The COMET Study: a prospective COhort of MEdical residenTs to assess professional, personal and psychological trajectories of residents in General Internal Medicine

Research legislation:	Ordinance on human research with the exception of Clinical trials (HRO) [1].
Type of Research Project:	Research project involving human subjects
Risk Categorisation:	Risk category A
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PROTOCOL SIGNATURE FORM

Study Title	The COMET Study: a prospective COhort of MEdical residenTs to assess professional, personal and psychological trajectories of residents in General Internal Medicine

The project leader (main center) and the investigator (at the local center/site) have approved the protocol version 5.0 (dated 07.01.2025) and confirm hereby to conduct the project according to the protocol, the Swiss legal requirements [1,2], the current version of the World Medical Association Declaration of Helsinki [3] and the principles and procedures for integrity in scientific research involving human beings.

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GLOSSARY OF ABBREVATIONS

BASEC	*Business Administration System for Ethical Committees*
CRF	*Case report form*
FOPH	*Federal Office of Public Health*
HRA	*Human Research Act*
HRO	*Ordinance on Human*

1 BACKGROUND AND PROJECT RATIONALE

1.1.1 Background

In the postgraduate medical training, medical residents have the choice of a large panel of different career paths. In Switzerland, they can train in 45 clinical and non-clinical specialties and, later, work in private practices or in hospitals [a]. This freedom of choice has led to a growing number of people favoring medical or surgical specialties over primary care ones (e.g., general internal medicine (GIM), pediatrics or psychiatry). This *over-specialization* of the medical profession collides with the needs of the healthcare system, which requires more primary care professionals to cope with the basic healthcare needs of the population.

Currently in Switzerland, as in many other western countries, our healthcare system faces, on one hand, the accrual of an ageing population presenting with multimorbidity and complex diseases and, on the other hand, a growing shortage of healthcare professionals, including GIM physicians[b]. Nevertheless, GIM faces critical challenges itself related to: 1) the retirement of the older generation (baby-boomers) and 2) the low number of young physicians embracing this specialization [c].

Residents deciding to specialize in GIM have different profiles and expectations. They are (most of them) *millennials*, reflecting the changes appearing in the society, having higher expectations regarding their work-life balance and searching for possibilities to conduct their training part-time and preferring to work in organizations (hospitals or private practices) that promote well-being and personal development of collaborators. These expectations have lately been exacerbated by the COVID-19 pandemic that resulted in fatigue of the healthcare professionals, burnouts and people leaving the field of healthcare. Overall there exists a crucial and urgent need to better diagnose the reasons for young physicians to embrace GIM, determine the evolution of their psycho-somatic health during their training, and understand why some of them decide to leave this specialty.

1.1.2 Rationale for the research project

The lack of GIM physicians is due to at least two main reasons:

- First, most residents aspire to a subspecialty career path, in contradictions with the needs of the healthcare system. Previous research has showed the importance to recognize and support residents all along their postgraduate training (by setting goals) to promote GIM over subspecialties.

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[a] https://www.siwf.ch/fr/formation-postgraduee.cfm# accessed online January 2024

[b] https://www.sbfi.admin.ch/dam/sbfi/de/dokumente/2016/02/gesamtsicht_aus-undweiterbildungmedizinimsystemdergesundheitsver.pdf accessed online January 2024

[c] FMH-Ärztestatistik 2021: Jeder vierte Arzt ist 60 Jahre alt oder älter (Schweizerische Ärztezeitung) accessed online February 2023

- Second, evidence shows that healthcare professionals' well-being and quality of life is at risk, which affects their activities and professional trajectories. This reflects on an increasing distress of medical residents, contributing to physician burnout, depression, and job dissatisfaction. These factors have been associated with negative effects on patient care, including medical errors, suboptimal care practices, and decreased patient satisfaction with medical care and to lower medical knowledge.

A better understanding of the issues encountered by residents engaging in GIM would help identify potentially modifiable aspects in their career decision making and inform post-graduate educators, practitioners, and those with a policy interest in the physician workforce to facilitate their work conditions and their quality of life.
Capitalizing on the potential annual recruitment of ~1300 medical residents in the Departments of internal medicine of more than 20 hospitals and policlinics in Switzerland, we will establish the COhort of MEdical residenTs (COMET) Study, in order to prospectively assess the determinants of medical residents embracing a GIM training, their psycho-somatic health and the reasons why they purse or not in this specialty. The COMET Study will further pave the way for collaborations with other services of internal medicine or general practices/policlinics engaging medical residents in Switzerland to extend the recruitment in other settings to obtain a better insight into residency in GIM.

2 PROJECT OBJECTIVES AND DESIGN

2.1 Hypothesis and primary objective

We hypothesize that among the GIM residents participating in the COMET Study there will be an interaction and possibly a correlation among psycho-somatic health, job satisfaction, and work-life balance factors. We aim to describe how these factors will evolve during time and how they will influence their career trajectory.

2.2 Primary and secondary endpoints

General Objective: To establish a longitudinal cohort of GIM residents.
Specific objectives:

1. To assess the trend in psycho-somatic health, job satisfaction, and work-life balance among GIM residents
2. To describe internal medical residents' career path and to follow their evolution over time

The factors that we will measure to evaluate the objectives above are regrouped in:

- General baseline factors: year of birth, sex, no. of children, relationship status, work position, years of experience as a resident in GIM (indexed full time), year of board certification (or projected year of certification), native language(s), level of education of parents, financial aspects (income aspirations and educational debt), country of graduation (MD), years since graduation from medical school, title, number of articles published, days of conferences attended over the last 12 months
- Job related factors: average clinical working hours per week, average number of patients to care for per day, irregular shifts: number of evening, night and weekend shifts, other working activities: protected research time, protected time for teaching, actual specialty goal, interest in other medical specialties, long-term goal, actual work life balance and work balance aspired to, intention to quit
- Pull-up and push-out factors: a list of 24 factors that influence for or against a career in GIM
- Factors related to the well being at work: Well-being will be assessed by the Physician Well-being Index (PWBI), professional fulfillment with the PFI (Professional Fulfillment Index), residents' satisfaction with the balance between their personal and professional life, overall Quality of Life
- Factors related to mental health: depressive symptoms, daily stress perceived, cognitive and affective empathy
- Factors related to physical health: physical activities, fatigue, sleep quality, auto-medication and personal healthcare expenses

2.3 Project design

The COMET Study will be a prospective cohort study collecting data investigating the pull-up and push-out out factors for pursuing a general internal medicine career and evaluating the health, social and professional pathways of GIM residents.
The study will collect information through regular assessment by multiple surveys.
The study will be conducted as a multi-center study initiated in the department of GIM at the Fribourg Hospital with the collaboration of the departments of internal medicine from the Lausanne University Hospital of (CHUV) and Universitätsspital Bern (Inselspital). This research project has been extended to multiple other national centers. Most of the other centers have desired to become a study site (indicated as "study site" in the protocol) with its own local PI: the departments of internal medicine of the Hospital of Nyon, Hospital La Tour, hospital Riviera-Chablais, Hospital of Neuchâtel, Hospital of Biel/Bienne, Baselland Cantonal Hospital, Baden Cantonal Hospital, Interlaken Hospital, Langenthal Hospital, Solothurn Hospital, Ente Ospedaliero Cantonale, St. Gallen Cantonal Hospital, Lucerne Cantonal Hospital, the University Hospital of Geneva (the medical policlinic and the department of general internal medicine) and the medical

policlinic of the Lausanne University Hospital (Unisanté). The heads of the departments of internal medicine of the Hospital of Yverdon, of the Hospital of Payerne and of the Aarau Cantonal Hospital, have agreed that their residents can be included in the study, they are therefore indicated as "annex centers", without providing a local PI.

3 PROJECT POPULATION AND STUDY PROCEDURES

3.1 Project population, inclusion and exclusion criteria

The project population includes all residents in GIM in the Departments of general internal medicine at the Hospitals of HFR-Fribourg (4 sites: Fribourg, Riaz, Meyriez, Tafers), the University Hospital of Bern (Inselspital) and the University Hospital of Lausanne (CHUV), as well as all the residents from all the other study sites and annex centers that are participating to the study, as noted above.

Inclusion criteria: All residents in GIM present during the recruitment period starting from July 2024 to July 2025 (The exact time plan will depend upon the approval from the ethic commission)

Exclusion criteria: Residents not exercising direct patient care. Severe mental or physical disability precluding informed consent or compliance with the protocol for prospective data collection

3.2 Recruitment, screening and informed consent procedure

The recruitment will take place in the GIM Departments of the hospitals cited above. Depending on the approval from the ethic commission we will than start to include all consecutive residents starting to work in each of the departments. For example there are specific periods in the year when most of the residents start their working position (1st of May or 1st of November), therefore we will start the recruitment by getting the list of all new residents beginning their residency from the departments' secretary. As all the departments participating in this study are dedicated to clinical work, almost every participant will be eligible to inclusion. Recruitment will be done directly (in presence or per email) by the respectively local PI. The participants of the annex centers are recruited directly by the project leader (Marco Mancinetti) either in presence or per email.

All candidates are provided with a participant information sheet and a consent form describing the study and providing sufficient information for them to take an informed decision about their participation in the study. Potential participants are thus given at least 24h, to decide whether they want or not to participate. The potential participants will have the opportunity to ask questions and will be included if the agree to sign the informed consent. The consent form is signed (with notice of date and time) by an investigator or one of her/his designees at the same time as the participant signs (with notice of date and time). A copy of the participant information and signed informed

consent form is given to the study participant. The consent form is retained as part of the study records.
The participants do not receive any compensation or payment for their participation to the study.
The informed consent documents will be done in the language preferred by the residents: either German or French

3.3 Study procedures

After recruitment every participant will be asked to fill an online survey every year for at least 4 years after recruitment. We are planning to start the recruitment either on May or November 2024. The study will than last at least until May/November 2028.
The survey will be administered through the survey function of the REDCap® (Research Electronic Data Capture) software. A monitoring of the response rate of the questionnaire will be performed regularly and reminders (maximum of 2 reminders) will be sent to each participant multiple times in order to assure a high response rate..
The survey will consist of multiple questionnaires based on the study measures as indicated below. Questionnaires will be based on validated surveys, including using questionnaires administrated in the CoLaus|PsyCoLaus study [d],an established population-based cohort recruiting participants in Lausanne since 2003.
Questionnaires will be made available in the language of choice of the participant: French or German.
3.3.1 Study measures:

1. **General questionnaires**
    - Socio demographic characteristics: year of birth, sex, no. of children, relationship status, work position, native language, level of education of parents, educational debt.
    - Previous educational and work experience: undergraduate medical education, years since graduation from medical school, scholarship (MD, PhD, number of articles published), days of conferences attended last year, years of experience as a resident in GIM, year of board certification (or projected year of certification).
2. **Job-related questionnaires**
    - Nature of patient care: average clinical working hours per week, average number of patients to care for per day (average during the past 3 months).
    - Document irregular shifts: number of evening, night and weekend shifts (average during the past 3 months).

[d] https://www.colaus-psycolaus.ch

- Other working activities: protected research time, protected time for personal education, protected time for teaching.
- Career interest: Actual specialty goal, long-term goal (clinical hospitalist, academic position, general practitioner, specialist, undecided, other), interest in other medical specialties
- Work life balance aspired to (wish to change to part-time/full-time)
- Intention to quit.
- Pull-up factors and push out factors to influence career decision (adapted from Hauer et al. [e])

3. **Well-being at work**
    - Well-being will be assessed by the Physician Well-being Index (PWBI) which has been largely used in its French and German version
    - We will use the Professional Fulfillment index (PFI) to evaluate professional fulfillment, work exhaustion, and interpersonal disengagement
    - Overall Quality of Life (QOL) will be measured by a single-item linear analogue self-assessment (LASA) using 1 question with linear visual scale from 0 to 100.
    - Residents' satisfaction with the balance between their personal and professional life will be assessed with one question with a 5 point Likert scale, as it has been used in a previous study.
4. **Mental Health questionnaires**
    - Depressive symptoms will be assessed with the Centre for Epidemiological Studies – Depression questionnaire (CES-D)
    - Daily stress perceived in the past month will be evaluated by the Perceived Stress Scale (PSS), used in French and German.
    - The inclination for burnout will be analyzed with the Maslach Burnout Inventory, which has been largely used in various languages – a particular attention will be laid on specific subgroups of the inventory: emotional exhaustion, professional efficacy and cynism.
    - The Questionnaire of Cognitive and Affective Empathy (QCAE) will be used to measure different dimensions of empathy. It has already been used in a French sample and it has been used in a cohort of medical students in Switzerland, which will be interesting to compare with our cohort of internal medicine residents.
5. **Physical Health questionnaires:**

[e] Hauer KE, Durning SJ, Kernan WN, Fagan MJ, Mintz M, O'Sullivan PS, Battistone M, DeFer T, Elnicki M, Harrell H, Reddy S, Boscardin CK, Schwartz MD. Factors associated with medical students' career choices regarding internal medicine. JAMA. 2008 Sep 10;300(10):1154-64. doi: 10.1001/jama.300.10.1154. PMID: 18780844.

- Physical activity will be evaluated asking the participating GIM residents to indicate the average number of steps taken per day for the current month, the previous month, and two months prior, according to the default health app on their smart-phone. The I-PAQ questionnaire on physical activity will also be used to complete the evaluation. This self-reported questionnaire assesses the type and duration of 70 kinds of (non)professional activities and sports during the previous week (during work and leisure time) (PAFQ) and has been validated in a Geneva study.
- We will evaluate fatigue with fatigue severity scale by Krupp and the Chalder fatigue scale, (validated as well in a Swiss-German cohort and in French).
- As shift work is an important part of residents' work schedule we will evaluate their sleep quality (Pittsburgh sleep quality index and insomnia severity index both largely used in multiple languages).
- We will collect health care utilization and expenses in the previous year according to the summary account of the health expenses and payments available from the participants' health insurer.

3.4 Withdrawal and discontinuation

All potential participants are informed that the participation in the study is voluntary, that they may withdraw from the study at any time by communicating their wish to the local PI (by phone or by email) and that withdrawal of consent will not affect their residency or their professional career. Subjects may leave the study if they wish, without consequence and without obligation to give a reason. If a participant withdraws consent for study participation, the data collected up to the time point of withdrawal will be used for the study.
Potential participants are informed that their data will remain coded in the database. If a participant ends the study prematurely, the central study team will record the date and reason for early discontinuation in the source document and the appropriate portion of the eCRF.
Investigators will make any reasonable effort to collect and report the end of study participation.

4 STATISTICS AND METHODOLOGY

4.1. Statistical analysis plan

This cohort study aims to be as comprehensive as possible in terms of participant inclusion. We acknowledge that the power of the individual analyses will largely depend on the number of participants.
Number of residents from the study sites and annex centers:

Fribourg (4 sites)	135
Bern	82
Lausanne Hospital	117
Lausanne Policlinic	60
Geneva Hospital	100
Geneva Policlinic	60
Neuchâtel	60
Biel/Bienne	32
Payerne	20
Yverdon	25
Nyon	25
La Tour	24
Riviera – Chablais	40
Baselland	65
Baden	75
Lucerne	60
St. Gallen	85
Aarau	50
Langenthal	25
Interlaken	30
Solothurn	50
Lugano (EOC)	80
Total	**1300**

Estimation of the number of residents: recruitment of 80% of 1300 residents will translate into an expected number of 1040 residents recruited. This number is susceptible to increase if other centers are included in the future.

To calculate the sample size needed to have enough power analyses, we will take two important measures from our questionnaires concerning depressive symptoms within the GIM residents'

population and match these values with a control general population taken from the CoLaus|PsyCoLaus study (www.colaus-psycolaus.ch) to see if a significant difference can be found. In a systematic review, the summary estimate of the prevalence of depression or depressive symptoms among resident physicians was 28.8% ranging from 13% to 39% when the CES-D questionnaire was used. As the reported prevalence of depression in a general population is 8.8% we would need at least a sample size of 214 residents to show a double prevalence (18%) in our cohort population.

We will also recruit enough participants to investigate significant changes in empathy. In fact, it has been shown that empathy levels wane during a doctor's professional trajectory. In a recent study investigating medical students' empathy, the values for their Cognitive Empathy (QCAE) had a median of 58.5 and an Affective Empathy reported at 35 and it has been suggested that the decline during medical school and residency can be expected to be as high as 10% between the first and last year of residency.

As we may expect a reduction in our residents' population, we would need a sample size of at least 60 residents to show a reduction of a 0.5 standard deviation in the QCAE Cognitive and Affective score of GIM residents compared to the data already available of a Swiss medical student population (80% power, alpha 0.05).

4.1.1 Planned analysis

Descriptive statistics will be calculated for all participants at baseline.

Linear, logistic, Poisson, and Cox-Proportional Hazard regression models will be used to establish cross-sectional and longitudinal associations, when needed. Models will be adjusted for potential confounders, such age, sex, number of years in postgraduate education.

Depending on the research question and written informed consent from the CoLaus|PsyCoLaus study, results from the present could be contrasted with those from the CoLaus|PsyCoLaus which recruited ~1,000 participants aged 18-35 from the general population between 2019-2023 (as many questionnaires will overlap between both studies).

Data Analysis will be performed with StataCorp 2021. *(Stata Statistical Software: Release 17. College Station, TX: StataCorp LLC.).*

4.2. Handling of missing data

As stated above, we are expecting an 80% of recruitment rate to attend a large number of participants. A certain amount of drop-outs due mainly to lost follow up can be expected: this is the reason of the recruitment of an initial large number. As this is an exploratory cohort study we will look in longitudinal trends of the data if, after a first evaluation of the possible correlation, a sufficient number of participants will follow-up. In order to ensure an adequate number we do not

exclude that subsequent rounds of recruitments will be necessary to reach the sample size. The structure of the study lends itself to be continued over time.

5 REGULATORY ASPECTS AND SAFETY

5.1 Local regulations / Declaration of Helsinki

This research project will be conducted in accordance with the protocol, the Declaration of Helsinki [f], the principles of Good Clinical Practice, the Human Research Act (HRA) [g] and the Human Research Ordinance (HRO) [h] as well as other locally relevant regulations.

5.2 Notification of safety and protective measures (HRA Art. 15, HRO Art. 20)

If, during the research project, circumstances arise which could jeopardise the safety or health of the participants or lead to a disproportionate relationship between the risks and burdens and the benefits, all the measures required to ensure protection are to be taken without delay.
The project leader (and if applicable the Sponsor) is promptly notified (within 24 hours) if immediate safety and protective measures have to be taken during the conduct of the research project. The Ethics Committee will be notified via BASEC of these measures and of the circumstances necessitating them within 7 days.

5.3 Serious events (HRO Art. 21)

No serious adverse event are imaginable for this study. However, it cannot be ruled out that answering the questionnaire may cause discomfort or cause or increase a feeling of distress. In this case, the principal investigator and/or the local principal investigator can be contacted by the participant to discuss how best to support them: either by stopping participation in the study and/or by referring them to the medical (and psychological) services (inside the hospital) for professional help.
If any adverse event would happen the project leader will make a causality assessment of the event to the trial intervention, labeling it as definitely, probably, possibly, unlikely, not related. Any event assessed as possibly, probably or definitely related will be classified as related to the trial intervention.

[f] https://www.wma.net/policies-post/wma-declaration-of-helsinki-ethical-principles-for-medical-research-involving-human-subjects
[g] http://www.admin.ch/opc/en/classified-compilation/20121176/201401010000/810.305.pdf
[h] https://www.admin.ch/opc/en/classified-compilation/20121177/index.html

The project leader will make a severity assessment of the event as mild, moderate or severe. Mild means the complication is tolerable, moderate means it interferes with daily activities, and severe means it renders daily activities impossible.
Any adverse event where it cannot be excluded that it is attributable to the intervention under investigation, will be documented and reported immediately (within a maximum of 24 hours) to the project leader and the Sponsor of the study and they will report these events to the Ethics Committee(s) concerned via BASEC within 7 days. Adverse events will be followed up until the resolution or stabilization.
A serious event is defined as any adverse event where it cannot be excluded, that the event is attributable to the sampling of biological material or the collection of health-related personal data, and which:
a. requires inpatient treatment not envisaged in the protocol or extends a current hospital stay;
b. results in permanent or significant incapacity or disability; or
c. is life-threatening or results in death
If a serious event occurs, the research project will be interrupted and the Ethics Committee notified on the circumstances via BASEC within 7 days according to HRO Art. 21 .

5.5 Amendments

Substantial changes to the project set-up, the protocol and relevant project documents will be submitted to the Ethics Committee for approval according to HRO Art. 18 before implementation. Exceptions are measures that have to be taken immediately in order to protect the participants.

5.6 End of project

Upon project completion or discontinuation, the Ethics Committee will be notified via BASEC within 90 days.
The Sponsor-Investigator may terminate the study prematurely according to certain circumstances, e.g.:

- Ethical concerns,
- Insufficient participant recruitment

Upon premature study termination or study interruption, the Ethics Committee will be notified via BASEC within 15 days (ClinO, Art. 38).
Health-related data at the end of the study will be handled as described in chapter 7.3 (Confidentiality and coding) and in chapter 7.4 (Retention and destruction of project data)

5.7 Insurance

In the event of study-related damage or injuries, the liability of the institution will provide compensation, except for claims that arise from misconduct or gross negligence (Sponsor: HFR, Department of general internal medicine, chemin des pensionnats 2-6, 1700 Fribourg, Switzerland; insurer: Zürich Versicherungs-Gesellschaft AG, Commercial Insurance, Switzerland, Postfach, CH-8085 Zürich).

6 FURTHER ASPECTS

6.1 Overall ethical considerations

This study is conducted respecting the World Medical Association Declaration of Helsinki, the ICH-GCP guidelines, as well as the regulatory and legal national applicable requirements. The authorization from the responsible Ethics Committee(s) was collected prior to the beginning of the recruitment. All protocol changes or unexpected problems concerning human participants will be reported during the conduction.
No specific risk has been identified. Conversely, the COMET study could have a significant impact in helping different stakeholder to address the problems exposed in the introduction

6.2 Risk-Benefit Assessment

The establishment of a longitudinal cohort of GIM residents is expected to result in substantial findings from which residents and different stakeholders in the healthcare system (residents' program directors, attending physicians, administrators, and patients) could benefit substantially in the future. There might be no immediate benefit for the individual participant.
Data collection will be protected according to GCP recommendations. Individual data will be anonymized and thus participants' identity will be protected.

7 QUALITY CONTROL AND DATA PROTECTION

7.1 Quality measures

Each data point recorded in the study database will have attached attributes identifying the code of the user who entered it with the exact time and date. Subsequent alterations of data entries will be recorded in an audit table, including the time, data field with the initial and altered value, and the identifier of the user who altered the data.
Before database lock, each investigator will validate the collected data with her/his signature.

For quality assurance, the Sponsor, the Ethics Committee or an independent trial monitor may visit the research sites for the purpose of audits, inspections and monitoring. Direct access to the source data and all study related files will be granted on such occasions. All involved parties will keep the participant data strictly confidential.

7.2 Data recording and source data

We will conduct a survey among residents in the GIM department using the public survey function of REDCap®, which allows collection of coded responses. Each participant will receive the survey online and will choose the preferred language to perform the questionnaires (French or German). Each survey will than be registered as an eCRF under a coded number (cf below section 7.3). The personal information, including minimal personal data (name, date of birth) and the information on the signed informed-consent (when, which site), as well as the attributed coded number, will be stored in a different database as "participant identification list".

Data management:

Data management will include the use of the REDCap® study database, which is a secure web application for building and managing online surveys and databases. REDCap® provides audit trails for tracking data manipulation and user activity, as well as automated export procedures for seamless data downloads to Excel, PDF and common statistical packages.

The information collected during this study will be entered into REDCap®.

Each data entry will have attributes attached to it identifying the user entering (or altering) it with the exact time and date.

For final analyses, data files will be extracted from the database into statistical packages to be analyzed.

The study database with all archive tables will be securely stored by the Sponsor-Investigator for at least 10 years.

Electronic Case Report Forms (eCRFs):

For each participant, an eCRF will be maintained, which will not identify participants by their name or birth date, but provide appropriate coded identification. All protocol-required questionnaires will be recorded in the eCRFs.

Source data:

All data captured in the eCRF will be itemized on a source data location list, which will be stored in the Investigator Site File at each study site. This list is highly site-specific and will reflect the work flow at the individual site, clearly indicating the source data location corresponding to each eCRF

entry. All the data will be directly entered into the eCRF by each participant by filling up the online questionnaire.

7.3 Confidentiality and coding

The principal investigator at each “study site” (cf section 2.3 above) will safeguard the confidentiality of participant data, ensuring that no participant information containing identifying data leaves the study site. The data coming from the “annex centers” will be stored at the main site under the responsibility of the project leader and his team.

Direct access to study-related records at the participating study sites will be permitted for purposes of monitoring, audits and inspections. The Sponsor-Investigator and the Ethics Committee will have access to all information necessary to accomplish their tasks.

Trial and participant data will be handled with uttermost discretion and accessible only to authorized personnel who requires the data to fulfil their duties within the scope of the study. On the eCRFs, participants will be identified only by a unique participant identification number. The format of the identification number will be a combination of the site and a consecutive participant number, such as FR-001, FR-002, FR-003, for the site Fribourg.

The participant identification list will also include the participant's contact email address and will be stored in a separate Excel file for each study site, under the responsibility of each local principal investigator, in a secure location accessible only to study staff. As discussed with the ethical committee, a copy of this list will be kept exceptionally at the main site, to allow the Project Leader to contact the participant in case they would show indices of psychological distress (i.e. if the survey scores would be pathological) as automatically reported by the eCRF software. As this is a longitudinal cohort study, it is reasonable to think that the participant will work in the future 4 years in different places than the site that have recruited them, thus complicating the follow up.

The copy of the participant identification list will be destroyed at the main site, directly after the end of the Study.

The data collected from the questionnaires will be stored in the eCRF as described above, which will be managed by the main site through the REDCap® licence of the University of Fribourg.

Only non-genetic and non-biological data will be collected and used in this study.

7.4 Retention and destruction of project data

All study data will be archived for 10 years after study termination or premature termination of the study. The Sponsor-Investigator and local study sites will maintain appropriate medical and research records for this study, in compliance with ICH-GCP as well as national regulatory and

institutional requirements for the protection of confidentiality of subjects. Biological material will be neither collected nor stored.

8 FUNDING / PUBLICATION / DECLARATION OF INTEREST

Funding: This study is partially funded by an unrestricted Grant from the Swiss Society of General Internal Medicine and by a HFR-Fribourg grant. The rest of funding will be assured by each site for what it concerns the secretary and organizational work.

Publications: The COMET study will strive for complete dissemination of all resulting data and publications after securing valuable intellectual property. The study sponsor will have the ultimate authority over any of the activities.

The findings will be presented at national and international medical conferences and published in peer-reviewed medical journals. We will make raw data available.

Declaration of interest: With regard to the intellectual concern and proprietary affairs, no conflict of interest exists.

Agreement between study sites: Agreement on study conduction (protocol, term, publication, confidentiality, data transfer) is defined in contracts (Clinical Study Agreements) between the Sponsor-Investigator and each local investigator / study site.

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