension). Pearson chi-square for categorical variables and student t-test were used to evaluate differences in subjects' baseline characteristics. Association tests between hypertension status (uncontrolled vs. controlled hypertension) were performed by separate logistic regressions including independent variables.

Results: Characteristics such as heavy alcohol consumption, BMI, glycemia, high sodium urinary excretion, ferritinemia and albuminuria were significantly positively associated with uncontrolled hypertension when adjusted for sex and age. Characteristics inversely associated with uncontrolled hypertension were education level such as apprenticeship and university degree, current smoker and high potassium urinary excretion.

Conclusion: Uncontrolled hypertension being associated with an increased risk of adverse cardiovascular outcomes and all-cause death, confirming, and identifying modifiable characteristics such as heavy drinking, obesity and bad dietary habits associated with poor blood pressure control emphasize that there is room for public health approaches to better control blood pressure in hypertensive population.

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Effects of Electronic Nicotine Delivery Systems (ENDS) for smoking cessation on weight gain – secondary analyses of the ESTxENDS trial

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Introduction: Previous data indicate that nicotine replacement therapy (NRT) moderately reduces weight gain after smoking cessation weight gain, which concerns many smokers. We aimed at testing the effect of electronic nicotine delivery systems (ENDS) on weight gain.

Methods: We included participants from an RCT on smoking cessation with ENDS and counseling (intervention group) or counseling with optional NRT (control group) with body weight measures at baseline and after 6 months. We assessed weight gain in an intention to treat analysis (ITT). We also performed a per-exposure analysis in the intervention group (continuing smokers, quitters, dual ENDS and tobacco users, ENDS-only users with or without nicotine) based on self-reported use within the 7-days before the visit. The linear regression models were adjusted for baseline demographics, weight, use of NRT, cannabis and alcohol use. We applied inverse probability weights to account for attrition.

Results: Among 1,246 randomized participants, 790 (63%) were weighed at 6 months. Median age was 40 (IQR 31 to 52 years) and 431 (55%) identified as men in our sub-study sample. After 6 months, 274 (62%) did not report smoking in the intervention and 148 (43%) in the control groups. In the intervention group were 87 (20%) smokers, 48 (11%) quitters (none reporting NRT use), 85 (19%) dual users, 184 (41%) ENDS-only users with nicotine, and 42 (9%) ENDS-only users without nicotine. In ITT analyses, mean weight gain after 6 months was similar in intervention and control groups (1.5kg [95% CI 1.2 to 1.8] vs. 1.8kg [95% CI 1.5 to 2.1], p=0.34). In per-exposure analyses of the intervention group, quitters and ENDS-only users without nicotine gained more weight (2.8kg [95% CI 1.6 to 5.7], p=0.04; 2.9kg [95% CI 2.0 to 5.4], p=0.02) than continuing smokers (1.2kg [95% CI -0.4 to 4.6]). ENDS-only users with nicotine (1.4kg [95% CI -0.6 to 4.2], p=0.77) and dual users (1.0kg [95% CI -0.4 to 4.2], p=0.62) had similar weight gain than continuing smokers.

Conclusion: On average, those who were randomized to ENDS use besides counseling for smoking cessation gained weight similarly to those receiving counseling alone. As ENDS raised the proportion of quitters, it might encourage smokers worried about weight gain to switch to ENDS. While using ENDS without nicotine was associated with weight gain in quitters, those using ENDS with nicotine had similar weight than continuing tobacco smokers.

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Exploring the gender differences in type 2 diabetes incidence in a population-based cohort using latent class analysis: an intersectional approach

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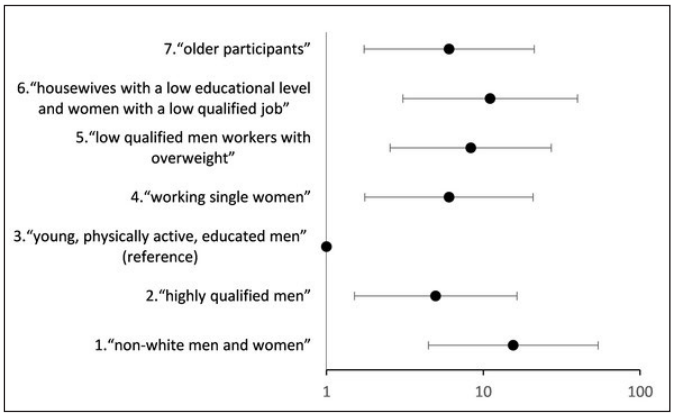
Introduction: Socioeconomic status and health-related behaviors create various risk patterns of developing type 2 diabetes (T2D). We hypothesize a gender difference in the distribution of these determinants of health and aim to disentangle their role from administrative sex in predicting the development of T2D.

Methods: Secondary data analysis of the CoLaus|PsyCoLaus study, an observational cohort study on determinants of cardiovascular and mental diseases. Participants were recruited from all the inhabitants of the city of Lausanne (CH) aged 35-75 years in 2003. We excluded participants with diabetes at baseline and/or with missing information about diabetes at baseline or follow-up. We first conducted latent class analyses using demographic (e.g., age, race), socioeconomic (e.g., employment, education), and health-related behavioral variables (e.g., physical activity), allocating individuals to the latent class for which they had the highest belonging probability. We then conducted logistic regression analyses to explore how these classes predicted the development of T2D at third follow-up (2018-2021), adjusting for T2D known risk factors. Third, we adjusted the model for sex to disentangle the influence of the socioeconomic gender differences.

Results: Of the 6734 participants enrolled at baseline, 98.0% (N=6597) were not diabetic. Of those without missing information at follow-up (N=3547), 3409 were included in our analyses (96.1%): 1893 women (55.5%), mean age 50.30 years (SD 9.8). Over a median follow-up time of 14.53 years, 255 (7.5%) participants developed T2D, of which 97 women (48.0%). We identified seven latent classes and labeled them using characteristics with high allocation probability (Fig 1). Using the class of "young, physically active, educated men" as reference, the risk of incident T2D (adjusted for sex and age) was higher in all other classes (Fig. 1).

Conclusions: Socioeconomic variables are not homogeneously distributed between men and women and show different risk patterns of developing T2D at different intersections. These patterns are only partly captured by traditional sex-stratified analyses.

Fig. 1: Adjusted odds ratio (with 95% Confidence intervals) for incident type 2 diabetes by latent class.



*adjusted for sex, age, cardiovascular disease at baseline, dyslipidemia, high blood pressure, positive familiar history for T2D, abdominal obesity, polycystic ovary syndrom, gestational diabetes, and menopause status.

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Geographical variation of common illnesses in Central Switzerland – A retrospective cohort study of the relative risk for pneumonia in the Canton of Lucerne

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Introduction:

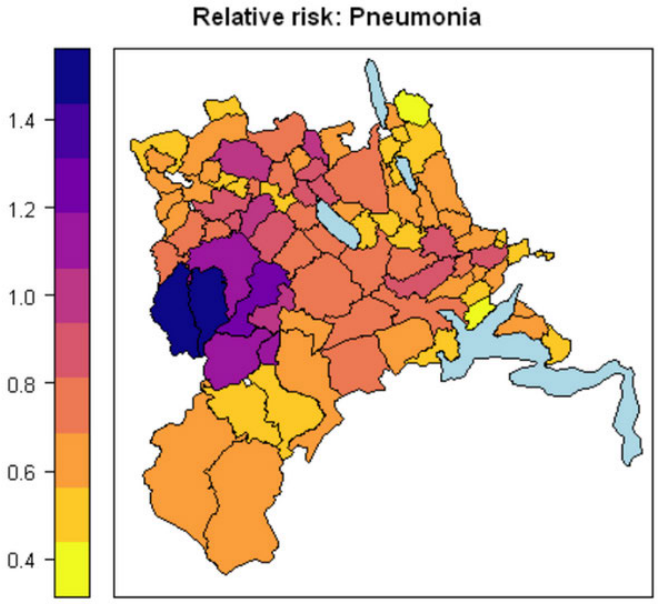
- The geographical distribution patterns of diseases in Switzerland are varied and etiologies unclear.
- There are studies that show impressive regional variations such as hysterectomy for benign uterine disease or mortality for cardiovascular disease[1, 2].
- Causes for regional variation of disease may vary and encompass genetics, socio-demographic factors, physician behavior, local health care infrastructure and environmental factors such as exhaust fumes and noise.
- The aim of this study was to analyze the geographical distribution pattern of common illnesses such as pneumonia in the Canton of Lucerne, the character of which our group has defined in an earlier publication[3].

Methods:

- The design was a retrospective, single center cohort study.
- The study center Luzerner Kantonsspital (LUKS) is the university-affiliated tertiary referral center for Central Switzerland with around 48'000 inpatients and 976'000 outpatient contacts per year. Regarding inpatients LUKS covered 71.3% within the Canton of Lucerne in 2013.
- Inclusion criteria were all inpatients of any age and both sexes with a main diagnosis of pneumonia according to ICD-10 GM (J12-J18) during the period of 2010-2019.
- The statistical analysis included a stepwise procedure first computing the mean of the expected number of pneumonia diagnoses for each community according to the BFS stratified according to age and gender. In a second step the population-adapted observed diagnosis-rate was compared to the expected diagnosis rate resulting in a risk difference per community.
- Disease Mapping was performed using the Besag-York-Moillé model using R software (INLA package; INLA=integrated nested Laplace approximation).

Results

- We observed 4898 patients (42.3% women) with pneumonia with a mean age of 64.9 years (range 0-103 years).
- The mapping results are depicted in Figure 1 with a relative risk above 1 mainly in communities in the area of Willisau.



- The relative risk varies from a minimum of 0.388 to a maximum of 1.483.
- Etiologies that might explain the differences in relative risk have not been analyzed in this study.

Conclusion:

- Our results show an impressive inconsistency in the geographical distribution of pneumonia in the Canton of Lucerne. Reasons for this distribution are not known.
- Further studies are warranted to analyse possible influencing factors such as genetics, socio-demographic aspects and environmental influences.

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Hospital outcomes in patients with alcoholic and non-alcoholic Wernicke Encephalopathy: an observational study

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Introduction: Epidemiological trends and in-hospital adverse outcomes in hospitalized patients with Wernicke Encephalopathy remain poorly explored. Therefore, we aimed to assess trends and hospitalization-associated outcomes in patients with Wernicke Encephalopathy.

Methods: In this retrospective cohort study, we used in-hospital claims data of patients hospitalized with Wernicke Encephalopathy in Switzerland between 2012 and 2020. Stratified by alcoholic and non-alcoholic induced Wernicke Encephalopathy, we estimated incidence rates (IR) and rate differences per 100,000 person-years among the overall Swiss population. Primary outcome was all-cause in-hospital mortality. Secondary outcomes included progression to Korsakoff Syndrome, length of stay at intensive care unit, and 1-year hospital readmission. We estimated odds ratios (OR) for binary and changes in percentage for log-transformed continuous outcomes.

Results: 4,098 of 4,393 hospitalizations (93.3%) with Wernicke Encephalopathy were alcohol-related. Incidence rates for hospitalizations per 100,000 person-years were 5.43 for alcohol-related Wernicke Encephalopathy and 0.93 in non-alcohol-related Wernicke Encephalopathy. The risk for in-hospital mortality was significantly lower in patients with alcoholic vs. non-alcoholic Wernicke Encephalopathy (3.2% vs. 8.5%, adjusted OR 0.38, 95%CI 0.23 to 0.62), but patients with alcoholic Wernicke Encephalopathy had higher risk for developing Korsakoff Syndrome (16.9% vs. 1.7%, adjusted OR 10.64, 95%CI 4.37 to 25.92) and for 1-year hospital readmission (31.6% vs. 18.7%, adjusted OR 1.4, 95% CI 1.04 to 1.88).

Conclusions: In this Swiss nationwide cohort study, Wernicke Encephalopathy was a rare but serious cause for hospitalization and mainly due to alcoholism. Patients with alcohol-related Wernicke Encephalopathy had lower risk for in-hospital mortality but were more likely to develop Korsakoff Syndrome and be readmitted to the hospital within 1 year.

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Iron biomarkers and cardiovascular risk factors: is it time to shift to the iron hypothesis?

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Background: The association between iron biomarkers and cardiovascular disease risk factors (CVD-RFs) remains unclear. We aimed to
1) evaluate the cross-sectional and longitudinal associations between iron status and CVD-RFs among pre and postmenopausal women, and
2) explore if these associations were modified by menopausal status.

Method: Cross-sectional and longitudinal analyses including 2542 and 1482 participants, respectively. Multiple linear regression and confounder-adjusted multilevel mixed-models were used to analyse the associations between iron, ferritin, transferrin and transferrin saturation (TSAT) and CVD-RFs. Variability of outcomes and iron markers between surveys was accessed using intraclass correlation coefficient (ICC).

Results: In the cross-sectional analysis, after multivariable adjustment, ferritin levels were positively associated with insulin, and transferrin levels were positively associated with glucose, insulin, total and HDL-cholesterol, and systolic and diastolic blood pressure. No association between TSAT and CVD-RFs was found. All iron biomarkers (serum iron, serum ferritin, transferrin, TSAT) showed low reliability, especially in the menopause transition group. In the longitudinal analysis, no significant association between iron biomarkers and changes in CVD-RFs were found, except for a negative association between transferrin and glucose and diastolic blood pressure. The associations did not change according to menopausal status.

Conclusion: We found few associations between iron markers and CVD-RFs among women both in cross-sectional and longitudinal analyses. The associations did not change according to menopausal status. Our results also showed that there is longitudinal variation of iron biomarkers indicating that one single measurement of iron is insufficient for adequate longitudinal analyses.

Keywords: iron biomarkers; menopause; cohort; cardio-metabolic risk factors

Table 1. Result of intraclass correlation, stratified by menopausal status, CoLaus study, Lausanne, Switzerland.

Menopause status	Baseline and first follow-up	Baseline and second follow-up	First and second follow-up
Glucose (mmol/L)			
Non menopause	0.30	0.40	0.24
Transition	0.37	0.47	0.43
Menopause	0.65	0.61	0.67
Insulin (mIU/mL)			
Non menopause	0.31	0.21	0.63
Transition	0.35	0.28	0.53
Menopause	0.41	0.30	0.55
SBP (mm Hg)			
Non menopause	0.67	0.52	0.58
Transition	0.57	0.54	0.63
Menopause	0.61	0.55	0.61
DBP (mm Hg)			
Non menopause	0.56	0.53	0.52
Transition	0.58	0.53	0.55
Menopause	0.54	0.44	0.55
HDL (mmol/L)			
Non menopause	0.76	0.70	0.60
Transition	0.75	0.72	0.80
Menopause	0.77	0.71	0.70
TC (mmol/L)			
Non menopause	0.60	0.69	0.64
Transition	0.55	0.57	0.57
Menopause	0.45	0.32	0.46
Ferritin (µg/L)			
Non menopause		0.48	
Transition		0.15	
Menopause		0.33	
Transferrin (mg/dL)			
Non menopause		0.46	
Transition		0.41	
Menopause		0.51	
TSAT (%)			
Non menopause		0.24	
Transition		0.20	
Menopause		0.43	
Iron (µg/dL)			
Non menopause		0.15	
Transition		0.17	
Menopause		0.34	

HDL-C: High Density lipoprotein cholesterol. SBP, systolic blood pressure; DBP, diastolic blood pressure; TC: Total cholesterol. Data for 1482 participants. An ICC ≥0.75 was considered excellent, between 0.40 and 0.75 good and <0.40 unsatisfactory.

Table 2. Results of linear regression analysis of the associations between iron biomarkers and cardiovascular risk factors at baseline, CoLaus study, Lausanne, Switzerland.

	Total, model 1		Total, model 2		Menopause, model 3		Non-menopause, model 3	
	Beta (95% CI)	P-value	Beta (95% CI)	P-value	Beta (95% CI)	P-value	Beta (95% CI)	P-value
Sample size	2542		2542		1421		1121	
Glucose (mmol/L)								
Ferritin	0.06 (0.01; 0.11)	0.007	0.02 (-0.01; 0.06)	0.20	0.01 (-0.04; 0.08)	0.88	0.03 (0.01; 0.08)	0.003
Transferrin	0.41 (0.16; 0.65)	<0.001	0.21 (0.03; 0.42)	0.03	0.50 (0.17; 0.83)	<0.001	0.01 (-0.19; 0.21)	0.93
TSAT	-0.15 (-0.24; -0.05)	<0.001	-0.05 (-0.12; 0.02)	0.17	-0.05 (-0.19; 0.08)	0.40	-0.05 (-0.12; 0.01)	0.17
Insulin (mIU/mL)								
Ferritin	0.06 (0.03; 0.10)	<0.001	0.03 (0.00; 0.06)	0.02	0.03 (0.00; 0.08)	0.07	0.03 (-0.01; 0.07)	0.12
Transferrin	0.50 (0.33; 0.67)	<0.001	0.43 (0.29; 0.60)	<0.001	0.48 (0.28; 0.73)	0.07	0.39 (0.19; 0.62)	<0.001
TSAT	-0.10 (-0.17; -0.04)	<0.001	-0.03 (-0.08; 0.02)	0.27	-0.03 (-0.12; 0.06)	0.41	-0.03 (-0.10; 0.04)	0.38
SBP (mm Hg)								
Ferritin	0.81 (-0.16; 1.79)	0.10	0.34 (-0.61; 1.32)	0.49	0.38 (-1.24; 1.93)	0.41	1.13 (-0.49; 1.78)	0.26
Transferrin	12.2 (7.28; 17.2)	<0.001	10.5 (5.65; 15.2)	<0.001	13.9 (3.61; 19.6)	<0.001	11.6 (5.00; 16.4)	<0.001
TSAT	-1.54 (-3.45; 0.37)	0.11	-0.28 (-2.14; 1.56)	0.64	-0.38 (-3.11; 3.60)	0.82	-0.77 (-2.53; 1.50)	0.44
DBP (mm Hg)								
Ferritin	0.78 (0.13; 1.49)	0.01	0.14 (-0.44; 0.83)	0.65	-0.11 (-1.04; 0.81)	0.39	0.50 (-0.10; 1.67)	0.25
Transferrin	7.73 (4.43; 11.0)	<0.001	7.53 (3.94; 10.3)	<0.001	7.17 (2.82; 12.2)	<0.001	8.35 (3.42; 12.4)	<0.001
TSAT	-0.96 (-2.23; 0.30)	0.13	-0.08 (-1.31; 1.13)	0.69	0.50 (-1.46; 2.44)	0.85	-0.34 (-1.93; 1.21)	0.493
HDL (mmol/L)								
Ferritin	-0.04 (-0.07; -0.01)	<0.001	-0.02 (-0.04; -0.001)	0.05	-0.05 (-0.10; -0.02)	<0.001	-0.004 (-0.03; 0.02)	0.96
Transferrin	0.21 (0.07; 0.35)	0.026	0.25 (0.12; 0.37)	<0.001	0.18 (0.00; 0.37)	0.03	0.30 (0.13; 0.47)	<0.001
TSAT	0.09 (0.04; 0.15)	<0.001	0.04 (0.003; 0.10)	0.09	0.03 (-0.04; 0.11)	0.51	0.05 (-0.01; 0.11)	0.09
TC (mmol/L)								
Ferritin	0.06 (0.01; 0.12)	0.02	0.03 (-0.03; 0.08)	0.25	0.05 (-0.03; 0.15)	0.13	0.005 (-0.08; 0.07)	0.89
Transferrin	0.48 (0.18; 0.79)	<0.001	0.66 (0.29; 0.89)	<0.001	0.48 (0.24; 0.94)	<0.001	0.73 (0.34; 1.11)	<0.001
TSAT	0.01 (-0.09; 0.13)	0.76	0.02 (-0.08; 0.14)	0.67	0.08 (-0.18; 0.19)	0.74	0.05 (-0.10; 0.17)	0.07

HDL-C, High density lipoprotein cholesterol; BMI, body mass index; SBP, systolic blood pressure; DBP, diastolic blood pressure; TC, Total cholesterol; TSAT, transferrin saturation. All iron biomarkers, insulin and hs-CRP levels were log transformed. Model 1 was adjusted for age. Model 2 was adjusted for age, BMI, smoking, and alcohol use, hs-CRP, eGFR, antidiabetic and antihypertensive drugs, prevalence of diabetes, CVD and menopause status. Model 3 was adjusted for age, BMI, smoking, and alcohol use, hs-CRP, eGFR, antidiabetic and antihypertensive drugs, prevalence of diabetes and CVD .Statistical analysis by multiple linear regression.

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Missed opportunities for stroke diagnosis: a gender perspective

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Introduction: Acute Ischemic Stroke Chameleons (AIS-C) are defined as missed Acute Ischemic Stroke (AIS). They represent 9% of stroke diagnose in Emergency Department (ED) and have a worse functional outcome than correctly identified strokes. To date, we don't know how sex and gender-related aspects influence stroke recognition. The aim of our study is to analyze if gender-related aspects of patients are associated with AIS-C, and thus to differences in the management and prognosis between men and women.

Methods: We performed a nested case control study, using data collected from March 2003 to December 2020 from the Acute STroke Registry and Analysis of Lausanne (ASTRAL), Switzerland. We identified 182 AIS-C and we randomly selected a sample of 182

controls (1:1 ratio) in the ASTRAL registry (n= 6007). We extracted available gender-related variables (civil status, living situation, education level, professional categories, being active, having children). We used logistic regression models to assess the association between sex variable and gender-related variables with AIS-C. We constructed a gender score: the gender-related variables were adjusted to the others and "sex" used as an independent variable in a logistic regression. The score reflects the probability of being a woman.

Results: AIS-C represented 3% of all AIS. Women represented 44% (n=80) of the total of AIS-C. Sex was not associated with AIS-C (OR 1.02, 95% CI 0.68-1.55). Gender-related variable associated with AIS-C was difference of civil status (being single compared being widowed OR 4.51, 95% CI 1.47-13.89). Interaction analysis showed differences according to the sex of the patient: women with middle professional category were associated with being AIS-C compared to women with low professional category (OR 3.93, 95% CI 1.19-13-03). Men with higher education had lower odds of being AIS-C compared to men with lower education (OR 0.31, 95%CI 0.10-0.92). The gender score for women was associated with lower odds of being AIS-C (OR 0.66 95% CI 0.46-0.94). For men the association was not significant but showed an opposite direction to that of women.

Conclusion: Sex is not associated with AIS-C but gender is. Gender and socio-economic factors influences women and men differently. Women are less protected by socioeconomic factors. Having a "feminine" gender score (unfavorable social characteristics) protects women from misdiagnosis while it has the opposite effect in men.

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Obtaining and displaying absolute risk estimates when comparing multiple treatments in network meta-analyses

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Introduction: To inform health care decisions, clinicians and patients need to compare absolute risk estimates of benefits and harms for each available option. This is particularly critical to inform shared decision-making. An increasing number of clinical decisions involve the comparison of multiple options (e.g. antihypertensives, antidepressants, antidiabetics, anticoagulants, etc.) Approaches to estimating absolute risks are well established for pairwise comparisons but more challenging when comparing multiple treatments.

Methods: We developed a methodological framework to obtain absolute risks of multiple treatments from network meta-analyses (NMA), using results from published NMA or when conducting a new NMA, by assuming transitive risk across all possible pairwise comparisons in the network. The investigator need only select the baseline risk for a chosen reference treatment to obtain unique absolute risks for all the other treatments, compared to the chosen reference. We applied this approach to two published NMAs of different baseline risks: using the estimates from an existing NMA when study-level data are unavailable and conducting an NMA de novo.

Results: When using the estimates from an existing NMA, the unique absolute risks are calculated using the summary effects of comparisons with the reference treatment and the baseline risk through a formula specific to the effect measure. When conducting a new NMA, the unique absolute risks are estimated from the model as a function of the odds ratios and the selected baseline risk. Results can be presented using a league table that depicts the odds ratio and risk difference in the upper and lower off-diagonal, respectively, and the absolute risks in the main diagonal. These estimates can then populate the summary of findings tables or evidence profiles, providing absolute differences between all treatment options to support decision-making. We have also designed an online presentation format - the MATCH-IT decision aids - in our MAGICapp authoring and publication platform.[1]

Conclusions: Using absolute risks for interpreting results from systematic reviews is necessary for clinical decisions when issuing recommendations for practice and in shared decision-making with patients. Our proposed framework allows obtaining absolute risks in the context of multiple treatments in a simple way.

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Prevalence of blood pressure raising drugs among hypertensive patients in a population-based setting. The CoLaus|PsyColaus study

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Objective: Assess the association between BP-raising drugs and
1) prevalence and
2) control of hypertension in a population-based study.
Our hypothesis was that people with hypertension and people treated but uncontrolled for hypertension would report a higher number of BP-raising medications.

Methods: Four survey periods (2003-2006, 2009-2012, 2014-2017 and 2018-2021) from a prospective cohort conducted in Lausanne, Switzerland. BP-raising drugs were self-reported, and compared between hypertensive and non-hypertensive groups, as well as between controlled and non-controlled hypertension groups.

Results: Overall, participants with hypertension took BP-raising drugs more frequently than participants without hypertension. The number of BP-raising drugs was also higher among participants with hypertension than without hypertension. After multivariate analysis, immunosuppressants, alpha agonists and NSAIDSs were associated with a higher likelihood of hypertension. On bivariate analysis, participants with treated and controlled hypertension consumed more frequently BP-raising drugs, and presented a higher number of BP-raising drugs than treated and uncontrolled participants. After multivariate adjustment, antidepressant use was associated with a higher likelihood of controlled hypertension [odds ratio and 95% confidence interval: 1.49 (1.15-1.93)], while no association was found for the other BP-raising drugs, presence of any BP-raising drug, or the number of BP-raising drugs.

Conclusion: BP-raising drugs are associated with a higher likelihood of hypertension, but not with a lower control rate.

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Prevalence of vaping-associated symptoms over six months among participants of a randomized controlled trial on smoking cessation with Electronic Nicotine Delivery Systems (ENDS)

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Introduction: Electronic nicotine delivery systems (ENDS) are increasingly popular for smoking cessation. Some people switching to ENDS report symptoms associated with ENDS use. We aimed at assessing the prevalence and changes in self-reported vaping-associated symptoms among participants of a large randomized controlled trial (RCT).

Method: We included 620 participants from the intervention group of the Efficacy, Safety and Toxicology of ENDS (ESTxENDS) RCT. These participants received ENDS, e-liquids, and smoking cessation counselling. Assessments were conducted 1 week and 6 months after target quit date. The following symptoms were assessed at each visit: dry mouth, mouth/throat irritation, cough, shortness of breath, headache, dizziness, and/or heart palpitations/tachycardia while vaping. We used descriptive statistics to report prevalence and multivariable adjusted mixed-effect models to analyze changes in symptoms in ENDS-only users. We used inverse probability weighting to account for attrition.

Results: In the intervention group, participants' median age at study entry was 38 (IQR=29-52) years; 53% identified as men. After 1 week, 405 (65%) ENDS-only users completed the questionnaire on vaping-associated symptoms. The most common symptoms were dry mouth (34%), mouth/throat irritation (23%), and cough (25%). Participants rarely reported headache (7%), shortness of

breath (3%), dizziness (4%), and heart palpitations/tachycardia (2%). After 6 months, 256 (41%) ENDS-only users completed the questionnaire. The most common symptoms were much less frequent than in the week 1 visit: dry mouth (18%), odds ratio (OR) for reduction=0.15, 95 % CI 0.07 to 0.31), mouth/throat irritation (11%, OR=0.14, 95 % CI 0.05 to 0.37), cough (12%, OR=0.25, 95 % CI 0.12 to 0.51). Other symptoms displayed no statistically significant changes after 6 months.

Conclusion: The most common vaping-associated symptoms were dry mouth, mouth/throat irritation, and cough. Reported prevalence at 6 months of these symptoms decreased by about half in ENDS-only users. Physicians who recommend ENDS as a smoking cessation strategy can alert patients to the possibility of these symptoms and their probable gradual reduction over time.

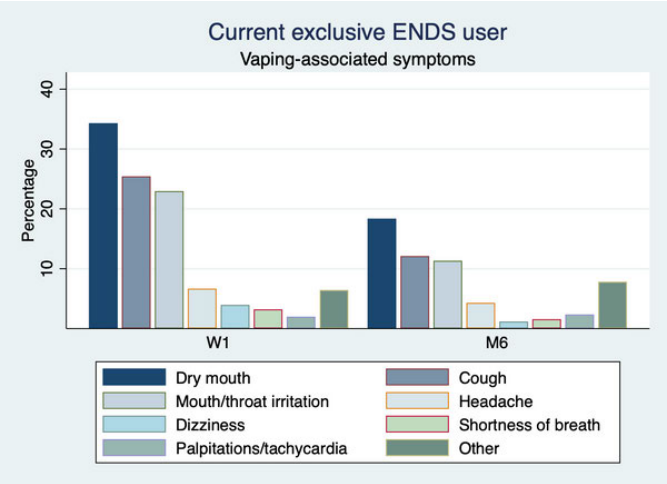

Figure 1) Vaping associated symptoms – Percentage
W1: one week after target quit date, M6: 6 months after target quit date

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Sweet dreams are made of this: association between diet and sleep quality

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Introduction: Numerous studies have emphasized the significance of nutrition on the quality of sleep, but little have evaluated the effect of various coexisting dietary markers on middle-aged adults. We aimed to assess the subjective sleep as defined by the PSQI index with different dietary markers among middle-aged, community-dwelling subjects.

Methods: Data from the first, second and third follow-ups of the CoLaus|PsyCoLaus study, a population based-study in Lausanne, Switzerland. Subjects were excluded if they had 1) no sleep data; 2) no dietary data; 3) extreme total energy intake values (<500 or >3500 kcal/day for women and <800 or >4000 kcal/day for men), or 4) no covariates.

Results: Data from 3857 (53% women, 57.2±10.4 years), 2370 (52% women, 60.7±9.5 years) and 1617 (52% women, 63.5±9.0 years) participants from the first, second and third follow-ups was used. After multivariable analysis, no significant associations were found between nutrients and sleep quality in both surveys (Table 1). Participants reporting low sleep quality tended to present a lower dietary quality as indicated by a lower Mediterranean diet score and a lower likelihood of consuming fish but the results were not consistent between surveys (Table 2). Correlations between PSQI score and consumption amounts of food categories showed negative associations with cheese and fruits (not shown).

Conclusion: People reporting low sleep quality tend to present a lower quality of dietary intake. Cheese and fruits appear to exert a beneficial effect on sleep quality. Those associations were inconsistent between surveys and should be explored in other settings.

Table 1: Multivariable analysis of the associations between sleep quality and nutrient intake, stratified by study period, CoLaus|PsyCoLaus study, Lausanne, Switzerland. Due to limited space, only the results for the first two surveys are presented.

	2014-2017			2018-2021		
	PSQI≤5 (n=1557)	PSQI>5 (n=793)	p-value	PSQI≤5 (n=1126)	PSQI>5 (n=491)	p-value
Nutrients (as % of TEI)						
Total protein	15.8 ± 0.1	15.7 ± 0.1	0.329	15.8 ± 0.1	15.7 ± 0.2	0.713
Vegetal protein	4.57 ± 0.03	4.49 ± 0.05	0.159	4.53 ± 0.04	4.49 ± 0.06	0.597
Animal protein	11.3 ± 0.1	11.2 ± 0.1	0.664	11.3 ± 0.1	11.2 ± 0.2	0.881
Total carbohydrates	45.0 ± 0.2	44.4 ± 0.3	0.205	43.8 ± 0.3	43.1 ± 0.5	0.169
Monosaccharides	22.9 ± 0.2	22.1 ± 0.3	0.033	22.4 ± 0.3	21.4 ± 0.4	0.046
Polysaccharides	21.9 ± 0.2	22.2 ± 0.3	0.461	21.3 ± 0.2	21.5 ± 0.4	0.612
Total fat	35.3 ± 0.2	35.4 ± 0.3	0.716	36.5 ± 0.2	36.2 ± 0.3	0.601
Saturated fat	12.8 ± 0.1	12.9 ± 0.1	0.394	13.3 ± 0.1	13.2 ± 0.2	0.741
Monounsaturated fat	14.5 ± 0.1	14.6 ± 0.2	0.844	15.1 ± 0.1	15.1 ± 0.2	0.870
Polyunsaturated fat	4.81 ± 0.04	4.88 ± 0.06	0.311	4.85 ± 0.04	4.84 ± 0.07	0.870

Table 2: Multivariable analysis of the associations between sleep quality and dietary intake, stratified by study period, CoLaus|PsyCoLaus study, Lausanne, Switzerland. Due to limited space, only the results for the first two surveys are presented.

	2014-2017			2018-2021		
	PSQI≤5 (n=1557)	PSQI>5 (n=793)	p-value	PSQI≤5 (n=1126)	PSQI>5 (n=491)	p-value
Dietary patterns/quality						
Mediterranean (Trichopoulo) [1]	4.12 ± 0.04	3.95 ± 0.06	0.028	4.01 ± 0.05	4.02 ± 0.08	0.927
Mediterranean (Vormund) [2]	4.86 ± 0.06	4.53 ± 0.09	0.002	4.60 ± 0.07	4.70 ± 0.11	0.436
AHEI	32.5 ± 0.3	32.0 ± 0.4	0.318	32.1 ± 0.3	32.2 ± 0.5	0.887
Dietary guidelines						
Fruits ≥ 2/day	1 (ref.)	0.71 (0.57-0.87)	0.01	1 (ref.)	0.95 (0.74-1.23)	0.715
Vegetables ≥ 3/day	1 (ref.)	0.77 (0.52-1.13)	0.175	1 (ref.)	0.68 (0.39-1.18)	0.170
Meat ≤ 5/week	1 (ref.)	1.01 (0.82-1.24)	0.908	1 (ref.)	0.75 (0.58-0.98)	0.032
Fish all ≥ 1/week	1 (ref.)	0.98 (0.78-1.22)	0.847	1 (ref.)	0.92 (0.70-1.21)	0.555
Fish not fried ≥ 1/week	1 (ref.)	0.74 (0.61-0.91)	0.004	1 (ref.)	0.94 (0.68-1.29)	0.687
Dairy ≥3/day	1 (ref.)	1.31 (0.91-1.89)	0.145	1 (ref.)	1.44 (0.89-2.34)	0.141
At least 3 guidelines	1 (ref.)	0.85 (0.67-1.07)	0.166	1 (ref.)	0.77 (0.57-1.05)	0.103
At least 3 guidelines	1 (ref.)	0.78 (0.60-1.01)	0.064	1 (ref.)	0.83 (0.64-1.08)	0.165

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A candidate Respiratory Syncytial Virus (RSV) prefusion F protein investigational vaccine (RSVPreF3 OA) is immunogenic when administered in adults ≥ 60 years of age: results at 6 months after vaccination

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Introduction: RSV infections are frequent and can lead to respiratory complications in older adults (OA). However, there is no licensed RSV vaccine yet. Here we present immunogenicity results up to month (M) 6 after vaccination with the RSVPreF3 OA.

Methods: In this phase 3 multi-country ongoing study (NCT04732871), adults ≥ 60 years of age were randomized (3:1:1) to receive RSVPreF3 OA and to be followed up for 3 years. All participants received a dose of RSVPreF3 on day (D) 1. Humoral immune (HI) and cell-mediated immune (CMI) responses were measured in subsets of participants at pre-vaccination (D1), D31 and M6. HI outcomes included RSV-A and RSV-B neutralizing antibody (NAb) geometric mean titers (GMTs) and RSVPreF3-specific immunoglobulin G (IgG) antibody geometric mean concentrations (GMCs). The CMI response was assessed in terms of frequency of RSVPreF3-specific CD4+ T-cells and CD8+ T-cells expressing at least 2 activation markers including at least 1 cytokine among CD40L, 4-1BB, IL-2, TNF-α, IFN-γ, IL-13, IL-17 (polypositive T-cells).

Results: A total of 1653 participants received a dose of RSVPreF3 OA. Of these, 987 participants were included in the HI subset and 566 in the CMI subset at D1. The RSV-A and RSV-B GMTs and RSVPreF3-specific IgG GMCs increased between D1 and D31 followed by a decline until M6. At D31, RSV-A and RSV-B NAb GMTs were 10.5-fold and 7.8-fold higher than pre-vaccination (Figure), and RSVPreF3-specific IgG antibody GMCs was 12.2-fold higher than pre-vaccination levels. At M6, the RSV-A and RSV-B GMTs were 4.4-fold and 3.5-fold, and RSVPreF3-specific IgG antibody GMCs were 4.7-fold above pre-vaccination levels. The RSVPreF3-specific polypositive CD4+ T-cell median frequency (events/10^6 cells) increased from 191 (below assay quantification limit) to 1339 at D31 and declined to 666 (above assay quantification limit) by M6. No RSVPreF3-specific CD8+ T-cell response was detected after RSVPreF3 OA vaccination.

Conclusion: In adults ≥ 60 years of age, 1 dose of RSVPreF3 OA was shown to be immunogenic, with both high HI and specific CMI responses at D31 post-vaccination and remained 3.5–4.7 fold above pre-vaccination levels at M6. This study will continue to monitor the immunogenicity of RSVPreF3 OA up to 3 years.

Funding: GlaxoSmithKline Biologicals SA (GSK study identifier: 212496)

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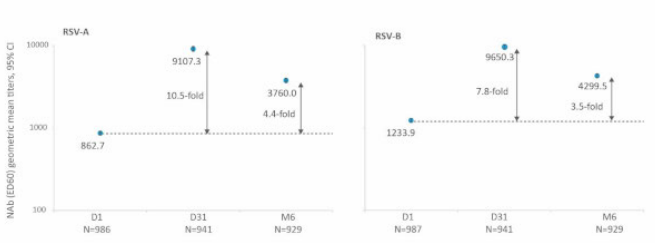

P81

A Respiratory Syncytial Virus (RSV) Prefusion F protein candidate vaccine (RSVPreF3 OA) is efficacious in adults ≥ 60 years of age (YOA)

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Introduction: RSV-associated acute respiratory infections (ARI), particularly lower respiratory tract diseases (LRTD), present a significant disease burden in older adults. Currently, there are no approved vaccines against RSV. We present results from an ongoing study designed to demonstrate the vaccine efficacy (VE) of the AS01E-adjuvanted RSVPreF3 OA in adults ≥ 60 YOA.

Methods: This ongoing, phase 3, observer-blind, placebo-controlled, multi-country study (NCT04886596) enrolled adults ≥ 60 YOA from the northern and southern hemispheres. Participants were randomized (1:1) to receive a single dose of RSVPreF3 OA or placebo before the RSV season. The primary objective was to demonstrate VE of a single dose of RSVPreF3 OA in preventing RSV-confirmed LRTD during one RSV season (criterion: lower limit of VE confidence interval [CI] > 20%). VE is reported also against severe RSV-confirmed LRTD, RSV-confirmed ARI, RSV-confirmed LRTD and RSV-confirmed ARI by RSV subtype (RSV-A and RSV-B), and RSV-confirmed LRTD by age, baseline comorbidity and frailty status. RSV-A/B was confirmed by quantitative RT-PCR.

Results: A total of 26,664 participants were enrolled, of whom 24,966 (RSVPreF3 OA: 12,467; placebo: 12,499) were included in the exposed set and 24,960 (RSVPreF3 OA: 12,466; placebo: 12,494) in the efficacy analysis. The mean age was 69.5 (±6.5) years and 51.7% were women. Over a median follow-up of 6.7 months (maximum 10.1 months), 47 RSV-confirmed LRTD episodes were reported (RSVPreF3 OA: 7; placebo: 40), resulting in a VE of 82.6% (96.95% CI: 57.9–94.1), thus the primary objective was met. Consistently high VE across the clinical spectrum of RSV disease, from RSV-confirmed ARI (71.7% [95% CI: 56.2–82.3]) to severe RSV-confirmed LRTD (94.1% [95% CI: 62.4–99.9]) was observed. High VE was seen in different age groups and regardless of RSV subtype, baseline comorbidity or pre-frail status (**Figure 1**). Cumulative incidence curves for RSV-confirmed LRTD and RSV-confirmed ARI showed persistent efficacy throughout the follow-up (**Figure 2**).

Conclusion: A single RSVPreF3 OA dose is highly efficacious against RSV-confirmed LRTD and RSV-confirmed ARI in adults ≥ 60 YOA, regardless of RSV disease severity, RSV subtype, baseline comorbidity and pre-frail status.

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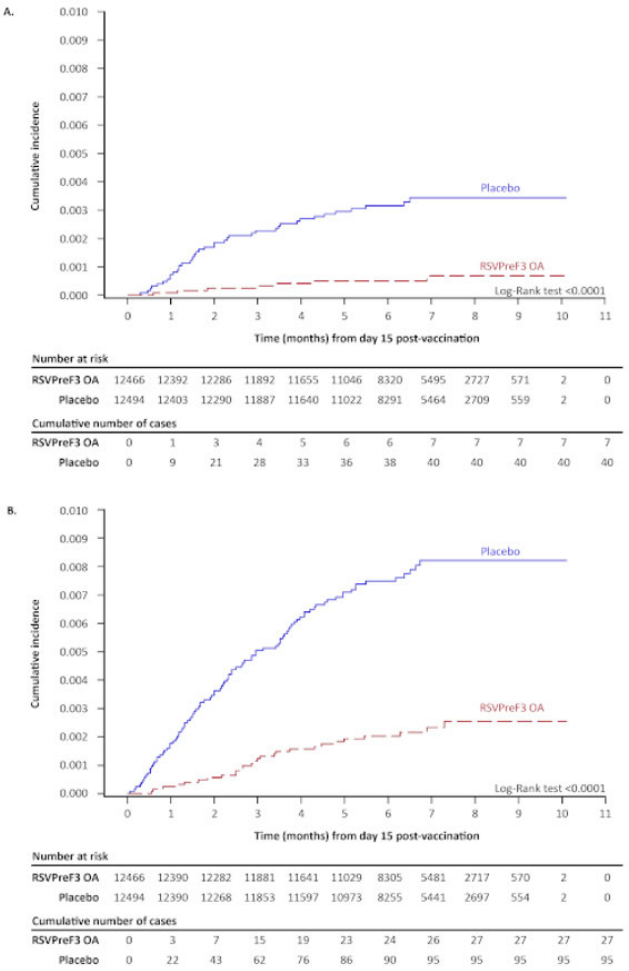
Figure 1. Vaccine efficacy against first episodes of RSV-confirmed LRTD and RSV-confirmed ARI (modified exposed set)

	RSVPreF3 OA				Placebo				Vaccine efficacy (%)	p-value
	N	n	T (p-yr)	n/T (n/1000 p-yr)	N	n	T (p-yr)	n/T (n/1000 p-yr)		
RSV-confirmed LRTD										
Overall	12466	7	6865.9	1.0	12494	40	6857.3	5.8	82.6 (94.1)	<0.0001
Severe	12466	1	6867.9	0.1	12494	17	6867.7	2.5		0.0001[a]
By subtype										
RSV-A	12466	2	6867.4	0.3	12494	13	6868.9	1.9	84.6 (80.9)	0.0074[a]
RSV-B	12466	5	6866.7	0.7	12494	26	6862.3	3.8		0.0002[a]
By age										
≥70 yr	5503	3	3015.0	1.0	5515	19	3020.9	6.3	84.4 (33.8)	0.0008[a]
≥80 yr	1016	2	551.4	3.6	1028	3	559.3	5.4		0.9931[a]
60–69 yr	6963	4	3850.8	1.0	6979	21	3836.4	5.5	81.0 (93.8)	0.0009[a]
70–79 yr	4487	1	2463.6	0.4	4487	16	2461.6	6.5		0.0003[a]
By baseline comorbidities										
Low/medium risk[b]	8235	4	4495.8	0.9	8367	23	4560.6	5.0	82.4 (82.9)	0.0004[a]
High risk[b]	4231	3	2370.0	1.3	4127	17	2296.6	7.4		0.0021[a]
No comorbidity of interest[c]	7529	6	4094.1	1.5	7633	22	4148.1	5.3	72.5	0.0040[a]
≥1 comorbidity of interest[c]	4937	1	2771.8	0.4	4861	18	2709.1	6.6	94.6	<0.0001[a]
By frailty[d]										
Frail	189	1	95.8	10.4	177	1	92.9	10.8	14.9	1.0000[a]
Pre-frail	4792	1	2577.6	0.4	4778	14	2545.3	5.5	92.9 (80.0)	0.0009[a]
Fit	7464	5	4182.7	1.2	7519	25	4208.5	5.9		0.0003[a]
RSV-confirmed ARI										
Overall	12466	27	6858.7	3.9	12494	95	6837.8	13.9	71.7 (70.6)	<0.0001[a]
By RSV subtype										
RSV-A	12466	9	6865.2	1.3	12494	32	6862.3	4.7	71.9	0.0004[a]
RSV-B	12466	18	6861.7	2.6	12494	61	6849.4	8.9		<0.0001[a]

0 20 40 60 80 100

Cases reported up to the efficacy data lock point of 11 April 2022. **N**, number of participants in the modified exposed set; **n**, number of participants with ≥1 RSV-confirmed LRTD (identified by the adjudication committee) or ≥1 RSV-confirmed ARI; **T**, sum of follow-up time (from day 15 post-vaccination until first occurrence of the event, data lock point or drop-out); **p-yr**, person-years; **n/T**, incidence rate of participants reporting at least one event. Error bars represent 96.95% confidence intervals (CI) for primary objective (RSV-confirmed LRTD, overall) and 95% CI for other endpoints. [a]Two-sided exact nominal p-value conditional to number of cases comparing incidence rates. [b]Charlson comorbidity index: low/medium risk, participants with baseline comorbidity score ≤3; high risk, participants with baseline comorbidity score >3. [c]Comorbidities of interest included chronic obstructive pulmonary disease, asthma, any chronic respiratory/pulmonary disease, chronic heart failure, diabetes mellitus type 1 or type 2 and advanced liver or renal disease. [d]Frailty status assessed using a gait speed test: frail, participants with a walking speed <0.4 m/s or not able to perform the test; pre-frail, participants with a walking speed of 0.4–0.99 m/s; fit, participants with a walking speed ≥1 m/s. **Note**: RSV subtype was unknown for 1 RSV-confirmed LRTD and 2 RSV-confirmed ARI episodes.

Figure 2. Cumulative incidence curves for RSV-confirmed LRTD (A) and RSV-confirmed ARI (B) reported up to the efficacy data lock point (modified exposed set)



P82

Colorectal cancer risk factors and use of screening tests: baseline results from a pilot randomized controlled trial

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Introduction: Screening for colorectal cancer (CRC) reduces incidence and mortality from CRC. Individual 15-year risk for CRC is influenced by genetics, lifestyle, and several diseases, and varies from <1% to >15%. Personalized screening could improve the risk-benefit balance of screening and optimize use of colonoscopy resources. We present the use of screening tests and CRC risk factors in Vaud canton.

Methods: Vaud citizens not yet invited to the Vaud Screening Program were mailed invitations for a pilot randomized controlled trial (Clinicaltrials.gov NCT05357508). We collected their history of CRC screening, CRC risk factors, intention for screening (on a scale of 1 to 5), knowledge about CRC screening, screening recommendations provided by physicians, and sociodemographic variables. Individual CRC risk was calculated using the QCancer calculator. We considered <3% as low, 3-6% as moderate, and >6% as high risk.

Results: Of 898 respondents, 51% were women and the average age was 52.6 (SD=2.9). Some 37% (n=336) were ineligible for screening (Table 1). Among eligible participants (63%), the mean intention for screening was 4.1 (SD=1.2); 42% preferred FIT, 25% colonoscopy, and 29% had no preference. Risk of CRC ranged be-

tween 0.9% and 7%, and 96% of all participants were at low risk (score <3). Most of those who had had a colonoscopy were at low risk (88%), and aged between 50-55 years (73%). The main sources of information about CRC screening were physicians (27%), participants' acquaintances (22%), newspapers (11%), and the internet (10%). One third (34%) of participants reported receiving suggestions to do screening from their physician. 52% of participants believed that screening was recommended for healthy people, 31% that it was recommended for people with CRC symptoms, and 17% responded that they didn't know.

Conclusion: In this population of primarily 50 to 54 year olds, the majority of persons already screened for CRC had done a colonoscopy, despite being at low risk. Most of those eligible for screening were at low risk, emphasizing potential of discussion regarding different screening approaches including FIT.

Table 1: Reasons for ineligibility for the Vaud colorectal cancer screening program among 336 potential participants (many reasons are possible).

Reason	n	%
Up to date FIT	37	11
Up to date colonoscopy	224	69
Genetic risk	41	13
Inflammatory bowel disease	6	2
Polyp surveillance	59	19
Other serious disease	2	1
Unexplained weight loss	7	2
Blood in stool	32	10
Changes in bowel habits	79	25

P83

Coronary artery calcium scoring for atherosclerosis screening in adults and its impact on cardiovascular primary prevention: a systematic review of RCTs and prospective cohorts

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Introduction: Coronary artery calcium (CAC) scoring by native computed tomography (CT) improves risk prediction of cardiovascular disease (CVD), but it remains unknown whether this leads to better prevention of CVD. We reviewed the impact of screening with CAC scoring in adults without known CVD on clinical events, cardiovascular risk factors (CVRF) modification and changes in health behaviour.

Methods: This is a systematic review of randomized controlled trials (RCTs) and prospective cohorts comparing adults without CVD undergoing CAC to a control group that either did not undergo CAC or where the participants and physicians were blinded to its result. We searched MEDLINE, EMBASE and Cochrane Central Register of Controlled Clinical Trials for eligible studies. Outcomes included clinical events (all-cause and CV mortality, cardiovascular events), changes in CVRF control at follow-up and changes in health behaviour.

Results: We identified 7 RCTs and 1 prospective cohort study, with participants ranging from 56 to 43,447 with a total 51,555. Populations were heterogenous with a mean age range of 42-64 years, % women ranging from 21-100% and mean baseline CAC from 1 to >100 Agatston units. Interventions following CAC scoring were heterogeneous as well and ranged from communications of results to participants only to statin therapy initiation with detectable CAC. The RCTs generally demonstrated improvements regarding blood pressure (BP) (range -2.0 to -2.2mmHg) and blood lipids (e.g. LDL cholesterol: range -6.8 to -52.2 mg/dl) in the intervention group compared to control. Results regarding change in adherence to or use of CV medication were more discrepant, with some studies showing a decrease and others an increase in use of or adherence to medication. No study found a significant effect on health behavioural changes. Due to low event rates, short follow-up and/or limited sample size, none of the studies demonstrated an effect on clinical cardiovascular events or mortality. Heterogeneity in interventions following CAC and studied outcomes did not permit pooling of results.

Conclusion: CAC screening appears to have a favourable effect on CVRF control and potentially on adherence to CV medication. The available evidence is insufficient to determine whether CAC screening has an impact on clinical events or mortality. More evidence regarding the impact on clinical outcome is needed to determine the clinical use of CAC scoring for screening purposes.

Table 1 Study characteristics

Study	Intervention/Control	Participants (%women)	Age	CAC-Score	Follow-up	Limitations
Muhlestein et al. (2022), RCT	Intervention: CAC and protocol-based Statin-recommendation communicated to participant and GP Control: PCE-Score and protocol-based Statin-recommendation communicated to participant and GP	n=601 (61%)	Range: 59 – 85y Mean: CAC: 61y Mean: Control: 61y	0 AU: 50% 1-100 AU: 36% >100 AU: 14%	12 months	Single health care system Self-reported questionnaires Treatment recommendations based on the 2013 AHA/ACC primary prevention guideline
Venkataraman et al. (2020), RCT	Intervention: CAC and commencement of atorvastatin and information of GP Control: Blinded CAC result and RF education only together with GP	n=450 (43%)	Range: 40–70y 40-49 y: 14% 50-59 y: 40% 60-70 y: 45%	>0 AU: 100% Median: 33 AU	12 months	Known inclusion criterion of CAC 1-400 AU 5% without FUP 11% of blood lipids required imputation Self-reported questionnaires with risk of recall bias
van der Aalst et al. (2020), RCT	Intervention: CAC and protocol-based recommendation of statins and ACEI to participants and GP Control: Screening by classical RF and guideline based preventive treatment recommended to participant and GP	n=43.447 (42%)	Range Men: 45-74y Range Women: 55-74y Median Women: 64y Median Men: 59y	>0 AU: Women: 52% Men: 69% <100 AU: 76% 100-399 AU: 15% >400 AU: 8.9%	5 years	Cross sectional analysis Self-reported questionnaire with risk of recall bias Not all risk increasing factors that codetermine the treatment indication were incorporated in the screening as they are not part of the SCORE calculation
Denissen et al. (2019), RCT	Same as van der Aalst et al.	n=600 (37%)	Range Men: 45-74y Range Women: 55-74y Mean: 64 y	>100 AU: 100%	Mean: 14.8 months	Comparison of increased risk participants Long FUP and self-reported questionnaires with risk of recall bias Possible exclusion of participants with low health literacy
Rozanski et al. (2011), RCT	Intervention: CAC and RF counselling with recommendation to share CAC-result with GP Control: RF counselling	n=2137 (48%)	Range: 45 - 86y Mean: 59y	>0 AU: 52%	4 years	Highly educated, fairly affluent, sufficiently motivated participants CAC not shared with GP directly Self-reported questionnaire with risk of recall bias
Lederman et al. (2018), RCT	Intervention: CAC and conventional screening with RF counselling and communicated to participant and GP Control: conventional screening with RF counselling	n=56 (100%)	Range: >55y Mean: Intervention: 64y Mean: Control: 66y	n=19 with mean 1.37 AU	12 months	Low CAC scores Few cardiovascular RF Small sample size Change in counselling protocol during ongoing trial Self-reported questionnaire with risk of recall bias
O'Malley et al (2003), 2x2 RCT	Intervention: CAC-Scanning and disclosure of results to participant and GP Control: Blinded CAC Subgroups 1: Intensive case-management with guideline-based recommendation of treatment 2: Usual care with guideline-based recommendation of treatment	n=450 (21%)	Range: 39-45y Mean: 42y	>0 AU: 15%	12 months	Low prevalence of modifiable RF and CAC Young army personnel Self-reported questionnaire with risk of recall bias
Chia-hsuan Chi et al. (2014), Observational study	Intervention: Patients who received a CAC ordered by their physician Control: Patients who were denied a CAC ordered by their physician	n=3814 (41%)	Range: 18-64y Mean: 53y	No information	6 months for therapeutic interventions	Observational study Only working, commercially insured participants Short follow-up with few CV events Possible risk misclassification Patients with denied CAC might have paid for them themselves

PCE: pooled cohort equation, CAC: coronary artery calcium, ACEI: Angiotensin-converting-enzyme inhibitor, AU: Agatston Units, y: years, GP: general practitioner, RF: risk factor, FUP: follow-up, SCORE: Systematic COronary Risk Evaluation

Table 2 Effect of CAC scoring on outcomes

	Change/Utilization of CV medication				Adherence to Medication				Behaviour changes				CVRF				Clinical events
	Overall	BP	Lipid	Diabetic	Overall	BP	Lipid	Diabetic	Smoking	Diet	Physical activity	«Well-beings»-Scores	BP	Blood lipids	Weight **	Glucose/ HbA1c	
Muhlestein et al.			-				↑							↑			*
Venkataraman et al.									↔	↔	↔	↔	↑	↑	↔		
van der Aalst et al.	-																
Denissen et al.	+	+	+		↔												
Rozanski et al.		+	↔	↔		↔	↔	↔	↔		↔		↑	↑	↑	↔	*
Lederman et al.		↔	↔							↔		↔	↔	↓	↔	↔	
O'Malley et al.									↔		↔	↔	↔	↔	↔	↔	
Chia-hsuan Chi et al.		↔	↔														↔

↑ Improvement or better controlled; ↓ less controlled; + increase; - decrease; ↔ no significant effect; * statistical power was insufficient for an adequate assessment; **weight-criterion includes BMI and/or weight and/or waist circumference; CV: cardiovascular; CVRF: cardiovascular risk factor; BP: blood pressure;

P84

Effects of Electronic Nicotine Delivery Systems (ENDS) for smoking cessation on olfactory function - secondary analyses of the ESTxENDS trial

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Introduction: Tobacco smoking is known to reduce olfactory function. The effect of smoking cessation interventions on olfactory function had never been tested within the context of a RCT. We tested the effect of ENDS added to standards of care smoking cessation counselling (SOC) (intervention group) compared to SOC alone (control group) on a measure of olfactory function at 6-months in a secondary analysis of a smoking cessation randomized controlled trial (RCT).

Methods: We consecutively included participants from the ESTxENDS RCT that underwent olfactory function testing at baseline and at 6-month follow-up. We measured olfactory function with the "Burghart's Sniffin' Sticks", pen-like odor dispensing devices. Using a four-alternative forced-choice paradigm, odor identification was assessed for 16 common odors, resulting in an olfactory identification score (OIS) ranging from 0 (worst) to 16 (best). We assessed differences of the OIS in an intention to treat analysis (ITT) after 6-month. Data were analyzed using linear regression models adjusting for baseline covariates and using inverse probability censoring weights (IPCW) to account for attrition.

Results: Among the 375 participants (n=186 in the intervention group, n=189 in the control group) that completed testing at baseline, 242 participants (65%, n=134 in the intervention group, n=108 in the control group) completed the testing at 6-month follow-up. Participants at baseline aged between 18 and 74 years with a median age of 36 years and 44.8% identified as women. After 6 months, 85 (46%) in the intervention group and 46 (22%) had quit smoking in the control group.
The mean (SD) OIS in the control group was 13.4 (2.0) at baseline and 13.2 (1.8) at 6-month follow-up. In the intervention group, it was 13.5 (1.5) at baseline and 13.6 (1.4) at 6-month follow-up. In ITT analyses with adjustment for baseline covariates and using IPCW, those randomized to the intervention group had a significantly higher mean OIS at 6-months follow-up (coefficient 0.41; 95% CI: 0.10 to 0.72; p=.009) and a significant improvement in mean OIS from baseline for 6-months follow-up (coefficient 0.42; 95% CI: 0.04 to 0.80; p=.03) compared to the control group.

Conclusion: In these secondary analyses of the ESTxENDS trial, participants allocated to ENDS added to SOC experienced improved olfactory function compared to those allocated to SOC alone. ENDS for smoking cessation improves olfactory function.

P85

Patients' perception of the management of an acute low back pain episode: a qualitative interview study

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Introduction: Studies indicate that psychological, interactive-educational, and behavioral factors play an important role in patients with chronic low back pain (LBP). To date, little is known about the patients' self-perceived factors that influence recovery during an acute LBP episode. This interview study assessed patients' experiences, perceptions, and expectations during their acute LBP episodes.

Method(s): Qualitative interview study of patients participating in the EMISI study, a randomized clinical study. Patients were recruited from general practitioners' practices, outpatient clinics, and emergency departments. The interviews were audio and video recorded, transcribed verbatim and analyzed using a content analysis method with the software MAXQDA 2020. The code list was based on a mixed inductive and deductive method reporting findings for emotions, expectations, information seeking, and impressions of the physician-patient interaction.

Result(s): In total, 15 interviews (30-60 minutes) were conducted (mean age 43.8 years, range 25-62 years). Patients reported very strong emotions when experiencing pain (Table 1). Patients mentioned anxiety (n=3), helplessness (n=3), anger (n=3), discomfort (n=4), and annoyance (n=4). Treatments that relieved pain included interventions recommended in the guidelines (physical therapy, pain medication, and heat) but also interventions not recommended by guidelines (activity restriction, massage). Three patients were expecting radiographic imaging (x-ray, MRI). Expectations included faster recovery, more effective pain medications, external problem solving ("pain should go away"), and the prescription of therapies (massage, chiropractor). Patients were seeking information and relaying on their experiences from past pain episodes. The role of the physician was important (n=3) and had a calming effect on patients (n=2). Important factors during the physician-patient encounter were good explanation (n=7), communication (n=1) and medical care (n=2).

Conclusion: Patients experience strong and threatening emotions during an acute LBP episode. The quality of the physician-patient encounter was important and major factors included good quality of communication, explanation, and medical care.

Table 1

	Emotion	Helpful§	Expectations	Information seeking	Physician encounter
Positive		Heat (n=3) Exercise / activity (n=1) Physical therapy (n=6) Pain medications (n=10) Meet the physician regularly (n=1) Trigger treatment (n=2)	Faster improvement (I want the pain to go away quickly) (n=1) Option for physical therapy (no option due to covid-19 pandemic, no physical therapist available) (n=1) Stronger pain medication (n=1) Prescription for massage / chiropractor (n=3) No (n=6) / Satisfied (n=1)	Videos (n=2) Previous good experience with massage (n=2) Previous good experience with exercise/activity (n=1) Previous back pain episode (n=3) Education in massage techniques (n=1) Physiotherapy (n=2) Osteotherapy (n=1) Recommendations from friends (n=1) Knowledge about medicine (n=1) Reading (n=1) Internet (n=1) Treatment plan from the study (n=1)	Friendly physician (n=1) Physician checked everything (n=2) Physician played an important role (n=1) Active listening (n=1) Calmed me down (n=2) Good medical care (n=2) Good explanation (n=7) Good communication (n=1) Prescribed the treatment (n=1) Satisfied with clinic (n=1) A lot of attention (n=1) A control is good to have reassurance (n=1)
Negative	Shame (n=1) Anxiety (n=3) Self-blame (n=1) Uncomfortable (n=4) Helpless / Hopeless (n=3) Devastating (n=1) Annoying (n=4) Limit daily activities (n=3) Anger / frustration (n=3) Influences concentration (n=1) Avoidance (n=1) Dizziness / Nausea (no appetite) (n=1) Burdening (n=1)	Massage (n=3) Bed rest / activity restriction (n=4) Acupuncture (n=1) Osteopathy / chiropractor (n=3)	X-ray / MRI (n=3) Taken seriously (n=1) and recommendations (n=1) Better medical evaluation work solution-oriented (n=1) That my problem is solved (n=2)		Physician played a minor role (n=3) Not helpful / not specific enough (n=1)

§positive, in agreement with guideline recommendations; negative not in agreement with recommendations

P86

Spatial analysis of 10-year predicted risk and incident cardiovascular atherosclerotic disease in an urban population: the CoLaus|PsyCoLaus study

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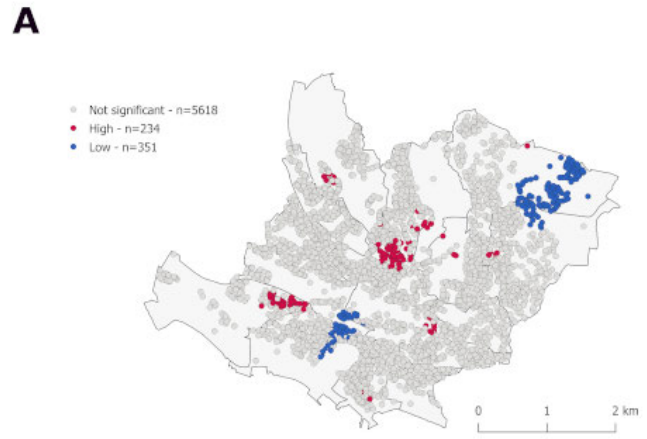
Introduction: Whether cardiovascular risk score geographically aggregates and informs on spatial development of atherosclerotic cardiovascular disease (ASCVD) remains unknown.

Methods: Using data from the CoLaus|PsyCoLaus cohort study, we first determined the spatial distribution of cardiovascular risk predicted in Lausanne, Switzerland, urban population, recruited between 2003-2006. We computed the Systematic Coronary Risk Evaluation Score 2 (SCORE2, including SCORE2-OP) in participants free from ASCVD. Second, we compared risk maps with clustering of incident ASCVD over a 10-year follow-up. Geographical distributions of risk and incident ASCVD were determined using Moran's I global and Getis-Ord local spatial autocorrelation statistics. Different models were tested to identify explanatory variables.

Results: 6203 individuals (54% women, mean age 52.5 ± SD 10.7) with a median follow-up of 10 years (IQR, 6-10) were included. Predicted risk and incident ASCVD marginally overlapped spatially (Figure 1). Age, body-mass index, and alcohol consumption explained most of the spatial distribution of predicted risk. High ASCVD prevalence clusters either persisted or were reinforced after adjustment for sex, behavioural, socio-economic, genetic, treatment and environmental covariates, while low prevalence clusters reduced. Incidence rate of ASCVD was 2.5% higher (IC95%, 1.4-3.7) in high-risk clusters compared to the rest of the sample.

Conclusions: We identified clusters of high and low incidence of ASCVD using a population-based cohort in an urban area. Geographical distribution of clusters of high risk score was not congruent with distribution of incident ASCVD, limiting the use of these risk scores to identify areas where ASCVD may develop. Further research should aim at identifying regional factors affecting ASCVD development beyond traditional risk factors

Figure 1. Dot maps of predicted risk (A), ten-year incident ASCVD (B) in the whole population at baseline - 2003-2006



Legend: Getis-Ord statistic. Geo-referencing at postal addresses. White dots show places where there is no spatial dependence. Red / Blue dots show individuals with a statistically significant positive / negative Z score (α=0.05), meaning that high / low values cluster, within a spatial lag of 600 m, and are found closer together than expected if the underlying spatial process was random. Pseudo-p based on a permutation inference with 999 permutations.

P87

Vitamin D deficiency in a refugee population in Geneva

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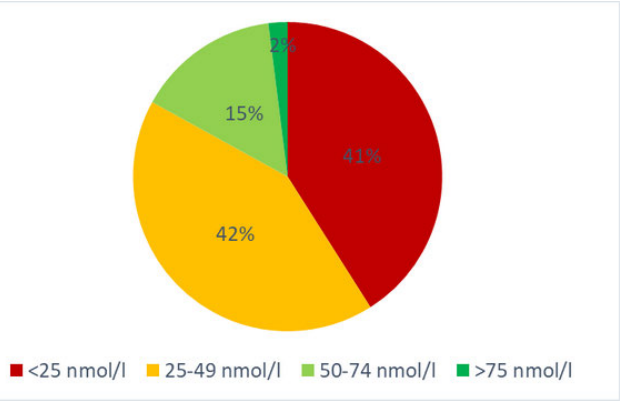
Introduction: Vitamin D deficiency (<50 nmol/l) is a global health burden, often underdiagnosed and potentially associated with osteomalacia when severe (<25 nmol/l). Migrants are known to be at an increased risk of vitamin D deficiency, compounding biological and environmental factors. However, since July 2022 diagnostic blood testing is only reimbursed in certain conditions in Switzerland. Given these new restrictions, we decided to retrospectively analyse vitamin D levels in a refugee population at the Migrant Health Program (Geneva University Hospitals).

Methods: During the month of August 2022, we recorded patients' vitamin D level on arrival in Switzerland as well as their gender, age and nationality. We then carried out summary statistical analysis with a quality control perspective.

Results: 349 patients were included, 44% female, with a mean age of 41. A third were from the Middle East, a quarter from Sub-Saharan Africa and a fifth from Asia. The mean vitamin D levels was 31.5 nmol/l and median 28 nmol/l. 84% were deficient (<50 nmol/L) and 41% were severely deficient (<25 nmol/L) (graph 1). Vitamin D levels were similar between the sexes and between geographical regions.

Conclusions: Our analysis shows the high prevalence of severe vitamin D deficiency (41%) in a refugee population in Geneva. Given its association with osteomalacia, it remains important to continue routine vitamin D blood testing and supplementation in this population.

Graph 1: Prevalence of vitamin D deficiency in a refugee population at the Migrant Health Program, Geneva University Hospitals



P88

Adolescent behavioral risk screening in primary care: physician's point of view

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Introduction: This study examines physicians' self-reported psychosocial risk behavior screening in adolescents and young adults. It aims to highlight which elements hinder or improve screening abilities.

Methodology: Data were obtained through an online self-reported questionnaire sent out to primary care physicians (PCP) in Switzerland in 2018. A total of 1824 PCP were contacted, with a 29% response rate. The questions were directed to child well visits and routine checkups. Participants were asked whether they screened youths from three age groups (10-14 y/o, 15-20 y/o and 21-25y/o) for the HEEADSSS items. Barriers to screening included primary consultation motive prioritization, insufficient consultation time, patient compliance, reimbursement, lack of skills related to adolescent health, lack of referral options.

Data were analyzed first through a bivariate analysis using the Chi-square test then through a multinomial logistic regression.

Results: The majority of physicians partook in preventive screening for 3-5 psychosocial risk elements. They reported the primary consultation motive as well as a lack of available time as having a high impact on their screening habits. Increasing physician's experience and having discussed confidentiality were related to an increase in the number of topics addressed. Having discussed confidentiality remained a significant variable throughout all analyses.

Conclusion: Most physicians screen youths preventively for at least three risk behaviors. Barriers such as lack of consultation time and prioritization issues were found to be critical according to physicians but did not hinder screening habits. The main element impacting screening habits in this study was self-efficacy, with physicians who felt lacking the necessary skill set screening less and those feeling experienced, screening for more topics.

P89

CAVOVID: Calcium Dobesilate in patients with COVID-19 - a study protocol

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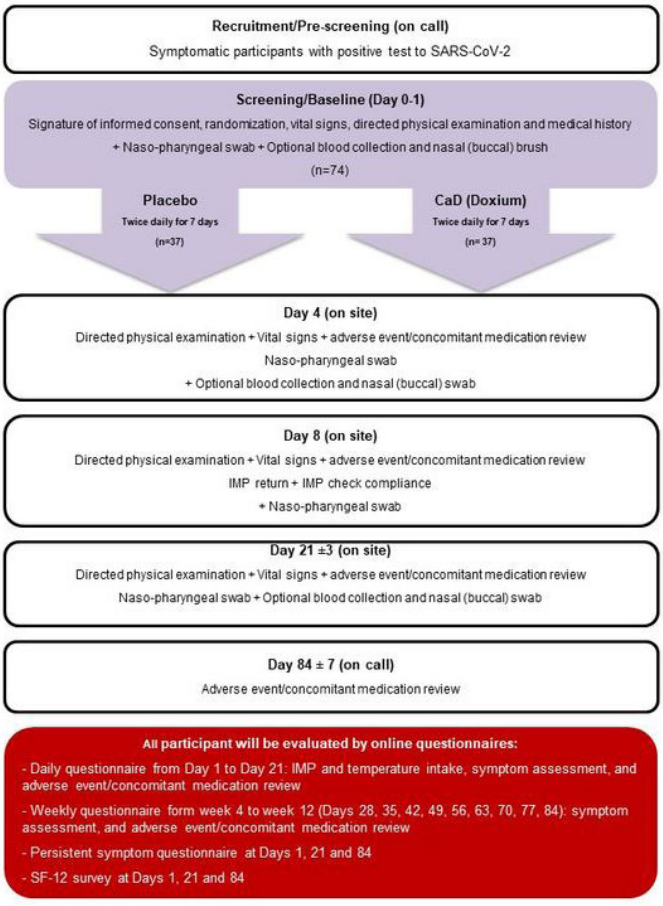
SARS-CoV-2, responsible for the COVID-19 pandemics, infects endothelial cells through angiotensin-converting enzyme 2 (ACE2) mediated viral entry, while heparan sulfate proteoglycans (HSPGs) provide the first anchoring sites on the cell surface and help the virus make primary contact with host cells [1].
In vitro results using viral pseudo typed particles demonstrated that calcium dobesilate (CaD) reduces the uptake of SARS-CoV-2 spike protein in cultured endothelial cells, by interfering with heparan-sulfate binding of the virus [2] . This is supported by data showing that CaD interferes with the heparan sulfate binding of VEGF [3] .This suggests that modification of heparan-sulfate or reduction of viral adhesion to heparan-sulfate may represent a viable therapeutic approach.
We have previously demonstrated the bioavailability of CaD in the nasal tissue and saliva after oral treatment.
We hypothesize that oral CaD treatment in early symptomatic phase may represent an interesting alternative for the treatment of early COVID-19 disease through its potential antiviral activity.
Enrollment to the study began in July 2022 and is expected to be completed in Q1 2023. Enrolled participants are randomized, in a ratio of 1:1 to either the treatment (calcium dobesilate, 2x500mg twice a day) arm or to the matching placebo arm.The treatment period is 7 days for both arms, followed by a 77-day observational period without treatment administration.
During the study, participants will be asked to complete online questionnaires using their personal smartphone or other electronic personal device. Online questionnaires include COVID-19 questionnaire (assessing symptoms, temperature measurement and reporting of concomitant medication and adverse events), COVID-19 persistent symptoms questionnaire and SF-12 survey. SARS-Cov-2 PCR assays will be performed through nasopharyngeal swabs collected at Day 1, 4, 8 and 21.
The primary endpoint is the reduction from baseline of RT-PCR SARS-CoV-2 viral load at Day 4. We estimate that a sample size of **74 patients (37 in each arm)** would provide an 80% power to detect a difference of 1 log (or 3 cycle thresholds, CT) in the mean reduction of RT-PCR SARS-CoV-2 viral load at Day 4 with a 1-sided significance level of 2.5%, assuming a standard deviation (SD) of 1.5 log (difference to detect of 0.67 SD).

This poster will focus mainly on presenting the study protocol, but may include some early results if already available.



P90

Change of long covid symptoms in the context of an interdisciplinary treatment

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Background: The prevalence of Long Covid syndrome, defined as the persistence of long-term symptoms such as fatigue, respiratory, cardiovascular or cognitive symptoms and an overall delayed physical and psychic recovery after COVID-19 disease, is around 15%. Current data show that affected individuals have reduced quality of sleep and life and are at higher risk of developing anxiety and depressive symptoms. The aim of this study was to assess psychological distress and quality of life as well as changes in these symptoms within during an interdisciplinary treatment.

Method: In addition to the physical examination, the mental state is assessed by validated questionnaires as part of the initial consultation in the Long Covid treatment. This results in an individual treatment concept with pacing therapy (occupational and physiotherapy) and, if necessary, psychological and complementary medical support. Following psychometric parameters were used: Sleep / Insomnia (ISI), Fatigue (FSS), Traumatization (IES-R), Anxiety (GAD-7) and Depression (HADS, PHQ-9), Somatization (PHQ-15) and Quality of Life (EQ-5D-5L). The survey was administered at Baseline (T0), second consultation (T1, 8-12 weeks), and third consultation (T2, 24-26 weeks). This retrospective evaluation included 578 (374 women; 204 men) for baseline and a total of 37 Long Covid patients for the T1 and T2 analysis. The latter was performed using linked t-tests.

Results: The mean of 570 subjects had pathologic fatigue scores (M = 47.6, SD = 12.5, cut-off ≥ 36) and 295 of 570 subjects (51%) had severe somatic symptoms (M = 15.1, SD = 5.7, cut-off ≥ 15). Quality of life was moderately impaired in 570 subjects (M = 18.3; 15 - 19 moderate problems). Mean scores of insomnia, anxiety, depression, and trauma were non pathological. From T0 to T1, fatigue (FSS) ($t = 1.85$; $p < .05$), quality of life (EQ-5D-5L) ($t = -1.94$; $p < .05$), somatic symptoms (PHQ-15) ($t = 2.97$; $p < .05$), and anxiety symptoms improved significantly. There were no significant changes from T1 to T2.

Conclusion: Long Covid patients had pathological baseline scores in fatigue and somatic symptoms. Across the interdisciplinary Long Covid treatment, psychological and somatic distress improved substantially. Thus, the outpatient consultation contributes importantly to the recovery of the performance of affected persons and to the prevention of psychosomatic problems in Long Covid syndrome.

P91

CHildren Of the Cohort (CHOC): the iceberg beneath the Mother to Child Transmission (MTCT) tip – a pilot study

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Background: As much of the focus is on mother-to-child HIV transmission (MTCT), children born to a man living with HIV, prior to the HIV diagnosis, not living with the parent or aged >18 years old may be undocumented by treating HIV physicians. Since the U=U campaign (undetectable=untransmissible) much has changed for People Living with HIV's (PLWH) sexuality but the effects on their parenting desire are uncertain.

Methods: A pilot study was conducted at the Lausanne University Hospital in Switzerland from September 1st to November 30th ‹22. PLWH enrolled in the Swiss HIV Cohort Study (SHCS) completed a questionnaire aimed to quantify and characterize their children (living and financial situation, HIV status and awareness of parental's serology) and their parenting desire. There were no exclusion criteria.

Results: Out of 196 participants with a median age of 50.6 years old (IQR 25; 80), 57 were female (29%), 44 of African origin (22%), 143 (72%) completed a post-mandatory education, 126 (64%) were employed. 83 men (42%) reported sexual relationships with men (MSM) and 115 participants (58%) were involved in a steady relationship. 96 participants (48%) had children, 14 of whom were MSM (14%). We identified 180 children whose median age was 22 years (IQR: 12; 31). The majority did not live with the parent (102, 56%) who still represented the child's most frequent financial support (104, 57%). Only three children (1.7%) were living with HIV and 60 knew their parent's HIV status (32%). While 52 participants (26%) reported the desire to have a child, the HIV diagnosis was described as a barrier for 16 of them (30%). 56 participants (28%) discussed parenthood with their HIV-physician; this was positively associated with their parenting desire (OR 4.13, 95% CI 2.09-8.16, p-value < 0.001) and to higher HIV influence on fertility planning (OR 2.69, 95% CI 1.19-6.03, p-value 0.02).

Conclusion: We found a parenthood rate of 1.8 children per participants, with a non negligible proportion of PLWH reporting a desire to have a child. While the HIV diagnosis represented an obstacle to family planning for a third of the participants who desired to have a child (16/52) it remains an underdiscussed subject as reported by 72% of our sample. Half of the participants account for their child's finances, a responsibility which could represent another psychological or financial burden. Identifying those individuals would enable the introduction of adequate supportive structures.

P92

Effect of e-cigarettes for smoking cessation on depressive and anxiety symptoms: secondary analyses of a randomized controlled trial

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Background: Previous observational studies showed associations between the use of e-cigarettes/electronic nicotine delivery systems (ENDS) and the occurrence of mental health problems. Robust empirical evidence of this association is still needed. Using a smoking cessation RCT, this study assessed differences in depressive and anxiety symptoms at 6-month follow-up between participants having received ENDS and smoking cessation counselling versus smoking cessation counselling alone.

Methods: This is a secondary analysis of the open-label pragmatic RCT ESTxENDS: Efficacy, Safety and Toxicology of ENDS as an Aid for Smoking Cessation. Adults smoking at least 5 cigarettes/day and willing to quit smoking were recruited from July 2018 until June 2021. The intervention group received 2 ENDS and e-liquids for 6 months for free plus smoking cessation counselling, while the control group only received smoking cessation counselling. Participants completed the Patient Health Questionnaire-9 (PHQ-9, score range 0-27) and the General Anxiety Disorder-7 (GAD-7, score range 0-21) to assess self-reported depressive and anxiety symptoms at baseline and 6-month follow-up visit. Data were analyzed using linear regression models adjusting for baseline covariates and using inverse probability weighting to account for attrition.

Results: We included 1243 participants (n=620 in the intervention group, n=623 in the control group) with a mean age of 41.1±13.5. A total of 910 participants (n=502 in the intervention group, n= 408 in the control group) completed the PHQ-9 at 6 months follow-up. The mean PHQ-9 scores at baseline were 4.4±4.2 in the intervention group (3.6±3.9 at 6 months) and 4.4±4.3 in the control group (4.0±4.2 at 6 months). There was no evidence for an effect of the intervention on the PHQ-9 score in the main adjusted model (coefficient -0.033, 95% CI -0.072 to 0.005, p=.091). A total of 881 participants completed the GAD-7 at 6 months follow-up. The mean GAD-7 scores at baseline were 5.5±4.4 in the intervention group (4.6±4.3 at 6 months) and 5.3±4.6 in the control group (4.6±4.4 at 6 months). There was no evidence for an effect of the intervention on the GAD-7 score in the main adjusted model (coefficient -0.0005, 95% CI -0.038 to 0.038, p=.981).

Conclusion: Among smokers participating in the ESTxENDS smoking cessation trial, there was no effect of e-cigarettes on depressive and anxiety symptoms at 6 months follow-up.

Trial Registration: ClinicalTrials NCT03603340

P93

Effectiveness of group psychotherapy for Long-Covid

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Background: The prevalence of Long Covid syndrome, or persistence of long-term symptoms such as fatigue, respiratory problems, or cognitive impairment after COVID-19 disease, is approximately 15%. Studies show reduced quality of sleep and quality of life in affected individuals and a higher risk of developing psychological symptoms such as depression or anxiety disorders. Interdisciplinary treatment and psychological counselling are provided for support. The aim of this analysis was to collect preliminary data on the effectiveness of group psychotherapy for Long Covid patients.

Method: In this preliminary analysis of an ongoing, single-arm group psychotherapy setting, 20 patients (16 women, 4 men) with Long Covid syndrome were included. The setting provides a peer exchange of experiences and teaches behavioural strategies for coping with the disease. At the start (T1) and end (T2) of therapy, validated questionnaires were used to assess sleep (ISI), fatigue (FSS), trauma (IES-R), anxiety & depression (HADS, GAD-7, PHQ-9), somatization (PHQ-15), and quality of life (EQ-5D-5L).

Results: At baseline T1, all subjects showed clinically relevant fatigue scores (M = 56.7, cut-off ≥ 36). Severe somatic symptoms were found in 13 subjects (65%) (M = 15.8, cut-off ≥ 15). Quality of Life was moderately impaired across the sample (M = 17.5). Mean scores on insomnia, trauma, anxiety, and depression did not prove pathological. However, a subset of 5 subjects (25%) showed pathological depression scores (PHQ-9). A pre-post therapy comparison (T1 vs. T2) in 12 patients (limited statistical power of 49%) showed a trend toward improvement in all measured dimensions, with statistically significant differences found in depression (PHQ-9) with $t(11) = 4.33$, $p = .001$, somatization (PHQ-15) with $t(11) = 3.00$, $p = .012$, and quality of life (EQ-5D-5L) with $t(11) = 2.28$, $p = .044$.

Conclusion: Long Covid patients showed pathological values in fatigue and somatic symptoms. In addition, a subgroup showed pathological depression values. In the course of the group intervention, psychological distress, especially depressive symptomatology, was reduced. Thus, the group therapy provides an important contribution to the prevention of additional psycho-psychiatric concomitant diseases.

P94

General practitioners' approach to tobacco cessation before and after a training intervention (The FIRST trial: interim analysis)

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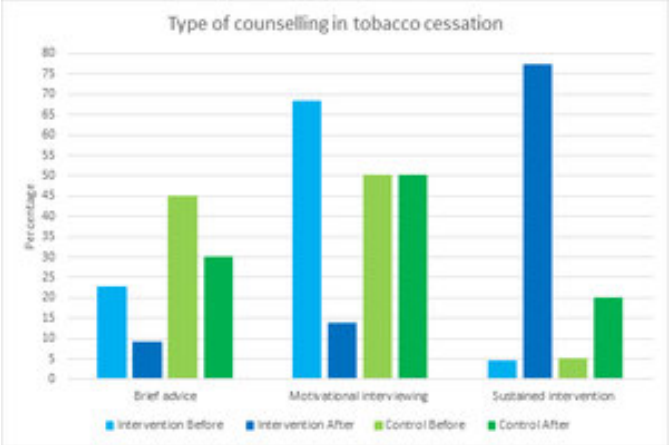

Figure 1

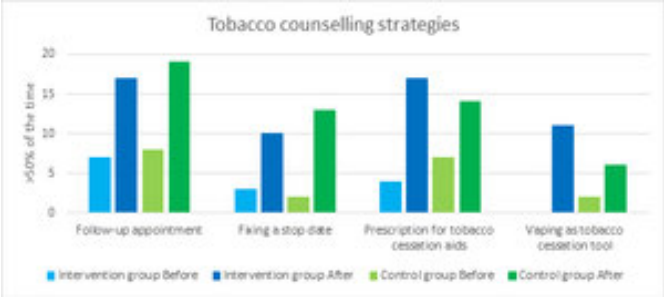

Figure 2

Introduction: Several effective interventions are available to help primary care patients to stop smoking, but they are underused. The ongoing FIRST trial (Clinical trials NCT04868474) assesses a training program encouraging GPs to use shared decision-making (SDM) that includes a decision aid and compares it to standard treatment options for tobacco cessation. In this abstract, we present the interim results regarding observed effects of the training on the types of counselling and strategies used in tobacco cessation by GPs.

Methods: GPs were recruited from French speaking Switzerland and the Lyon area, France. GPs were randomized at enrolment to either control group: a 45-minute update on tobacco cessation treatment options without trying to modify their routine or to the intervention group: update plus training to use SDM and a decision aid. GPs in both groups completed questionnaires before and straight after the training. Questionnaires focused on the type of counselling they used most often: sustained intervention, brief advice or motivational interviewing and post training which they intend to use. Counselling strategies, namely frequency of follow-up appointments, fixing a stop date, prescription of aids and use of vaping products as a tobacco cessation tool were also explored. We conducted simple descriptive analysis.

Results: Of the 42 GPs who completed the training, 22 were intervention and 20 control; 62% were women, 21% were aged >50 years, and 69% practiced in an urban area. The majority of GPs were based in Switzerland (33 vs 9 from Lyon). When asked before training which type of counselling they used, 23% of intervention and 45% of the control group declared brief advice, a further 68% and 50% respectively, used motivational interviewing and 5% in both groups used sustained intervention. After training, this changed to 77% intending to use sustained intervention in the intervention group vs 20% in the control group, who still favoured motivational interviewing at 50% (Figure 1). Counselling strategies were also affected by training, increasing intended use for all types in both groups (Figure 2).

Conclusion: Intended practices of GPs enrolled in the FIRST trial were influenced by both trainings. Notably, intention to provide help with tobacco cessation appeared to increase, with the distinction of the control group favouring motivational interviewing compared to sustained intervention in the intervention group.

P95

Is subclinical hypothyroidism associated with increased risk of heart failure? An individual participant data analysis from 12 prospective cohorts

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Introduction: Subclinical hypothyroidism (SHypo) might be associated with an increased risk of heart failure (HF), especially at higher thyroid-stimulating hormone (TSH) concentration. More evidence with longer follow-up is now available to clarify whether a threshold of TSH exists above which the risk of HF increases.

Methods: After a systematic review of the literature, we performed a two-stage individual participant data analysis of multiple prospective cohorts. SHypo was defined as TSH of 4.50-19.9 mIU/L with normal free thyroxine concentration and euthyroidism as TSH 0.45-4.49 mIU/L. We predefined baseline TSH categories as of 4.50-6.99, 7.00-9.99, and 10.00-19.99 mIU/L. We fitted Cox-proportional hazard models separately for each study and used a random effects model to pool the estimated hazard ratios adjusting for age and gender.

Results: In the preliminary data of 12 prospective cohorts from Australia, Europe, North and South America, we analyzed 49,892 adults (median age 69 years [range 21-98 years], 47% female). In total, 3816 individuals (7.6%) had SHypo, the majority with a TSH between 4.50-6.99 mIU/L (N=2011). There were 5,146 HF events during a median follow-up of 4.3 years. In age- and sex-adjusted analyses, the hazard ratio (HR) for HF events was 1.10 (95% confidence interval [CI] 0.94-1.29) for the overall SHypo compared to euthyroidism. In stratified analyses, the HR for HF events was 0.98, 95% CI 0.88-1.10 for TSH 4.5-6.9 mIU/L and 1.61 (95% CI 1.23-2.13) for a TSH ranging from 7.00-9.99 mIU/L when compared to euthyroidism. The association found in the group 7.00-9.99 mIU/L was robust after adjustment for CV risk factors (HR 1.66, 95% CI 1.24-2.23) and after excluding the use of thyroid medication (HR 1.99, 95% CI 1.01-3.92) or those with preexisting HF (HR 1.66, 95% CI 1.16-2.36). In a post-hoc analysis, the risk of HF was 1.43 (95% CI 1.11-1.84) in those with a TSH 7.00-19.99.

Conclusion: Subclinical hypothyroidism with TSH values above 7 mIU/L is associated with an increased risk of HF events, whereas there is no risk for the vast majority of SHypo individuals with a TSH below 7 mIU/l when compared to euthyroidism.

P96

Prevalence of nicotine product use among patients seen in primary care: cross-sectional data from Sentinella

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Introduction: General practitioners (GPs) play an essential role in delivering cost-saving interventions to reduce the burden of tobacco in the population. We analyzed the current prevalence of nicotine use (with and without tobacco) and status of smoking cessation efforts in general practice, with a focus on time spent discussing tobacco cessation and the prescription of pharmacologic quit aids.

Methods: Cross-sectional study of patients consulting pediatricians and GPs in the national Sentinella network. GPs were asked to collect data from 30 consecutive patients ≥ 12 years of age seen for non-urgent consultations. Data collected from the GPs were their gender and average time spent providing smoking advice in minutes. Data collected for each patient included year of birth, gender, tobacco use or electronic nicotine delivery system and if positive clarification as to which one.

Results: We analyzed a cohort of 2438 patients, of whom 519 (21%) used a nicotine product within the last 7 days (Table 1). Among the 106 who planned to quit, 16 (15%) planned to use a pharmacological nicotine substitute, 9 (9%) varenicline, 6 (6%) a vape and 5 (5%) bupropion. Moreover, 236 (45%) of 519 patients using nicotine products received 1-5 min of cessation advice, 80 (15%) 6-10 minutes and 18 (3%) more than 10 minutes. No discussions were reported by 164 (30%) of them.

Table 1

Characteristics	Number	Percent
Prevalence by gender		
- Women	250/1330	19%
- Men	269/1155	23%
Prevalence by age category		
- 12-18 years	15/203	7.4%
- 19-40 years	129/418	31%
- 41-65 years	236/857	28%
- >65 years	139/960	14%
Tobacco products		
- Cigarettes	387/2438	16%
- Rolled cigarettes	46/2438	2%
- Joint with tobacco	33/2438	1%
- Other	54/2438	2%
Nicotine products without tobacco		
- Vape with nicotine	25/2438	1%
- Vape without nicotine	12/2438	0.5%
- Nicotine replacement therapy	10/2438	0.4%
- Other	2/2438	0.1%
Plans to quit in ≤3 months		
- Yes, to quit	106/2438	4%
- Yes, to cut back	43/2438	2%
- No or missing	370/2438	15%

Conclusion: The use of nicotine products remains common among primary care patients, the majority of whom smoke cigarettes. Nicotine products without tobacco remain relatively rare. After the consultation, 1 in 5 patients using nicotine products planned to quit, the majority without a prescription quit aid.

P97

Primary health care needs of gender and sexually diverse people In Geneva

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Background: Gender and sexual diversity (GSD) individuals are at increased risk of negative health outcomes and suffer health inequities and discrimination, including in health care setting. Therefore, many GSD individuals do not seek healthcare for fear of being discriminated against, and do not disclose this part of their identity to their health care providers, leading to diagnostic errors. The objective of our study was to identify and improve understanding of the primary health care needs of GSD individuals.

Methods: This qualitative study relied on individual semi-structured interviews with a purposive sample of GSD individuals recruited through social media, community associations and medical offices in Geneva. Interviews were based on the critical incident technique. Thematic analysis of interview content took place involving all researchers. Community members were involved at each step of the project.

Findings: Interviews took place with 19 GSD individuals who self-identified as cisgender (8), transgender (3), non-binary transgender (3), non-binary (2), intersex (1) and in questioning (3). They self-categorized as being gay (5), lesbian (5), bisexual (2), pansexual (4), queer (3), lesbian non binary (1) and in questioning (1). Their age ranged from 25 to 56 years (mean 36.31). 102 critical incidents were identified and the majority of incidents occurred in primary or emergency health care settings (54.9%). The main primary care consultation challenges for GSD patients were: revelation of GSD status, feeling discriminated against, and dealing with physician embarrassment or lack of competence regarding GSD health issues. These challenges impacted negatively their medical care and health prevention measures. Improving health professionals' knowledge related to GSD health issues was the main need expressed by participants. Furthermore, inclusive language and appropriate, non-judgmental reactions to patients' disclosure of their GSD identity appears to be essential. Participants provided many practical, individual and structural solutions for equitable and inclusive health care.

Conclusion: Exploring health experiences of GSD patients in primary care identified that disclosure of GDS status and finding a health care provider competent to answer to their specific needs remain a constant challenge for GSD patients. Training primary care professionals in GSD health must be improved to provide safe care for GDS individuals.

P98

Shared decision making for tobacco cessation counseling in primary care: the patient's perspective. A qualitative study

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Introduction: Smoking cessation provides substantial health benefits. Medications for smoking cessation can double quit rates. The majority of Swiss smokers expect a discussion about smoking cessation with their general practitioner (GP) but only a small number receive a prescription. The FIRST study aims to increase smoking cessation using a decision aid (DA) showing the different quitting methods and a half-day GP training course on shared decision making (SDM).
This qualitative study nested in FIRST explored the reactions of a purposive sample of participants to the discussion they had with their GPs about smoking cessation. In the intervention group, we asked participants about the acceptability of a more proactive offering of treatment and the helpfulness of our DA. In both, the intervention and control groups, we explored participants' expectations regarding the role of their GP in tobacco counselling.

Methods: As part of the FIRST randomized controlled trial, we conducted qualitative semi-directed interviews with study participants in both arms (adults, daily smokers at any level of motivation for quitting) between 11.2021-10.2022. Interviews were over the phone, 5-16 weeks after a routine visit with their GP. Data were analyzed using thematic data analysis assisted by the MAXQDA software. We followed COREQ standards.

Results: Among 20 participants, 8 were in the control and 12 in the intervention group. The average age was 49 years old and 55% were female. The average interview length was 15.5 minutes.
Among intervention group, seven participants appreciated the DA, two participants didn't find it helpful and three didn't recall using it.
Participants in both groups felt their GP provided strong moral support. They felt that the most important factor influencing smoking cessation was their own motivation. Seven participants wanted to receive a medication to stop smoking. At the time of conducting the interviews, one participant received a prescription in the control and four in the intervention group.

Conclusions: Most participants in the intervention group appreciated the DA. Participants across both groups expected their GP to provide moral support but not necessarily treatment to quit smoking.
The perspective of the FIRST study results could be that an early explanation of treatment options to all smokers may encourage them to ask for it when they are ready to quit smoking.

THEMES	SUB-THEMES
Acceptability of the decision aid used in the intervention group	• Usefullness, usability and value (n=7) • No utility (n=2)
Discussion about tobacco	• Discussion about tobacco cessation after study inclusion (n=5 in control group and n=10 in intervention group) • Discussion about medication after study inclusion (n=2 in control group and n=7 in intervention group)

Patients' expectations regarding the role of clinicians in tobacco counselling	• The influence of the general practitioner (n=7 in control group and n=12 in intervention group)
	• The influence of the specialist (n=5 in control group and n=7 in intervention group)
	• Willingness to receive a medication:
	  • yes (n=2 in control group and n=5 in intervention group)
	  • no (n=4 in control group and n=7 in intervention group)

Quit attemps	• Facilitators due to physical condition (n=11) and social motivation (n=9) • Barriers linked to psychological dependence (n=12), to fear of physical (n=6) or psychological (n=4) changes and to costs (n=2) • Advantages (n=6) and disadvantages (n=15) of the vape

Table: Themes and sub-themes raised in qualitative interviews (n=20)

P99

A Swiss COhort of Healthcare Professionals and Informal CAregivers (SCOHPICA) to address the health workforce crisis: description and preliminary results

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Introduction: Worldwide, HCPs are affected by turnover, staff shortages, low job satisfaction and burnout, and healthcare stakeholders stress the lack of data to tackle this crisis. In that context, we implemented the Swiss COhort of Healthcare Professionals and Informal Caregivers (SCOHPICA) to study the trajectories, intentions to leave/stay in the job/profession, and well-being of healthcare professionals (HCPs), and their determinants.
This presentation describes the methods and main results of SCOHPICA's baseline survey on HCPs.

Methods: SCOHPICA is a prospective open cohort with an embedded mixed methods design. Using an electronic self-reported questionnaire, the baseline survey was implemented between October 1, 2022 and January 31, 2023. It targeted a minimum of 1500 HCPs. Follow-up surveys will take place yearly, with an online life history calendar (LHC) implemented in 2023. Participants will be invited for focus groups or interviews every two years. Any type of HCP working with patients in all healthcare settings and sectors in Switzerland (regardless of employment status) is eligible. Outcome variables are trajectories, intentions to leave/stay in job/profession and well-being, and independent variables are organizational (e.g. work-life balance, leadership), psychosocial (e.g. recognition, sense of belonging), psychological (e.g. burnout, job satisfaction), occupational (e.g. current job, specialization) and sociodemographic determinants. Descriptive and regression analyses will ex-

amine the baseline data, and sequence analysis and clustering will be used for longitudinal data analyses. Qualitative analyses will apply interpretative phenomenological analysis and solution-focused approaches.

Results: By January 19, 2023, 1727 HCPs had already answered to the survey. Preliminary results will be presented at the conference.

Conclusions: Using an innovative methodology, SCOHPICA will gather new evidence to support the monitoring, planning and management of the health workforce. Moreover, this evidence is essential for policy interventions fostering a resilient health system capable to deliver high quality of care. Hence, the data will be made available online to the public. To complement this data, data will also be collected among informal caregivers, key but often neglected health system actors, and their recruitment will start in spring 2024.

P100

Barriers and facilitators for conducting research in palliative care as perceived by the interprofessionnal team: an observational study

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Introduction: Conducting studies in palliative care has been shown to be difficult for several reasons. It has been highlighted that the interprofessional team caring for the patients in palliative care units may contribute to the lack of studies in this population. However, research is fundamental in order to improve the quality of care and the quality of life of patients. Our aim was to identify obstacles and facilitators to the involvement of palliative care team members in research projects.

Methods: We performed an observational study with qualitative and quantitative components to identify which barriers and facilitators are encountered by palliative care team members. This was done through a questionnaire that included multiple choice questions, Likert scales and the opportunity to comment certain answers in free text fields. This questionnaire was sent via email to all professionals working in the palliative care division of the Geneva University Hospitals (physicians, nurses, care assistants, social workers, physiotherapists, dieticians, psychologists, and occupational therapists).

Results: Out of the 107 questionnaires sent to the interprofessional team, 51 people responded. 75% were interested in research, but only 47% had ever participated in a research project. The barriers identified were mainly a lack of training on how to conduct a study for 75% of the participants, lack of time for 89% and funding for 55%. Certain representations of patients at the end of life by members of the interprofessional care team such as the fear that their condition will deteriorate too quickly in relation to the duration of the study, was also identified as a barrier for 80% of the professionals. The main facilitators were the acknowledgement that research improves the quality of care (97%) and the appreciation that patients are respected in their autonomy and should be able to participate in research projects if they wish to (86%).

Conclusions: In order to promote research, the interprofessional palliative care team would benefit from time, funds and training to carry out studies. The establishment of a professional network to guide and share experiences around research would also be a good way to integrate a research culture with the aim of improving the quality of patient care.

P101

Communication between primary care providers and hospitals: the hospitalists' view

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Introduction: Due to the increasing fragmentation of the healthcare system, effective communication and data exchange between primary care physicians (PCPs) and hospital physicians is both central and challenging. Given the increasing fragmentation of health care (1) and the resulting rise in health care costs due to insufficient information exchange (2), effective and secure transmission of patient data is of great importance (1). The hospitalists view of communication between PCPs and hospitals was assessed in this Central Switzerland survey.

Objectives: The objectives of this survey are to examine the satisfaction with the current state of communication between hospital physicians and PCPs and to identify potential opportunities for improvement. In addition, it was examined whether web-based portals ("LUKSLink") support the communication between hospital physicians and PCPs in a meaningful way.

Methods: The survey was sent via email to hospitalists (November 2021 to February 2022). The questionnaire contained 17 questions with single- and multiple-choice answers and some offered free text entry. Descriptive statistics and regression analyses were performed using the statistical program R.

Results: In total, 276 of 1134 physicians from six different hospitals in Central Switzerland responded. This results in a response rate of 24.3%. The main results were:
1) the majority of hospital physicians are satisfied with the general communication (58.7%) with PCPs as well as with their communication in case of referrals(52.5%);
2) the preferred information channel for referral letters is e-mail (212, 76.8%), followed by electronic portals (181, 65.5%) such as LUKSLink;
3) the three most important information contents hospital physicians need from primary care physicians in referral letters are: Medication list, diagnoses and the reason for referral.

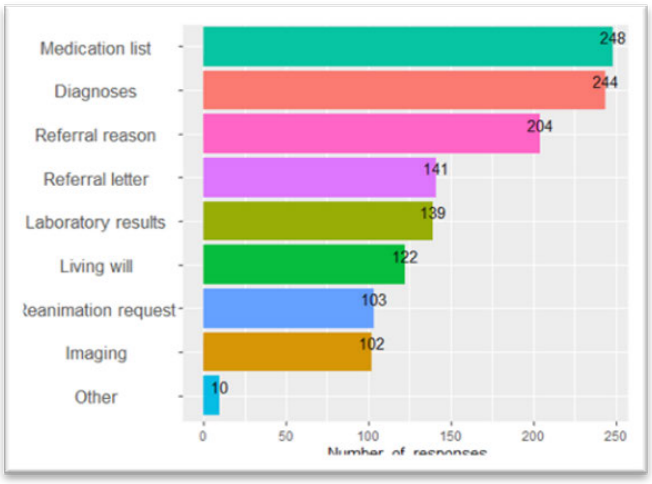

Figure 1 The most important information content in a referral letter from hospitalists' view

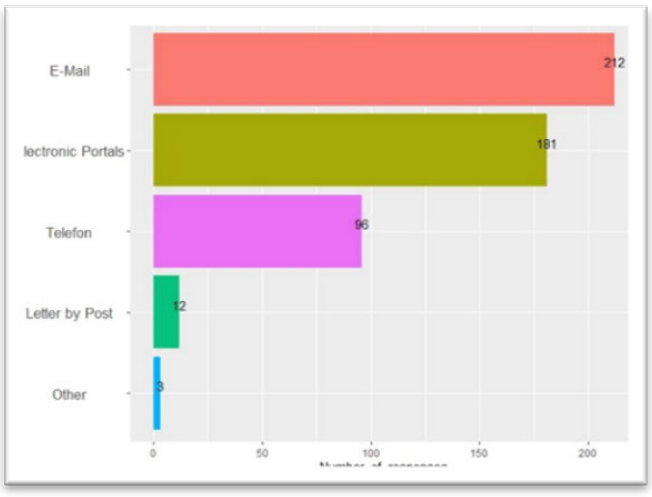

Figure 2 The hospitalists' preferred information channel for referral

Conclusion: The results of this study show that the majority of hospitalists in Central Switzerland are satisfied with the current state of communication between hospitals PCPs. In addition, preferences regarding the content and preferred communication channel for referral letters from PCPs to hospitalists could be determined.

P102

doMESTIC RedPIM – study of medication safety in home care, reducing potentially inappropriate medications: a structured approach to interprofessional medication management for home care clients

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Introduction: Recent Swiss publications indicate that medication-related problems (MRPs) are especially frequent among home care clients, who are predominantly elderly, multimorbid and polymedicated.[1,2] Interfaces of care are common, necessitating timely, complete and accurate communication of medication-related information.
In this study, we aimed to pilot-test a standardized approach to interprofessional medication management of home care clients, focusing on deprescribing.

Method: Home care clients of Spitex Bern, ≥64 years and taking ≥4 prescribed medications were assessed for their medication-related risk and subsequent need for a medication review, using the 10-item doMESTIC RISK tool.
For qualifying patients, pharmacists among 14 pharmacies performed a structured medication review, addressing resulting questions/suggestions to their primary care provider (PCP) using a standardized form.
Answers and the ultimate therapeutic decision by PCPs were communicated on the same form.

Results: With informed consent, nurses initiated 106 risk analysis; 75 (71%) could be completed by pharmacists. 26 patients scored <5, not necessitating a medication review.
49 patients qualifying for a medication review were on average 84.0±7.7 years (65-103) and took 11.2±4.5 prescribed medications regularly (2–24), with an additional 2.8±3.5 as-needed (0–14) and 0-5 over-the counter medications.
Pharmacists identified 120 potential MRPs (2.4/patient) with 64 potential interventions. Of those, 46 prioritized interventions concerning 20 patients were communicated to PCPs. The most commonly suggested interventions were dose reduction (27%) and therapy stop (23%), most often based on (potential) contra indications and potentially inappropriate medications.
While only 45% of pharmacy requests (9/20 patients) were answered by PCPs, acceptance rate for the remaining suggestions was 57% (26/46 interventions), predominantly generic substitution and dose reduction (7 medications). Three medications were deprescribed.

Conclusions: In a structured medication management program, pharmacists identified various potential medication therapy improvements in collaboration with home care nurses and PCPs. However, there is a lack of medical information accessible to all members of the healthcare team, limiting the pertinence of suggested interventions. Communication needs improvement and reimbursement should be discussed.
This project was funded by the KHM's Fonds interprofessionalité.

P103

Effects of the implementation of a standardized algorithm for medical inpatients on incidence, treatment and outcomes of delirium

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Introduction: With the aim to optimize delirium management, an algorithm was introduced in general internal medicine wards of a Swiss University Hospital in 2018. We evaluated the impact on incidence, therapeutic measures, and outcomes of delirium in a real-world setting.

Methods: Retrospective before-after study of patients aged ≥65 years hospitalized in general internal medicine. During 2018, an interprofessional delirium algorithm with recommendations for screening, prevention, and treatment was introduced. We compared the delirium incidence and other secondary outcomes (i.e. length of stay, mortality, use of pharmacological and non-pharmacological interventions among delirium patients) between the calendar year 2017 and 2019, first unadjusted using chi-squared tests or t-tests, and second adjusted for potential confounders using generalized estimating equations, clustering for individual patients.

Results: Of 4855 cases (2253 in 2017, 2602 in 2019), delirium incidence was 9.5% in 2017 and 11.0% in 2019 (p=0.08). Among 499 patients with delirium, length of stay (10.2 vs. 9.6 days, p=0.44) and mortality (10.3% vs 10.1%, p=0.95) were similar in 2017 and 2019; use of antipsychotics decreased (81.0% vs. 68.0%, p=0.035), while use of non-pharmacological interventions increased (Table). In multivariate analyses, the reduction in length of stay was

-0.28 days (95% confidence interval [CI]: -0.91-0.35; p=0.38) in 2019 compared to 2017, hospital mortality remained unchanged (odds Ratio [OR] 1.04 (95%CI: 0.77-1.40; p=0.81) and use of antipsychotics was markedly reduced (OR 0.67 (95%CI: 0.54-0.82; p<0.001)

Conclusion: A higher incidence of delirium was observed after the introduction of an evidence based delirium algorithm, potentially reflecting increased diagnostic awareness. While the intervention resulted in a shift from pharmacological to non-pharmacological treatment, mortality and length of stay in delirium patients remained unchanged.

Table: Outcomes in the pre- and post-intervention period

	2017	2019	p-value
	Subgroup of cases with delirium		
	n=213	n=286	
Deaths	22 (10.3)	29 (10.1)	0.95
Length of stay, days	10.2 (±0.44)	9.6 (±0.53)	0.44
	Random sample of cases with delirium		
	n=100	n=100	
Pharmacological interventions	84 (84.0)	74 (74.0)	0.08
Antipsychotics	81 (81.0)	68 (68.0)	0.035
Benzodiazepines	19 (19.0)	28 (28.0)	0.13
Melatonin and other	7 (7.0)	11 (11.0)	0.32
Non-pharmacological interventions	83 (83.0)	89 (89.0)	0.22
Communication	72 (72.0)	70 (70.0)	0.76
Orientation	52 (52.0)	34 (34.0)	0.010
Delirium validation tests (4AT, CAM)	4 (4.0)	47 (47.0)	<0.001
Involvement of relatives	3 (3.0)	31 (31.0)	<0.001
Somatic support	6 (6.0)	31 (31.0)	<0.001
Safety measures	76 (76.0)	84 (84.0)	0.16
Other	8 (8.0)	15 (15.0)	0.12

Numbers are presented as n (%), or mean (± standard deviation). Abbreviations: 4AT= Screening test for delirium, CAM= Confusion Assessment Method.

P104

Hospital@Home - improving discharge management of complex and multimorbid patients hospitalized in internal medicine wards

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Introduction: The early transition phase from hospital to home is particularly vulnerable. More than 20% of patients hospitalized in acute care internal medicine wards are rehospitalized within 30 days. Potential reasons for avoidable rehospitalizations include complications and loss of information between in- and outhospital caretakers. The aim of this pilot study was to assess the feasibility of a hospital@home intervention during this delicate transition.

Methods: Our team assessed the procedures, processes and interdisciplinary collaboration and made adjustments for the Hospital@Home program. The interprofessional program aims at improving transition of care for patients with a high risk for rehospitalization. The interventions include daily phone calls, individually adjusted interventions, and home visits if needed. The primary outcome of the randomized clinical study is to reduce unplanned rehospitalizations

in multimorbid patients. We hypothesize that a 5-day intervention by a multi-professional care team in 1362 patients will result in a reduction of rehospitalizations within 30 days by at least 25%.

Results: In December 2022, we enrolled 10 patients with a high risk for re-hospitalization in a pilot study (50% women, mean age 78.3 years (SD 8.5), mean BAARS score 7.7 (2.8), mean HOSPITAL score 4.2 (1.6). Patients were hospitalized for a mean of 12.3 days (12.5), 50% had heart failure, 40% had active cancer disease, 10% were living alone, and in 60% Spitex outpatient care was established. In total, 3 patients were rehospitalized within the first 18 days (30%). Reasons for rehospitalization were new viral infection, pain exacerbation, and aspiration. One patient withdrew the consent. On average, the study team performed 5.2 (1.8) planned phone calls and 0.4 (0.7) unplanned phone calls per patients. Patients were very satisfied or satisfied with the intervention. Table 1 summarizes feedback that contributed to the improvement of the program.

Conclusion: Hospital@home interventions are feasible, and patients are satisfied with the intervention. Although phone calls are well intended, they may also cause stress to patients. Thus, interventions need to consider patients' needs and preferences. Due to complex patient situations, phone calls also proved to be very challenging. As such, participating health professionals must be well-trained and excellent interprofessional collaboration is essential.

ID	Focus Follow Up Calls	Feedback
1	Digestion/Diarrhea and nutrition	Patient: glad for the possibility to call the hotline number (if needed)
2	Follow-up hypertension, treatment uncomplicated urinary tract infection at home	Patient: Blood pressure adjustments at home significantly more comfortable than at the hospital. Worries about missing phone calls
3	Weight, diuretics dosage, oxygen device consultation	Patient: H@H calls gave me confidence about the diuretics dose
4	Fatigue counseling, counseling relatives, organization of psychooncologist appointments, Spitex subsequently organized	H@H: Many phone calls, time-consuming to organize Spitex, deterioration of general condition during the five days despite the calls/interventions. Rehospitalization necessary because of new infection of respiratory syncytial virus (RSV).
5	Complex care situation, prescription of pressure ulcer mattress, communication with Spitex	Spitex organization: Gap in communication abut mobilization between nursing department and Spitex.
6	Digestion / constipation	Husband appreciated H@H intervention very much. In particular, follow up calls provided him a sense of security. Rehospitalized as a result of aspiration.
7	Follow-up hypertension	Participation discontinued on 4th follow-up day, patient fell during unscheduled follow-up call, outpatient treatment necessary (emergency department)
8	Weight, diuretics, coordination follow-up appointment in cardiology	Patient: Glad because the H@H team was able to schedule an urgent outpatient appointment. H@H team stopped medications due to persistent hypotension.
9	Coordination of follow-up appointment, Sending discharge documents to primary caregivers	Patient and his wife: Grateful for assistance with appointment coordination. Patient was electively referred to psychiatry within the 30 days by the attending psychiatrist.
10	Weight, adjustment of diuretics, additional coordination of follow-up appointment. Home visit was required	Home visit with H@H team, private care provider (Spitex), and patient. Clinical assessment of respiratory situation resulted in adjustment of the medication. The feedback was very positive. Advice/training was also provided on site.

P105

HYpertensive Patients dedicated interprOfessional model (HYPO) - Developing an interprofessional digital care pathway for optimizing the care of patients with hypertension in Swiss primary care settings (protocol)

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Introduction: Hypertension is a well-known chronic condition and risk factor for heart, brain, and kidney disease. Prevalence in Switzerland is high and despite prolonged treatment, more than 50% of Swiss adult patients do not reach blood pressure targets. Recent studies show that telehealth including team-based care is an effective and safe alternative to clinic-based care for improving blood pressure control and patient-centered care for hypertension. As we move toward a more digitalized and connected healthcare system, patients are becoming empowered, with the ability to share self-generated data and participate in decision-making to inform their health journey. The aim of this project is to develop and pilot a digital platform that coordinates patient-centered care of hypertension within an interprofessional care pathway and allows a targeted and detailed exchange of information between general practitioners (GPs), pharmacists, and patients.

Methods: The project is based on the iterative process of the Information System Research (ISR) Framework. At first, the end users of the platform (GPs, pharmacists, and hypertensive patients) will be involved in a national survey to identify unmet needs in the care of hypertension and assess opportunities for interprofessional collaborations. For the second phase, a sample of end users will be invited to co-design the digital platform and its functionalities. The prototype will be launched in a case series study to analyze the patient journey and experiences. Guidelines for the treatment of hypertension and information about the patient's journey will be integrated in the digital platform as interprofessional care pathway. This will help to coordinate care of hypertension in primary care settings. In the last part of the project, the developed digital care pathway(s) will be tested in a pilot study using an effectiveness-implementation hybrid design and a mixed-methods approach.

Result: Presentation of the project phases, based on the iterative process of the ISR-Framework.

Discussion: A digital team-based care for hypertension, aiming to empower the patient, could improve blood pressure control and therefore reduce burden of cardiovascular disease management in Swiss primary care settings. This project will be followed by a largescale efficacy study.

P106

Interprofessional care in palliative care units seen by caregivers: a qualitative study

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Introduction: According to the WHO, the goals of palliative care are to improve the quality of life of patients and that of their families who are facing challenges associated with a life-threatening illness, whether physical, psychological, social or spiritual. In palliative medicine, interprofessional collaboration is central to the overall care of patients. However, there is a scarcity of medical evidence or guidelines on how to work effectively in an interdisciplinary team in palliative care units. In this context, it seems difficult for the members of palliative care teams to optimize their collaboration. The aim of this project is to explore healthcare professionals' experiences and define the factors that promote and hinder the implementation of interprofessional collaboration in palliative care.

Design: We conducted three focus groups in which four health care professionals per group were recruited from acute palliative care units. Participants were recruited by purposeful sampling amongst doctors, nurses, physiotherapists, occupational therapists, spiritual caretakers, social assistants and music therapists. The data collected is currently being analyzed on a narrative basis, compared and critiqued using previously published literature on the subject.

Results: Our preliminary results show that consistency within the team's composition was defined as an essential element to an effective interprofessional collaboration. A general agreement on the patient's objectives and goals of care also facilitated the collaboration between the different members of the interprofessional team. The main barrier was the lack of knowledge about the work/activity conducted by the different team members. Finally, healthcare professionals felt that it would be essential to implement measures that would improve the collaboration of the interprofessional team in palliative care units. This could be something as informal as a "coffee meeting" during which each member could present his/her work or something more educational such as interprofessional skills training.

Conclusion: Communication between different members of each team is a key factor in effective interprofessional collaboration. Within a team, knowledge of how each member works is essential

for an effective collaboration. Our preliminary data highlights that training in interprofessional collaboration would be greatly appreciated by healthcare professionals and could result in better patient care.

P107

Interprofessional collaboration during a specialized mobile palliative care service pilot in rural Lucerne

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Introduction: Interprofessional collaboration (IPC) in outpatient palliative care is critical to ensure good quality of care in the home care sector. In rural Switzerland, due to the decentralisation of different healthcare institutions, communication and collaboration in outpatient palliative care are hindered. Moreover, shortcomings in IPC may lead to inadequate patient treatment in the home care setting. We investigated facilitators and barriers (FaB) of IPC among healthcare professionals involved in a 6-months pilot phase of a newly implemented specialised mobile palliative care service (SMPCS) in rural Lucerne.

Methods: This case study uses a mixed-methods approach to collect (i) qualitative data on FaB as perceived by nurses and primary care physicians (PCPs), and (ii) quantitative data across the entire IPC using a validated questionnaire, expanded by nine additional questions about the pilot project.

Results: In total, three nurses and three PCPs were interviewed. Preliminary results suggest that nurses and PCPs rate their IPC as satisfactory. Suggested facilitators of IPC are (i) personal meetings between PCPs and nurses in advance of the project start to introduce the SMPCS pilot and (ii) to define responsibilities and coordination. Further facilitation is identified if the cooperation was previously established or if healthcare professionals had previously known each other, especially IPC between nurses and PCPs. Possible barriers are a deficit of palliative care knowledge among PCPs, and a lack of skills about the competencies of professionals involved. To obtain more information about professionals› experiences with IPC during the pilot, the questionnaire was sent to 39 professionals from seven different occupations, of whom 17 completed the questionnaire.

Conclusion: This study gives first valuable insights into FaB in respect of IPC during a SMPCS pilot in rural Lucerne. A stable team with members who know each other and their individual responsibilities appears to be a critical component for success. For further similar projects and the broad rollout of the SMPCS, IPC should be promoted prior to the pilot phase of an SMPCS.

Keywords: Interprofessional collaboration, specialised mobile palliative care, pilot phase, Lucerne, rural area.

P108

Shadowing: an anthropological detour to learn interprofessional collaboration and reflect on person-centered care

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Introduction: Interprofessional collaboration is essential for optimal quality care[1]. One core competency is the aspiration to ensure patient, family and community-centered care[2]. To achieve the early acquisition of these skills, the Department of Family Medicine (DMF) at Unisanté has integrated shadowing as a pedagogical method during the one-month practice internship of family doctors (3rd year of master) at the University of Lausanne. Shadowing suggests following, observing and interacting with patients in their daily life, with minimal impact on the normal course of their activities. The educational benefits include increased understanding and respect for the roles of other health professionals, teamwork and communication skills, and reflect about one owns position with respect to others, patient and family[3].

Method: In 2021, a first pilot project took place with volunteers. The pedagogical concept was assessed with questionnaires filled out by students and family doctors teaching in practice and focus group discussions. The teaching team followed up and adapted the content of shadowing and initiated a second pilot project with a larger group of randomly selected participants. The same evaluation was completed. Shadowing has been introduced for all students in June 2022 and remains evaluated in the same way.

Results: Since April 2021, 175 students enrolled, 104 completed the evaluation form and 6 participated in a focus group. 81% of shadowing took place with adults and 19% with pediatric patients.
57% of students felt their thinking was stimulated. Shadowing allowed better understanding how care is organized around a patient in the community (56%) and feeling the patient's point of view (63%).
70% reported that interviews with other health professionals helped to better understand their respective roles. Several students think that shadowing should take place earlier in their studies. Overall, student satisfaction increased since the global introduction of shadowing in June 2022.
53 family doctors teaching in practice responded to the questionnaire. 57% acknowledged the need to introduce shadowing in family medicine clerkships and 91% felt that family medicine is an ideal place to teach interprofessional collaboration.

Conclusion: Shadowing as a teaching method is not fully appreciated by all students and presents some organizational challenges. Nevertheless, it appears to be effective in stimulating thinking on interprofessional collaboration.

P109

What do we know about the patient journey through the health system after hospital discharge?

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Introduction: Transition of care between hospital and ambulatory settings is a high-risk period for patients. Interprofessional communication, care coordination and partnership with patients are key components for patient safety but there are weaknesses at interfaces. The aim of this qualitative study was to describe patient's itinerary through the health system after hospital discharge.

Method: Type 2 diabetic patients with at least two comorbidities, and returning home after hospital discharge were recruited during their hospitalization at the Geneva University Hospitals. A qualitative longitudinal research approach was adopted with four individual semi-structured interviews over a period of two months after discharge. Interviews were based on a guide, transcribed verbatim and analyzed by themes. Patients' journeys through the health system were represented by "patient journey mappings" in order to visualise healthcare professionals (HCP) encountered over time.

Results: Twenty-one participants were included (12 men), with a mean age of 65 years old (SD:9; min-max: 45-86) from October 2020 to July 2021. Seventy-five interviews were conducted with a mean duration of 41 minutes (SD:11). During the two months following discharge, participants had 230 cumulative encounters with HCP, such as pharmacists, general practitioners (GP), home nurses, specialized physicians (e.g. diabetologists) and other HCP (e.g. physiotherapists) and 5 patients were rehospitalized. The pharmacist was the first HCP encountered by participants. Every patient saw at least once their pharmacist and 16 at least once their GP. Planning ambulatory care prior to discharge, interprofessional collaboration, help of informal caregivers and trust in known HCP allowed the patient to better navigate the health system. Other factors such as time-consuming organization of different appointments, fragmentation of care, lack of communication between HCP and contradictory information from different HCP were perceived by patients as barriers to continuity of care.

Conclusion: Upon discharge, patients have multiple encounters with several HCP and physicians have a central role for ensuring continuity of prescription. Other HCP, such as pharmacists, are easily accessible to patients and contribute actively to insure a safe medication use. Participants paid attention to care coordination and interprofessional communication, which are known to reduce patient burden and ensure patient safety.

P110

Facilitating the use of clinical data for research: building a data dictionary at a university-affiliated tertiary hospital in Switzerland

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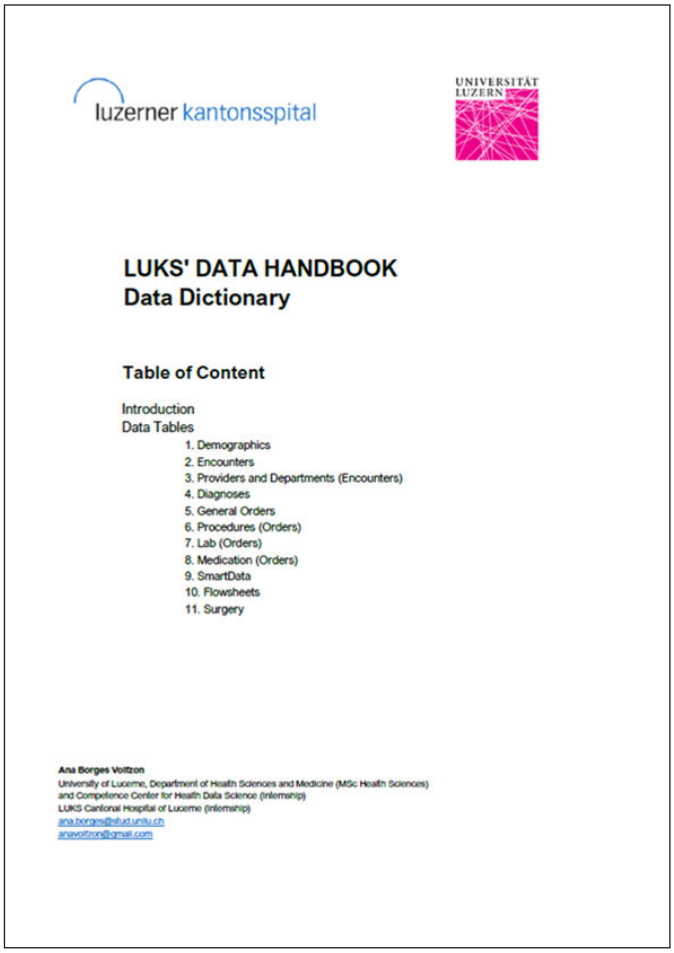
Introduction: The amount of data routinely generated in healthcare institutions is huge and continually growing (1). This is also the case at the Luzerner Kantonsspital (LUKS), a university-affiliated tertiary referral hospital. Its modern and complex information systems generate and store clinical, laboratory, imaging, and administrative data. Thus, physicians and researchers may not know the details and the extension of this comprehensive database. Aiming this issue, a data dictionary was built, in order to serve as a "menu" of the most used and relevant data for clinical research. This will facilitate and expand the use of hospital data for research.

Methods: Based on the national (2) and international literature (3) and the expertise of the Business Intelligence (BI) team, more than 3'000 variables were pre-selected to be analyzed. Each variable was carefully evaluated in terms of its relevance and quality of data. The selected variables were thematically organized and edited in order to provide an easy and efficient usage experience by researchers.

Results: The product generated is the LUKS' Data Handbook, a document containing the most useful data from LUKS Clinical Information System (LUKiS, by Epic). The 423 variables are displayed in 11 thematic lists of variables: Demographics, Encounters, Providers/Departments, Diagnoses, General Orders, Procedures, Lab, Medication, SmartData, Flowsheets, and Surgery. For each variable, an intuitive description of its content and its type are also displayed. Healthcare providers and researchers can consult the document in order to better understand the structure of the data available in LUKiS as well as sharpen the selection of variables suitable for their research.

Conclusion: The LUKS Data Handbook is an essential tool for physicians and researchers that want to use clinical data for research purposes. By facilitating and expanding the selection and use of data, it also foments research in the healthcare sector, which is usually very focused and engaged in the health assistance mission. The processes are also replicable by other healthcare institutions, and the data directory can be built based on one's own research interests and needs. In the context of educational healthcare institutions, like university-affiliated hospitals, this product is especially useful and significant by being an educational research incentive.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LUKS' DATA HANDBOOK
Data Dictionary

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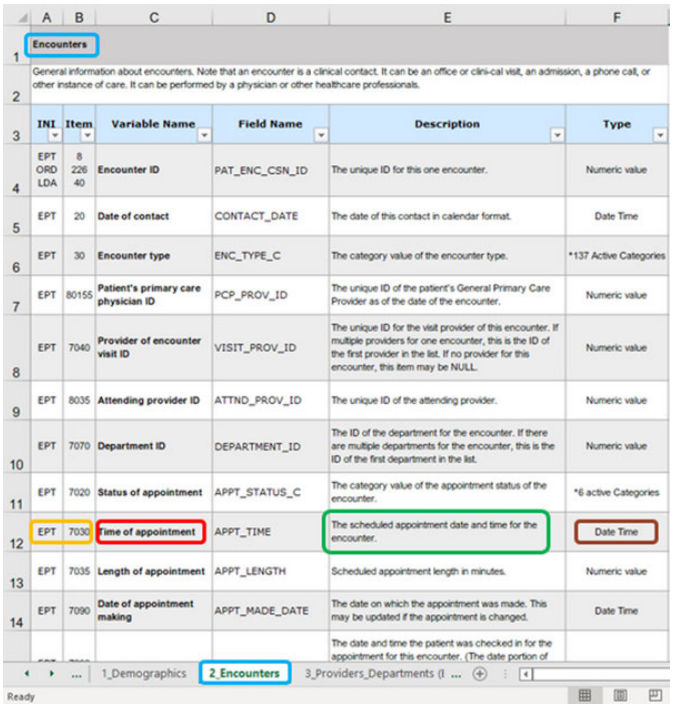
Encounters

General information about encounters. Note that an encounter is a clinical contact. It can be an office or clini-cal visit, an admission, a phone call, or other instance of care. It can be performed by a physician or other healthcare professionals.

INI	Item	Variable Name	Field Name	Description	Type
EPT ORD LDA	8 226 40	Encounter ID	PAT_ENC_CSN_ID	The unique ID for this one encounter.	Numeric value
EPT	20	Date of contact	CONTACT_DATE	The date of this contact in calendar format.	Date Time
EPT	30	Encounter type	ENC_TYPE_C	The category value of the encounter type.	*137 Active Categories
EPT	80155	Patient's primary care physician ID	PCP_PROV_ID	The unique ID of the patient's General Primary Care Provider as of the date of the encounter.	Numeric value
EPT	7040	Provider of encounter visit ID	VISIT_PROV_ID	The unique ID for the visit provider of this encounter. If multiple providers for one encounter, this is the ID of the first provider in the list. If no provider for this encounter, this item may be NULL.	Numeric value
EPT	8035	Attending provider ID	ATTND_PROV_ID	The unique ID of the attending provider.	Numeric value
EPT	7070	Department ID	DEPARTMENT_ID	The ID of the department for the encounter. If there are multiple departments for the encounter, this is the ID of the first department in the list.	Numeric value
EPT	7020	Status of appointment	APPT_STATUS_C	The category value of the appointment status of the encounter.	*6 active Categories
EPT	7030	Time of appointment	APPT_TIME	The scheduled appointment date and time for the encounter.	Date Time
EPT	7035	Length of appointment	APPT_LENGTH	Scheduled appointment length in minutes.	Numeric value
EPT	7090	Date of appointment making	APPT_MADE_DATE	The date on which the appointment was made. This may be updated if the appointment is changed.	Date Time
				The date and time the patient was checked in for the appointment for this encounter. (The date portion of	

1_Demographics | 2_Encounters | 3_Providers_Departments (I ...

Ready

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Telemedicine follow-up at hospital discharge, a solution to support transition care: the HH x SAT pilot project

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Introduction: Transition care after hospitalization is a vulnerable period for patients. A Swiss study shows that less than half of the patients (47.8%) feel ready for discharge (1). Once at home, they are at risk of clinical deterioration and may have difficulties reaching for medical advice.
In May 2022, the HH x SAT project brings together inpatient and outpatient services of the Geneva University Hospitals (HUG) and Geneva's main home care provider **imad**. It aims to use telemedicine during hospital-home transition to facilitate discharge for patients with semi-acute care without indication for rehabilitation, permit earlier discharge for patients with acute treatment but without the need of the hospital technical platform, and support coordination with home nurses and primary care providers (PCP).

Methods: The telemedicine team was composed of 6 primary care physicians from the HUG, having access to the electronic health record. During the hospitalization, patients were identified by inpatient physicians and "patient itinerary manager" (IPM). A first appointment was scheduled for the telemedicine team, with a delay individually assessed. During the first appointment, the need of telemedicine follow-up and its intensity was also assessed with the patient, the home nurses and the PCP. The HH x SAT project also included an on-call service for home nurses, 7/7 from 11am to 7 pm.
Data was collected prospectively by IPM and physicians.

Results: During the first 6 months, 151 patients were included in the HH x SAT follow-up, for a total of 316 scheduled consultations. Internal medicine was the main provider (60.2%), followed by geriatrics (22%). Patients had a mean age of 75 years and 48.8% were women. Main diagnosis were very diverse. 10 re-hospitalizations (6.6%) included 2 "impossible home care" and 4 led to a rehabilitation stay. Most patients had 1 or 2 telemedicine consultations. 90 calls from home nurses were managed. 1 led to an emergency referral, and 65.6% were subsequently referred to their PCP. 131 days of hospitalization were spared. Overall financial report including spared hospitalization days was positive.

Conclusion: A telemedicine consultation with a team of primary care providers having access to the electronic patient record is a promising solution to secure the hospital-home transition, support home nurses and patients, and coordinate care with outpatient structures including PCP. More information on its impact on quality of care is needed.

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The use of chatbots in medicine: the post-COVID experience

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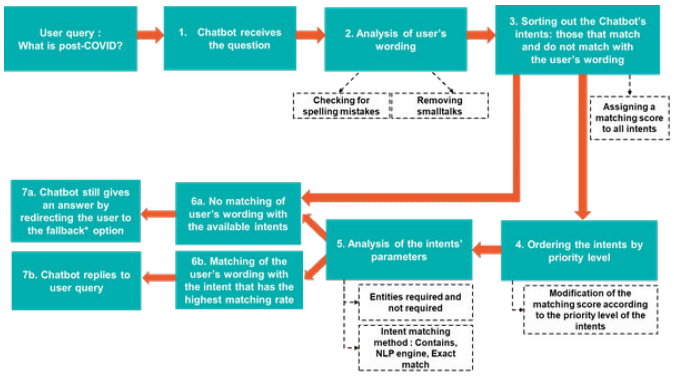
Introduction: Post-COVID condition has now affected millions of individuals, resulting in fatigue, neurocognitive symptoms and an impact on daily life (1). The past few years have seen an increase in online misinformation in general, and more specifically around post-COVID given the little knowledge on this disease to date (2). The RAFAEL platform (https://rafael-postcovid.ch) is an ecosystem addressing post-COVID condition, integrating online information, webinars and chatbot technology to answer to a large number of individuals in a time-limited and resources-limited setting. Chatbots have been used in some chronic conditions but mostly for research purposes and not in clinical settings (3). We describe here the development, deployment and use of RAFAEL to address emerging and chronic conditions, with easy access to verified information and a limited use of resources.

Methods: The RAFAEL online platform and chatbot were developed in Geneva, by primary care, pediatric and communication experts in collaboration with patients. The specific strategy behind the RAFAEL Chatbot balanced an accessible interactive approach with medical safety, aiming to relay correct and verified information in the management of post-COVID condition. The use of the chatbot technology and the answers provided were monitored by community moderators and healthcare professionals, creating a safe fallback for users.

Results: To date, the chatbot has had 23'438 interactions, with 71.4% matching rate and 72.7% positive feedback rate. Overall, 4'549 unique users interacted with the chatbot with 5.1 interactions/user, and 6'836 stories triggered. User queries included questions about post-COVID symptoms (66.5%), of which fatigue was the most predominant query (22.9% of symptoms-related stories). Additional queries included questions about consultations (6.5%), treatment (6.2%), and general information (6.3%).

Conclusion: The RAFAEL Chatbot was the first Chatbot developed to address post-COVID condition in children and adults. Its innovation lies in the use of a scalable tool to disseminate verified information in a time- and resources-limited environment. The use of machine-learning helps professionals gain knowledge about a new condition while addressing patients' concerns. Lessons learned from RAFAEL will further encourage a participative approach to learning, and could potentially be applied to other chronic conditions.

Fig 1. RAFAEL chatbot algorithm and pathway



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A case of *Malaria tertiana* caused by *Plasmodium vivax* – an example of how climate change is affecting the outbreak of infectious diseases?

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Learning objectives: As a result of climate change and humanitarian crises, health practitioners worldwide are facing growing incidences of infectious diseases such as malaria. Practitioners need to become acquainted with the epidemiology of malaria endemic regions, clinical and diagnostic implications, and specific treatments for the different *Plasmodium* species.

Case: A 19-year-old Afghan refugee fled to Switzerland by air, after a 10-day interim stay in Pakistan. Ten months later he experienced fever, flu-like symptoms and myalgia. On his second visit to the general practitioner, the patient was referred to the local hospital where he tested positive for malaria. Hospital admission followed due to high fever, hemodynamic instability and difficulty swallowing medication. Further evaluation revealed thrombocytopenia, hemolysis and splenomegaly. The Giemsa blood smear showed parasitemia of 1%, with microscopy confirming Plasmodium vivax. Clinical improvement occurred within 24 hours after artesunate therapy, enabling a treatment with chloroquine. After five days, parasitemia was no longer detected. Since *P. vivax* can cause relapses, adding primaquine is essential. Symptoms improved quickly and the patient recovered fully within one month.

Discussion: Malaria should be suspected in patients with fever and a travel history to endemic regions. *Malaria tropica* (*P. falciparum)* occurs mainly in sub-Saharan Africa, within one month after exposure. In contrast, *M. tertiana (P. vivax and ovale)* is prevalent in the Indian subcontinent and can develop months after transmission. Although *P. vivax* is regarded as a "milder" variant, our patient developed severe *M. tertiana* after a 10-month incubation

period and initial delay in diagnosis. Since Afghanistan and Pakistan are endemic for *P. vivax*, our patient could have contracted malaria in either country. In recent years, the Indian subcontinent has been hit by extreme weather conditions, linked to climate change. Pakistan, has been deluged by flooding, consecutively from 2020 to 2022. This has led to the expansion of breeding grounds for the *Anopheles* mosquito and outbreaks of *M. tertiana*. Afghanistan is also facing a humanitarian crisis with migration to adjourning countries like Pakistan and beyond. Primary care physicians can expect to see a rise in malaria cases from this region.

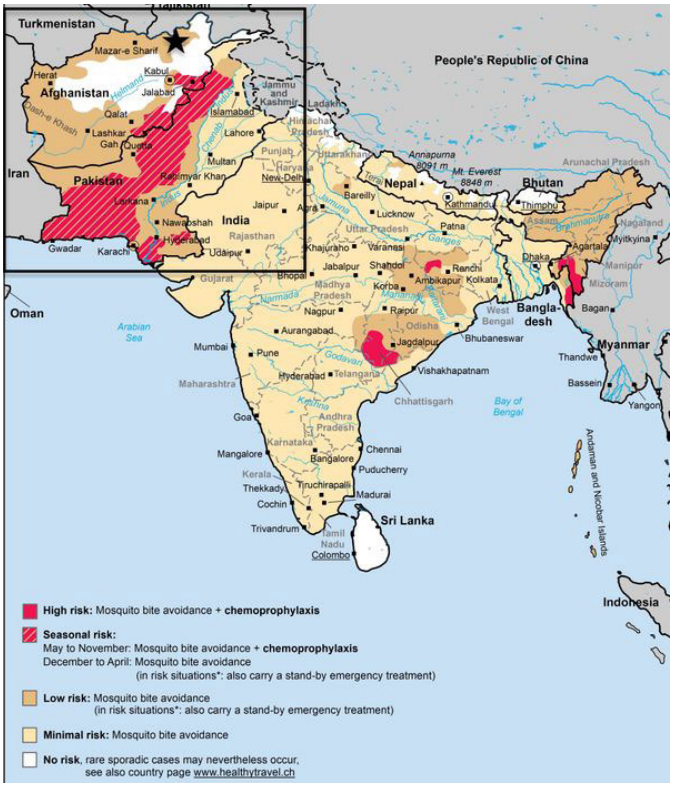

Figure 1. Malaria map of South Asia. box = region of interest

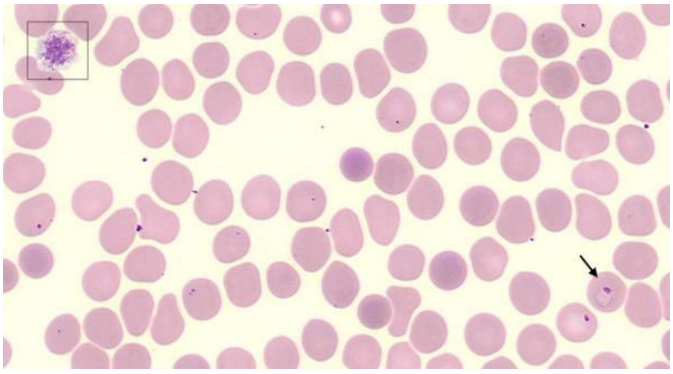

Figure 2. Giemsa smear of P. vivax. arrow = trophozoite; box = schizont

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Addiction to fossil fuels: what is the physician's role to address this very common disorder?

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Introduction: Addiction to fossil fuels has been framed by scholars as a key driver in environmental changes. It involves more than 99% of people living in Western Europe. Whereas it is not included in the ICD11 or in the DSM5 of mental disorders, it shares many similarities with drug and alcohol use disorders. Among other, it involves maladaptative psychological patterns, and the risk of harming others. This study aims at describing these analogies, understanding how physicians perceive them, and what role they think they have in addressing this very common disorder.

Method: We conducted a multimodal data collection. We first conducted a literature review whose results were discussed in a focus group with a panel of general practitioners. Moreover, we used a questionnaire to explore knowledge, attitudes and practices, and proposed solutions implementable in clinical setting among physicians and nurses in our hospital.

Results: The literature review has been completed and dozens of references have been selected. The results of the focus group and the questionnaire are expected in March 2023.

Conclusions: We found that there is little doubt in the general and medical literature about the fact that addiction to fossil fuels is a concrete and concerning health issue, yet insufficiently addressed in clinical setting. We are currently exploring the various reasons to explain this mismatch and defining the best ways of integrating this issue with patients.

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Choosing greenly: a multidisciplinary, champion-based approach for reducing the environmental impact of healthcare

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Natural environmental is a key determinant for human health. Climate change and other environmental deterioration represent a major threat to global health with potentially severe social and economic consequences. The interplay of climate change and health is bidirectional as the healthcare sector is a major contributor to greenhouse gases (GHG) emissions in addition to be at the frontline to mitigate its impact. Health institutions and professionnals are expected to endorse a leading role in the transition towards a carbon neutral society. We present here a project aiming at reducing GHG emission in a large Swiss Hospital.

Method: Choosing Greenly is an interdisciplinary and project whose main purpose is to curb the carbon footprint of Geneva University Hospitals (HUG) toward a Net-Zero pathway. It takes place in various clinical settings. It includes the following work packages: a) educational and motivational interventions to build up capacities and foster an institutional culture of ecoresponsible healthcare delivery run by champions within interprofessional teams at an institutional level; b) transition in anesthetic gases use to implement GHG neutral practices; c) reduction in water and energy use related to hemodialysis; d) targeted use of energy-costly investigations in emergency setting. Specialists in lifecycle analysis and behavioral changes will partner healthcare professionals in the implementation of these interventions.

Results: We expect to deliver the following outputs: 1) information to all of the 7'500 healthcare professionals about the links between human activities, environmental change, and health; 2) 15% reduction in energy use and GHG emission related to healthcare delivery in the pilot units; and 3) integration of environmental dimensions in new clinical guidelines production.

Conclusions: Adding to interventions on non-clinical aspects (mobility, building, purchase policies, etc.), this project aims to stimulate healthcare professionals and hospitals leadership in ecoresponsible service delivery to contribute to the urgently needed global effort at the whole-of-society level.

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Anxiety and adherence to preventive measures: evolution of citizen reactions during the COVID-19 pandemic

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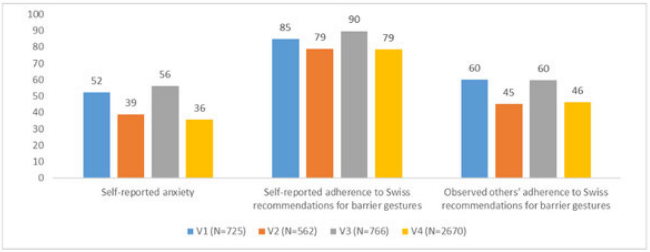
Background: Good communication between health authorities and citizens is key for the impact of preventive measures during a pandemic. As anxiety can influence communication, we aimed to evaluate associations between anxiety levels in the population and their respect of Swiss federal preventive measures during the COVID-19 pandemic.

Methods: Observational study of four cross-sectional online surveys of a convenience sample of adults in the Canton of Vaud, Switzerland. Questionnaires were distributed through social media and websites during four periods: version (V) 1) 17.04-14.05.2020; V2) 15.05-22.06.2020; V3) 30.10-2.12.2020; and V4) 18.06-30.12.2021. Participants reported anxiety, self-adherence to pandemic measures and their observation of others' adherence. We used multivariable logistic regression to assess associations and the influence of demographic factors.

Results: After exclusion of 2383 questionnaires (incomplete, age <18 years, residence outside Vaud), we analyzed data from 4723 participants. Their mean age was 47 years and 64% were women. Mean anxiety across the 4 periods was 42 on a scale of 0-100. It was significantly higher in women and during periods 1) and 3) (corresponding to peaks in COVID-19 incidence). Federal recommendations were also better followed (self-reported and observed) at those times (Fig. 1). A 2.9-point increase in the anxiety score was associated with a 10-point increase in the personal adherence score after adjusting for period, gender, age, education, and health literacy (p<0.001).

Conclusion: Higher anxiety levels during the Covid-19 pandemic were associated with increased self-reported and observed adherence to federal recommendations. Authorities should take into account population anxiety levels in the planning and design of pandemic communication. Adapting communication to population subgroups should be considered for future health crises.

Fig. 1 Canton Vaud citizens' self-evaluation of anxiety and adherence to federal recommendations during different phases of the Covid-19 pandemic



Participants were asked to scale their answers from 0 to 100. We report the mean value of their answers. V1-4: version 1-4 of the survey.

Exact wording of questions:

Self-reported anxiety: To what extent do you feel anxious about the new Covid-19 virus? *From not at all (0) to very anxious (100).*

Self-reported adherence to Swiss recommendations for barrier gestures: How closely have you followed the Swiss federal recommendations regarding barrier gestures in public places when in contact with strangers? *From not at all (0) to in all situations (100).*

Observed others' adherence to Swiss recommendations for barrier gestures: To what extent did you find that other people followed the Swiss federal recommendations regarding barrier gestures in public places? *From not at all (0) to in all situations (100).*

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Digital interventions for psychiatry in Switzerland: clinicians' perspective on promises and ethical challenges of eHealth

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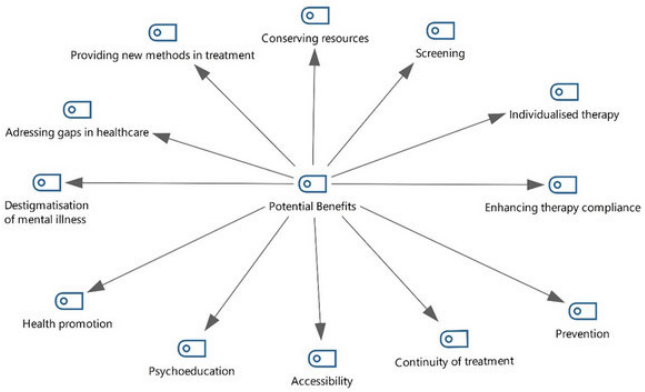
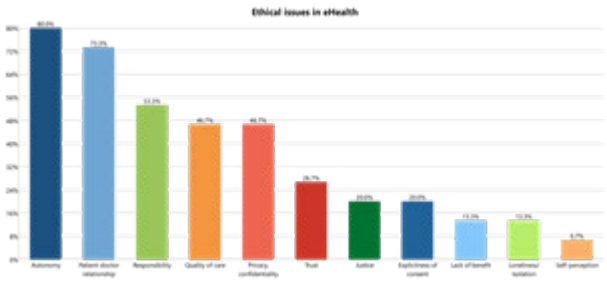
Introduction: Recent decade is an explosion of digital technology for mental health.The technology has been developed on a large scale from messaging chat bots to virtual realities, from direct-to consumer apps to fully integrated in the clinical care tools.

Methods: A semi-structured interviews with mental health practitioners (senior-level psychiatrists or clinical psychologists) working in of teaching hospitals in Switzerland were conducted from March 2019 to April 2020.The interview guide featuring open-ended questions.All interviews were conducted until data saturation was reached(N=20).The interviews lasted for 35–55 minutes each and were audio-recorded.The anonymized transcripts were imported into the qualitative data analysis management software MAXQDA. The usual standards for qualitative analysis in medicine were applied to the content analysis.

Results: This study examined experiences with the use of health apps among mental health specialists in Switzerland.While many people use health apps, a substantial portion of mental health specialists do not use digital technologies with their patients.Only 40% of responders, however, had not used mHealth apps. Our participants reported their use of diverse digital technologies and discussed the potential of such technologies in healthcare (Fig1).Common reasons for not using such technologies included the lack of evidence, the lack of legal and clinical recommendations, the incompatibility of the apps with clinical needs due to their design, the high costs of research and technical development and the lack of support for technology implementation.The main ethical issues which were identified are shown below (Fig2).

Conclusion: eHealth technologies raise a panoply of ethical dilemmas and practical obstacles in the medical practice.They are increasingly empowering patients to initiate, participate, and guide their own care as well as to manage their own medical data. Although an important goal of the emerging technology is to promote the patient autonomy, some caution is warranted in light of how these severe and persistent mental illnesses may adversely impact the clinician/caregiver-patient relationship.To overcome the existing obstacles, interviewees highlighted the demand for a great deal of reorganization, which must be implemented in accordance with the principles of biomedical ethics.





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A case of a „2:1 lock-in phenomenon" due to mode switching failure in a dual-chamber pacemaker

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Learning objectives: The "2:1 lock-in phenomenon" occurs due to an automatic mode switch (MS) failure during atrial flutter in patients with an implanted dual-chamber pacemaker. Diagnosis is confirmed by device interrogation. In this rare phenomenon where every second atrial event is falling in the post ventricular atrial blanking period (pVAB) due to a synchronous atrial flutter cycle. This malrecognition of the atrial events results in the failure of mode switch and therefore rapid ventricular pacing leading to palpitations and even tachycardia induced cardiomyopathy.

Case: A 88-year old women with a history of sick-sinus syndrome and an implanted DDD pacemaker presented to the emergency room (ER) with palpitations since a few hours. The initial 12-lead electrocardiogram (ECG) showed an atrial flutter with intrinsic 2:1 conduction (as seen in figure 1). Blood analysis showed mildly elevated troponin with no significant change after 2 hours and normal standard laboratory test including TSH . During the emergency stay the patients ECG changed to broad complex tachykardia (as seen in figure 2). The following pacemaker interrogation showed the correct diagnosis of the so called "2:1 lock-in phenomenon" with rapid ventricular pacing. An anticoagulation was established as well as an anti-arrhythmic therapy with beta-blocker, under which conversion into sinus rhythm could be archieved. Changes of pacemaker programming where evaluated by the cardiologist in a follow up consultation.

Discussion: We show a case of the 2:1 lock-in phenomenon seen on a 12-channel ECG with simultaneous documentation at device interrogation confirming the diagnosis. To avoid this kind of detection failure programming changes to enhance the chance of flutter detection are necessary. Most of the current pacemaker models provide special device algorithms for '2:1 lock-in' recognition and a termination. It is important to recognise this kind of mode switching failure in order to avoid severe heart failure in case of persistent tachykardia.

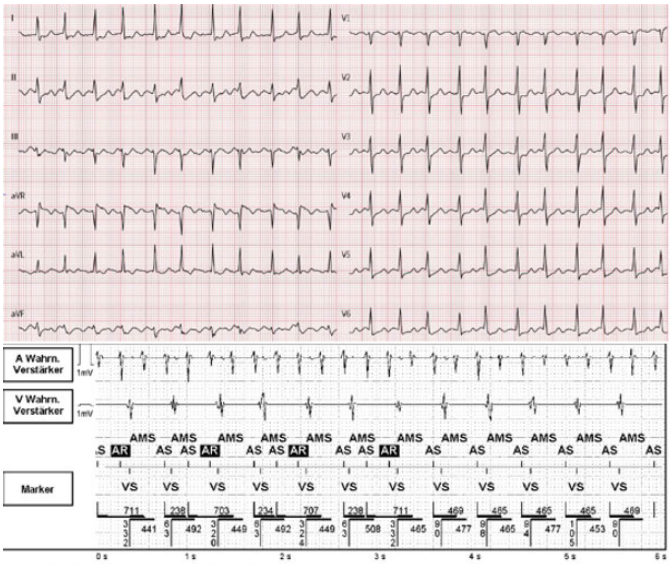

Figure 1: Atrial flutter on a 12-channel ECG with pacemaker interrogation below sensing the tachycardia and conducting mode switch

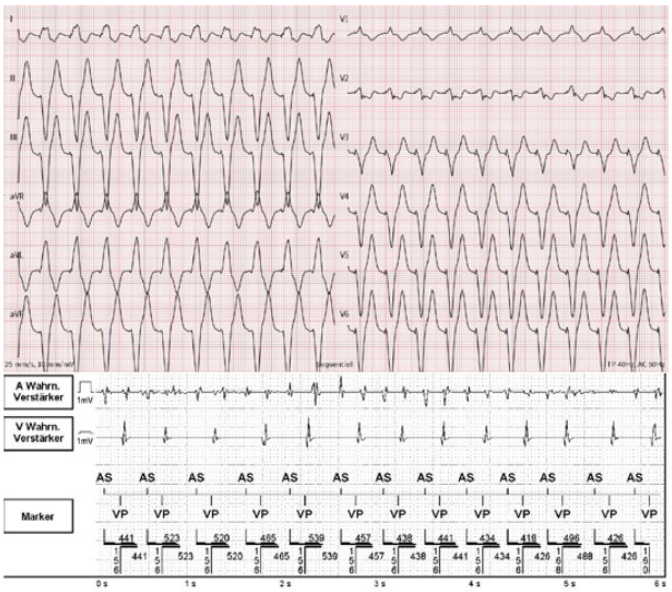

Figure 2: 12-channel ECG showing ventricular pacing with pacemaker interrogation below showing 2:1 lock-in phenomenon

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A case of COVID-19 associated secondary sclerosing cholangitis

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Learning objects: Secondary sclerosing cholangitis in critically ill patients (SSC-CIP), even though being a rare entity, is an important differential diagnosis of cholestasis in ICU patients, particularly when cholestasis persists after recovery from the critical event. We are now observing cases of COVID-19 patients developing SSC during ICU treatment. The outcome of SSC-CIP is poor because it can rapidly progress to cirrhosis. Liver transplantation should be discussed in an early stage of the disease. The optimal therapeutic strategy for this disease remains unclear.

Case: A 69 year old man was hospitalized in our ICU with a Covid-19 pneumonia associated ARDS and the need for long term ventilation and vasopressor support. During intensive care he developed a cholestasis (hyperbilirubinemia of 59 µmol/L, ALP 1161 U/L, GGT 1055 U/L. ASAT 99 U/L and ALAT 138 U/L) which persisted after recovering from the infection without any pre-existing liver disease. Abdominal ultrasonography showed only cholecystolithiasis without signs of inflammation and no further pathologic findings. Laboratory tests for underlying causes (autoimmune or acute viral hepatitis A-E, primary biliary cirrhosis, hemochromatosis, or alpha-1 antitrypsin deficiency, acute EBV, CMV, Lues or HIV infection) didn't show pathological results. The MRCP showed irregular intrahepatic bile ducts with a beaded appearance. SSC-CIP was suspected - a rare complication which can occur in ICU patients. Pathogenesis is believed to involve ischemic injury of intrahepatic bile ducts associated with prolonged hypotension and mechanical ventilation. A treatment with ursodeoxycholic-acid and cholestyramine was established as the patient was suffering from pruritus. In the following two years he was hospitalized three times with cholangitis (with E. coli and E. faecalis found in blood cultures) which was treated with antibiotics. ERCP with papillotomy, extraction of so-called biliary casts and balloon dilatation was performed. Despite this intervention he developed liver cirrhosis. Now liver transplantation will be discussed.

Discussion: Further studies are needed to understand if there is a direct causal role of the SARSCoV-2 virus in COVID-19-associated SSC-CIP. A liver transplantation should be considered in all patients with SSC-CIP with rapidly progressive hepatic fibrosis and liver failure. The outcome of liver transplantation for COVID-19-associated SSC-CIP though remains to be determined.

P120

A case of paraneoplastic Lambert-Eaton myasthenic syndrome in limited disease small cell lung cancer

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Learning objectives: The Lambert-Eaton myasthenic syndrome (LEMS) is a rare auto-immune disorder of neuromuscular junction transmission. The pathogenesis is based on paraneoplastic or idiopathic generation of autoantibodies directed against the presynaptic voltage-gated calcium channels (VGCC) leading to their inactivation, inhibition of acetylcholine release with subsequently muscle weakness. Some tumors, especially small cell lung cancer (SCLC), express the VGCC on their surface, which can trigger the production of anti-VGCC-antibodies.

Case: A previously healthy 60-year old woman was referred for the evaluation of worsening proximal muscle weakness in her legs and a dry mouth for about 4 months. Neurological examination revealed symmetrical paresis of the upper and lower extremities (M3-4), weak mastication, pronounced dysarthria as well as extinguished deep tendon reflexes. There was no ataxia, nor were there alterations in sensation, consciousness or cognition. Further work-up showed reduced CMAPamplitude in the ENMG. Spinal and cerebral MRI were normal. The titers for VGCC- and onconeural antibodies were elevated and a diagnosis of LEMS was made. Computertomography revealed a large pulmonary tumor mass with extensive mediastinal lymph node metastasis in this patient with a smoking history of 30 pack-years. Bronchoscopy confirmed the suspicion of small-cell lung cancer. A diagnosis of limited-disease SCLC (LD-SCLC) was retained and curative-intent chemoradiotherapy was started. The patient's LEMS was treated with high dose corticosteroids and amiframpidine, a potassium channel blocker, with rapid improvement of symptoms. After completion of chemoradiotherapy, 4 weeks of physical rehabilitation and tapering of prednisone, the patient had regained independence in activities of daily life. One month after completion of radiotherapy, restaging showed a subtotal regression of the tumor manifestations and titers of autoantibodies had returned to normal. Weaning of amiframpidine and regular follow-up of the SCLC is ongoing.

Discussion: We present a case of paraneoplastic LEMS in a patient with LD-SCLC. Proximal muscle weakness, autonomic dysfunction and extinguished muscle reflexes in combination with positive anti- VGCC-antibodies and characteristic ENMG findings are typical features of LEMS. The treatment is tumor-oriented, immunosuppressive and symptomatic. It can lead to rapid improvement and often to complete resolution of the LEMS symptoms.

P121

A case of severe symptomatic hyponatremia due to a possible incipient adrenal crisis in a patient with immune checkpoint-inhibitor induced hypophysitis

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Learning objectives: To recognize an incipient adrenal crisis without concurrent hypotension in a patient with severe symptomatic hyponatremia.

Case: A 72-year-old woman presented to the emergency department with a history of malaise and diarrhoea for about a week. On admission, she was confused with GCS 14. Blood pressure at admission was 136/56 mmHg and heart rate was 86/min, temperature 36,5°C.
Medical history was significant for an immune checkpoint inhibitor-induced hypophysitis with secondary adrenal failure and thyrotropic deficiency after receiving treatment with nivolumab and ipilimumab for a metastatic melanoma. Medication included 20 mg hydrocortisone and 50 mcg levothyroxin daily.
A CT head ruled out an acute cerebral haemorrhage. Blood chemistry revealed an undetectably low serum sodium (< 100 mmol/l) and a serum osmolality of 214 mosm/l. Unfortunately, cortisol levels were not assessed at admission. A severe symptomatic hypoosmolar hyponatremia was diagnosed and an infusion of saline 3% was started. Concurrently, clinically suspecting an incipient addison crisis, 100 mg hydrocortisone was administered intravenously as a bolus followed by 50mg every 6 hours. fT4 was within normal range (11.5 pmol/l) and oral levothyroxine was continued at the usual dose.
The patient was admitted to an intensive care unit (ICU). The infusion therapy was continued with saline 0,9%, later switched to a balanced solution and eventually to a glucose 5%-solution due to a rapidly rising sodium-value. When additionally polyuria ocurred, a treatment with desmopressin intravenously was started. The therapy with hydrocortisone was tapered off during the course of the ICU stay. After 4 days, patient was transferred to a medical ward with a serum sodium of 125 mmol/l. After 7 days on a medical ward, she was released from the hospital with a serum sodium of 131 mmol/l and a complete resolution of the neurological symptoms.

Discussion: We describe a case of a severe symptomatic hyponatremia due to a possible incipient adrenal crisis precipitated by an acute viral infection and failure to increase the oral hydrocortisone therapy according to sick day rules in a patient with immune checkpoint-inhibitor induced hypophysitis. In this situation, the early recognition of an incipient adrenal crisis with normal blood pressure and initiation of an adequate intravenous high dose therapy with hydrocortison can prevent the development of a fulminant adrenal crisis with hypotension.

P122

A dangerous two-hit event in a young man

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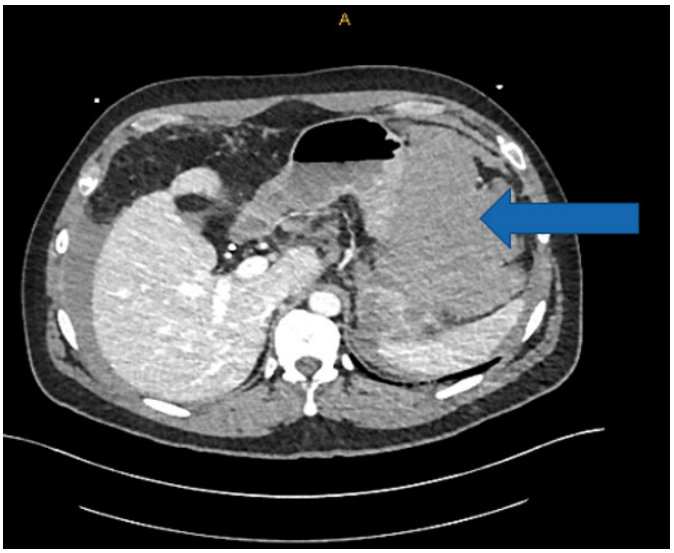
Learning objectives: Splenic artery aneurysm (SAA) is a rare but life-threatening condition as it has a definite risk of rupture.

Case: A 39-years old man was referred to our emergency room with acute onset of abdominal pain, syncope and paresthesia of the right arm. Apart from slight anemia (Hb 99g/l) and leukocytosis (11.4 $x10^9$/l) all other standard emergency parameters were normal. Only Troponin T (high sensitive) was elevated at 63ng/l. However, ECG was inconspicuous. Emergency CT scan ruled out pulmonary embolism, aortic dissection, active bleeding or intestinal organ perforation. However, it showed a large mass associated to the stomach and a partially thrombotic aneurysm of the splenic artery with no signs of active bleeding (Fig.). Tentative diagnoses were a Gastrointestinal stroma tumor (GIST), Mucosa associated lymphoid tissue (MALT-) Lymphoma or Hematoma. From the personal history it was known that he had intolerance to certain food ingredients and recurrent pain in the stomach region. A prior CT scan performed for an uncomplicated pancreatitis one year before showed no abnormalities. A biopsy and gastroscopy with endosonography were scheduled for the next working day to confirm the diagnosis of a potential tumor. Around 30 hours after an uneventful surveillance the patient had a seizure and went hypotonous and tachycard. Due to instable hemodynamic conditions and drop of Hb to 45g/l despite massive catecholamine use and volume management the patient underwent immediate emergency laparotomy with splenectomy and ligature of the splenic artery. After 10 days he was able to be released and was in good condition in a 3-months follow-up control.

Discussion: A symptomatic SAA has a high risk of rupture. It can present with hypovolemic shock and acute abdomen. In our case it was clinically and radiographically challenging as the new detected mass was initially interpreted as a tumorous lesion associated to the stomach. Together with the known stomach pain, intolerance to certain foods (e.g. gluten) and the initial possible GIST or (MALT-)lymphoma our thinking and clinical approach was biased towards tumor diagnostic. Retrospectively, it is hypothesized that the patient suffered from a post-pancreatitic SAA that had ruptured twice. The large mass must be considered retrospectively as a hematoma that might have compressed and stopped bleeding from the first rupture (first hit). The second hit (re-rupture) then led to hemorrhagic shock.



Hyperdense Mass

P123

A different presentation of Tubulointerstitial Nephritis and Uveitis syndrome (TINU) mimicking of Sjögren's syndrome

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Learning Objectives: Tubulointerstitial nephritis (TIN) and uveitis syndrome (TINU) is an uncommon disease identified mainly by two entities specified in its name: TIN and uveitis[1]. This reported TINU case with overlap of symptoms with Sjögren's disease underlines that TINU might have different clinical features. This report also points out a new perspective on approaches in uncommon clinical presentations of patients with oculo-renal involvement.

Case: A 55-year-old female patient was referred to our rheumatology clinic. In the first evaluation; she reported dry eyes and mouth; she also had a history of idiopathic unilateral anterior uveitis. After seeing an increased creatinine level (2.64 mg/dL), we consulted the case with the nephrology unit. 24 Hour urine collection revealed 848 mg proteinuria per day. Ophthalmologic examination revealed anterior uveitis. Schirmer test and Tear Break Up Time Test confirmed dryness in both eyes. Rheumatologic findings, proteinuria and increasing creatinine levels necessitated a renal biopsy which revealed TIN with eosinophilic infiltration. Furthermore, salivary gland biopsy was performed which didn't show any specific findings. Anti-SSA and anti-SSB were negative in the extractable nuclear antigen (ENA) panel. After ruling out differential diagnoses, TINU syndrome was left over, as a diagnosis of exclusion. We commenced prednisolone with a dose of 0.5 mg/kg/day. ESR normalized after two weeks and creatinine levels dropped. Uveitis went into remission.

Discussion: This case demonstrated an uncommon clinical presentation compared to other TINU cases, due to sicca symptoms. There is only one reported case in which a patient was presented with sicca symptoms and diagnosed with TINU syndrome. [2] In the diagnostic approach to TINU syndrome; exclusion of diseases such as sarcoidosis and Sjögren's disease is necessary since oculo-renal involvement might be seen in the course of these diseases. Although Sjögren's disease might be suspected in this patient with sicca symptoms, salivary gland biopsy and the ENA panel were not compatible with Sjögren's. As there was no granuloma formation in the kidney biopsy, TIN could not be attributed to sarcoidosis or Sjögren's disease. Fluorodeoxyglucose positron emission tomography also ruled out sarcoidosis. Negative direct immunofluorescence and normal serum complement levels ruled out Lupus and IgG4-related disease. Drug related TIN was unlikely as she had no drug history.

P124

A first case of locally prepared enteral tube feeding in Xiengkhouang Provincial Hospital in Laos

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Learning objective: In patients who are unable to eat sufficiently due to e.g. endotracheal intubation or dysphagia, without gastrointestinal obstruction, enteral nutrition through a nasogastric tube is indicated. Swiss projects can help to achieve one of the World Health Organization`s goal to eliminate all forms of malnutrition. Kantonsspital Winterthur (KSW) supports its partnership hospital, Xiengkhouang Provincial Hospital (XKHPH) in Lao PDR, to implement enteral tube feeding with formula made of local food products.

Case: A previously healthy, unvaccinated 40-year old man was hospitalized for generalized tetanus at the intensive care unit (ICU) of XKHPH. He suffered from frequent attacks of painful all-body muscle spasms, rigidity of jaw and neck as well as difficulties with swallowing which prohibited adequate food intake. Supportive treatment was started with morphine and high dose diazepam, given intravenously and through a nasogastric tube. Compromized breathing and an unsecured airway led to intubation and mechanical ventilation on the second day. Initially, following local habit, sugared water was administered through the nasogastric tube to `feed` the patient. We asked the family to buy food products at the market place (bananas, eggs, tofu, coconut milk, Figure 1). The ICU nurses subsequently prepared the enteral tube formula from these local products according to a recipe previously developed by the Division of Clinical Nutrition and the hospital dietary kitchen of KSW (Figure 2). On the third day, we could start with the tube feeding, slowly increasing the volume of each bolus over the next 24 hours. Unfortunately, our patient died 4 days after admission to the ICU due to progressive multiorgan failure.

Discussion: Because of limited financial resources at XKHPH, artificially produced enteral tube feeding is too expensive to use in standard medical care. Therefore, a nutrition project has been initiated by its partnership hospital KSW. In this project, the family of the patient is involved to buy the nutritional ingredients for enteral tube feeding and the medical staff is trained to coordinate the process and prepare the tube feeding.

KSW Kantonsspital Winterthur

ອາຫານເສີມສຳລັບສົ່ງທາງທໍ່ກະເພາະ ສຳລັບຜູ້ໃຫຍ່ 750 ml
Sondennahrung Laos für Erwachsene = 750ml

ສ່ວນປະສົມ:

112 gr / 6 ບ່ວງແກງ	ຖົ່ວດິນ (ບ່ວງແກງກ້ານສັ້ນ)
487 gr / 9 ½ ບ່ວງແກງ	ນ້ຳກະທິໝາກພ້າວ
75 gr / 1 ໜ່ວຍໃຫຍ່	ໝາກກ້ວຍ
90 gr / 1 ½ ໜ່ວຍປານກາງ	ໝາກນາວ
225 gr / 4 ໜ່ວຍໃຫຍ່	ໄຂ່ໄກ່
75 gr / ½ ຈອກ	ນ້ຳ
7.5 gr / 1 ບ່ວງແກງ	ນ້ຳມັນແກ່ນດອກຕາເວັນ/ ນ້ຳມັນພືດ
75 gr / 2 ½ ບ່ວງແກງ	ເຕົາຫູ້ / ເຕົາຮວຍ

ການກະກຽມ:

- ປີ້ນໝາກນາວ ເອົານ້ຳ
- ທຸບໄຂ່ຜິດໃສ່ໃນຖ້ວຍ.
- ປອກໝາກກ້ວຍ ແລະຕັດເປັນຕ່ອນໜາປະມານ 2 ນິ້ວມື.

ການປຸງແຕ່ງ:

- ຂົ້ວໄຂ່ໃສ່ໝໍ້ຂ້ວງໝຸງແຕ່ໃຫ້ສຸກ ແຕ່ບໍ່ໃຫ້ຂົ້ວດິນ, ບໍ່ໃສ່ນ້ຳມັນ ຫຼືເອົາໄຂ່ດິບໃສ່ເລີຍ ຖ້າສົດ.
- ເອົາສ່ວນປະສົມທັ້ງໝົດໃສ່ເຄື່ອງປັ່ນນຳກັນ ແລ້ວປັ່ນໃຫ້ລະອຽດ, ຫລັງຈາກນັ້ນ ໃຫ້ຕອງ.
- ໃຫ້ອາຫານປະສົມນີ້ແກ່ຄົນເຈັບທາງທໍ່ກະເພາະ ຫລືໃຫ້ຕົ້ມເອງກໍ່ໄດ້.

Figure 1. Laotic recipe of local ingredients for enteral tube feeding

Swiss-Lao Hospital Partnership
Xiengkhouang Provincial Hospital-Kantonsspital Winterthur

Nasogastric tube feeding adults

Patients 1

food item	amount in gram	Energy in kcal pro 100g	Total Energy in kcal	Protein pro 100g	Proteine caloric value in kcal (1g/4kcal)	Fats pro 100g	Fats caloric value in kcal (1g/9kcal)	Carbohydrates pro 100g	Carbohydrates caloric value in kcal (1g/4kcal)
sunflower oil	1	899	8.99	0.00	0.00	99.90	8.99	0.00	0.00
coconut milk	65	214	139.10	2.00	5.20	23.00	134.55	3.00	7.80
banana	10	94	9.40	1.00	0.40	0.00	0.00	23.00	9.20
lemon juice	12	21	2.52	0.00	0.00	0.00	0.00	6.00	2.88
fresh eggs	30	161	48.30	13.00	15.60	11.00	29.70	1.00	1.20
peanuts	15	601	90.15	26.00	15.60	48.50	65.48	11.20	6.72
water	10	0	0.00	0.00	0.00	0.00	0.00	0.00	0.00
tofu	10	81	8.10	8.10	3.20	4.80	0.70		0.00
			0	0.00	0.00		0.00		0.00
			0	0.00	0.00		0.00		0.00
			0	0.00	0.00		0.00		0.00
			0	0.00	0.00		0.00		0.00
			0	0.00	0.00		0.00		0.00
Total	153		306.56		40.01		239.42		27.80
daily calory need of adult at 1000 mg/d			100.0%		13.06%		78.10%		9.07%
					total g Protein		total g Fts		total g Carbohydrates
					10.01		26.60		6.95

Preparation: Mix all ingredients	amount in g (=ml)	total calories in kCal	Protein in g	Fats in g	Carbohydrates in g
	1	2.00	0.07	0.17	0.09
	10	20	0.65	1.74	1.82
	50	100	3.27	8.69	9.12
	100	200	6.54	17.39	18.24
	150	301	9.81	26.08	27.35
	200	401	13.08	34.77	36.47
	250	501	16.36	43.47	45.59
	300	601	19.63	52.16	54.71
	350	701	22.90	60.85	63.83
	400	801	26.17	69.55	72.95
	450	902	29.44	78.24	82.06
	500	1002	32.71	86.93	91.18

Figure 2. Enteral tube formula

P125

A painful handshake!

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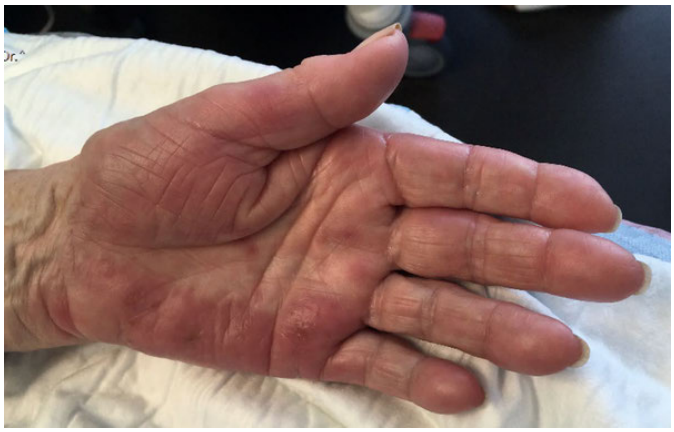
Learning objectives: Herpes simplex virus type 1 (HSV-1) infection has a high prevalence of about 66% of the population worldwide. Primary infection occurs mostly in childhood through the orolabial mucosa and results in chronic infection in sensory ganglia. Although HSV-1 infection can be variable, e. g. herpes keratitis, disseminated disease in neonate, meningitis and herpes simplex encephalitis, the cutaneous manifestation as cold sores and eczema herpeticum is most common.

Case: We report the case of a 79-year-old woman who presented with fatigue, dry cough and very painful pruritic palmoplantar papulo-erythematous exanthema for about 2 weeks. She had no relevant past medical history or medication use. In particular, there was no history of atopic disease, only a nickel allergy was known. Skin examination showed furthermore hyperthermic, pressure-dolent small vesicles mainly on both palms, less extensive plantar without other mucocutaneous or conjunctival involvement. Laboratory results revealed an elevated CRP (125 mg/l), a mild normocytic anemia and thrombocytosis without other significant findings. SARS-Cov2-PCR-test was negative and a chest radiograph showed no pneumonia. The increased CRP and the general symptoms resolved spontaneously within 3 days, so that we interpreted these signs and symptoms in the context of a viral upper respiratory tract infection. As the skin findings persisted, further dermatologic examination was performed. Blood results showed no evidence for HIV, syphilis, thyroid dysfunction or zinc deficiency. The clinical suspicion of subacute eczema was confirmed histologically. In addition, a HSV-1 superinfection was detected by PCR swab. We started a peroral antiviral therapy with valacyclovir 500mg twice daily for 10 days and moisturizing skin care. The eczema showed improvement without lichenification, infiltration or recurrence.

Discussion: In the present case we see a patient with a viral respiratory tract infection and consecutive HSV-1 reactivation presenting as palmoplantar eczema herpeticum. Differential diagnosis include subacute eczema with HSV-1 superinfection, which seems less likely because of the absence of any eczema prior to the viral respiratory tract infection. In case of recurrent HSV-1 infections or severe courses, immunodeficiency disorders should be excluded.



Palmar exanthema with vesicles

P126

A rare case of paraneoplastic opsoclonus-myoclonus syndrome

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Learning Objectives: Opsoclonus-myoclonus syndrome is a rare neurologic disorder with a typical clinical presentation. Etiology is usually paraneoplastic or, in rare cases, due to infectious diseases. Diagnosis is usually made clinically, but can be assisted by serological testing and liquor analysis (CSF) in selected cases. Treatment is experimental and difficult. Prognosis is still unknown.

Case: A 64 year old female patient presented to the emergency room with a history of nausea and emesis for one week. Upon presentation, the patient was afebrile, in reduced general condition, but neurologically inconspicuous. The patient history showed a small cell lung cancer (SCLC) in remission, diagnosed one year ago for which she underwent a radio-chemotherapy 8 months ago. A chest CT Scan one month ago showed no signs of recurrence. A MRI neurocranium scan revealed no signs of metastases. 5 days later the patient presented a new bilateral rapid ocular flatter, 7 days later myocloni of upper and lower extremities.
After ruling out an infection of the neurocranium by CSF analysis, **a paraneoplastic opsoclonus-myoclonus** syndrome was assumed, with typical positive Hu-antibodies in serum; these remained negative in CSF. An additive PET-CT showed no local recurrence, but a positive signal of the right ovary. High-dose steroid therapy and symptomatic therapy with clonazepam were started and the patient was transferred to University Hospital Zurich for IVIG and plasmapheresis, which could not be started due to the poor patient`s general condition, leading to regionalization to Winterthur Cantonal Hospital, where she underwent right ovariectomy, where SCLC was detected histologically. Furthermore, despite negative PET/CT results, wedge resection of the previous cancer site was performed, in hope of removing any possible subclinical recurrence. However, histology showed no malignancy. The patient soon showed further deterioration, palliative chemotherapy was initiated.

Discussion: Paraneoplastic syndromes are very rare. After exclusion of an infection, the presence of an underlying malignancy must be assumed until disproven. The clinical syndrome may precede the tumor diagnosis by years. Treatment is similar to the tumor treatment and is often difficult with an uncertain prognosis.

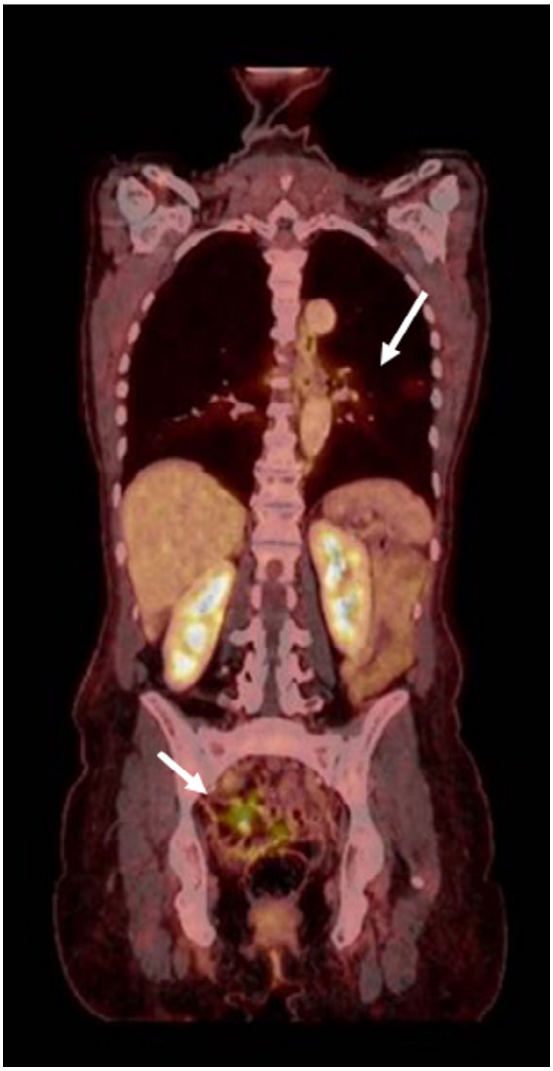

Figure 1: No recurrence of radiated SCLC in left anterior lower lobe, suspect lesion in right ovar PET/CT

Liquor	Unit	Upper normal limit	Value upon presentation
Macroscopy			clear
Leuc-mononucl.	µl	<5	**20***
Leuc-polynucl.	µl	<5	1
Protein	mg/l	120 - 600	595
Glucose	nmol/l	2.5- 3.9	3.1
Lactat	nmol/l	0.6-2.2	1.7
Gram staining			no bacteria
Hu-antibody	Titer	<100	<100
Ri-antibody	Titer	<100	<100

Table 1: liquor analysis, * isolated mononucleosis

P127

A rare cause of B symptoms

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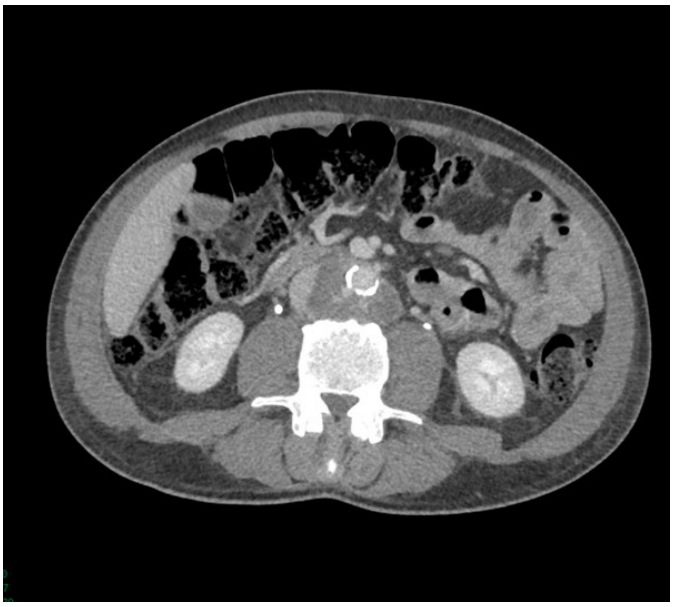
Learning objective: Complicative course of salmonella infection.

Case: Referral by a general practitioner of a 65-year-old male with known Diabetes type 2 and arterial hypertension because of severely reduced general condition since 1 month, B symptoms, lumbar back pain and occasionally diarrhea. He presented with pain on percussion over the flanks. Laboratory revealed elevated inflammatory markers (CRP 153 mg/L, leukocytosis 12.3 G/L). Urine analysis was normal. CT scan showed an infrarenal mass with arrosion of the aortic wall with multiple covered perforation sites. Blood cultures and stool samples showed salmonella typhimurium. The findings were interpreted as salmonella aortitis with dorsal rupture of a mycotic aneurysm. Emergency resection and debridement of the lesion and aortic reconstruction were performed. Intraoperative bacteriology confirmed salmonella species. After 2 weeks on intravenous antibiotic therapy (ceftriaxone) the patient could be discharged and therapy could be switched to oral ciprofloxacine for a total of 12 weeks.

Discussion: Our case presents salmonella bacteremia with aortitis as a rare cause of B symptoms. Globally salmonellae are common pathogens for food poisoning. In Switzerland, there are 1200 to 1500 notifiable salmonellosis per year. Salmonella can be differentiated as S. typhi/paratyphi and non-typhoidal salmonellae (NTS) as e.g. S. typhimurium. Typically, NTS gastroenteritis occurs 8 to 72 hours after exposure, but less than 1% of NTS enteritides result in bacteremia. The prognosis is influenced by host risk factors (age, immunosuppression, recent antibiotic therapy) and by Salmonella serotype. Endovascular infections (especially in atherosclerotic vessels) may occur in up to 20% of patients with Salmonella bacteremia.
Our patient had B symptoms and lower back pain. Gastroenteritic symptoms were absent at the time of presentation, which is not typical for salmonellosis and made the diagnosis challenging. B symptoms can be considered in context of bacteremia and back pain corresponds to the mycotic aneurysm. Bacterial translocation occurred probably on a previously low symptomatic enteritis. As risk factors the patient had Diabetes mellitus and moderate atherosclerosis.
Although the term "B symptoms" originates from lymphoma diagnostics (and the mass in the CT in our case was firstly interpreted as lymphoma), our case shows that there are other causes.



Perforation site and infrarenal mass on computet tomography

P128

A rare cause of nonbacterial thrombotic endocarditis - marantic endocarditis

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Learning objectives: Nonbacterial thrombotic endocarditis, Marantic endocarditis.

Case: 61 year-old woman was admitted with out of hospital cardiac arrest because of massive pulmonary embolism, and treatment with ECMO was initiated. PET-CT scan identified a tumor of the ovary and the ovary tube (Figure 2), and there were signs of peritoneal carcinosis. Due to the general condition of the patient surgery could not be performed, and rehabilitation was started.
In the rehabilitation clinic the patient suffered a stroke, and echocardiography showed endocarditis of the aortic valve (Figure 3). MRI of the head revealed multiple emboli. However, blood cultures remained negative, and the antibiotic therapy with ceftriaxone was stopped, and the diagnosis of marantic endocarditis was considered. Further complication was thrombocytopenia due to disseminated intravascular coagulation, treatment with heparin was initiated. In general consent with the patient and er family palliative comfort therapy was initiated, and the patients died on day 26 of hospitalization.

Discussion: Patients with cancer are in a hypercoagulable state, and nonbacterial thrombotic endocarditis was first described by Ziegler in 1888 (1), and identified in 1954 by Angrist and Marquiss as systemic embolization associated to malignancy (2, 3). The vegetations in marantic endocarditis consist of degenerative platelets interwoven with strands of fibrin. Therefore, the vegetations are superficial and the underlying valve shows normal tissue, or only subtle histological evidence of abnormal collagen and elastic fibers. The pathogenesis is not fully understood, and most patients are in their fourth and eighth decades of life. The prevalence is estimated between 0.9 to 1.6% in autopsy series. The diagnosis of marantic endocarditis is challenging because there are no pathognomic signs or symptoms. Transesophageal echocardiography is the gold standard for detecting marantic endocarditis.
The treatment of marantic endocarditis is to treat the underlying tumor and the DIC. For the DIC the preferred agent is heparin. Vitamin K antagonist should not be used in this condition. Although, prognosis is depending on the underlying tumor, in most cases it is very poor.

P129

A rare cause of reversible painless vision loss

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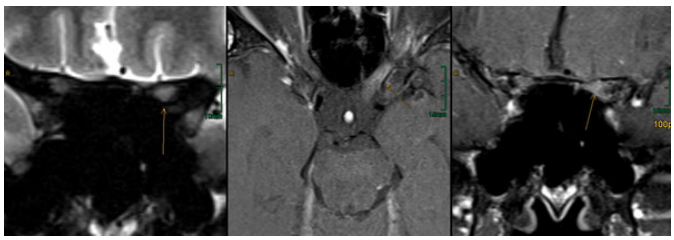
Learning objectives: To recognize neurosarcoidosis as a rare, but potentially reversible cause of painless vision loss.

Case: A 49-years old woman presented to our emergency department with left sided monocular vision loss. The ophthalmologic examination revealed bilateral panuveitis and papillitis. Both did not fully explain the complete vision loss.
A Computer tomography scan to rule out a stroke or left-sided carotid artery pathology was unremarkable but accidentally found mediastinal and hilar lymphadenopathy suspicious for sarcoidosis or lymphoma. The clinical and laboratory findings were not suggestive for a giant cell arteritis. Cerebro-spinal fluid analysis showed a moderate macrophagic pleocytosis with slightly elevated lactate and total protein and slightly reduced glucose quotient. Oligoclonal bands were negative, but the immunoglobulin-quotient was pathological. (An empirical antiviral and antibiotic therapy to treat a potential meningitis and could be stopped after negative viral and microbiological work-up). Polymerase Chain Reaction for Mycobacterium tuberculosis was repeatedly negative in sputum culture. Anti-**M**yelin **O**logodendrocyte **G**lykoprotein (MOG)- and anti-**N**euro**m**eyeltis **op**tica (NMO)-antibodies were negative, too. A brain Magnetic resonance imaging (MRI) scan confirmed a florid optic neuritis (figure 1). Already on the day after initiation of intravenous high-dose methylprednisolone vision started to improve. At dismissal, the patient reported a normalized visual function. A per-oral steroid tapering scheme over a 6 months period was proposed.
A biopsy of the pathological lymph nodes showed epithelioid granulomas (figure 2) without signs of malignancy. Serum Neopterin and sIL2-receptor were increased, 25-OH vitamin D was severely decreased. Most likely diagnosis was therefore neurosarcoidosis.

Discussion: Neuro-sarcoidosis is a rare extra-thoracic manifestation of sarcoidosis. Involvement of the central nervous system and especially cranial nerves is frequent (II, VII, VIII). The diagnosis of neurosarcoidosis is based on the clinical, laboratory, radiological and histopathological findings. Acute treatment consists in steroids and eventually plasmapheresis in resistant cases. The course of the disease can be monophasic, but immune-suppressing drugs are needed in case of steroid-dependency.

Fig 1: MRI inflammation of left optical nerve (arrow)



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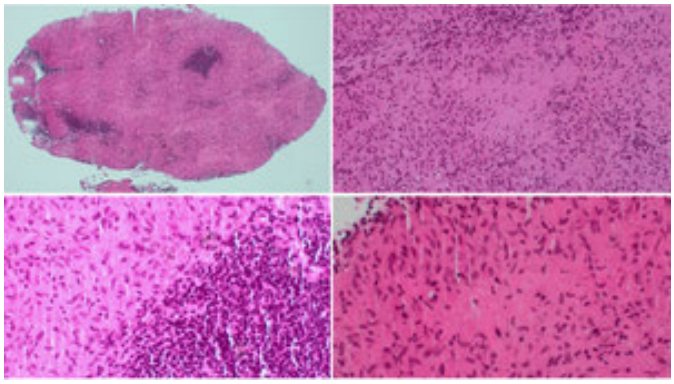

Fig 2: Lymph node with epitheloid cell granuloma (stain H&E)

P130

Always trust the patient's history and examination: a false positive hair ethylglucuronide dosage in a dialysed alcohol abstinent patient with a high vinegar intake

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Learning objective: To remember that laboratory tests can be misleading with important clinical consequences.

Case: A 48 years old man was referred for alcohol evaluation, because of a positive hair Ethyl Glucuronide (ETG) sample (more than 600 pg/mg) 1 month after a mixed liver and kidney transplantation. His medical history included a hepatic liver cirrhosis from metabolic syndrome and alcohol toxicity, a dialyzed renal insufficiency, and a tuberculosis treated for 9 months before and after transplantation. Before it, he underwent the usual evaluation, including a full substance use and psychiatric assessment. He met the criteria of alcohol abstinence for more than 6 months, having no unstable psychiatric disease and a supportive social environment (married with 2 children). He had been an excessive drinker, without criteria of alcohol dependence and had been able 3 years ago to stop his consumption within a few weeks without help, medication or withdrawal symptoms.
The transplantation team became preoccupied because of the GGT elevation and high ETG result. They suspected a relapse to alcohol use, challenging the declarations of the patient and his wife.
The clinical evaluation showed no symptoms or signs of alcohol use (facial erythema, hypertension, breathanalysis), and the patient and his wife explained he was doing well, abstinent from alcohol. A precise dietary history allowed to find an important daily ingestion of white wine vinegar at about 1 tablespoon per day (14.8 ml). The second hair ETG level 3 months after transplantation was at 517 pg/mg, the third 6 months after was negative.

Discussion: We concluded that the patient was abstinent, having no clinical argument to think otherwise and that the ETG dosage was not compatible with the patient and relative's history, nor with the normal clinical examination, and was an exceptional false positive. Still, the patient and the specialist were constantly challenged by the transplantation team. Hair ETG has been found in literature to accumulate in case of advanced renal insufficiency[1]. As even so source of ethanol should exist to create ETG. The patient's diet was found to contain uncommon vinegar quantity, that we hypothesize to explain that.[2] The favourable evolution, and the discussion between the addiction and the transplantation team made that the latter was reassured about the patient's abstinence. This was very important since the patient felt unfairly accused and stigmatized.[3]

P131

Amlodipine-induced hyponatremia and cholestasis: a case report with a review of the literature and of pharmacovigilance registries

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Learning objectives: Amlodipine is a safe drug commonly used in the treatment of hypertension with only very rare and severe side effects reported (1). Here it is described an unusual case of two rare side effects induced by amlodipine: hyponatremia and cholestasis. In fact, according to the World Health Organization pharmacovigilance registries, only 338 (0.3%) cases of hyponatremia and 256 (0.2%) cases of biliary disorders out of a total of 106,937 side effects have been reported up until now (2).

Case: A 91-year-old Caucasian Swiss woman known for hypertension, osteoporosis and chronic cholestasis of unknown origin, treated with monthly ibandronate 150mg and daily amlodipine 10mg, aspirin 100mg, metoprolol 25mg and calcimagon D3®, was admitted to the hospital on May 23rd 2022 in order to be submitted to a kyphoplasty of an osteoporotic L5 vertebral fracture. At admission, blood analysis showed sodium levels at 118mmol/L and osmolality at 246mosmol/kg. The urine analysis showed sodium at 21mmol/L and osmolality at 240mosmol/kg. Since the patient was asymptomatic, euvolemic, with no signs of organ dysfunction, the patient was diagnosed with hyponatremia due to the syndrome of inappropriate ADH secretion (SIADH) and put on water restriction. The following days, the sodium levels improved. Patient was discharged on June 9th 2022 and on her first outpatient appointment, the patient presented high levels of gamma-GT 550U/L and of alkaline phosphatase 199 U/L and normal transaminase and sodium levels. As the patient also presented unexplainable lower limb edema, amlodipine was considered as a possible cause and was therefore stopped. The following days, the leg edema resolved as well as the liver enzymes. Fluid restriction was progressively decreased and eventually stopped as the sodium levels remained normal.

Discussion: Amlodipine works as an anti-hypertensive drug by inhibiting calcium channels leading to peripheral vasodilation, but it can also act as a diuretic by having a sodium depleting effect in the kidneys, increasing the risk of hyponatremia (3). The mechanism responsible for the SIADH is not clearly understood. As to amlodipine hepatotoxicity, it can occur as cholestasis or transaminitis, rarely mediated by one of its metabolites (4). Side effects can appear the following days up to several years later (4). In conclusion, even though a high clinical suspicion is needed, amlodipine must be considered as a rare cause of hyponatremia and cholestasis.

P132

Amoebiasis presenting as colitis and complicated appendicitis

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Learning objectives: Amoebic infections are increasingly found in returning travelers. Symptoms, if present, can range from mild diarrhea to severe colitis with bowel necrosis or extra intestinal manifestations.

Case: A 31-year cold woman presented with acute non-bloody diarrhea and persistent abdominal pain days after she travelled to Bhutan and India. Her medical history was uneventful. The pain was initially only associated with bowel movements, later constant in the lower right abdomen.
Clinical examination showed diffuse lower abdominal tenderness but no peritonitis. A gynecologic examination was unremarkable without signs of adnexitis and the cervical swab showed no STDs. Laboratory investigations showed hypokalemia and inflammation. An abdominal ultrasound, a confirmatory CT scan, und later an MRI, showed severe right sided colitis with typical signs of appendicitis and perityphlitic abscess. Conservative therapy with metronidazole and ceftriaxone was started. Surgery was delayed due to the massive intestinal inflammation und the risk of hemicolectomy and ileostomy thereafter. Due to the retrocecal location, CT-controlled drainage was not feasible.
The stool analysis revealed entamoeba histolytica and coli. As the inflammation and pain decreased, we switched from ceftriaxone to co-amoxicillin. After 10 days of metronidazole, we switched to paromomycin for endoluminal decolonization. Appendectomy is planned.

Discussion: This case shows a young, healthy woman with severe amoebic colitis and complicated appendicitis. The occurrence of both, colitis and appendicitis, could be a coincidence, however the appendicitis was more likely caused by amoebas also. Indeed the unanticipated histologic finding of amoebae in appendectomy samples has previously been reported. This case also illustrates, that delayed surgery is feasible even in the presence of perityphlitic abscess if the patient is clinically stable and shows no signs of peritonitis.

P133

Atropa belladonna intoxication: a case report

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Learning Objectives: Atropa belladonna intoxication leads to a central anticholinergic syndrome, presenting with mydriasis, tachycardia, hypertension, dry skin, confusion, agitation, hallucinations, and potentially coma. This is due to competitive inhibition of acetylcholine muscarinic receptors and, in higher doses, of the nicotinic acetylcholine receptors. **Physostigmine, an indirect parasympathomimetic** inhibiting acetylcholinesterase and thus increasing acetylcholine concentration in the synaptic cleft, **is used as the therapeutic measurement.**

Case: A 71-year-old retired chef presented to the emergency department with acute confusion after accidentally eating 10-15 deadly nightshades (Atropa belladonna) in the nearby forest. Clinically, he was subfebrile, slightly hypertonic, tachycardic, and showed a striking mydriasis and motor agitation. Laboratory tests did not reveal any abnormalities, nor did the blood gas analysis. Due to urinary retention an indwelling catheter was inserted. The patient described the complaints as lightning bolts shooting through his body.
After telephone consultation with the local toxicology centre, 1 mg of lorazepam and 0.5 mg of neostigmine were administered, under which a progression of the symptoms was documented, which is why the patient was transferred to the in-house intensive care unit. Here, cholinergic therapy with physostigmine and initially continuous sedation with midazolam and propofol were administered. In total, 48 hours of sedation were necessary with recurrent severe restlessness and great suffering of the patient. Suicidality was credibly denied, so that the patient could be discharged without residual symptoms after three days of monitoring.

Discussion: Atropa belladonna is a poisonous plant whose fruits, leaves, and roots contain alkaloids. This nightshade plant is found throughout Switzerland with a flowering period from July to August and is recognized by its shiny, black berries. **Acute poisoning, most often occurring in children, can lead to a severe, potentially deadly anticholinergic syndrome.** The lethal dose is not sufficiently clarified. Therapy includes both symptomatic treatment and administration of the antidote physostigmine.

organ	symptoms
brain	agitation, hallucinations, coma
eyes	mydriasis, glaucoma
skin	decreased sweat secretion, hot and red skin
mouth	dry mouth, decreased salivation
lungs	bronchial dilatation
heart	tachycardia, hypertonia
bladder	bladder atony
gastrointestinal tract	intestinal atony

Table 1: anticholinergic syndrome: organ dysfunction and symptoms

P134

Beri-Beri Heart Disease after bariatric surgery - a rare cause due to vitamin B1 deficiency

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Learning objectives: Beri-Beri Heart Disease, Bariatric Surgery, Heart Failure

Case: A 49 year-old woman presented with increasing dyspnea and orthopnea for 6 months. There was no history of infection or travelling. Echocardiography showed endomyocardial fibrosis with apical thrombosis (Figure 1), left atrial dilatation, and a restrictive diastolic pattern. A heart CT scan showed no signs for a coronary artery disease (Figure 2). Heart MRI examination confirmed endomyocardial fibrosis from the left apex to midventricular (Figure 3). Infectiology screening was negative, as was rheumatological examination. The patient had a history of cholecystectomy 1998, a gastric banding in 1997, a distal gastric bypass operation in 2004, and re-operation of the gastric bypass in 2012.
Therefore, we performed an extended lab examination, where low Vitamin A levels of 0.43 umol/l, low Vitamin C (31ug/l), and a low Vitamin B1 of 29 nmol/l were detected. Therefore, the diagnosis of severe Vitamin B1 deficiency was made (Beri-Beri Heart Disease), and after high-dose substitution the patient was discharged in good condition.
Discussion: Beri-Beri Heart Disease due to Vitamin B1 deficiency was first described in 1947 by Burwell and Dexter (1). Beri-Beri Heart Disease is a distinctive clinical entity that also includes right heart failure. There are two forms of Beri-Beri, the dry Beri-Beri and wet Beri-Beri. The dry one usually affects the nervous system, where the wet one affects the cardiovascular system.
A meta-analysis revealed that 27% of the patients undergoing bariatric surgery experienced a significant Vitamin B1 deficiency (2). Thamine is absorbed in the jejunum, and there is a reserve of 2 weeks. The cardiac symptoms of Beri-Beri heart disease are associated with normal left ventricular output. However, a restrictive pattern of the left ventricle can be seen leading to symptoms of left heart failure. Systolic murmurs are common. The ECG is usually normal as in our case. The most common rhythm disorder is atrial fibrillation. QRS complex remain most of the time normal. Treatment of Beri-Beri heart disease is similar to acute heart failure treatment combined to supplements with vitamin B1 (i.v. or i.m.) Undiagnosed Beri-Beri Heart Diseases has high mortality. Eric et al (3) described 72 deaths among 301 cases. The cardiac disease is completely reversible after substitution of vitamin B1. After 6 months of replacement of vitamin B1, no symptoms are seen in 80% of the cases.

P135

Better look twice: beware of hasty diagnosis of incomplete right bundle branch block

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Learning objective: Brugada syndrome (BrS) is a channelopathy with increased risk of ventricular tachycardia (VT) and sudden cardiac death (SCD). While diagnosis is easy in type 1 electrocardiogram (ECG) pattern it may be challenging in type 2 and 3 ECG pattern, resembling incomplete right bundle branch block (iRBBB).

Case: A 21-year-old healthy female was examined with ECG due to temporary rapid pulse a few days after COVID-19 booster vaccination. ECG showed sinus rhythm with heart rate of 76 b.p.m. and mild ECG changes suggestive of iRBBB (***Image 1A***). Medical and family history was negative and cardiac work-up (echocardiography, stress test) revealed normal findings. To exclude rare differential diagnosis of type 2 BrS ECG pattern (***Image 2***) additional flecainide provocation test (2 mg/kg) was performed, which showed transition to both J point and coved ST elevation (type 1 BrS ECG pattern, ***Image 1B***), thus diagnosis of BrS was made. Genetic screening could not detect BrS specific mutations. Prophylactic implantation of a cardioverter/defibrillator (ICD) was not indicated, but avoidance of certain drugs (see below), cocaine, cannabis and excessive alcohol intake was recommended, as well as treatment of fever with antipyretic drugs.

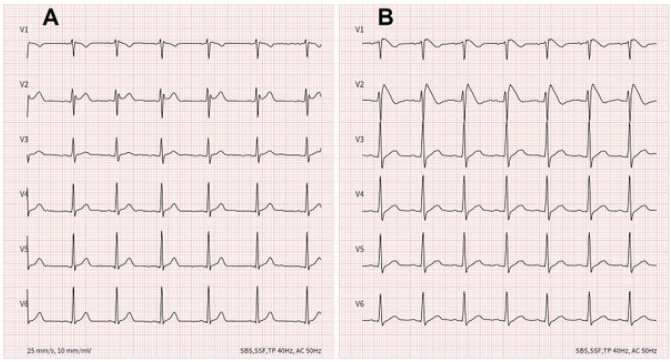

Image 1

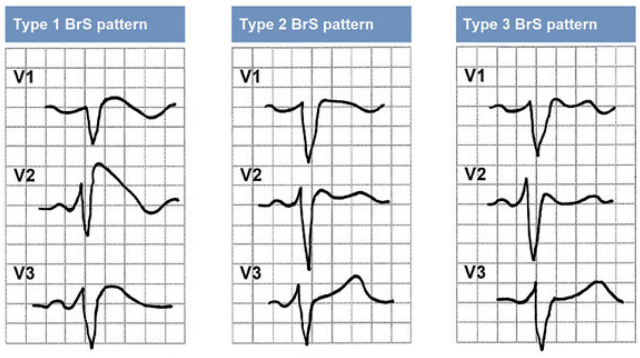

Image 2

Discussion: BrS is a channelopathy causing abnormal electrical activity of the heart leading to increased risk of VT and SCD. Diagnosis is made in symptomatic and asymptomatic patients without other heart disease with spontaneous type 1 ECG pattern (J point

elevation of > 2 mV with coved ST elevation and T wave inversion in at least one precordial ECG lead V1 or V2) or sodium channel-blocking drug or fever induced type 1 ECG pattern. Latest European guidelines recommend drug provocation test in the absence of spontaneous type 1 ECG pattern primarily in patients with documented VT, arrhythmic syncope, or positive family history. Genetic testing of BrS associated mutations (most frequently *SCN5A* gene loss-of-function mutation) is positive only in about 20% of patients. Treatment is avoidance of drugs that may induce ST-segment elevation (e.g., class I antiarrhythmic drugs, psychotropic drugs, and some anesthetics; see *brugadadrugs.org*) cocaine, cannabis and excessive alcohol consumption, and strict treatment of fever with antipyretic drugs. Implantation of an ICD is recommended in patients with BrS and survived cardiac arrest and/or documented spontaneous sustained VT. Regular monitor ECG follow-up is advised.

P136

Cefepime-associated encephalopathy on Outpatient Antibiotic Treatment (OPAT)

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Learning objectives: Cefepime is a fourth generation cephalosporin, active against *Pseudomonas aeruginosa*. Neurotoxicity including encephalopathy has been reported with cefepime use. There is little data for therapeutic drug monitoring during outpatient antibiotic treatment (OPAT) with cefepime.

Case: We report a 70-year-old man with an osteomyelitis of the ischium with *Pseudomonas aeruginosa* who was on OPAT with Cefepime 6 g/d for 5 weeks. He was admitted to the emergency department in a disoriented state with a fluctuating speech disorder. An elevated creatinine was noted, consistent with an acute on chronic renal failure. After exclusion of an acute ischemia or intracerebral hemorrhage by computed tomography and magnetic resonance imaging a cefepime intoxication aggravated by the acute on chronic kidney insufficiency was the most likely differential diagnosis. Further workup showed no epileptic activity in the electroencephalogram but a pattern of metabolic encephalopathy, consistent with the differential diagnosis. The diagnosis was confirmed by a markedly elevated serum cefepime concentration of 214 mg/L (proposed normal value during continuous infusion < 35 mg/L, normal through level < 20 mg/L). Hemodialysis was initiated leading to a rapid decline of the cefepime concentration (0.5 mg/L, after 72 hours). The patients› neurological symptoms improved in parallel gradually with a slight delay.

Discussion: Cefepime is used for treatment of *Pseudomonas aeruginosa* infections. Adverse reactions including encephalopathy, aphasia, myoclonus and nonconvulsive status epilepticus have been reported. The mechanism of neurotoxicity is not fully understood. Severe intoxication can occur, but there is no data on therapeutic drug monitoring during cefepime OPAT. Regular controls of the kidney function is warranted, particularly in elderly patients with preexisting renal insufficiency. Continuous veno-venous hemodialysis successfully eliminated cefepime and led to normalization of the neurological status of the patient.

P137

CYP3A4 inhibition and therapeutic drug monitoring of everolimus in a patient with CHAI-disease

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Learning objective: Effective immunosuppression with everolimus (EVE) in comedication with a CYP34A inhibitor requires therapeutic drug monitoring (TDM) with dose reduction at the start of comedication to avoid overdose, but also adequate dose escalation after discontinuation of the CYP34A inhibitor to avoid subtherapeutic concentrations with relapses of the underlying disease.

Case: A 33-year-old female patient with **CHAI**-disease (1), an autoimmune lymphoproliferative syndrome due to CTLA4 haplo-insufficiency with severe gastrointestinal, hematologic, immunologic, and dermatologic involvement was referred to our ward with a history of generalized exfoliative exanthema. The patient was immunosuppressed with glucocorticoids and EVE (therapeutic trough level (TL): 3-7ug/l), and comedicated with fluconazole (FCZ) for oral thrush and skin candidiasis. In order to prevent overdose at already supratherapeutic TL of 7.4ug/l, the daily EVE dose of 3.5 mg was reduced during FCZ comedication, leading to a TL of 2.5mg on the day of FCZ therapy cessation. Two days later, the patient was highly febrile, had elevated inflammatory parameters and progressive oedematous, erythematous and exfoliative skin on the upper extremities and face.
The TL was redetermined (again, with a lab delay of two days) and corresponded to the lowest norm with 3.0ug/l, which is why we assumed an inflammatory relapse of CHAI-disease in the context of subtherapeutic EVE concentrations. The adequate increase of EVE to control the dermatologic symptoms occurred shortly before transfer of the patient to the university hospital for the already planned potentially curative haemotopoietic stem cell transplantation for CHAI-disease.

Discussion: Immunosuppressed individuals without appropriate prophylaxis develop oropharyngeal candidiasis in 25-35% (2). CYP3A4-inhibiting drugs such as FCZ are often used for treatment in this setting and can lead to overdose and toxicity of comedicated substrates of CYP3A4, which include many immunosuppressants. Close TDM of the CYP3A4 substrate should not be limited to the time of initiation of comedication with a CYP3A4 inhibitor but is also essential during the phase of cessation of CYP3A4 inhibition, because CYP3A4 substrate levels may fall into the subtherapeutic range when CYP3A4 inhibition is discontinued. In our case, this led to a relapse of the severe underlying autoimmune disease.

P138

Fixation error in a patient with drug abuse history

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Learning objectives:
- In Patients with known drug abuse health care workers are in danger of cognitive bias leading to misdiagnosis and inadequate treatment that may be fatal for the patients outcome.
- In case of thyroid storm it is important to search for the underlying disease of hyperthryroidism as well as its trigger of exacerbation.

Case: We report the case of a 39-year-old patient brought to the emergency department at night by the ambulance service on suspicion of intoxication with LSD. A history of drug abuse is reported. The patient was confused and disoriented (GCS 13). He showed agitation and aggressive behaviour with psychotic symptoms, tachycardia and rattled breathing. A cranial computer tomography scan revealed no abnormalities. The patient was given sedative and antipsychotic medication and was admitted to the intensive care unit. Intubation was needed because of ventilatory failure. Next morning, a significantly decreased thyroid stimulation hormone was detected in the blood sample. By measuring significantly increased free thyroid hormone levels we diagnosed thyroid storm and therefore established therapy of hyperthyroidism.
Later the patient reported that he had already noticed increased sweating, restlessness and weight loss a few weeks earlier. By positive TRAK antibodies Graves hyperthyroidism could be confirmed as underlying condition. During the first days of ICU stay, the patient had a fever and we realized Janeway lesions. We assume that the endocarditis caused by staphylococcus aureus was the final trigger of thyroid storm.

Discussion: Thyroid storm is an acute life-threatening exacerbation of hyperthyroidism. It can occur spontaneously or be caused by factors such as severe illness, exposure to iodine or drug-induced. It is important that patients receive immediate intensive medical care. In our case, we were initially misled by the drug history, the report of the paramedics and relatives. This is called fixation error. It is important that you do not let yourself be biased by a history of drug abuse. If the diagnosis in this patient had not been made so early, the patients outcome could have been fatal.

P139

Flash news: Popeye is in jail? A puffy hand and feet syndrome case

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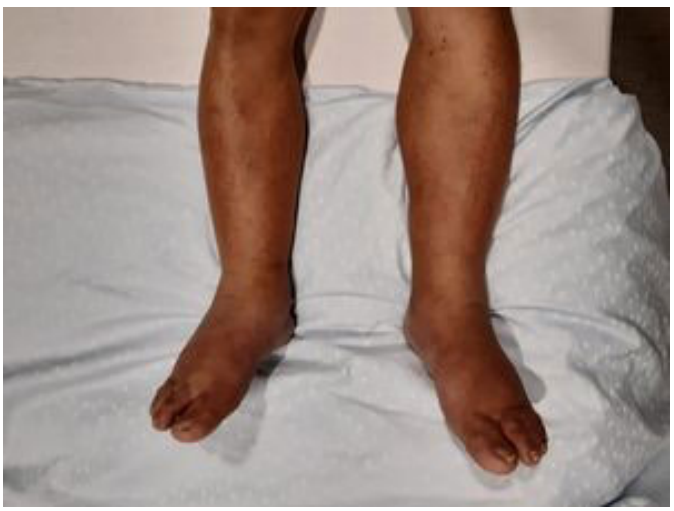
Learning objectives: differential of oedematous syndromes, cutaneous complications among intraveinous drug users

Case: 48 y.o male is admitted to prison medical unit in HUG for lower extremities oedema investigation. He presents with a first episode of isolated symmetric non pitting and painless oedematous syndrome, involving both limbs up to mild calves, and both dorsum of hands. He reports previous intravenous substance use (diacetylmorphine), last injection 4 months ago. He›s on opioid agonist therapy ever since. Injections sites preferences were in between fingers, toes, along palmar and plantar surfaces. He reports nodules in groin area from «old needle debris». He once heard from a fellow users he had « Popeye hands ». Extensive systematic history, physical examination and laboratory findings ruled out systemic causes of bilateral inferior limb oedema. No other causes of lymphatic obstruction or damages were found, except the recurrent injections. Duplex ultrasound examination revealed well perfused lower extremities and no deep veinous thrombosis. Transthoracic echography showed an healthy heart. Radiographic workup revealed 7 remains of needles, somehow, sparing vascular walls. We retained a puffy hand and feet syndrome. Giving the patient risk factors, we added screening for STDs and discussed immunization against HBV. We started compressive treatment allowing a modest effect on oedema.



Discussion: The puffy hand syndrome was first described in 1965, in USA in prison setting. Defined as a symmetric painless erythema and oedema of the hands in patients with a history of intravenous drug use. Expresses a lymphatic occlusion and progressive destruction by sclerosis causing chronic lymphedema. It's a clinical diagnosis, but diagnosis of exclusion and a rare chronic complication of intravenous substance use despite the cessation. It's an interesting clue for a patient's past or ongoing substance use, and to indentifiy other linked comorbidities. Management is symptomatic, there is no curative treatment. The prevalence of heroin users remains approximative since the population is hard to reach by statistical studies. In the 90's, estimation of 30 000 people dependant on heroin and/or cocaine. 0,7% population declare heroin consumption once in their lifetime. In swiss safe drug injection centres, 30% consume heroin, 20% of all users report iv consumptions of substances. Remember to shake hands with patient maybe the diagnosis lies (hides) in their hands!

P140

From bad to worse: Distributive shock after Cerebrolysin® and Actovegin® Infusion

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Learning objectives:
- Most common causes of distributive shock are sepsis and anaphylaxis. Less common causes include neurogenic shock due to spinal cord injury, endocrine disorders and adverse reactions to drugs and toxins.
- Careful history taking is the key in the diagnostic approach.

Case: A 22-year old female from the Ukraine was admitted to our hospital with fever, diarrhea and extensive vomiting. For treatment of severe migraine, she had received four off-label infusions of Actovegin® (calf blood extract) and Cerebrolysin® (neuropeptide) during the week before admission. Personal history was otherwise unremarkable.
Clinical examination revealed a hypotensive, tachycardic and febrile patient in distributive shock (SOFA Score 6 points). Laboratory studies showed thrombocytopenia (69G/L), neutrophilia (15.5G/L), elevated levels of C-reactive protein (135mg/L), acute renal injury (creatinin 192umol/L) and acute liver injury (INR 2, ASAT 385U/L, ALAT 269U/L, Bilirubin 23umol/L).
Suspecting a septic pattern in the context of severe gastroenteritis, fluid resuscitation, noradrenaline, empiric antibiotic therapy (ceftriaxone and metronidazole) and steroids were started and the patient was transferred to our intensive care unit. Computed tomography of the thorax and abdomen revealed no infectious focus. Blood, urine and stool cultures remained sterile. Viral testing was negative for CMV, EBV, HIV, HAV/HBV/HCV and SARS-CoV-2. Ultrasound of the liver including elastography was unremarkable. Thyroid and adrenal function were normal.
Vomiting and diarrhea stopped quickly and the patient reached hemodynamic stability within 24 hours. Antibiotic therapy was discontinued. Inflammation, platelet count, liver and renal markers normalized and the patient was discharged in good condition.
Since, despite intensive investigations, no other explanation could be identified, we strongly suspect a toxic reaction to the infusion of Cerebrolysin® and Actovegin®. Similar severe adverse reactions have been described previously (1-3).

Discussion:
- Careful history taking including the review of the patient's medications is of major importance, in particular in patients presenting with an unclear clinical picture.
- Although a neuroprotective effect of Cerebrolysin® and Actovegin® is under debate, no evidence supports their use for the treatment of migraine.

P141

Gas in the hip joint

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Learning objectives: Gas in the hip joint.

Case description: A 87-year-old woman was referred to the emergency room by the general practitioner for right hip pain without trauma. The pain was getting worse over the last two weeks, especially during movement. At last, the patient could not move herself without pain. There was no fever but a continual weight loss during the last month. There were no symptoms present for a respiratory or abdominal Infection. In the physical examination hip palpation was painful, as well as flexion above 50°. There was no rash or local inflammation signs present. The peripheral pulses were palpable. Blood work showed an elevated CRP-level over 200 mg/l. Conventional X-ray of the hip showed a massive emphysema of the soft tissue with an air-fluid level. CT-scan showed a massive abscess with possible connection to the colon. The patient was hospitalized five months ago due to a sealed perforated diverticulitis. Back then performed CT-scan showed a possible osteomyelitis of the sacrum. The patient then refused an operation and an antibiotic therapy was prescribed but the patient was lost to follow up. An operation as the only curative therapy now was discussed with the patient and family members but again declined. We initiated a palliative care plan and pain management and the patient was discharged to a retirement home. She died three weeks after diagnosis.

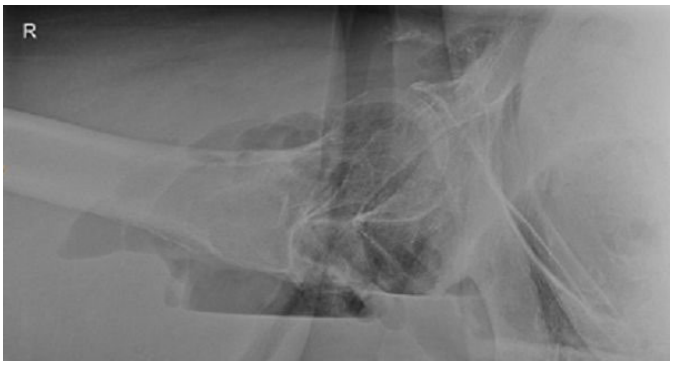

Fig 1: Rx right Hip at the emergency department with air-fluid-level

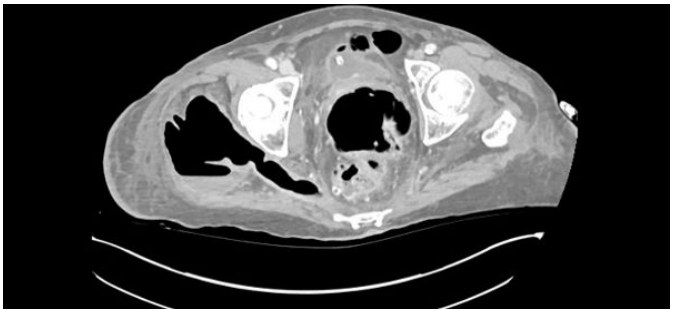

Fig 2: CT-Abdomen with the massive abscess and possible fistula to the colon

Disscusion: We describe a very rare case of complicated perforated diverticulitis with abscess to the hip joint. Abscesses occur in 16 to 40 percent of patients with complicated acute diverticulitis[1]. Percutaneous drainage is recommended for abscesses larger than 4 cm in addition to antibiotic treatment[2]. Further treatment with surgery or drainage was not wished by this patient. Fistula to the bladder is well known, but abscesses to the hip joint is a very rare complication of this common disease. In literature only a few cases were described, commonly treated with antibiotics and surgery.

P142

Hepatitis E hidden behind suspected drug-induced liver injury

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Learning objective: Hepatitis E and drug-induced liver injury can present very similar. If the cause of an acute hepatitis is unclear, hepatitis E should be considered, even if no travel history or consumption of raw pork has been reported.

Case: A 65-year old asymptomatic patient was referred to the emergency department from the rehabilitation centre due to elevated liver function tests. He was alert, afebrile, normocardic and normotensive. Physical examination revealed no icterus or abdominal pain. He presented with slight pain at the left jaw where he had undergone surgical removal of a squamous cell carcinoma two weeks earlier. He was treated with antibiotics consisting of imipenem and clindamycin due to a surgical site infection.
Laboratory findings included severely elevated aspartate transaminase (AST), alanine transaminase (ALT) and bilirubin (Table 1). Albumin concentration was 27 g/L (normal range 35-52 g/L) and the INR was 1.0 (normal range <1.3). Liver ultrasound was unremarkable.
Drug-induced liver injury was suspected and treatment with imipenem as well as all other potentially hepatotoxic drugs (clindamycin, paracetamol, metamizol) were stopped. Hepatitis B and C virus serology resulted negative. The patient had previously been vaccinated against hepatitis A.
Additional serological tests were performed and revealed positive Anti-HEV IgM and Anti-HEV IgG (Figure 1). The serum HEV-RNA-PCR was positive (5.02 x 10^6 GEq/mL) and confirmed the diagnosis of an acute hepatitis E. ALT and AST peaked on day 3 after admission. The AST/ALT ratio (De Ritis ratio) was 0.6 indicating an acute hepatitis with good prognosis. Liver function test results decreased spontaneously in the subsequent course of the patient's illness. No consumption of raw pork within the last 2-6 weeks prior to admission had been reported.
Discussion: Even if drug induced liver injury is suspected, further diagnostic tests, especially a hepatitis E screening should be evaluated, as the clinical and laboratory presentation can appear very similar.

	Bilirubin	AST	ALT	AST/ALT	GGT	AP
Normal range	<24 µmol/L	11-34 U/L	9-59 U/L	0.6-0.8	12-68 U/L	40-130 U/L
26. JAN	9.7	32	24		30	58
28. JAN	7.2	37↑	35		107↑	80
Date of admission: 10. FEB	39.4↑	1098↑	1702↑	0.6	2899↑	614↑
11. FEB	38.7↑	1182↑	1899↑	0.6	2891↑	616↑
12. FEB	42.4↑	1293↑	2217↑	0.6	2917↑	652↑
13. FEB	35.9↑	1017↑	1929↑	0.5	2493↑	550↑
14. FEB	34.2↑	678↑	1639↑	0.4	2408↑	531↑
11. MAY	3.6	26	19		22	90

Table 1: Course of bilirubin, aspartate transaminase (AST), alanine transaminase (ALT), γ-glutamyltransferase (GGT) and alcalic phosphatase (AP). JAN: January, FEB: February

Figure 1: Course and peak of alanine transaminase (ALT) and aspartate transaminase (AST), time point of sampling and diagnosis of Hepatitis E virus (HEV), JAN: January, FEB: February, DOA: date of admission

P143

Human adenovirus-induced fulminant hepatitis: think of the rare ones!

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Learning objectives: When faced with acute liver failure (ALF), rare infectious causes like adenovirus should be considered, especially in immunocompromised patients. Contacting liver transplant centers early is vital. Autopsy can be crucial in determining the cause of death and impact of novel treatments.

Case: A 75-year-old woman was referred to our hospital with fever, asthenia, and confusion, lasting for two days. History included chronic pericarditis and refractory multiple myeloma (MM) with several previous treatments, including a recent treatment with a bispecific antibody. Laboratory findings showed elevated transaminases (AST 1396 U/L, ALT 943 U/L) and cholestasis (GGT 348 U/L, ALP 496 U/L) with normal bilirubin. C-reactive protein was increased (200 mg/L), a complete blood count revealed bicytopenia. Initial obstructive cholangitis suspicion was ruled out, autoimmune and viral hepatitis serologies were negative. Evolution was rapidly unfavorable with the development of ALF and death.
Autopsy revealed panlobular hepatocellular necrosis with mild portal tract inflammation. The few remaining viable hepatocytes showed intranuclear inclusions, highly suggestive of a viral infection. PCR performed on tissue was positive for type 2 adenovirus, as well as immunohistochemical (IHC) staining.

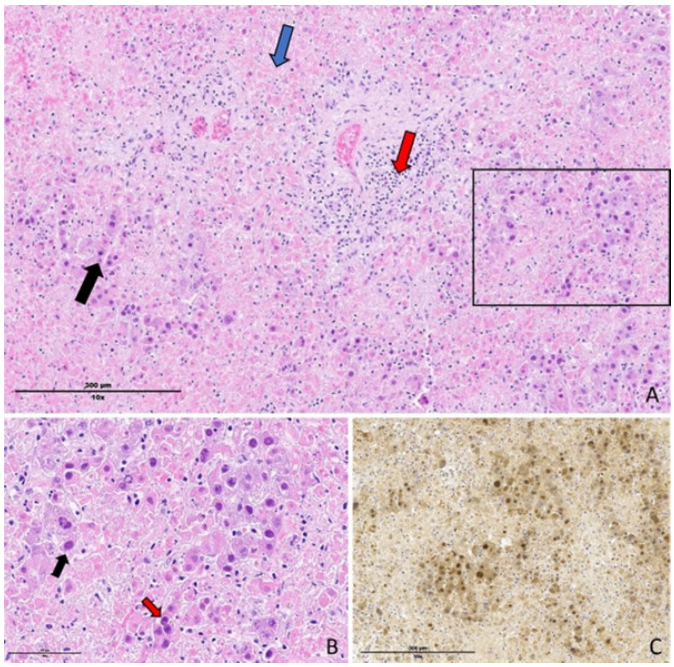
Discussion: Adenovirus infection is a rare disease leading to mild infection in immunocompetent patients; in immunocompromised patients it may be severe and present as pneumonia, colitis, or hepatitis. PCR testing on blood is the diagnostic gold standard. During the workup of ALF, besides drug-induced injury, autoimmune disease, and vascular obstruction, it is important to consider rarer etiologies, including unusual viral agents, especially in patients with hematologic malignancies, or under immunosuppressive therapies. Treatment options include reducing immunosuppression, antiviral agents, intravenous immunoglobulin infusion, and liver transplantation (LT). Prognosis of adenovirus-induced hepatitis is poor, related to frequently delayed diagnosis and limited treatment options, as in our patient who was not eligible for LT. Autopsy played a central role in determining the cause of liver failure and underlines the importance of an interdisciplinary approach.

Figure

A) HE stain, liver. Arrows: blue) necrosis red) lymphocytes black) surviving hepatocytes.

B) Inset from A. Arrows black) smudged chromatin red) inclusions.

C) Adenovirus IHC.



P144

Hypomagnesemia-induced cerebellar syndrome

T. Kellerhals[1]

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Learning objective: Even though magnesium (Mg^{2+}) is the fourth most abundant cation in the human body, its homeostasis and disorders are less well known. We present a patient with an acute cerebellar syndrome due to severe hypomagnesemia.

Case: A 61-year old male patient was referred to our emergency department due to a cerebellar syndrome with dysarthric speech and ataxia that started a few days prior to admission. The patient has been under antibiotic treatment with doxycycline and hydroxychloroquine for the last three weeks after surgery for a mycotic aortic aneurysm due to *Coxiella burnettii*. He has suffered from permanent nausea with anorexia for two weeks, and so stopped his antibiotics two days prior to admission. He regained his appetite within four days. Dysarthria and ataxia worsened two days after admission.

	Day 0	Day 4	Day 8
Sodium (136-146 mmol/l)	140	139	134
Potassium (3.6-5.1 mmol/l)	3.0	3.2	4.6
Calcium (2.2-2.65 mmol/l)		1.76	2.27
Magnesium (0.73- 1.06 mmol/l)		0.22	1.05

Table 1: Laboratory results on day 0, 4 and 8

During diagnostic work-up, – cerebral CT and MRI scan were unremarkable, there was no fever or meningism, laboratory results showed no infection and paraneoplastic antibodies were negative – a combined dyselectrolytemia with mild hypokalemia, moderate hypocalcemia and severe hypomagnesemia struck, see table 1. Dysarthria and ataxia improved – at least partially – after supplementing the deficient electrolytes, see figure 1 for synopsis of timeline.

Figure 1: Timeline of events

Discussion: 18 cases with a similar clinical presentation in conjunction with hypomagnesemia can be found in the medical literature, under the designation "hypomagnesemia-induced cerebellar syndrome (HICS)". Hypomagnesemia can develop from renal or gastrointestinal loss, malnutrition and as a side effect of different drugs such as proton-pump-inhibitors (PPI), diuretics, chemotherapeutics or certain antibiotics. Magnesium is vital for numerous enzymatic reactions and a deficit can also lead to combined electrolyte disorders. In our patient, we assume that hypomagnesemia developed due to long-time PPI use, chronic diarrhoea and antibiotic-associated anorexia combined with increased magnesium demand after refeeding. Timely recognition and supplementation of hypomagnesemia can improve prognosis in HICS, however many patients do not recover completely.

P145

Lemierre's syndrome – a rare but feared complication of pharyngitis

V. Hoffmeister[1], T. Kellerhals[1]

[1]Kantonsspital Uri, Innere Medizin, Altdorf, Schweiz

Learning objective: The paradigm of antibiotic treatment in streptococcal tonsillopharyngitis has changed in the past years. Nonetheless, there are severe complications, one of them being Lemierre's syndrome. We present a case of the "forgotten disease", that is special in two ways: manifestation of Lemierre's syndrome secondary to acute mononucleosis in a post-tonsillectomy patient.

Case: A 29-year old male patient presented to our emergency department with throat pain for a week and aggravation on the right side, high fever, chills and general weakness for 3 days. On admission the patient was febrile with otherwise normal vitals. Red flags in physical exam were poor general condition, one sided submandibular swelling with tenderness on palpation and trismus. Mclsaac Score was 4 points, a Streptococcal group A throat swab was positive. Assuming complications of a simple pharyngitis, a cervical CT scan was conducted, showing thrombosis of angular, facial and retromandibular vein, see Figure 1.

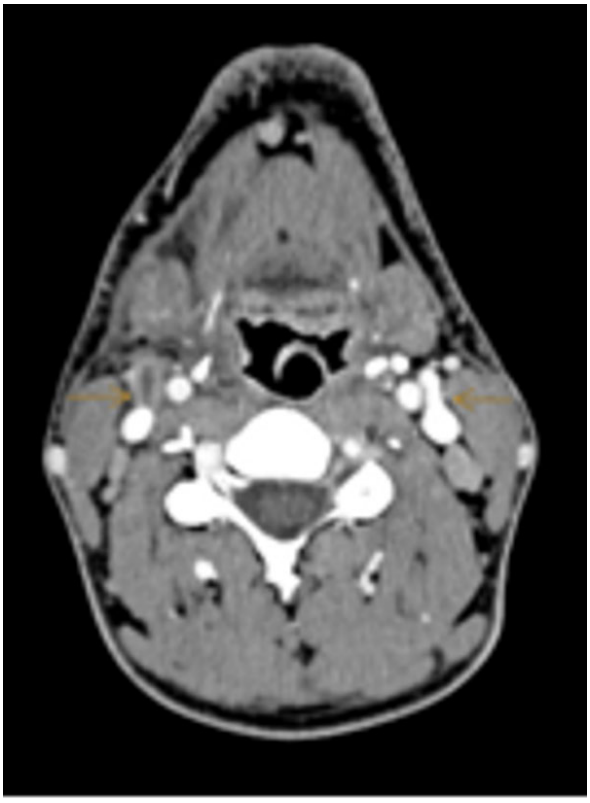

Figure 1: cervical CT scan showing right-sided thrombophlebitis Suspecting Lemierre's syndrome, we added a thoracic CT scan that demonstrated bilateral pulmonary noduli consistent with septic emboli, which confirmed diagnosis. Additionally, EBV-IgM showed a positive result. Antibiotic therapy with Piperacillin-Tazobactam was initiated as well as therapeutic anticoagulation with unfractionated heparin. Fever subsided quickly but right-sided swelling increased at first due to obstructed venous out-flow, see Figure 2. After four weeks of antibiotic therapy the patient recovered completely.

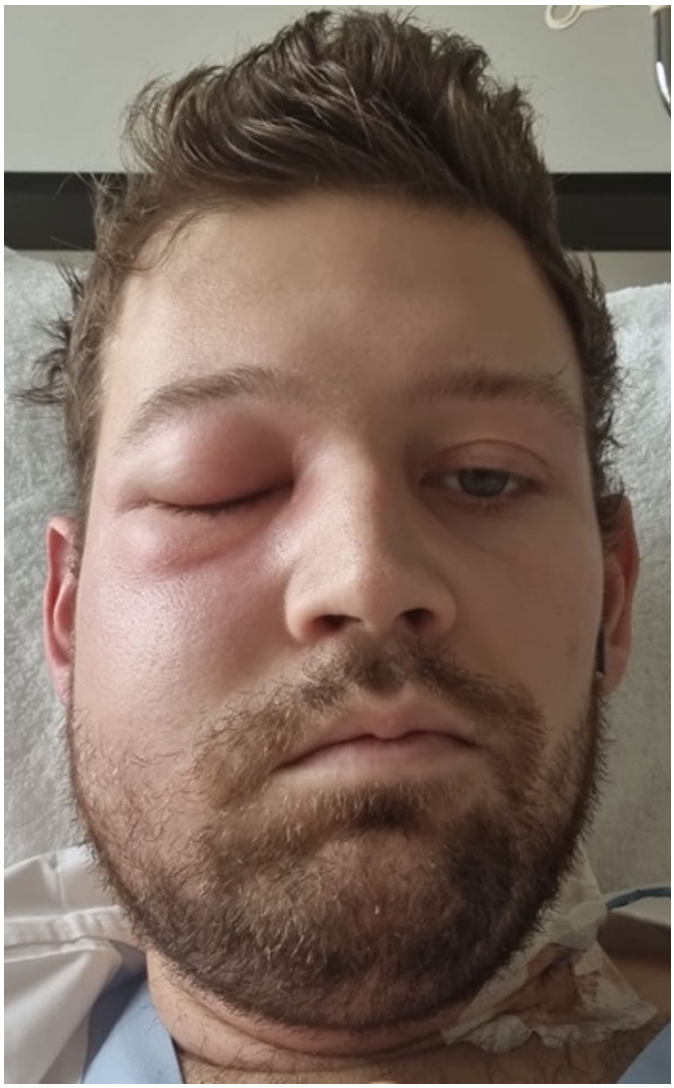

Figure 2: clinical presentation on day 4 (informed consent was given)

Discussion: Lemierre's Syndrome is a rare clinical condition with an increase in prevalence in the last decades and mortality of 5%.

The disease also known as postpharyngitis anaerobic sepsis is the result of a pharyngeal infection, e.g. due to EBV, weakening mucosal tissue and allowing invasion of mostly Fusobacterium necrophorum. Infection spreads per continuitatem or lymphatic/haematogenous resulting in thrombosis of jugular vein. Septic emboli can lead to severe consequences such as respiratory insufficiency and multi-organ failure. Treatment of septicaemia and thrombosis consists of beta-lactam antibiotics plus metronidazole. Anticoagulation therapy is controversial. In times aiming towards reducing antibiotic use, it is even more crucial recognizing severe complications and inducing fast and targeted therapy.

P146

Liver cirrhosis at 30 years of age?! and what's actually behind it

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Learning objectives:
- in patients with Budd-Chiari-syndrome one should look for an underlying myeloproliferative neoplasm even if peripheral blood counts are within normal range
- the JAKV617F-mutation can help in the diagnosis of an occult myeloproliferative neoplasm

Case: A 30-year-old woman without comorbidities was referred to our emergency room due to suspected liver cirrhosis. In the clinical examination we found a distended abdomen consistent with ascites, jaundice and an enlarged liver. Laboratory showed elevated liver enzymes, INR and cholestasis parameters. The analysis of the ascites fluid revealed an elevated Serum-ascites albumin gradient (SAAG) reliable with a portal hypertensive genesis. The ultrasound of the abdomen showed a decompensated liver cirrhosis with splenomegaly and marked ascites. All laboratory test for the broad spectrum of causes of liver cirrhosis (including serology for hepatitis A-E, HIV, antibodies for autoimmune disorders, Echinococcus serology, Ferritin, Ceruloplasmin, Alpha1-antitrypsin, Alpha-1-Fetoprotein) were unremarkable. The following magnetic-resonance-cholangiopancreatography (MRCP) showed a thrombosis in the right liver vein and a partial thrombosis of the vena cava inferior with corresponding hypoperfusion of the right lobe of the liver. This eventually led to the diagnosis of Budd-Chiari-syndrome (BCS).
Because myeloproliferative neoplasms (MPN) represent a major risk factor for BCS (1), a coagulation workup was done, which revealed a positive Janusin-Kinase2 (JAK2)V617F-mutation on the background of normal peripheral blood counts. In the following bone marrow biopsy, an increased morphologically conspicuous megakaryopoesis compatible with an MPN not otherwise specified (MPN-NOS) was detected. The patient is now treated with Ruxolitinib.

Discussion: MPN is the most frequent underlying prothrombotic factor in patients with BCS. However, it is not uncommon for these patients to lack the characteristic diagnostic feature of increased peripheral blood counts, possibly due to congestion and blood accumulation in the liver and spleen (1). Those so-called "occult MPN" are therefore more difficult to diagnose. Among patients with BCS, a high frequency of JAK2V617F-mutations (30-45%) could be detected, which confirmed the association between MPN and BCS (2,3). Thus, physicians should consider the possibility of JAK2V617F-mutations in patients with BCS, even if there are no hematologic abnormalities.

P147

Myocarditis and Pericarditis following COVID-19 immunisation in elderly patients: evaluation of case-reports received by Swissmedic

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Introduction: «Myocarditis and pericarditis» became an important safety issue of the mRNA-based Covid-19 vaccines with main focus on young male patients, which are predominantly affected (Ref. 1). So far, little is known about similar cases following vaccination in elderly people, while suspected cases with fatal outcome were recently published (Ref. 2).

Methods: Evaluation with descriptive statistics of case-reports from the Swiss pharmacovigilance database in elderly patients (≥ 65 years).

Results: By the end of 2022, Swissmedic received 32 case-reports of myocarditis (n=9), pericarditis (n=14) or perimyocarditis (n=9) in elderly patients. Of these, 20 cases were reported in association with the Moderna Covid-19 vaccine and 11 with the Pfizer-BioNTech vaccine. Based on criteria of the US-CDC (Ref. 3), the clinical diagnosis of myocarditis and/or pericarditis was mostly judged as 'probable' (n=11) or 'confirmed' (n=10). More myocarditis cases (5/9) and perimyocarditis (4/9) remained clinically unconfirmed, as compared to pericarditis (2/14).
The age of patients ranged between 65 and 88 years (mean=72 years) and more events were reported in men (n=21; 65.6%) than in women (n=9; 28%).
Pre-existing cardiovascular diseases were recorded in 13 of the 32 patients. At the time of reporting, 22 cases were clinically recovered or recovering. However, 6 cases needed ICU-treatment and 1 case had a fatal outcome.
More cases were reported after the second vaccine dose (n=16; 50%) as compared to the first (n=9; 28%) or the third dose (n=4; 12%). The time-to-onset (TTO) ranged from <1 to 327 days (median=14.5 days), with a faster onset of symptoms after the second vaccine dose (median TTO=11.5 days) or third dose (median TTO=12.5 days), as compared with the first dose (median TTO=22 days).

Conclusions: Our findings enhance the safety knowledge regarding elderly. Reports of confirmed myocarditis and/or pericarditis were received in temporal association with mRNA Covid-19 vaccines. Most cases had a favorable outcome, whereas some cases had a severe clinical course. Hence, these diagnostic entities should be considered and thoroughly clarified in elderly patients with suggestive cardiac symptoms following vaccination. Furthermore, a safety monitoring of this age-group appears mandatory.

P148

Organizing pneumonia secondary to an infectious aetiology with Actinomyces species: a case report

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Learning objective: Organizing pneumonia (OP) is a diffuse interstitial lung disease affecting the distal bronchioles, respiratory bronchioles, alveolar passages, and alveolar walls and characterized by the formation of organized buds of granulation tissue obstructing the alveolar lumen and bronchioles. The associated symptoms and radiology are nonspecific.

Case: 66-year-old otherwise healthy female was referred to us because of a persistent dry cough of 3 months. Initial symptoms were shortness of breath, and 4kg weight loss after upper respiratory infection. She was started on treatment for pneumonia with clarithromycin and subsequently with Augmentin for 10 days with lack of response. because of persistence of the symptoms a 5 days steroid therapy was given. Chest radiograph performed on referral revealed right parenchymal infiltrates. Pulmonary function showed slightly reduced diffusion capacity of 72%. The eosinophil count was normal by slightly elevated CRP. CT scan of the chest showed multiple, dense subpleural consolidations and peripheral fibrosis pattern. A diagnosis of organizing pneumonia or COP was suspected but for further investigation bronchoscopy was performed. The lavage showed lymphocytic alveolitis compatible with moderate chronic inflammatory response, microbiology revealed no microorganism. However, Actinomyces graevenitzii was identified in EBUS-TBNA and in TBB samples. Consequently, a treatment with long-term (6-12 months) antibiotic therapy with co-amoxicillin was initiated. In the absence of clinical and objective improvement after 4 weeks an additional anti-inflammatory therapy with corticosteroids over the course of 6-12 months was reconsidered. Diagnosis of OP secondary to infectious aetiology caused by Actinomyces species was made.

Discussion: COP is categorized as an idiopathic interstitial pneumonia whereas secondary OP is associated with a variety of diseases including infections, malignancies, radiation injury and connective tissue diseases, among others. COP is diagnosed in appropriate multidisciplinary clinical, radiographic, and pathological setting after excluding diseases associated with secondary OP. Patients with OP present with cough, shortness of breath and a restrictive pattern on pulmonary function testing. Bronchoscopy is an important tool in the evaluation of patients with OP. The management of secondary OP requires treatment of the underlying disease as in this case, whereas COP usually responds to steroids only.

P149

Paraneoplastic dermatomyositis retrospectively explains multisystemic problems causing repeated hospitalisations: a case report

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Learning Objective: Dermatomyositis (DM) is a rare inflammatory disease characterised by dermal rashes and proximal myositis. In rarer cases, internal organs such as the oesophagus, heart and lung can be affected[1]. Diagnosis is primarily based on clinical findings and laboratory results such as elevated creatinine kinase (CK) or autoantibodies[2]. DM is associated with various malignancies, hence such malignancies should be ruled out.

Case: A 83-year-old female presented with weakness, muscle pain and shortness of breath. The patient had recently been hospitalised three times because of atrial fibrillation with consecutive heart failure. Dysphagia and computed tomography (CT) findings suggesting interstitial lung disease (ILD) had been documented.
Clinical examination revealed a symmetric reduction in strength, motion-dependent pain of the proximal muscles and basal crackles on pulmonary auscultation. A reddened and oedematous face with accentuation in the periorbital area (heliotrope rash) and an erythematous rash over the upper chest and back (shawl sign) were observed. Later, a maculopapular rash over the knuckles (Gottron's papules), calcium deposits on the palmar side of the left hand (calcinosis cutis) and paronychial telangiectasias appeared.
Laboratory analyses showed elevated erythrocyte sedimentation rate and muscle enzymes. Antinuclear antibodies and anti-transcriptional intermediary factor (TIF) 1-γ antibodies were positive, which is a profile particularly associated with malignancy[1]. A punch biopsy of the lip revealed an interface dermatitis.

Parameter	Unit	Reference Ranges	Patient Values
Total leukocyte count	G/L	6.4 – 10.5	8.8
C-reactive protein	mg/l	< 10	39*
Erythrocyte sedimentation rate	mm/h	< 20	110*
Creatinine kinase	U/l	30 – 135	258*
Aspartat aminotransferase	U/l	<36	52*
Alanine aminotransferase	U/l	<35	24
Lactate dehydrogenase	U/l	120-246	287*
Antinuclear antibodies	Titer	<160	1280*
Anti-transcriptional intermediary factor 1-γ antibodies		Negative	Strongly positive

Table 1. Relevant laboratory values and serologic results. *-values indicate elevated results.

Upon diagnosing DM, high dose therapy with steroids and a search for malignancies were initiated. The CT scan exhibited enlarged subcarinal lymph nodes, two metastases suspicious lesions in both pectoral muscles and pulmonary fibrosis. Lymph node cytology showed a synaptophysin-positive malignant small cell lung carcinoma.
Because of a kidney injury neither a steroid-sparing immunosuppressive therapy nor a chemotherapy were feasible. The patient's condition worsened, and she died seven days after the initial diagnosis of DM.

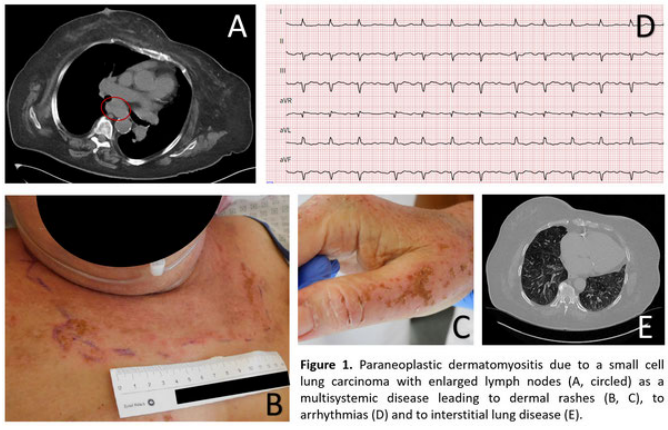

Figure 1. Paraneoplastic dermatomyositis due to a small cell lung carcinoma with enlarged lymph nodes (A, circled) as a multisystemic disease leading to dermal rashes (B, C), to arrhythmias (D) and to interstitial lung disease (E).

Discussion: We diagnosed paraneoplastic DM with small cell lung carcinoma. The multisystemic aspect of DM had been described months before with dysphagia due to oesophageal muscular affection, treatment-resistant arrhythmias due to heart involvement and dyspnoea due to ILD. Consideration of the multisystemic aspect could have led to earlier diagnosis of DM and the associated carcinoma.

P150

Prolonged pancytopenia and agranulocytosis due to metamizole

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Learning objectives: Despite its ban in many countries, metamizole is used extensively in many Swiss clinics and hospitals. It can cause life-threatening agranulocytosis lasting up to several weeks. Therefore, it should not be used as a painkiller of first choice. Exposed patients presenting with a sore throat should be evaluated for agranulocytosis.

Case: A 42-year-old previously healthy woman took metamizole for three weeks due to painful cervical disc herniation. She presented to the emergency department with a sore throat and fever. She showed a tender and swollen neck, CRP was 360 mg/l and neutrophilic granulocytes 0%. Blood cultures grew streptococcus pneumoniae, which led to the diagnosis of metamizole-induced agranulocytosis complicated by bacterial tonsillitis. CT scan of the neck and fiber endoscopic examination did not show an abscess. Even with antibiotic treatment, severe pain in the tonsillar region persisted and the patient later also developed pneumonia.
Despite intermittent treatment with GCSF, agranulocytosis persisted for 25 days, in addition thrombocytopenia with a nadir of 16 G/l as well as anemia in need for transfusion developed. A bone marrow biopsy on day 12 after admission showed inexistent granulopoiesis, as well as decreased megakaryopoiesis and erythropoiesis. Further differential diagnoses for pancytopenia were evaluated. Neither an infectiological or rheumatological workup, nor the excision of a cervical lymph node led to another diagnosis. On day 21, a PET scan showed strong activation of the bone marrow and Waldeyer's tonsillar ring with no evidence of vasculitis or arthritis. On the same day monocytes and thrombocytes increased, and two days later, neutrophilic granulocytes finally began to rise. Subsequently all hematologic lines quickly recovered and the patient rapidly improved.

Discussion: Metamizole is increasingly prescribed as a pain killer, even though the severe hematological side effects are well known. Fortunately, agranulocytosis often resolves after a few days, however, this case illustrates, that it can persist for many weeks, putting patients at risk for fatal outcome.
We strongly suggest that metamizole should not be used uncritically as analgesic of first choice. However, in selected clinical settings this drug still plays a useful role.

P151

Pulmonary emphysema in non-smoker leads to diagnosis of Birt-Hogg-Dubé syndrome in swiss family: a case report

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Learning objective: The trias of pulomary and renal cysts combined with fibrofolliculomas can lead to the diagnosis of Bird-Hogg-Dubé Syndrom. Especially if these terms occur over several generations within one family.

Case: A 80-year old woman was evaluated in the department of pneumology for shortness of breath. Clinical observation showed a vesicular breath sound with an SpO2 of 93%, the vital signs were normal. Multiple papules on the neck and head were noted. Spirometry and bodyplethysmography showed signs of a moderate hyperinflation and diffusion interference, which matches with the diagnosis of a cystic pneumopathy with bullous emphysema in the computer tomography. Incidentally, renal cysts were described.

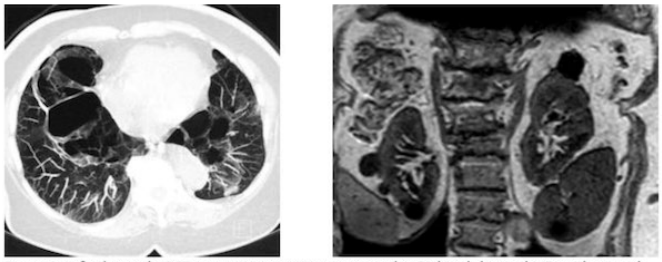

Figure 1. Left: thoracal HRCT presenting a cystic pneumopathy. Right: abdominal MRI with several renal cysts

The patient already has had two pneumothoraces but interestingly had no history of nicotine. Her mother had been told to have also a "smoker's lung" even she had never smoked.Shortly after, the patient's son was evaluated for COPD as well. He also presented no history of smoking, lung auscultation with regular breath sounds and eye-catching fibrofolliculomas on head and neck.

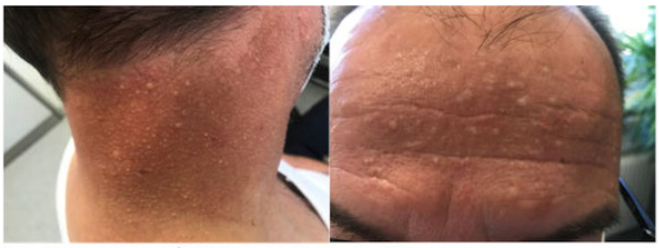

Figure 2: Fibrofolliculoma/trichodiscoma on head and neck

His pulmonary CT scan also showed signs of early emphysema, which on a closer look appears to be cystic structures, and an abdominal MRI presented several renal cysts. With the same striking symptoms of a pulmonary emphysema without smoking, which were mistakenly diagnosed as such and should rightfully be described as cysts, dermal lesions and renal cysts over at least two, probably three generations we stated our suspected diagnosis of Birt-Hogg-Dubé syndrome. A punch biopsy of the son's skin lesions confirmed a typical fibrofolliculoma/trichodiscoma.

Discussion: Birt-Hogg-Dubé syndrome is an autosomal dominant tumor syndrome that is characterized clinically by skin fibrofolliculomas, as well as pulmonary and renal cysts. The pulmonary cysts can radiologically be misdiagnosed as an emphysema and spontaneous pneumothoraces often occur. Since the renal cysts have a lifetime risk of 12-34% of developing benign or malignant renal tumors regular screenings are advised[1]. Demonstration of fibrofolliculomas on a skin biopsy or detection of a pathogenic FLCN mutation confirm the diagnosis of BHD in patients with clinical suspected disease[1]. Fibrofolliculomas can be treated by laser therapy but have a high recurrence rate.

P152

Severe inflammatory neck pain in the context of hypomagnesemia - a case report

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Learning objectives: An acute episode of Calcium Pyrophosphate Crystal Deposition disease (CPPD) can be triggered by hypomagnesemia, and both, proton pump inhibitors (PPI) and thiazide diuretics may lead to hypomagnesemia. A combination of both substances may even exacerbate this phenomenon and lead to the onset of CPPD resembling vertebral osteomyelitis.

Case: A 79 year old woman presented to the emergency department with increasing neck pain that had begun two weeks prior to the visit. She had visited another hospital the month prior due to an activated arthritis of her left hand and was treated with high dose corticosteroids accompanied by PPI. Relevant past medical history included arterial hypertension (treated with a thiazide diuretic) and peripheral artery disease. The clinical examination showed pain and tenderness of the paravertebral muscles. Neurological deficits were absent. Neck stiffness and fever were absent. Blood analysis showed an elevated CRP of 187.6 mg/l and LDH of 351 U/l with multiple electrolyte imbalances including hypokalemia of 2.6 mmol/l, reduced ionized calcium of 1.83 mmol/l (normal range 2.10-2.65 mmol/l) and significant hypomagnesemia of 0.19 mmol/l (normal range 0.7-1.0 mmol/l) (Figure 1). ECG showed paroxysmal atrial fibrillation and a prolonged QTc interval of 565ms. As an infectious disease such as a vertebral osteomyelitis was first suspected, intravenous antibiotics were started and CT imaging was performed showing multisegmental degeneration of the cervical vertebrae and calcium pyrophosphate deposits in the connective tissue around the dens consistent with a crowned dens syndrome (Figure 2). Antibiotics were ceased and treatment with colchicine and physiotherapy quickly lead to an improvement of the symptoms and a normalization of the inflammation. Due to the rapid recovery, CPPD was considered the most likely diagnosis secondary to hypomagnesemia (with secondary hypocalcemia), exacerbated by the combined medication of a PPI and a thiazide diuretic. They were both stopped and IV and oral electrolytes were supplemented to normalize the dysbalance, which subsequently also lead to a normalisation of the prolonged QTc interval to 451ms.

Discussion: Although a rare manifestation, CPPD can occur in the cervical spine and may be misinterpreted as infective vertebral osteomyelitis. As hypomagnesemia is a possible risk factor for CPPD, it should be actively investigated in patients being treated with PPIs or thiazide diuretics.

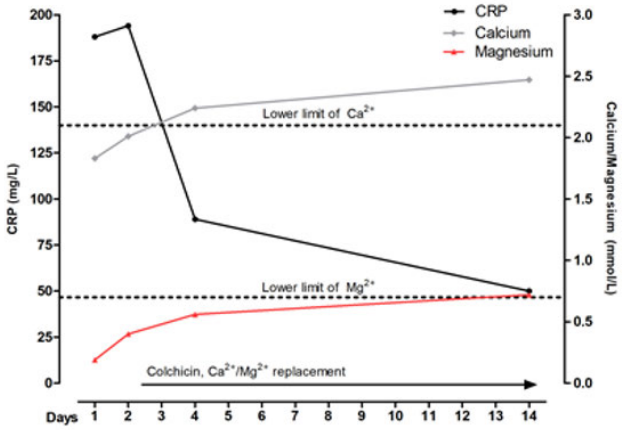
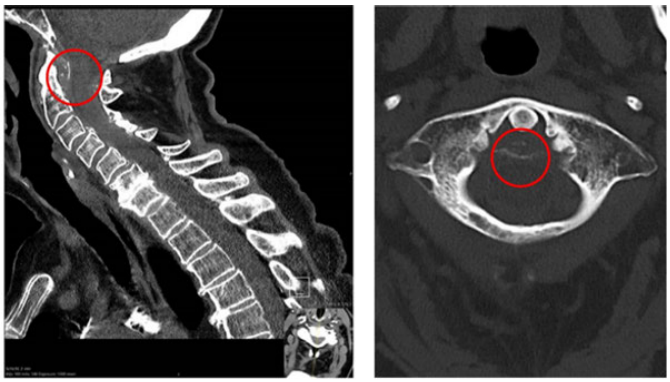


Figure 1: Blood values during hospitalisation



Figures 2: CT-Image depicting calcification of the cruciform ligament (red circle) surrounding the dens (crowned dens syndrome)

P153

The Sinclair-Method is an effective and evidence-based treatment for alcohol use disorder

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Learning objectives: The Sinclair Method (TSM) for the treatment of alcohol use disorder (AUD) was discovered by the Finnish neuroscientist Dr. David Sinclair in the 1990s. It is scientifically substantiated by numerous experimental and clinical studies.[1]
It is a drug-mediated change of those brain functions, which contributes to the development of alcohol dependency. By means of blocking the opioid system during active drinking, the usual endor-

phin release under alcohol consumption is suppressed and thus attenuating the reward system. This leads over time to a "reverse learning process", compromising those nerve pathways, which are responsible for the loss of control and craving.
You don't need to be a psychiatrist or a specialist in addiction medicine to use TSM. It can be easily performed by general practitioners or specialized nurses. Very helpful and improving patients complience are specific Chats and Social Media Groups, e.g. for dealing with side effects of the Nalmefen medication.

Case: A 28 years old man with progressive AUD for the last ten years. The drinking pattern was determined by episodic binge drinking, in change with abstinent periods. This pattern caused a severe controversial issue in his family, who didn't want to invite him anymore for family celebrations. ADHS was diagnosed in late childhood and treated with Ritalin®. Further medication was Mirtazapine.
The patient was introduced to TSM by explaining the pathophysiological pathways in the brain and how they can be reversed. He was instructed to take one tablet of Nalmefen (Selincro®) one hour before he intends to drink alcohol. His compliance was excellent, resulting in a significant change of his drinking pattern, which means maximum one or two units per day - a "miracle" for the whole family.

Discussion: More than 80 experimental and clinical trials have documented long-term success in reducing drinking and craving in more than 75% of cases. In Switzerland Selincro® was approved in 2014. It is hard to understand that TSM could not be established as a standard treatment for AUD despite the scientific evidence. Possible explanations could be the unwillingness of relativizing the goal of abstinence.
TSM is good medical practice and treats alcohol use disorder as a medical problem and not as a psychological condition. The guidance of the patient must be based on the research findings of Dr. Sinclair, including the understanding of the reversed learning process of drinking.[2]

P154

Treatment induced neuropathy of diabetes versus diabetic neuropathy

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Learning objectives: Treatment induced neuropathy of diabetes (TIND) is a rare disease that clinically resembles diabetic neuropathy. With pathophysiological processes still not fully understood, management of this small fiber neuropathy remains challenging.

Case: A male patient in his sixties has been admitted to for an extensive neurological work up due to progressive asymmetrical distally accented pain in both feet and legs. The pain was described as burning, stabbing and throbbing, has started around two months prior to hospitalization, and has since been progressive. Conventional pain relievers did not help in pain reduction, pregabalin at a dose of 3 x 75 mg per day, however, has slightly reduced his symptoms.
Of notice, the patient had started insulin treatment due to a newly diagnosed late-onset diabetes around six months before hospitalization. The HbA1c has dropped from over 14 % to around 6 % in a few months using a continuous glucose monitor.
The neurological workup revealed an unremarkable cranial nerve status, moderate tendon reflexes at the arms and weak or absent reflexes at the legs as well as unremarkable motor and sensory function, (including preserved vibration sense). The cerebrospinal fluid showed slightly elevated albumin and immunoglobulins without indication for intrathecal immunoglobulin synthesis. A sudoscan showed relevant damage of the small nerves in all four extremities.
Upon increasing the dose of pregabalin and adding duloxetine 30 mg, the patient reported improvement of the symptoms.

Discussion: Because TIND shares similar symptoms with diabetic neuropathy and is thus hard to distinguish from one another it is often underdiagnosed. It is usually caused by a rapid correction of HbA1c and more commonly found in diabetes type 1 patients. With potentially years of undiagnosed diabetic metabolism with consequent glucose toxicity, a clear sign of small fiber damage and the acute onset of symptoms, we concluded that TIND was very likely in our patient's case. Management of TIND is challenging, though to date there is no evidence based standard care and only symptom-oriented therapy, which consists mainly of tricyclic antidepressants, anticonvulsants, and SNRIs. It is hypothesized that the magnitude of HbA1c correction correlates with the severity of TIND symptoms. Thus, in patients with severe hyperglycemia changes in glycemic control should be stepwise and not rapid, however, to date no guidelines exist how to avoid TIND.

P155

Ventriculoperitoneal shunt infection in a patient with migratory abdominal pain – PET-CT to the rescue?

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Learning objectives: Patients with a ventriculoperitoneal (VP)-shunt infection do not always present with headaches. Occasionally, their first symptom includes acute abdominal pain and even guarding. These patients are at risk to be misdiagnosed with gastrointestinal disease, leading to a delayed or wrong therapeutic approach. Could ^{18}F-FDG PET/CT (PET/CT), combined with clinical information be useful as a diagnostic tool in these cases?

Case: A 23-year-old patient with a VP-shunt, implanted 2 months before the current event, presented to the emergency room four times over the course of a month with migratory abdominal pain and guarding (Figure 1). Neurological symptoms were absent. The laboratory tests showed an elevated CRP at each visit [peak on visit 2: 121.1mg/l (normal range < 10.0mg/l)]. In total, 3 ultrasounds, 2 CT scans and 2 MRIs of the abdomen were performed, with inconclusive results. In particular, there was no evidence for appendicitis, cholecystitis or pelvic inflammatory disease.
Due to clinical and radiological signs pointing towards peritonitis, several courses of empiric antibiotic treatments were initiated with a prompt, but not lasting improvement of the symptoms. Hence, a PET/CT was performed which showed an elevated tracer uptake surrounding the intraabdominal tip of the shunt. The subsequent VP-shunt puncture showed no increased cell count, but growth of coagulase-negative staphylococci. Appropriate antibiotic treatment with flucloxacillin was started and the shunt was removed.
Finally, growth of a methicillin-susceptible *Staphylococcus epidermidis* in sonication fluid culture of the shunt tip, confirmed the diagnosis of a VP-shunt infection.

Discussion: Migratory abdominal pain, originating from migratory local peritonitis caused by the free-floating shunt, can be the first symptom of a VP-shunt infection. PET/CT is a diagnostic adjunct to facilitate the diagnosis in combination with a VP-shunt puncture.

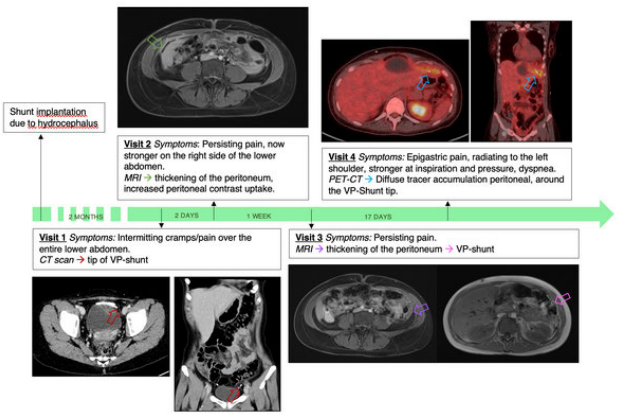

Figure 1

P156

When crouch gait reveals Crohn's disease

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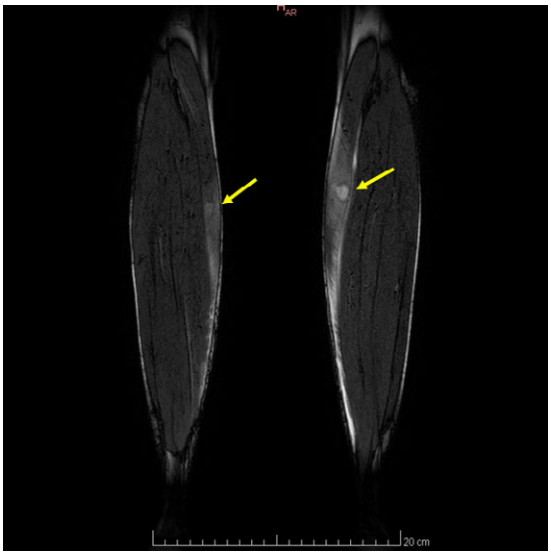
Learning objectives: Inflammatory bowel diseases are often associated with a constellation of extraintestinal manifestations (1). We report the case of a man with gastrocnemius myositis revealing Crohn's disease (CD). After a first description in 1976 (2), it was named "gastrocnemius myalgia syndrome" (GMS) in the early 2000s. In our case, we discuss the role of antiproteinase 3 anti-Neutrophil Cytoplasmic Antibodies (Anti-PR3-ANCA) in the diagnosis of CD.

Case: A previously healthy 28-year-old man presented to ED with lower limbs pain and crouch gait. He walked on tiptoes and could not extend his knees. On palpation, there was exquisite tenderness and one nodule on each calf with no Erythema Nodosum. Neurological examination was normal. Biological data showed: WBC 13.5 G/L, Hb 128 g/L, platelets 691 G/L, CRP 115 mg/L. Creatine kinase (CK), LDH, thyroid and renal function were normal. HIV, EBV, HAV, HBV, HCV serologies were negative. Anti-PR3-ANCA were 27.4UI/L (N<5). This clinical picture was suggestive of GMS associated with CD. Fecal calprotectin was increased up to 751 mcg/g (n<50). MRI showed bilateral centimetric lesions within both mesial portions of gastrocnemius muscles (figure1). A CT-scan showed a subpleural parenchymal condensation of the right lower lobe and thickening of the transverse colon. A calf muscle biopsy showed focal necrotizing myositis. Lung and colonic biopsies confirmed the diagnosis of CD. Steroid therapy and Infliximab were introduced. Three months later, the patient was totally asymptomatic and the thoraco-abdominal CT-scan was strictly normal.

Discussion: The prevalence of extraintestinal manifestations in CD ranges from 21 to 40% (3). Muscular involvement often manifests in the orbital muscles and rare cases of poly- and dermatomyositis have been reported (4). About 20 cases of GMS have been reported, typically affecting the lower limbs bilaterally. Muscle biopsies show patterns ranging from non-necrotizing or necrotizing vasculitis to granulomatous myositis. CK levels are normal in all reported cases as in our patient, which seems a typical feature. Our patient had pulmonary lesions associated with Anti-PR3-ANCA, which appear to be of interest for CD diagnosis with 45% sensitivity and 96% specificity (5). They are also useful to assess disease severity and extension (6). As it often precedes digestive features or is the predominant symptom, GMS should be recognized by internists to prompt the diagnosis of CD.



P157

When you least expect it: the tiger man sign as a rare indicator of the cause of severe hypercalcemia

E. Crisman[1], I. Bosma[2], K. Frontzek[3], B. Klaser[2], M. Osthoff[1]

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Learning objectives: Sarcoidosis is a rare cause of hypercalemia. History and clinical judgement remain a fundamental cornerstone. 18F-FDG PET/Computed tomography (CT) may aid in the diagnosis of suspected sarcoidosis.

Case: A 68-year-old man presented to the emergency department because of weakness, recurrent falls, appetite loss, weight loss of 30 kg over the last 3 months, vomiting and confusion since a week. His past medical history included diabetes mellitus type 2 and arterial hypertension. His medication included 5600 E of vitamin D daily. On admission, disorientation and psychomotor slowing was noted. Laboratory findings were significant for hypercalcemia (corrected calcium 3.63 mmol/l; normal range: 2.10 – 2.55 mmol/l), hyperphosphatemia (1.84 mmol/l; normal range: 0.74 – 1.52 mmol/l), high vitamin D levels (25-OH-vitamin D 118 ug/l; 1,25-OH-vitamin D > 200ng/l) and suppressed parathyroid hormone. Computed tomography showed no evidence of lymphoma or sarcoidosis.
Initially, we assumed symptomatic hypercalcemia secondary to vitamin D intoxication and established intravenous hydration and treatment with zolendronic acid. Subsequently, his calcium levels dropped.
He remained disoriented and was dependent on support in everyday activities. The patient was transferred to a rehabilitation hospital.
After a week, he was referred back with increasing hypercalcemia and loss of strength. On examination, muscle weakness and edematous swelling of forearms and hands was noted (Figure 1 A), with absent intrinsic muscle reflexes and an inability to mobilize independently. Importantly, his CRP level remained moderately elevated.
Due to the severe proximal myopathy, bilateral forearm swelling of unknown origin and hypercalcemia with elevated 1,25 vitamin D, we ordered a PET-CT to search for granulomatous diseases. Indeed, disseminated linear heterogeneous uptake in skeletal muscles ("tiger man" appearance) was detected raising the suspicion for muscular sarcoidosis, supported by evidence of granulomatous myopathy in a muscle biopsy (Figure 2 A/B). There was no evidence of cardiac, pulmonary or ocular sarcoid involvement. After initiation of high-dose steroid therapy, an immediate clinic improvement was noted (Figure 1 B).

Discussion: Sarcoidosis may be difficult to diagnose, especially in the absence of characteristics pulmonary findings. 18F-FDG PET/CT may help to identify occult lesions. The tiger man sign is highly suspicious of muscular sarcoidosis.

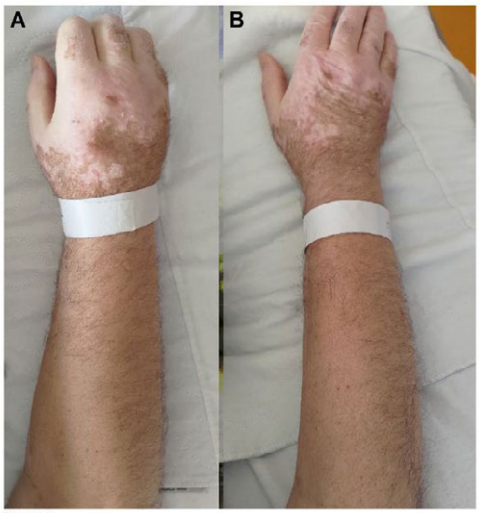

Figure 1
A): Edema and swelling of right forearm and hand;
B): Reduction of edema 3 days after the start of corticosteroid treatment

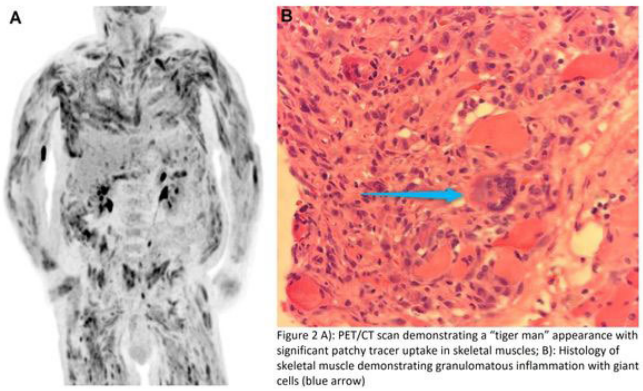

Figure 2 A): PET/CT scan demonstrating a "tiger man" appearance with significant patchy tracer uptake in skeletal muscles; B): Histology of skeletal muscle demonstrating granulomatous inflammation with giant cells (blue arrow)

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P158

A randomized double-blind ascending-dose placebo-controlled study of N-desmethylclobazam in patients with peripheral neuropathic pain

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Introduction: Neuropathic pain prevalence is 8% of the European population. More than half of patients are non-responders to available treatments because of their relative efficacy and side effects such as sedation. N-desmethyl clobazam (NDMC) is a benzodiazepine drug, devoid of sedative effect, which has shown antihyperalgesic effect in preclinical models. NDMC represents a first in class drug with an allosteric modulator mechanism on the GABAA receptors which are key receptors in the modulation of the pain signal at the level of the spinal cord. The proof of concept of GABAergic modulation in neuropathic pain patients needed to be confirmed in neuropathic pain patients.

Method: Randomized, double-blind, placebo-controlled, 4-arm, and sequential parallel study testing 40, 60, 120 mg of NDMC vs placebo in neuropathic pain patients. The 3 dosing sequences were separated by two interim analyses to check the safety and the PK linearity of the increasing dosages of NDMC. The primary outcome was the mean change in the weekly average daily intensity of pain on a Numerical Rating Scale (NRS) between the end of the study (V7) and baseline (V1). Secondary outcomes were the mean change in the weekly average daily subjective sedation on a NRS between V7 and V1 and steady-state and V7 NDMC plasma concentrations.
Due to a lower recruitment rate than expected, related to Covid-19 pandemia, an interim analysis was carried out at half of the needed inclusions. This decision was coherent and possible in the context of a phase IIa study.

Results: At the time of the interim analysis, only 33 of the required 76 patients were included. The improvement in pain score on placebo was -1.53 units, whereas it was -2 units on NDMC; the difference between the two treatment groups was not statistically significant (p=0.46). There was no evidence for higher magnitude of efficacy according to the dose groups but the Pearson correlation calculated between the steady state concentrations of NDMC in plasma and the change in pain score suggested an inverse (expected) relationship, but not statistically significant. NDMC was well tolerated and the CNS adverse events were not increased in NDMC compared to placebo group. Sedation and PK data are currently being analyzed.

Conclusion: At this stage the lack of statistical power does not allow strong conclusions to be drawn. Further analysis of these results will help refine the proof of concept of GABAergic modulation in neuropathic pain patients.

P159

Acute effects of intravenous DMT in a randomized placebo-controlled study in healthy subjects

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[1]Universitätsspital Basel, Klinische Pharmakologie und Toxikologie, Basel, Schweiz, [2]Universitätsspital Basel, Department Biomedizin, Basel, Schweiz, [3]Psychiatrische Universitätskliniken Basel, Neurobiologisches Labor Transfakultäre Forschungsplattform, Basel, Schweiz

Background: *N,N*-dimethyltryptamine (DMT) is unique among classic serotonergic psychedelics because of its short-lasting effects when administered intravenously. Despite growing interest in the experimental and therapeutic use of intravenous DMT, there are little current data on its clinical pharmacology.

Methods: We conducted a double-blind, randomized, placebo-controlled crossover trial in 27 healthy subjects to test different intravenous DMT administration regimens in 5-h sessions that were separated by at least 1 week. Outcome measures included subjective, autonomic, and adverse effects, pharmacokinetics of DMT, and plasma levels of brain-derived neurotropic factor (BDNF) and oxytocin.

Results: Low (15 mg) and high (25 mg) DMT bolus doses rapidly induced very intense psychedelic effects that peaked within 2 min. DMT perfusions (0.6 or 1 mg/min) without a bolus induced slowly increasing and dose-dependent psychedelic effects that reached plateaus after 30 min. Both bolus doses produced more negative subjective effects and anxiety than perfusions. After stopping the perfusion, all drug effects rapidly decreased and completely subsided within 15 min, consistent with a short early plasma elimination half-life ($t_{1/2\alpha}$) of 5.0–5.8 min, followed by longer late elimination ($t_{1/2\alpha}$ = 14–16 min) after 15–20 min. Subjective effects of DMT were stable from 30 to 90 min, despite further increasing plasma concentrations, thus indicating acute tolerance.

Conclusions: Intravenous DMT, particularly when administered as a perfusion, is a promising tool for the controlled induction of a psychedelic state that can be tailored to specific needs of patients and therapeutic sessions.

P160

Acute effects of MDMA and LSD co-administration in a double-blind placebo-controlled study in healthy subjects

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Introduction: There is a renewed interest in the use of lysergic acid diethylamide (LSD) in psychiatric research and practice. While the acute subjective effects of LSD are mostly positive, negative subjective effects including anxiety may occur. The induction of positive acute subjective effects is desired in psychedelic-assisted therapy because positive acute psychedelic experiences are associated with greater therapeutic long-term benefits. 3,4-methylenedioxymethamphetamine (MDMA) produces marked positive subjective effects and is used recreationally with LSD as “candy flip”. The present study aimed to investigate whether co-administration of MDMA could be used to enhance the acute subjective effects of LSD.

Methods: We used a double-blind, randomized, placebo-controlled, crossover design with 24 healthy subjects (12 women, 12 men) to compare the co-administration of MDMA (100 mg) and LSD (100 µg) with MDMA or LSD alone or placebo. Outcome measures included subjective effects, autonomic effects, endocrine effects and pharmacokinetics.

Results: MDMA co-administration with LSD did not change the quality of the acute subjective effects compared with LSD alone. However, the duration of the acute subjective effects was longer after LSD-MDMA co-administration compared with LSD (or MDMA) consistent with higher plasma concentrations of LSD (maximum plasma concentration; Cmax and area under the plasma concentration-time curve; AUC) and a longer elimination plasma half-life of LSD when MDMA was co-administered. The LSD-MDMA combination increased blood pressure, heart rate, and pupil size more than LSD. Both MDMA and the MDMA-LSD combination increased oxytocin more than LSD.

Conclusion: Co-use of MDMA (100 mg) does not improve the acute effects and safety profile of LSD (100 µg). Combined use of MDMA and LSD is unlikely to provide relevant benefits over LSD alone in psychedelic-assisted therapy.

P161

Apixaban's Physiologically-based Pharmacokinetic model validation in hospitalized patients in the OptimAT study: a first step for larger use of a priori modelling approach at bed side

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Introduction: When direct oral anticoagulants (DOACs) are used in real-world conditions, substantial interindividual variations in plasma concentrations can be observed for the same dose, leading to a risk of over or under-exposure. Physiologically-based pharmacokinetic (PBPK) models incorporate substrate specific properties obtained from in vitro experiments to predict the dose-concentration relationships in vivo (1). Beyond their use by pharmaceutical companies PBPK models are increasingly studied in academic research and could help many physicians by guiding prescription in vulnerable populations in hospital settings. The goal of the present observational study is to elaborate and validate a PBPK model for hospitalized patients on apixaban in a tertiary center.

Methods: This observational study took place in the Geneva University Hospitals in the context of the OptimAT study (NCT03477331). It prospectively included 100 patients, 18 years and above, treated with apixaban for a minimum of 48h prior to inclusion. Apixaban determination in dried blood spots (obtained at 0, 0.5, 1, 2, 3, 4, 6 and 8h), was performed using a fully validated LC-MS/MS method. A previous apixaban PBPK model (2) (Simcyp®, version 21) was refined to our population using Simcyp® geriatric population and individual matching for patient's age, weight and renal function. The primary endpoint was the ratio between geometric mean of predicted (P) and observed (O) AUCtau. The model was considered to be validated clinically if the 95% confidence interval around the mean was included within the margins set to 20%. Non-compartmental analysis of observed data was performed using PKanalix®,version 21.

Results: P/O ratio for AUCtau filled the prespecified criteria for validation with the refined model (1.00 ; IC90% 0.99-1.02) (table 1, figure 1). Results for other PK parameters are summarized in table 1.

Conclusions: Apixaban's exposure was accurately predicted in a cohort of acutely ill hospitalized patients. The study supports the evidence that PBPK is a promising tool for model-informed prescription in a clinical setting. Virtual twining in integrating individual's phenotyping for metabolism and transporter's enzymes represents the next step in this process.

Table 1. Comparison between observed and predicted PK parameters for the final apixaban's model.

Population	AUC_{tau} (ng/ml·h) (geometric mean, IC 90%)	Cmax (ng/ml) (geometric mean, IC 90%) 90%)	Tmax (h) (geometric mean, IC 90%)	t1/2 (h) (geometric mean, IC 90%)
OptimAT (observed)	1591.80 (1488.75-1701.99)	182.95 (172.09-265.40)	1.80 (1.64-1.97)	13,42 (8,61-20,91)
Geriatric* adapted to OptimAT population (predicted)	1599.80 (1576.12-1623.84)	164.58 (162.22-166.97)	2.88 (2.85- 2.91)	12.51 (12.24-12.79)
Ratio P/O	**1.00 (0.99-1.02)**	**0.90 (0.88-0.91)**	**1.60 (1.59-1.62)**	**0.93 (0.91-0.95)**

* Simcyp® original population

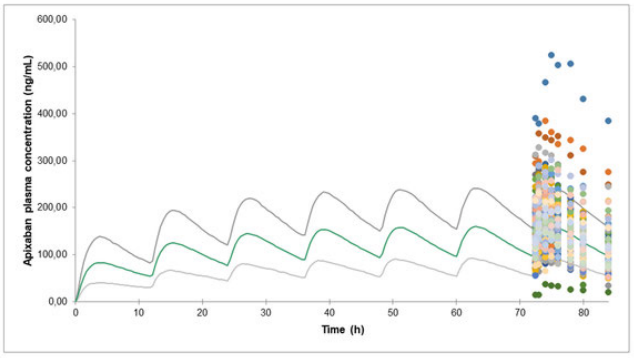

Figure 1. Observed apixaban plasma concentrations from the OptimAT study vs predicted apixaban plasma concentrations with the finale model in geriatric population adapted to OptimAT population. In green = mean concentration. Dark grey = 95th percentile. Light grey = 5th percentile.

P162

Biochemical follow-up of patients with a Pheochromocytoma/Paranganglioma: a Swiss retrospective study

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Background: Patients previously affected with a PHEO/PGL (Pheochromocytoma/Paraganglioma) or carrying a genetic mutation predisposing to a PHEO/PGL have a definite risk of relapse. Recommendations edicted by the Endocrine Society propose lifelong annual biochemical testing to assess for recurrent disease. The aim of this study was to establish the performance of this monitoring and to determine the frequency of testing that would be optimal to detect tumor relapse.

Methods: This retrospective study used our clinical PPGL laboratory database, established at CHUV since 2008. Plasma free and total metanephrines were measured in 3295 samples from 568 patients of whom 220 are at risk and monitored for a possible tumor development. This cohort includes 312 PHEO and 106 PGL. Among them, 109 patients harbored a known mutation (MEN2, NF1, SDHx and VHL). 14 % (15/91) of PGL were malignant and 6.7 % (21/291) for PHEO (Plasma metanephrines (free and total) were determined by LC-MS/MS. Biomarkers trajectories were followed during 3-13 years and described using longitudinal mixed-effect modeling and log transformed concentration for normality curves.

Results and conclusion: Free Plasma metanephrines (MNs, composed of Normetanephrine, Metanephrine and Methoxytyramine, NMN, MN, MT) concentration slopes monitored before surgery are significantly higher than in patients that will not undergo surgery and this apply for total MNs as well. This tendency appears several years before surgery.
Currently, decision for surgery is based when the cut-off values of MNs are reached. Probability for a surgery is 75 % ,65 % and 50 % when URL is reached for NMN, MN and MT, respectively.
Continuous measurements of biomarkers in patients at risk of developing a PPGL (inherited cause, follow-up after surgery) would better predict a PPGL than measuring only a target concentration based on URL.

P164

Development and validation of a multiplex HPLC-MS/MS assay for the monitoring of JAK inhibitors plasma concentrations abrocitinib, baricitinib, fedratinib, ruxolitinib, tofacitinib and upadacitinib

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Introduction: Janus kinase inhibitors (JAKi) are small molecules orally used to treat autoimmune and myeloproliferative disorders,

and are associated with erratic drug absorption. Dose-dependent efficacy and tolerability issues can be addressed by therapeutic drug monitoring (TDM), using plasma concentration measurement for drug exposure optimization. Individualized JAKi dosages meet all the conditions for drugs with narrow therapeutic indexes. A highly sensitive and selective analytical method using multiplex high performance liquid-chromatography coupled to tandem mass spectrometry (HPLC-MS/MS) was developed for the simultaneous quantification of abrocitinib, baricitinib, fedratinib, tofacitinib, ruxolitinib, and upadacitinib in plasma.

Methods: Human plasma samples are subjected to protein precipitation with methanol at a ratio of 3:1 v/v, using stable isotopically labelled internal standards to compensate for analytical variability. The separation of JAKi was performed on a Xselect® HSS T3 3,5 µm, 2,1x75 mm C18 column (Waters, USA) using a mobile phase composed of H2O/formic acid 0.1% (solvent A) and acetonitrile/formic acid 0.1% (solvent B) in gradient mode. The drugs were monitored in the positive electrospray ionization mode. The detection was performed on a triple-stage quadrupole Quantiva™ MS/MS detector (Thermo Scientific, USA). The method is extensively validated according to FDA guidance, SFSTP and ICH guidelines. As part of laboratory internal quality control the method was applied on patients' samples receiving JAKi for various conditions.

Results: Selectivity (including absence of cross-talk), carry-over, sensitivity (lower limits of quantification 0.5-2.5 ng/ml) were established across the clinically relevant concentration ranges (upper limits of quantification 200-1000 ng/ml) and the run lasts for 7 minutes. Repeatability (<15 %) and short-term stability (96h) were assessed for all studied molecules. The applicability of the method has been demonstrated in all analyzed human plasma samples.

Conclusions: We developed a highly sensitive method to quantify several JAKi in human plasma that are increasingly used for many pathologies. After validation, this assay could be implemented for clinical guidance to improve their effectiveness and safety. Population pharmacokinetic-pharmacodynamic analyses of JAKi is planned to complete the research program in order to streamline TDM as an essential approach to precision medicine.

P165

Generative artificial intelligence for the simulation of virtual patient profiles in non-linear mixed effects modeling

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Introduction: Non-linear mixed effects (NLME) models are the gold standard for pharmacometric modeling. They simultaneously describe the pharmacokinetic (PK) and -dynamic (PD) data from all patients within a population in a system of ordinary differential equations (ODEs), while also accounting for inter-subject variability and residual error by estimating subject-specific fixed effects (covariates such as sex or weight) [1]. The resulting population PK (PopPK) models are an estimated description of the fate of a drug within the body and its effects. In this study, we create artificial patients from an existing original patient population using Generative Adversarial Networks (GANs), and compare the estimated PK parameters. GANs are powerful machine learning algorithms that are able to learn the underlying probability distribution of a dataset and, based on that, create new artificial data samples [2, 3].

Methods: We created a dataset of 20 original patients (10 males, 10 females) with a random age, and sex-specific, normally distributed height and weight. We simulated blood concentration after extravascular administration of 300 mg of an imaginary drug with first order absorption, one compartment distribution and linear elimination. Weight was set as a covariate for volume of distribution (Vd). Artificial patients were generated by Wasserstein GAN (WGAN) [4] with gradient penalty (GP) [5]. We estimated and compared the PopPK parameters for the original and artificial patient population using Monolix (2021R1, Lixoft, Anthony, France).

Results: WGANs are able to learn temporal progression of the concentration of the drug in the blood, the covariate distribution, as well as the influence of the covariates on PK parameters. The estimated PK parameters of the original and artificial patient population are comparable. Due to the small sample size, the estimated parameter deviate from ground truth in both models.

	Ground truth	20 original patients	20 artificial patients
Fixed Effects			
ka_{pop}	**0.5**	0.28	0.29
Vd_{pop}	**14**	8.41	8.25
Body weight on Vd	**0.75**	0.36	0.32
Cl_{pop}	**5**	5	5.17
Standard Deviation of the Random Effects			
ω_{ka}	**0.2**	0.3	0.37
ω_{Vd}	**0.3**	0.077	0.16
ω_{Cl}	**0.2**	0.16	0.17
Error Model Parameters			
Additive	**0.2**	0.2	0.25
Proportional	**0.1**	0.097	0.078

ka: absorption rate constant; Vd: volume of distribution; Cl: clearance

Conclusion: Generative artificial intelligence can be used to simulate patients with the same underlying statistical distribution as the original patient population. Future applications could include augmenting data sets from underpowered clinical trials or sparse sampling strategies.

P166

Impact of ileostomy reversion on tacrolimus and everolimus blood concentrations: a case report

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Learning objectives: Ileostomy reversion can increase drug absorption. For molecules with a narrow therapeutic range, there is a risk of toxicity. In these situations, when therapeutic drug monitoring is available, close monitoring of drug concentrations is warranted after surgery.

Case description: A 56-year-old woman known for familial colorectal polyposis, multi-organ transplantation (duodenum, small intestine, right colon, pancreas, spleen), and ileostomy on tacrolimus (TAC) prolonged-release tablets 6mg qd and everolimus (EVR) 5mg bid, was admitted electively for ileostomy closure and colonic continuity restoration. By 48h after surgery, TAC whole blood trough concentration (Ct) increased significantly (28.7 µg/l; target Ct 3-5 µg/l at 48h). EVR trough Ct increased 96h after surgery (**Table 1**). The patient experienced symptoms, such as hypertension, headache, and nausea, consistent with TAC toxicity. Both treatment dosages were decreased.
A pre-analytical error was ruled out. Hematocrit values were stable. Medication nonadherence was excluded and no pharmaceutical modification was reported. Despite the presence of CYP3A4/5 and Pgp inhibitors, no new drug treatment or medication changes could explain the sudden increase in TAC Ct. Furthermore, no diet or transit changes occurred after the intervention.

	2 months before intervention (BI)	1 week BI	Intervention	2 days AI	4 days AI	14 days AI
TAC* (µg/l)	2.6	1.9	3.9	28.7	32.0	4.8
EVR** (µg/l)	11.2	4	14.5	10.7	28.1	12.4
TAC dosage	8mg qd	6mg qd	6mg qd	6mg qd	6mg qd	3mg qd
EVR dosage	5mg bid	5mg bid	5mg bid	5mg bid	5mg bid	4.5mg bid

*Electrochemiluminescence Immunoassay (ECLIA) measurement
** Liquid chromatography-mass spectrometry (LC/MS)

Table 1. Drug dosage and trough Ct before and after intervention

Discussion: This is the first reported case of high TAC and EVR Ct after reversion of ileostomy. Pharmacokinetic factors, such as oral bioavailability, contribute to the interindividual variability in drug concentration. TAC is absorbed from the duodenum to the ascending colon. Ileostomy reversal could increase colonic absorption of TAC and contribute to the increased TAC trough Ct and risk of toxicity. We did not find data on EVR absorption, however in this

patient, the increase in EVR concentrations is likely explained by the same mechanism.
Close monitoring of EVR and TAC concentrations appears to be extremely important after ileostomy closure and restoration of continuity.

P167

In vitro screening of putative inhibitors and substrates of UGT2B10 from transplant setting

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Background and purpose: Allogeneic hematopoietic stem cell transplantation (HSCT) is often used for treating malignant and non-malignant hematological diseases (e.g. leukemia and thalassemia) in children. Wide range of medication is used prior to and after HSCT, including conditioning chemotherapy (e.g. busulfan and cyclophosphamide) and supportive care drugs (e.g. paracetamol, lorazepam) and immunosuppressants (e.g. mycophenolic acid) as well as antifungal agents (e.g. voriconazole). Some of the administered drugs are hepatotoxic and may play a role in the incidence of sinusoidal occlusion syndrome (SOS). It was shown that a genetic variant in gene encoding the enzyme UGT2B10 can predict incidence of SOS. In this *in vitro* study, we screened drugs prioritized using an *in silico* pipeline in order to assess their potential of being substrates and/or inhibitors of UGT2B10[1].

Experimental approach: An analytical method for *in vitro* screening of the substrates and inhibitors of UGT2B10 was developed and validated. Cotinine was used as a substrate with recombinant UGT2B10, and its metabolite cotinine-glucuronide was quantified through LC-MS/MS. First, incubation time, DMSO proportion, and cotinine concentration were optimized. Then, paracetamol, lorazepam, mycophenolic acid and voriconazole-n-oxide were tested *in vitro* for their inhibitory potential of UGT2B10. Half-maximal inhibitory concentration (IC50) and inhibition constant (Ki) were determined for compounds showing inhibition. Finally, to determine potential substrates, each compound was incubated with recombinant UGT2B10 to identify the corresponding glucuronide metabolite through LC-MS/MS. Proper replicates, negative and positive controls are included in each experiment.

Key results: We report lorazepam (Ki = 0.25 ± 0.17 mM; IC50 = 0.01 mM) and mycophenolic acid (Ki =0.72 ± 0.54 mM; IC50 = 0.38 mM) as inhibitors of UGT2B10. Paracetamol and voriconazole-n-oxide did not show any inhibition. None of the tested compounds featured a metabolism through UGT2B10.

Conclusion and implications: Mycophenolic acid and lorazepam showed inhibition of UGT2B10 at therapeutic concentrations. It is known/likely that these molecules also inhibit homologous isoform UGT2B7. Further exploration of clinical relevance and screening of voriconazole as substrate of UGT2B10 is ongoing.

P168

Influence of SARS-CoV-2 infection on hepatic function impairment after paracetamol use: a case-control study

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Introduction: Reduced glutathione (GSH) is essential in the detoxification of the highly reactive paracetamol metabolite N-acetyl-p-benzoquinone imine (NAPQI),[1] and GSH deficiency may be associated with an increased risk of paracetamol-related hepatotoxicity.[2] Total GSH blood levels were found to be decreased in patients with Covid-19, with lower levels being observed in more severely ill patients.[3] This retrospective case-control study aims to investigate if SARS-CoV-2 test status combined with other clinical data is predictive for an impairment of liver function following paracetamol intake.

Methods: The study population consisted of patients tested for SARS-CoV-2 by Reverse Transcription Polymerase Chain Reaction nasopharyngeal swab test between February and November 2020 at the Insel Hospital Group (Bern). We included patients with alanine transaminase (ALT) ≤ 90 IU/L (2x upper limit of the norm (ULN)) and alkaline phosphatase (ALP) ≤ 200 IU/L (2x ULN) before paracetamol treatment. We defined cases as subjects with ALT > 135 IU/L (3x ULN) or ALP > 200 IU/L (3x ULN) up to 3 days after paracetamol treatment. Controls remained at ALT and ALP ≤ 2x ULN during and after paracetamol treatment. Cases and controls were matched in a 1:3 ratio. We applied different statistical models (multivariate logistic regression, decision trees, k-nearest neighbor and decision trees) to identify features, including demographics, laboratory values, and SARS-CoV-2 test status, predictive for elevation of liver enzymes. We selected biologically plausible features with high data availability and removed one feature out of every pair with a Spearman correlation coefficient |>0.2|.

Results: A total of 90 cases and 270 matched controls were included, and 13 features were used for modeling. The resulting decision tree has an overall balanced accuracy of 77.6%. Laboratory values indicative of liver function before start of paracetamol therapy (mean ALT, minimum international normalized ratio (INR)) and body mass index (BMI) contributed most to the classification, whereas SARS-CoV-2 test status seemed to carry the least predictive value of all included variables.

Conclusion: These results indicate that SARS-CoV-2 test status is no risk factor for elevation of liver enzymes after paracetamol treatment. Indicators of overall liver health, such as ALP, INR, and BMI need to be examined closely before initiation of paracetamol treatment.

P169

Ketanserin reverses the acute effects of lysergic acid diethylamide in healthy participants

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Introduction: Lysergic acid diethylamide (LSD) is being investigated in substance-assisted therapy. Therapy sessions with LSD are long, due to its duration of acute action of 8-11 h. LSD acutely produces an altered state of mind primarily through serotonin i.e. 5-hydroxytryptamine-2A (5-HT2A) receptor agonism (Holze et al., 2021). However, it is not clear whether its effect duration can be shortened using the 5-HT2A receptor antagonist ketanserin. Molecular dynamics simulations hypothesized that a lid is formed by an extracellular loop at the entrance to the 5-HT2A binding pocket (Wacker et al., 2017), which could therefore trap LSD at the receptor. On the other hand, the time course of the acute subjective action of LSD indicates that it acts only as long as it is present in the body (Holze et al., 2021). Therefore, no special mechanisms at the receptor would be needed to explain its duration of action in humans. The present study hypothesis was that ketanserin (40 mg p.o.) administered 1 h after LSD shortens the acute subjective and autonomic effects of LSD (100 µg p.o.) compared with LSD (100 µg p.o.) followed by placebo in healthy humans.

Methods: The study used a randomized double-blind, placebo-controlled, cross-over design with two experimental test sessions in 24 healthy volunteers (12 men, 12 women). Psychometric data were assessed, as well as autonomic effects and plasma concentrations.

Results: Ketanserin strongly and significantly reduced the LSD effect duration from 8.5 ± 2.2 h to 3.5 ± 1.3 h (mean ± SD; t(23) = -1.6, p = 0.001) compared with placebo (Figure 1). Similarly, ketanserin significantly reversed LSD-induced overall autonomic effects such as rate pressure product (t(23) = -3.7, p = 0.001), and mydriasis (t(23) = 3.1, p = 0.005). Pharmacokinetic parameters of LSD and its main metabolite 2-oxo-3-hydroxy LSD (O-H-LSD) remained unaffected by ketanserin administration.

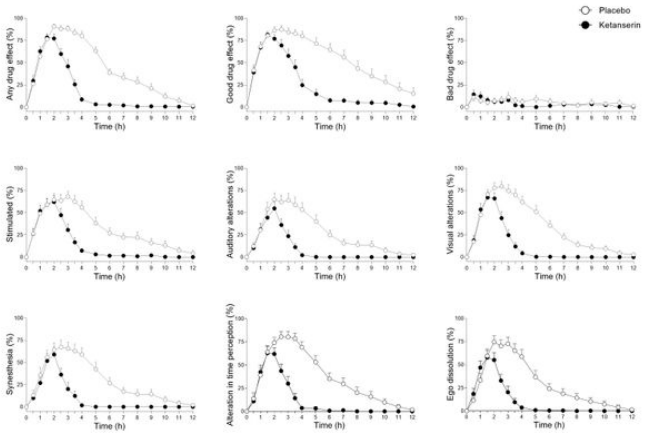

Figure 1. Acute subjective effects of LSD over time on Visual Analog Scales (VASs).

LSD was administered at t = 0 h. Ketanserin or placebo was administered at t = 1 h. The data are expressed as the mean ± SEM in 24 subjects.

Conclusions: The study findings are consistent with a competitive interaction of ketanserin and LSD at the 5-HT2A receptor and the view that LSD produces its effects only when present at the receptor. Moreover, ketanserin can be used clinically, as a planned or as a rescue option to shorten the effect duration of LSD in humans.

P170

Population pharmacokinetics of oral ivermectin in venous plasma in healthy volunteers in Kenya in preparation for BOHEMIA cluster randomized controlled trial

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Introduction: Malaria is preventable and treatable, and yet it remains a significant global public health problem. Despite the large-scale implementation of preventive strategies such as nets or sprays the worldwide decline in malaria incidence is stalling, particularly in Africa. Sustained control and elimination is not considered achievable, unless new ways of controlling the disease and its vector are developed. A promising new strategy in malaria prevention is vector control through mass drug administration (MDA) of ivermectin (IVM). IVM mode of action is independent of insecticide resistance, having the potential to directly address malaria residual transmission.
BOHEMIA trial aims at evaluating MDAs of IVM for malaria control in Africa. Two phase III MDA cluster randomized controlled trials (cRCT) will be conducted. Participants will either receive: 1IVM 400 µg/kg single dose humans; 2) IVM 400 µg/kg single dose to humans and livestock; or 3) albendazole 400 mg. In preparation for the BOHEMIA cRCT, a phase II clinical trial was carried out in Kenya to assess the pharmacokinetics (PK) of two different IVM dose regimens. Evidence from previous studies shows 300 µg/kg IVM given once a day for 3 days results in a significant reduction in mosquito survival up to 28 days. However, MDA strategies may operationally struggle to deliver high coverage and adherence rates using a 3 day regimen. For this reason, an open-label RCT was designed to compare the population PK of single high-dose of IVM 400 µg/kg to the 3-day regimen of 300 µg/kg of IVM.
Methods: Healthy adult individuals from Kenya (n=30) participated in the phase II clinical trial, randomized to receive either IVM once (1x400 µg/kg, n=12), IVM on 3 consecutive days (3x300 µg/kg, n=6), albendazole once (400 mg, n=6) or no treatment (n=6). Participants' blood plasma was sampled regularly for up to 28 days. IVM was quantified by LC-MS/MS and analysed by population PK analysis.
Results: The plasma PK parameters were as follows: apparent population clearance 7.5 L/h (interindividual variability: 0.21), central and peripheral volumes of distribution were 196 L (0.22) and 288 L (0.16), respectively. The PK model accurately depicted population PK for oral ivermectin.

Conclusion: IVM single dose can be more attractive than 3 doses strategy as it produces similar exposure while maintaining easier feasibility of MDA campaigns, is more affordable and likely to yield higher compliance at the community level.

P171

Real-life therapeutic concentration monitoring of long-acting cabotegravir and rilpivirine in Switzerland

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Introduction: SHCS879 is an ongoing nationwide multicenter observational study within the Swiss HIV Cohort Study (SHCS) for the prospective therapeutic drug monitoring (TDM) of people living with HIV (PLWH) on long-acting injectable cabotegravir and rilpivirine (LAI-CAB/RPV).

Methods: The study uses an integrated strategy of treatment monitoring based on TDM, relevant clinical factors related to patient characteristics, and potential drug-drug interactions.

Results: As of January 2023, 570 blood samples have been collected from 158 PLWH, mostly male (83%), white (61%), and with a median age of 45 years (range: 26-76). In addition, 46% are overweight (BMI 25-30 kg/m^2), while 11% are obese (BMI > 30 kg/m^2). Figure 1 shows that 46% of RPV trough concentrations (Ctrough) are below the threshold recommended for therapeutic response (i.e. 50 ng/mL),[1] while 19% are below the first quartile (i.e. 32 ng/mL) based on data from phase III trials.[2, 3] For CAB, 34% of Ctrough are below the first quartile (i.e. 1120 ng/mL),[2, 3] and 14% are below the 4 x protein-adjusted 90% inhibitory concentration (i.e. 664 ng/mL).[4, 5] Overall, 6% and 14% of PLWH had more than one Ctrough below the lowest threshold either for CAB or RPV, while 15% had at least one sampling with both CAB and RPV Ctrough below these thresholds. Although no virologic failures have been observed in the study participants, LAI-CAB/RPV was discontinued in two individuals due to repetitive low Ctrough which raised the concern of developing resistant viral strains. Low drug concentrations in presence of other risk factors (i.e. virus sub-type, RPV resistances and BMI > 30 kg/m^2) have indeed been associated with an increased risk of virological failure.[6]

Conclusion: These interim data show a large variability in CAB and RPV Ctrough with some individuals having repeatedly low concentrations. Further observations are warranted to evaluate the clinical relevance of TDM in PLWH under LAI-CAB/RPV.

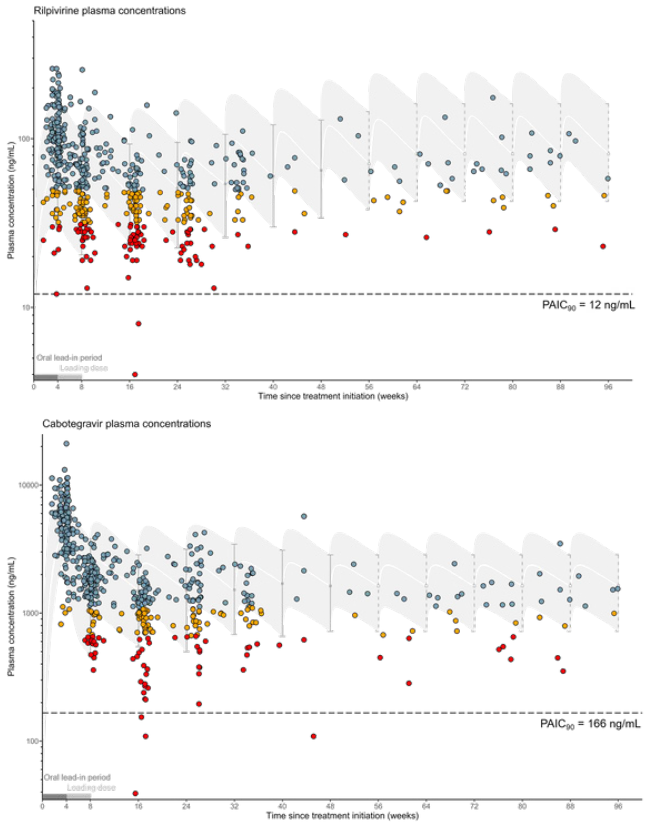

Figure 1. Observed plasma concentrations for CAB and RPV, along with usual concentration ranges (median, 5 and 95 percentiles) from the ATLAS-2M[7] trial. Ranges are prolonged beyond 48 weeks and extrapolated according to reported data (dashed intervals).[3, 8] Orange dots correspond to concentrations below the threshold of 1120 ng/mL for CAB,[2] and 50 ng/mL for RPV.[1] Red dots correspond to the concentrations below the threshold of 664 ng/mL for CAB,[4, 5] and 32 ng/mL for RPV.[2]

P172

Toxicity profile of supratherapeutic loperamide: a systematic review

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Introduction: The over-the-counter antidiarrheal loperamide is an opioid with a favorable safety profile at therapeutic dose thanks primarily to its low bioavailability. Recently, severe toxicity following high-dose loperamide misuse was reported. Systematic data on the dose-toxicity profile of these exposures are lacking so far.

Methods: Systematic review of publications on supratherapeutic loperamide with a focus on the exposure-toxicity relationship. In this interim analysis, we included reports published until March 2022 and identified by a systematic search of two databases (Medline, Embase). Supratherapeutic exposure was determined by reported dose or measured concentration. The primary outcome was the poisoning severity score (PSS), secondary outcomes consisted of the initial and maximal QRS and QTc. Associations of dose and concentration with endpoints were investigated using bivariate correlation analysis and multivariate ordinal logistic or linear regression adjusted for demographics, risk-increasing co-ingestions and comorbidities.

Results: 97 patients (63% male, median age 31) from 75 case reports and 8 case series were included. The number of publications peaked in 2018 (n=16). As exposures occurred typically after chronic misuse, substance use disorder was frequently reported (68%), while self-treatment of diarrhea syndromes was uncommon (9%). The median reported daily dose was 200 mg. Patients with severe symptoms (PSS 3, 58%) or fatal outcome (PSS 4, 12%) had ingested higher doses (median (range): 225 (20–800) mg) compared to those with non-severe symptoms (PSS 0-2, 30%, median dose (range): 160 (14–400) mg, p=0.006). Most frequent life-threatening symptoms were arrhythmias with polymorphic ventricular tachycardias, most frequent signs in non-severe presentations were syncope and ECG abnormalities (QTc/QRS prolongation or Brugada syndrome). On multivariate analysis, severity (but not QRS/QTc) was positively associated with higher dose (OR 1.07, 95%CI: 1.03-1.11, per 10mg dose unit, n=86) and with higher drug concentrations (OR 1.08, 95%CI: 1.01-1.2, unit: µg/dl, n=30).

Conclusion: In this preliminary analysis, supratherapeutic loperamide exposure occurred mainly as chronic ingestions in patients with substance use disorders. Nearly two thirds of patients experienced life-threatening symptoms such as ventricular arrhythmias or had a fatal outcome. The risk for more severe outcomes increased with loperamide dose and concentration.

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P173

Enantioselective separation of Omeprazole and 5-hydroxyomeprazole in human plasma using column switching approach: a snapshot of CYP2C19 activity

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Introduction: Cytochrome P450 2C19 (CYP2C19) is highly variable due to genetic and environmental factors. CYP2C19 phenotyping using omeprazole is widely used prior to the prescription of drugs substrate of this enzyme. The metabolism of omeprazole is, to a large extent, dependent on CYP3A4 and CYP2C19. Studies have demonstrated that omeprazole enantiomers show a clear in-vivo and in-vitro difference in their metabolism.

Objectives: We developed and validated a bioanalytical method for a stereoselective analysis of omeprazole and 5-hydroxy-omeprazole in human plasma using two-dimensional liquid chromatography-mass spectrometry to select the best enantiomer for CYP2C19 phenotyping.

Methods: The chromatographic equipment, an Agilent 1290 series LC system, was annexed to Agilent 1100 series LC gradient pump. The UHPLC system was coupled to a SCIEX QTRAP 6500 mass spectrometer equipped with an electrospray ionization source operating in positive polarity. Online extraction was first achieved on an achiral Discovery HS C18 trapping column for purification (20x2.1mm ID, 5um particle size, Supelco) and subsequent forward flush elution to a chlorinated phenylcarbamate cellulose-based chiral column (150x2mm ID, 3um particle size, Lux Cellulose-4, Phenomenex) using a six-port switching valve. Finally, omeprazole and 5-hydroxy-omeprazole enantiomers were separated on the chiral column using a gradient mobile phase composed of water and acetonitrile.

Results and conclusion: The total run-time was less than 8 min. This innovative strategy involves a minimal carryover and good preservation of the lifetime of columns. The tested range was 0.5-200 ng/mL for both analytes. This method was fully validated and featured good performance in terms of trueness (87.9-97.1%) and precision (4.8-13.7%). The mean extraction recoveries were 69 and 77% for omeprazole and 5-hydroxyomeprazole, respectively. Finally, this procedure was successfully applied to pharmacokinetic study samples and will be assessed in further studies as a potential metric of CYP2C19 activity.

P174

Improving data collection as part of pregnancy safety studies: towards standardization of data elements in pregnancy reports from public and private partners

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Introduction: The Swiss Federal Office of Public Health (FOPH) is evaluating the needs for a national registry on drug use in pregnant women. The goal is to improve drug safety in this population. In Europe, the EU-funded ConcePTION project, aims to change the way drug use during pregnancy is studied. Both initiatives require exploration of how standardizing data collection and analysis by different stakeholders would allow for meta-analyses from studies within the same therapeutic area. To do so, a reference framework of Core Data Elements (CDEs) recommended for studies on drug safety during pregnancy was previously developed. The aim of this study was to explore the possibility of adherence to the CDE items in a real world setting of data collected by different Data Access Providers (DAPs) using multiple sclerosis studies as a pilot.

Methods: Four pregnancy registries (Gilenya, Novartis; Aubagio, Sanofi (OTIS); Aubagio, Sanofi; the Dutch Pregnancy Drug Register [Lareb]), two enhanced pharmacovigilance programs (Gilenya PRIM, Novartis; MAPLE-MS, Merck) and four Teratology Information Services participated in the study. The CDE includes 51 items covering administrative functions, the description of medical history, maternal illnesses arising in pregnancy, delivery details, pregnancy and infant outcomes. Each DAP classified the variables from their databases for each CDE item as follows: 1) variable taken from an existing field 2) variable derived by combining data from other fields; 3) similar variable but with divergent definition; 4) missing variable.

Results: The majority of the DAP's data variables were either directly taken (85%, n=305/357) or derived by combining different variables (12%, n= 42/357) to conform to the CDE variables and definitions. For very few of the DAPs variables, adherence to the CDE items was not possible, either because of divergent definitions (1%, n=3/357), or because the variables were missing (2%, n=7/357).

Conclusion: A very high proportion of variables from The DAPs matched the CDE items, indicating that alignment of definitions and harmonization of data analysis by different stakeholders could be feasible. Since pregnancy safety data collection is a global challenge, the FOPH should consider the methods developed by ConcePTION in their efforts to consolidate a private-public nationwide registry of drug exposure in pregnancy in Switzerland.
This study was conducted as part of the the IMI-Conception project (IMI 821520).

P175

Pharmacodynamic interaction between capecitabine and folic acid: a case report and literature review

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Learning objective: Capecitabine toxicity may be enhanced by folic acid (B9) supplementation.

Case: A 48-year-old woman, known to be folic acid deficient and supplemented with 5 mg/d of B9 was diagnosed with right colic adenocarcinoma. A right colectomy and terminal ileostomy were performed and adjuvant chemotherapy (CAPOX protocol) with capecitabine (CAP) 3000 mg/day for 21 days and oxaliplatin 200 mg on day 1 was initiated. Preliminary dihydropyrimidine dehydrogenase (DPD) genotyping indicated an indeterminate genotype and DPD phenotyping measured normal activity of the enzyme. The identified MTHFR variant was not associated with increased CAP toxicity. On protocol day 2, severe nausea, vomiting, diarrhea and herpetic stomatitis were reported, but no evidence of myelotoxicity. The patient was hospitalised and CAP was stopped after 9 days, nevertheless, the digestive symptoms persisted.
A pharmacodynamic interaction between CAP and B9 was suspected, increasing the severity of the adverse effects of CAP. Those of acyclovir, used to treat herpetic stomatitis, may have contributed to the persistence of digestive symptoms, but they resolved 1 week after cessation of B9 supplementation and despite continued acyclovir administration. The 2nd cycle of chemotherapy was performed with 5-FU alone and was well tolerated without recurrence of symptoms.

Discussion: CAP, which is not cytotoxic, is converted to cytotoxic 5-FU in three enzymatic steps, the last of which occurs preferentially in the tumour. 5-FU is then catabolised by DPD to a less toxic metabolite. 5-FU inhibits thymidylate synthase (TYMS) by covalent binding. TYMS is required for pyrimidines/DNA synthesis and is essential in the endogenous folate pathway. B9 stabilises the covalent bond between 5-FU and TYMS, thereby potentiating the cytotoxic effects. Despite the widespread co-administration of 5-FU and leucovorin (a reduced form of B9), the association of CAP and B9 is less common.
Two cases of CAP toxicity with B9 supplementation have been reported in the literature. A relationship between serum B9 and the severity of CAP toxicity is also described with a 9% increase in the risk of severe toxicity for every 10 nmol/L increase in serum B9. The most common management strategy is B9 avoidance combined with CAP dose reduction in subsequent cycles. Therefore, physicians should be aware of the risk of adverse effects of CAP when co-administered with B9 and consider stopping B9 supplementation.

P176

The impact of metronomic chemotherapy such as vinorelbine plus capecitabine in the therapeutic arsenal of breast cancer (Algerian experience)

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Introduction: Metronomic oral chemotherapy is an alternative to conventional conventional chemotherapy; it is a treatment administered in reduced doses and repeated regularly like a metronome

Materials and methods: Retrospective study from June 01 to December 31, 2021 (6 months) on 06 women aged 65 and over with advanced breast cancer collected in the medical oncology department of the Annaba cancer center.

Results: The average age of 69 years. ¾ of the cases were from Annaba. Infiltrating ductal carcinoma was the most common histological type (75%), 60% of tumors had SBR grade III. 2/3 of the tumors were metastatic from the outset, with bone involvement being the most frequent metastatic localization (60%), surgery is performed in 50% of cases, while radiotherapy was indicated in 30% of the population. Metronomic oral chemotherapy such as capecitabine + vinorelbine in combination was administered to all patients with a total of 33 courses (5-8), All patients were evaluable for response and toxicity: One objective response (complete and partial) is observed in 75% of cases, concerning therapeutic tolerance; 40% of cases presented grade 1 and 2 side effects such as fatigue in 60%, anorexia in 20%, diarrhea in 10% and vomiting in 10%. We did not record any grade ¾ toxicities. Currently: 65% of patients alive, 15% lost sight of and 20% dead.

Conclusion: Unlike conventional chemotherapy, metronomic chemotherapy acts primarily on the tumor microenvironment through at least two known mechanisms; anti-angiogenic action and anti-tumor immunity with better tolerance.

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P177

Breast cancer in elderly women: impact of geriatric assessment in therapeutic management in eastern Algeria (about 74 cases) multicenter study

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Introduction: Oncogeriatrics is a subject of the future, but above all immediate! Any doctor can identify at least 30% of his activity with patients ≥ 65years old suffering from cancer and who require a geriatric evaluation.

Materials and methods: From January 2018 to December 2019; 74 patients aged 65 and over with locally advanced and / or metastatic breast cancer underwent a specialized geriatric evaluation.

Results: In our multicenter study; more than half (56.8%) of patients with advanced breast cancer were under the age of 75 at admission. 59.4% of the population had a performance status equal to 1 at the time of diagnosis. More than two thirds of the elderly patients were dependent at the first consultation; with different degrees. The G8 questionnaire was used in the entire study population, of which 64.4% revealed geriatric vulnerability or fragility. The average G8 score was 12.9 with extremes (8-17). 82.4% of the patients presented co-morbidities ranging from one to five defects of different severity, a small percentage of grade 3 comorbidities compared with grade 2 and a total absence of grade 4 co-morbidities. The main co-morbidities grade 3 morbidities encountered: renal pathology (5.4%); heart (2.7%); gait disturbance (2.7%); dysthyroidism (2.7%). The analysis of the general condition of the patients evaluated by the G8 score and the presence or absence of co-morbidities distinguished three groups: harmonious aging 35.2%; vulnerable 47.3% and a fragile group 17.5%.

Tableau: Répartition des malades en fonction des résultats de l'évaluation gériatrique.

Evaluation gériatrique	74	100%
Groupe « vieillissement harmonieux » : G8 ;14 +co-morbidités grade 0-1	26	35,2%
Groupe « Vulnérable » : G8 ; 14+co-morbidité grade 2	35	47,3%
Groupe « fragile » : G8 ; 14+ co-morbidité grade 3 (≤2)	13	17,5%
Groupe «trop malade » : G8 ; 14+co-morbidité grade 3 (>2)	0	0%

Conclusion: Integrate the geriatric assessment into the decision-making process of patients ≥ 65 years old with cancers in Algeria and develop the scales of this assessment for better management of this age group.

P178

Characteristics of patients who reach ST-REHA 300-minutes requirement for geriatric rehabilitation: a preliminary analysis

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Introduction: ST REHA financing structure for inpatient geriatric rehabilitation is based on structural, procedural, and staff requirements to reach a 300-minutes threshold of therapies (e.g., physical and occupational therapy, nutritional, psychological, and social interventions, etc) to obtain reimbursement. However, little is known about the proportion and characteristics of older patients meeting or not this threshold, as well as about their respective functional gains.

Study objectives:
1. To determine the proportion of patients who meet the 300-min weekly threshold over their geriatric rehabilitation stay
2. To investigate the clinical characteristics of these patients
3. To compare functional gains in patients who succeed or not the 300-min threshold.

Method: Enrolled patients (N=646) were those consecutively admitted over a 6-month period (January 2022-June 2022) to a swiss geriatric rehabilitation center. Socio-demographic, health, and functional status characteristics at admission and discharge were retrieved from electronic medical records. Bivariable analysis was performed.

Results: Overall, 47/646 (7.3%) patients reached the 300-min threshold of weekly therapy. Compared to patients who did not reach this threshold, those who succeed were younger (median age 80.8 vs 85.0 p=.003), more frequently men (53.2% vs 38.1%, p=.041), with more severe comorbidities (median CIRS score 20.0 vs 19.0, p=.038), nutritional (MNA<7, 68.9% vs 43.0%, p=.004), functional (FIM ADL score 22.0 vs 28.0, p=.03) and mobility (FIM mobility score 14.0 vs 17.0, p<.001) impairments but no difference in cognitive and affective status at admission. Successful patients remained with lower functional (FIM ADL score 29.0 vs 34.0, p=.02) and mobility (FIM mobility score 20.0 vs 24.0, p<.01) performance at discharge than those of patients who did not reach ST REHA 300-min threshold, but the magnitude of gain in functional (delta FIM ADL 3.0 vs 3.0, p=.35) and mobility (delta FIM mobility 4.5 vs 5.0, p=.48) performance was similar in both groups.

Conclusions: Less than 10% of enrolled patients reached ST REHA 300-minutes threshold defined for geriatric rehabilitation. Successful patients were more severely impaired at admission but the magnitude of their functional and mobility gains did not differ from those of patients who did not meet this threshold. Overall, these preliminary results strongly question the scientific basis of ST REHA 300-minutes arbitrary threshold.

P179

Diagnostic algorithm for malignant breast tumors in people aged 65 and over "difficulties encountered" (case series)

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Introduction:
Today, cancer is undoubtedly the most dreaded disease and it is assimilated to a real modern scourge. The elderly are largely under-represented in clinical studies and the optimal diagnostic modalities in this population are poorly codified.

Materials and methods :
Our work is extended over three years from January 2016 to December 2018 at the level of medical oncology services in eastern Algeria.
This is a multicenter descriptive and analytical study of 74 advanced cases of breast cancer.

Results :
The median age was 72 years old. The proportion of family history of cancer was 20.7%. The average consultation time was 12.6 months with a median of 5.5 months. The breast nodule was the main mode of revelation of this cancer (81%). More than half of our population presented with left breast cancer. The proportion of non-specific infiltrating carcinoma was high (78.3%). HR was positive in 63.5%, Her 2neu in 8.1%. and KI67 was measured for only 31 patients.
Bone (52.7%) and pulmonary (43.2%) metastatic sites were the most frequent. 75.6% stage IV versus 24.4% inoperable stage III.
82.4% of the patients presented co-morbidities and the geriatric evaluation distinguished 03 groups; harmonious aging 35.2%, vulnerable 47.3%, fragile 17.5%.

Conclusion :
The prognosis of breast cancer seems generally more pejorative in the elderly (delay in care "delayed diagnosis" and often sub-optimal treatment, while certain histological characteristics are more favourable). It is therefore urgent to build clinical research and oncogeriatric studies to improve the care of the elderly.

P180

Immune-senescence, mitochondrial dysfunction and frailty syndrome: more than an association?

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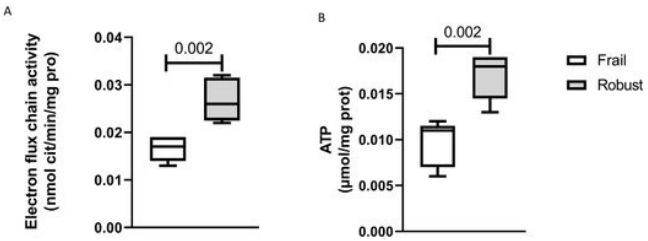
Here we studied the association between immune-senescence, mitochondrial dysfunction and frailty syndrome in older community dwelling frail adult age and gender matched with robust subjects. We enrolled 20 frail and 20 age and gender matched robust community dwelling older adults. T cells phenotype, answer to immune stimulation, cytokine production and immune cells mitochondrial function was measured.
In frail subjects both CD4+ and CD8+ T cells were decreased as respect to robust subjects, whether the ratio between CD4 and CD8 T cells was not significantly different. Naïve and memory T cells, as well as T cells expressing ICOS were similar between the two groups. Whereas both CD4 and CD8 T cells expressed lower levels of CD28 in frail as respect to robust subjects (Table 1).

Table 1. T cells phenotype in frail and robust older subjects. Mean and SD with CI are shown, for Gaussian variables. Median, 25th and 75th percentiles are shown for non-Gaussian variables, indicated with *. P values were calculated by one-way ANOVA for Gaussian variables and by the U Mann-Whitney test for non-Gaussian variables.

T cell type (% of lymphocytes)	Frail (20)	Robust (20)	P value
CD8+ T cells	21.5±15.7 (13.7-29.3)	38.8±22.2 (27.4-48.2)	0.014
CD8+CD45 Ro+ T cells*	14.8 (5.7-23.3)	8 (0.9-28.9)	0.602
CD8+ CD45Ra+ T cells *	1.6 (0.6-3.1)	0.6 (0-2.2)	0.211
CD4+ T cells	21.3±15.5 (13.6-29)	38.3±23.6 (27.3-49.4)	0.013
CD4+ CD45Ro+ T cells	12.9 (2.3-19.7)	26.3 (1-28.9)	0.871
CD4+ CD45Ra+ T cells*	1 (1-1.5)	0.4 (0.1-2.3)	0.620
CD4+/CD8+	1±0.1 (1-1.1)	1 ± 0.1 (0.9-1.1)	0.781
C8+/ICOS+	35.5±5.4 (24.2-46.9)	26.8±(17.2-36.3)	0.218
C4+/ICOS+	2.9±0.9 (1.1-4.7)	2.7±0.7 (1.1-4.2)	0.842
CD8+/CD28+	24.5±4.5 (15-34)	38±4.8 (27.9-48.2)	0.048
CD4+/CD28+	24.9±4.6 (15.2-35.5)	39.7±5.2 (28.8-50.6)	0.041

Despite the difference in immune phenotype, there was no significant difference in serum levels of the measured cytokines between frail and robust subjects. The stimulus of ICOS was effective in reducing TNFα production in frail and robust patients, whereas T cells from robust patients produced more IL-17 after CD28 stimulus as respect to T cells from frail subjects. In order to evaluate a possible impairment in mitochondrial function in frail subjects, we measured their electron flux chain and ATP level showing that both the parameters were significantly reduced in frail subjects (Figure 1).

Figure 1. Mitochondrial activity in PBMCs from frail and robust older subjects. Panel A. The box and whiskers plot shows the electron flux chain activity (shown on the y-axis) in mitochondria from frail and robust subjects. Panel B. The box and whiskers plot shows the ATP level (shown on the y-axis) by mitochondria from frail and robust subjects. Box and whiskers are drawn with the Tukey method, median, interquartile range maximum and minimum values are shown. P values were calculated by one way ANOVA.



According to our findings, the imbalance between CD4+ and CD8+ cells may not be regarded as a marker of frail aging, thus confirming the hypothesis raised by clinical longitudinal studies showing no survival advantage in the increased CD4/CD8+ T cells ratio [1,2]. Whereas the reduction of T cells may be associated to frail aging.
Despite the literature shows that mitochondrial function declines with age and may play a role in age associated increase in inflammation and immune-senescence [3] there are not studies investigating this relation in frailty in humans.
Here we show that mitochondrial function is compromised in frail subject, suggesting that mitochondrial dysfunction may be considered as a hallmark of frailty and targeted as possible therapeutic intervention.
In conclusion, we suggest that changes in T cells profiles are not associated with frailty syndrome, however changes in the amount of T cells, their answers to immune stimuli and reduced mitochondrial activity in PBMCs may be considered as a hallmark of frailty.

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