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Master Thesis in Medicine, Number 336

The TOPIC study (Thoracic Pain In Community)
Step 2

Implementation study of a clinical prediction score to rule out cardiogenic chest pain in community: Cluster randomized trial

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Summary

This protocol details the phase IV study aiming to assess both impact and implementation of a new clinical prediction rule (CPR) only based on patient's history and physical examination in order to help general practitioners ruling out a cardiac origin to chest pain without further investigations. It is built upon the data of the TOPIC (Thoracic Pain In Community) study run in 2001 to measure occurrence and aetiologies of chest pain in primary care. Internal and external validation studies have been done by now. The current study is a prospective cohort cluster randomized trial with two arms: on one hand general practitioners aided by the CPR and on the other hand general practitioners working according to their usual clinical practice. The target population is patients consulting primary care settings and reporting any type of chest pain. We will measure the acceptability, satisfaction and use of the CPR by physicians and intend to show that it can spare useless extra investigations without compromising patients' management and outcome. To reach this goal, 300 general practitioners and 15,000 patients are needed. Inclusion and exclusion criteria are defined. The follow-up lasts 9 months and the main endpoints measured are hospitalizations, diagnostic of coronary artery disease, extra investigations and referrals run to determine the origin of chest pain. We will also assess use, acceptability of the CPR and satisfaction among the physicians selected to use it. An intermediate analysis is planned at 3 months and stopping rules are defined. A case report form has to be filled in for each patient with chest pain. No adverse events are expected. Independent reviewing and follow-up will insure correct management of the patients enrolled. The current protocol will be submitted to an ethical committee.

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Synopsis

Study subject	Clinical prediction rule to help general practitioners rule out a serious cardiac condition in primary care patients complaining of chest pain.
Study title	Implementation study of a clinical prediction score to rule out cardiogenic chest pain in community: cluster randomized trial.
Investigators	Principal investigator: to be defined Investigators: to be defined
Study centre	Institute for General Medicine, University of Lausanne, Switzerland
Study place	Western Switzerland private primary care settings ; Department of Ambulatory Care and Community Medicine, University of Lausanne
Study period	To be defined
Objectives	1. To measure the acceptability, satisfaction and use of the clinical prediction rule by general practitioners in primary care patients complaining of chest pain. 2. To show that using the cardiovascular clinical prediction rule as an assistive tool to rule out coronary heart disease in primary care practice can spare useless extra investigations, without compromising patient's management and outcome.
Methodology	Prospective cohort cluster randomized trial
Number of patients	15,000 patients
Number of physicians	300 physicians
Selection criteria	Inclusion criteria: patients aged 18 years and over reporting any type of chest pain, even if chest pain is not the main complaint, if it is revealed by systematic anamnesis or if there is yet a known history of chest pain or cardiovascular disease. Exclusion criteria: patients unable to communicate with physicians, for whom follow-up may not be feasible, obvious traumatic or extrathoracic origin to chest pain, psychiatric severe comorbidities, refusal or impossibility to consent.
Duration	At most 9 months follow up per patient
Reference	Usual primary care practice
Evaluation	- Hospitalizations, severe CHD at 9 months - Number and type of extra investigations and referrals - Use/non use of the CPR, acceptability and satisfaction
Statistical method	STATA (data analysis and statistical software)

Abbreviations

CHD	Coronary Heart Disease
CPR	Clinical Prediction Rule
CRF	Case Report Form
GP	General Practitioner

1. Background

1.1 Fundamentals

Chest pain is a common complaint in primary care patients (1 to 3% of all consultations) (1) and its aetiology can be miscellaneous, from harmless to potentially life threatening conditions. In primary care practice, the most prevalent aetiologies are: chest wall syndrome (43%), coronary heart disease (12%) and anxiety (7%) (2). In up to 20% of cases, potentially serious conditions as cardiac, respiratory or neoplasic diseases underlie chest pain. In this context, a large number of laboratory tests are run (42%) and over 16% of patients are referred to a specialist or hospitalized (2).

A cardiovascular origin to chest pain can threaten patient's life and investigations run to exclude a serious condition can be expensive and involve a large number of exams or referral to specialist - often without real clinical need. In emergency settings, up to 80% of chest pains in patients are due to cardiovascular events (3) and scoring methods have been developed to identify conditions such as coronary heart disease (CHD) quickly and efficiently (4-6). In primary care, a cardiovascular origin is present in only about 12% of patients with chest pain (2) and general practitioners (GPs) need to exclude as safely as possible a potential serious condition underlying chest pain. A simple clinical prediction rule (CPR) like those available in emergency settings may therefore help GPs and spare time and extra investigations in ruling out CHD in primary care patients. Such a tool may also help GPs reassure patients with more common origin to chest pain.

1.2 Study clinical prediction rule

In order to help GPs rule out a serious cardiac condition in patients complaining of chest pain, several CPRs have been developed in the last few years, two of them in Switzerland (7, 8) and Germany (9, 10). They are only based on patient's history and physical examination and aim to define the risk of cardiac origin to chest pain.

The Swiss CPR allows points to each of the seven following items: known cardiovascular risk, men over 55 years or women over 65 years, personal history of cardiovascular disease, substernal pain (two points each), duration of pain from 1 to 60 minutes, increasing with effort, absence of tenderness at palpation (one point each). Cut-off point for the low-risk group is 5. This rule showed a sensitivity of 97.6% and a specificity of 71.3% in ruling out CHD, a negative likelihood ratio of 0.033 and a negative predictive value of 99,5% in the derivation cohort. External validation has been done using the cross-country cohorts and showed a sensitivity of 85,6% a specificity of 47.2%, a negative predictive value of 94.8% and a negative likelihood ratio of 0.305 for the Swiss CPR (N.B.: inclusion criteria in both German and Swiss studies were not the same, which may explain at least part of the difference between results of internal and external validation studies) (8).

German investigators have also run a further external validation study with a new cohort that confirms the validity of their CPR. The Marburg Heart Score showed a sensitivity of 89.1%, a specificity of 63.5%, a positive predictive value of 23.3%, a negative predictive value of 97.9%, a positive likelihood ratio of 2.44 and a negative likelihood ratio of 0.17. Germans also noticed that GPs whose clinical judgment was aided by the score showed a higher sensitivity (90.0 versus 82.9%) and specificity (66.8 versus 61.8) than those working without the score, but the difference was not

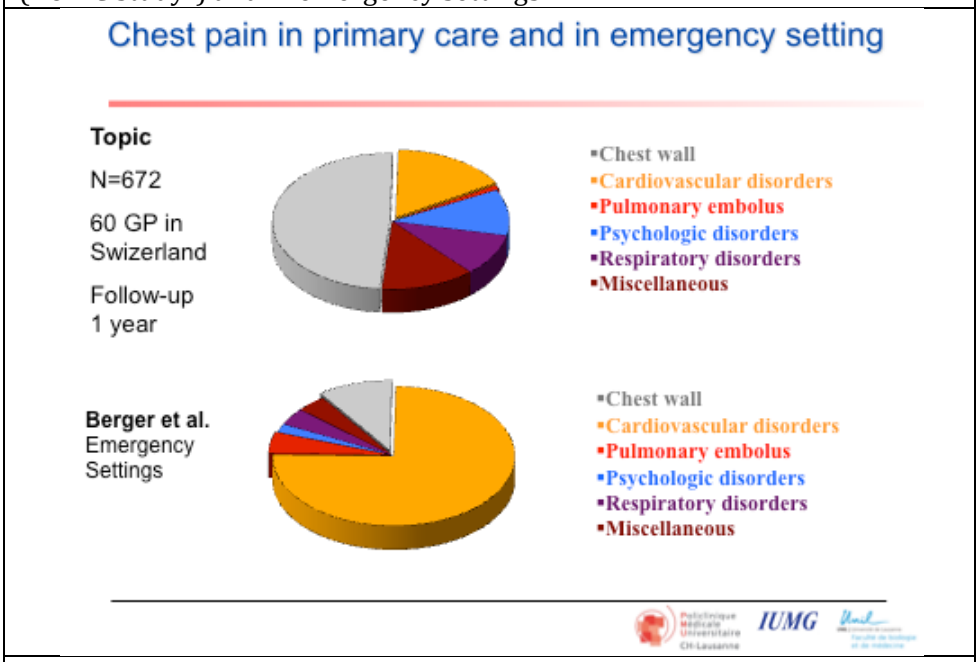
significant (11). More results should soon confirm safety and robustness of such CPRs, especially the final results and publication of the Marburg Heart Score.

Both CPRs aim to define low-risk patients and rule out CHD without further investigations. We strongly believe that using such CPRs may improve the management of chest pain in primary care in the same way the D-dimers test does in ruling out venous thromboembolism without computer tomography or ultrasound (since it has high sensitivity and negative predictive value). Moreover, it may reduce extra investigations and costs for patients of equivalent risk of cardiogenic chest pain.

We however remember that such CPRs are not valid for patients with chest pain in emergency settings or at the cardiologist office, as there are already scoring methods and diagnostic tools available and validated to rule out CHD in those structures. Besides, the prevalence of diseases is not the same in primary care (low prevalent setting) than in more specialized settings (**Figure A**). Specialists and hospitals usually get a minor part of general population, as patients have often already been selected in primary care settings, while GPs have to deal with the whole population - with early, untypical and unselected symptoms - and its own repartition of diseases. It is therefore worth having an assistive tool such as a CPR especially developed for general practice and its own needs.

We are now waiting for the last results from the international collaborating studies, confirming validity of those CPRs for primary care practice. Next step is to run an implementation study to show that the cardiovascular CPR can be applied and is effective as an assistive prediction tool for GPs. The current protocol describes the phase IV study aiming to measure use of such a CPR among GPs and its impact on everyday primary care practice (extra-investigations, referrals, patients outcome).

Figure A: Comparison between chest pain aetiologies in primary care (TOPIC study[1]) and in emergency settings[2]



(1) Verdon F, Herzig L, Burnand B, et al. Chest pain in daily practice: occurrence, causes and management. *Swiss Med Wkly*. 2008;138(23-24):340-347.
(2) Berger A, Stauffer J, Eckert P, et al. Epidémiologie des douleurs rétrosternales aux urgences. *Forum Med Suisse*. 2002;8(38S).

1.3 Study rationale

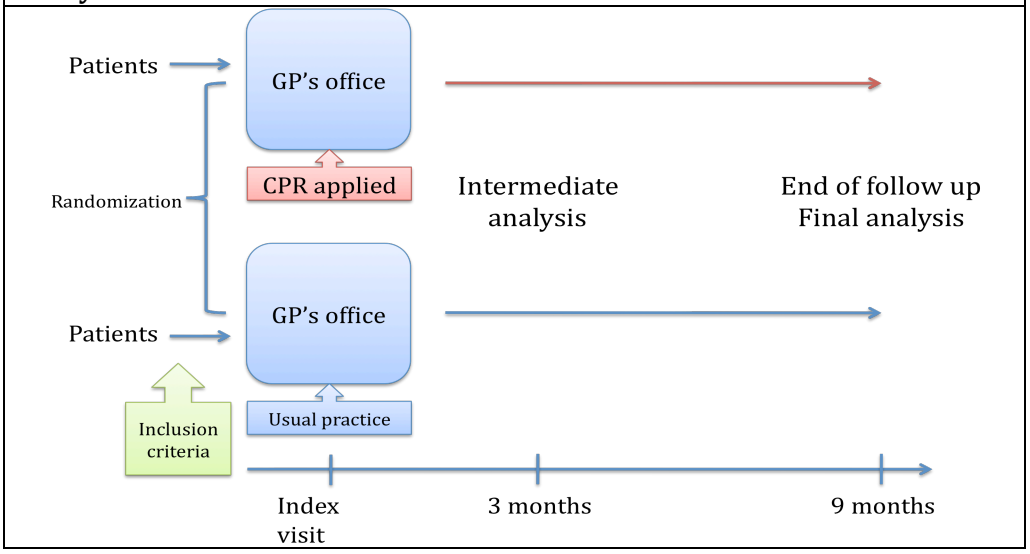
The study is a phase IV study and will take place in Swiss primary care settings. Target population are patients over 18 years consulting GPs and reporting any type of chest pain. We built a two arms trial to compare management of chest pain either in usual practice or aided by the cardiovascular CPR.

We chose a cluster randomized trial design and the intervention will be performed at the level of GP's offices. Randomization within the same health care unit and intervention performed at patient's level would have led to an important selection bias. This would have made impossible to guarantee an equivalent management of patients within the same arm as well as a strict distinction between the two arms.

GPs will therefore be enrolled in a prospective study and randomized either to use the Swiss CPR as an additional tool for the management of chest pain or go on with their usual practice. Each GP will have to include a defined number of patients complaining of chest pain.

Follow-up will concern number and type of paraclinical tests run by GPs, referrals and patient's outcome. We will also appreciate the use of the CPR, its acceptability and the satisfaction among the selected GPs. An intermediate analysis is planned during follow-up and stopping rules are defined in case of necessity.

Study scheme



2. Objectives

- To measure the acceptability, satisfaction and use of the CPR by GPs in primary care patients complaining of chest pain.
- To show that using the cardiovascular CPR as an assistive tool to rule out CHD in primary care practices can spare useless extra investigations, without compromising patient's management and outcome.

3. Study design

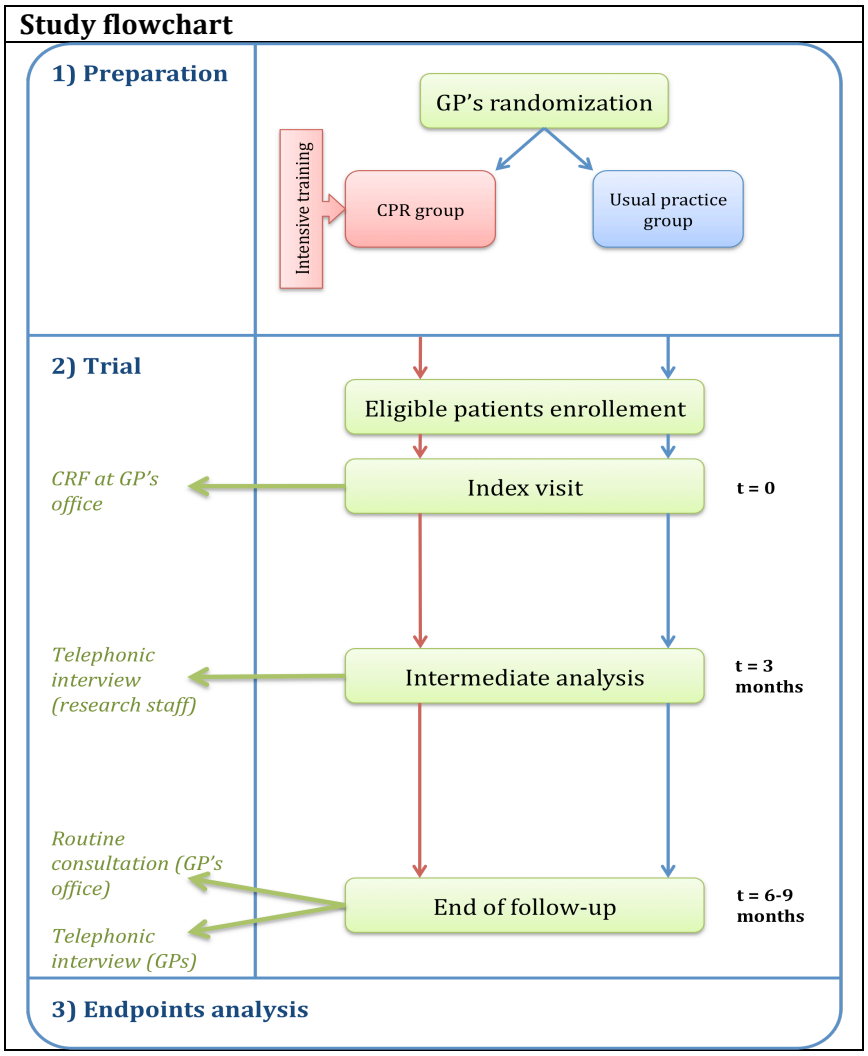
3.1 Overall description

This trial aims to assess implementation of a new cardiovascular CPR in primary health care. It is built as a prospective cohort study of primary care patients with chest pain. The cluster randomized trial design allows us to randomize GP's offices in two groups, one using the CPR in daily practice and the other working without, according to usual care practice. Thus, randomization and intervention are targeted at the level of GP's offices. Patient's outcome however is measured at the individual's level thanks to a case report form (CRF). Use of the CPR is measured directly by a few questions intended for GPs.

GPs selected to use the cardiovascular CPR will get intensive training to make as sure as possible that they use it in an equivalent way (see Annex 1 for description of GPs training). GPs of the usual practice group should not be aware of the CPR and will not get any information about it. In both groups, GPs will have to fill in a CRF for each patient complaining of chest pain.

Follow-up ends nine months after patient's index visit. An intermediate analysis is planned at three months. Members of research staff are designed to make sure that case report forms are complete for each patient and will get in touch with every agreeing patient at three months (intermediate analysis). GPs will assure the follow up until nine months (end of follow up) either by telephonic interviews or usual consultation. The research staff will control the follow up and remember GPs if necessary.

Independent physicians will review a defined randomized number of cases. They will control patient's condition at the end of the follow-up, validate the correct management of patients and verify the validity of the initial diagnosis of cardiogenic chest pain.



3.2 Endpoints

In order to assess implementation and effectiveness of the cardiovascular CPR (targeted at GPs) on the management of chest pain and patient's outcome, we will measure:

- Hospitalizations, severe CHD at 9 months among patients included
- Number and type of extra investigations and referrals run by GPs to manage patient's chest pain
- Use/non use of the CPR by GPs, acceptability and satisfaction

3.3 Randomisation

Participating GPs will be split in two groups by simple randomisation, one using the cardiovascular CPR for each patient complaining of chest pain (intervention group) and the other working with usual clinical practice (control group). Randomisation will be performed with a table of random numbers by a member of the research team not involved in the current study and blinded to the identity of GPs.

3.4 Study duration for subjects and stopping rules

The study duration is of 9 months for subjects, from index visit to end of follow-up. Study ends with routine consultation at GP's office 6 to 9 months after index visit or, if no consultation is scheduled, with telephonic interview at 9 months.

Intermediate analysis is done at 3 months and *stopping rules* are:

- The CPR is so effective that is has to be applied to control group
- There is no significant difference between intervention and control group or no data indicating that a difference may be expected at the end of complete follow-up
- Non use of the CPR by GPs of the intervention group
- Unexpected unfavourable effect on patients

3.5 Data collected in the CRF

A case report form (CRF) has to be filled in by all the GPs for each patient included to define patient's characteristics, current pain, personal history of cardiovascular disease and risk factors. It will also provide investigators with information regarding complementary investigations, referrals or hospitalizations for each patient at the time of index visit.

GPs of the intervention group will be asked to calculate the risk of cardiogenic chest pain for each patient with the CPR. The CRF also includes questions directly addressed to GPs to appreciate use, satisfaction and acceptability of the CPR.

GPs who belong to the usual care group will have to evaluate the risk of cardiogenic chest pain according to their clinical judgement only.

As all the items of the CPR are part of usual practice (patient's history and physical examination) investigators will be able to calculate patients' risk of cardiogenic chest pain a posteriori in the usual care group with the data collected in the CRF.

(See Annex 2 for complete CRF)

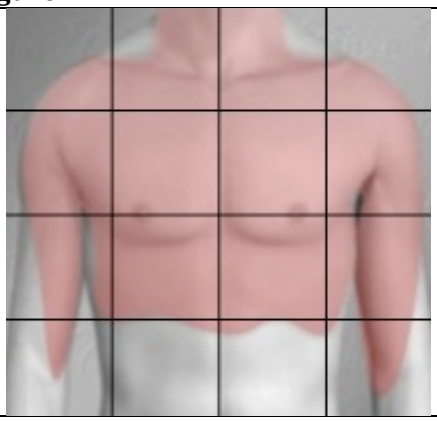
4. Study population

Target population are inhabitants of Switzerland who consult primary care settings.

4.1 Inclusion criteria

Adults (aged 18 years and over) reporting any type of chest pain (defined as a superficial or deep pain in the area indicated in ***Figure B*** *(page 12)*, with or without posterior irradiation and/or irradiation in arms) will be asked to enter the study. Subjects will be enrolled even if chest pain is not the main complaint, if it is revealed by systematic anamnesis or if there is yet a known history of chest pain or cardiovascular disease. Telephonic interviews, emergency consultations and home visits will also be included.

Figure B



4.2 Exclusion criteria

Patients unable to communicate with physicians (language barriers), patients for whom follow-up may not be feasible, obvious traumatic or extrathoracic origin to chest pain, severe psychiatric comorbidities, refusal or impossibility to consent will be excluded from the current study.

4.3 Withdrawal criteria

As the only intervention in this study is to calculate a risk thanks to a CPR and to collect information regarding patient's characteristics and use of the CPR, no withdrawal criteria are established. Patients are free to drop out the trial at any time and just need to inform their physician so that no new information is communicated to the data centre.

In case of patient's withdrawal no replacement procedure is planned. A complete analysis of patient's characteristics will be performed in order to avoid any bias induced by the loss of patients.

4.4 Selection and recruitment procedure

Swiss GPs and physicians of the Department of Ambulatory Care and Community Medicine in Lausanne will be contacted and asked to participate the study. Starting from a defined date, each GP will enrol a defined number of patients reporting any type of chest pain, according to inclusion criteria.

Sampling of all the GPs recruited will be performed in order to assess characteristics of participants (age, place, type of practice) and minimize cohort effect. Investigators may decide to use pre-existing GPs network such as Sentinella, which can insure correct sampling of Swiss GPs.

5. Study CPR

GPs selected to use the cardiovascular CPR as an assistive tool will have to calculate the risk of cardiac origin to chest pain for each patient. According to Gencer and al. (8), the Swiss CPR is the following:

Swiss Heart Score	
Men over 55 years, women over 65 years	2 points
Known cardiovascular risk	2 points
Personal history of cardiovascular disease	2 points
Substernal pain	2 points
Duration of pain from 1 to 60 minutes	1 point
Increasing with effort	1 point
No tenderness at palpation	1 point
Total < 5 points: low risk of cardiogenic chest pain Total 5 to 7 points: intermediate risk of cardiogenic chest pain Total > 7 points: high risk of cardiogenic chest pain	
- *Sensitivity 97.6%, specificity 71.3%, negative likelihood ratio 0.033, negative predictive value 99,5% (derivation cohort)* - *Sensitivity 85.6%, specificity 47.2%, negative likelihood ratio 0.305, negative predictive value 94.8% (validation cohort)*	

Except filling in the CRF and – for GPs allocated to the intervention group - calculating the risk of cardiogenic chest pain, taking history of the patient, examination, and further investigations have to be done as usual by GPs, according to their scientific knowledge and clinical experience.

Intensive training will provide GPs of the intervention group all information concerning aim, performance and limitations of the cardiovascular CPR as an assistive, prognostic tool (see Annex 1). Diagnosis and treatments should not be altered.

N.B. Investigators may choose to use the Marburg Heart Score instead of the Swiss Heart Score according to the not yet published results of Marburg's last external validation study. This will be decided before submission of the current protocol to the ethical committee.

Marburg Heart Score	
Men over 55 years, women over 65 years	1 point
Known clinical vascular disease*	1 point
Pain worse during exercise	1 point
Pain not reproducible by palpation	1 point
Patient assumes pain is of cardiac origin	1 point
Total ≤ 2 points: low risk of cardiogenic chest pain * Coronary artery disease, occlusive vascular disease or cerebrovascular disease	
Sensitivity 89.1%, specificity 63.5%, negative likelihood ratio 0.17, negative predictive value 97.9% (results to be published)	

6. Evaluation criteria

Aiming to assess both implementation of the cardiovascular CPR and its potential effect on chest pain management, evaluation criteria are split in two classes. On one hand, criteria concerning use of the CPR, evaluated by few questions in de CRF directly addressed to GPs. On the other hand, criteria aiming to measure impact of the CPR on chest pain management and patient's outcome. These are to be filled in by GPs for each patient complaining of chest pain at the time of the index visit (CRF) and at the end of follow-up (6 to 9 months), and by research team for intermediate analysis.

Implementation:	
Acceptability of the CPR	- Use/non use of the CPR - Reassurance with low-risk result
Satisfaction	- Discrete visual analogue scale
Impact:	
Extra investigations of chest pain	- None - ECG - Thoracic radiography - Laboratory (CRP, FSC, CK, D-dimers, Troponines, BNP) - Cardiac stress test - Others (precise)
Referral	- None - Hospital / emergency setting - Cardiologist (less than 6 hours, less than one week, more than one week, telephonic interview) - New consultation - Other (precise)
Patient's outcome at 9 months	- Hospitalisation(s) during follow-up - CHD / no CHD, with degree of certainty (discrete visual analogue scale)

7. Data collection and management

7.1 Source data

- CRF filled in by GPs for each patient included at index visit (see Annex 2, in French)
- Intermediate analysis questionnaire (see Annex 3, in French)
- End of follow up questionnaire (see Annex 3, in French)

7.2 Documents storage and keeping

The documents collected during the current study are the CRF, questionnaires filled in by research team at 3 months and end of follow up questionnaires for each patient included. All the files regarding the current trial will be kept at the Institute of General Medicine, University of Lausanne, Switzerland.

GPs have to send index visit CRF to research team once a week, as well as end of follow up questionnaires (routine consultation 6 to 9 months after index visit or telephonic interview). Questionnaires for intermediate analysis at 3 months will be filled in by research team during a telephonic interview and kept in the research department.

A single code will be attributed to each patient and GP, so that complete anonymity is insured. Patients' details will be known only by their GP to insure maximal confidentiality. Each GP makes a ranking list of participating patients with name, code and phone number to assure the follow up. Furthermore, and only with patients' consent, mobile phone number is attached to identification code to allow the research team to contact patient in case of incomplete CRF. Mobile phone numbers will be deleted after intermediate analysis.

8. Adverse events management

8.1 Adverse events in the current study

The current study aims to measure implementation of a cardiovascular CPR and its impact on chest pain management in primary care. We will measure several endpoints in both intervention and control group. We therefore expect some minor changes in GPs behaviour regarding investigations and diagnostic approach, as those using the CPR will be provided with additional information concerning patient's risk of cardiogenic chest pain. Those changes will be measured during follow-up.

To avoid misuse of the CPR, GPs selected to use the CPR will undergo intensive training (see Annex 1). Moreover, except calculating the risk of cardiogenic chest pain, GPs are asked to take care of patients according to their scientific knowledge and clinical experience. We therefore do not expect any adverse event due to the CPR itself for patients included in the trial.

8.2 Monitoring of adverse events

Intermediate analysis is done at 3 months after patients index visit to display any unexpected effect of the CPR. In case of unfavourable effect for patients included, study will be immediately stopped. For stopping rules, please refer to *Chapter 3.4*.

9. Quality control and assurance

9.1 Monitoring

Follow-up will last 6 to 9 months, with intermediate analysis at 3 months. To insure the data collection and avoid loss of follow-up, a member of research team will phone patients at 3 months and will also contact GPs at 9 months to insure closing of the follow-up.

Quality control will be provided by an independent GP and a hospital internist not aware of the current study. They will both review 20% of the cases, randomly

selected, to insure correct management of patients and validity of the data collected before analysis. Both reviewing and follow up should certify as surely as possible and without any invasive procedure the correct diagnosis and management of patients' complaint.

9.2 Audit and inspection

This trial, as an implementation study of a CPR, does not involve any treatment or drug. Audit and inspection are therefore not strictly required.

10. Statistics

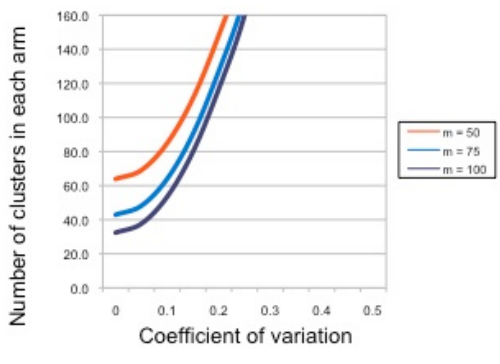
10.1 Number of subjects

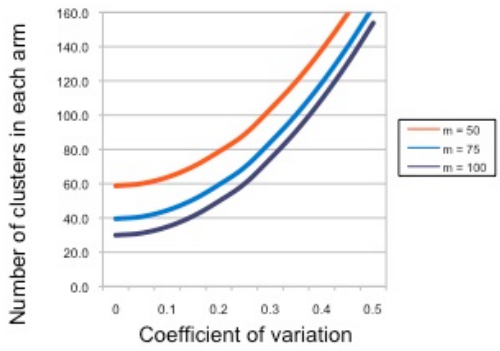
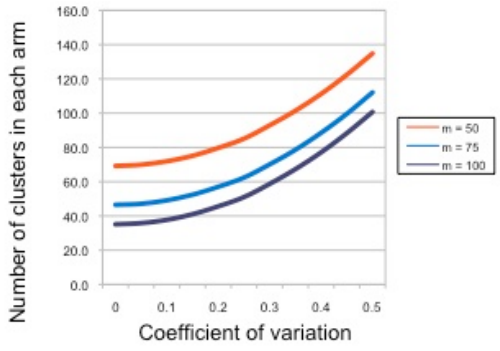
Calculation of the number of subjects is based upon the TOPIC study, targeting the same population of patients with chest pain. We used a sample size calculation table for cluster-randomized trial to calculate the number of clusters needed with different values of subjects per cluster (m value). Calculation has been made for different variables up to the endpoints of the study. We chose the following variables for the calculation of the number of subjects: number of paraclinical tests, number of referral to specialist, number of hospitalisations.

All the true proportions for each variable in the control arm of the sample size calculation table come from the TOPIC study results. We then decided a reasonable decrease expected in the rate of paraclinical tests, referral and hospitalisations while using the CPR, which led us to the expected proportions in the intervention arm

In the TOPIC study, investigators reported 42% (284/672) of patients with paraclinical tests, 16% (110/672) with referral to specialist and 8% (53/672) hospitalised up to 12 months of follow-up (2).

To choose the number of cluster needed in each arm of the trial we took a coefficient of variation of 0.2. Final decision about number of subjects per cluster and number of clusters was based upon practical considerations so that recruitment procedure remains comfortable for GPs and to limit its duration.

Paraclinical tests Control arm: 42% (TOPIC) Intervention arm: 38% expected *4% reduction expected in CPR group*	

Referrals Control arm: 16% (TOPIC) Intervention arm: 13% expected *3% reduction expected in CPR group*	
Hospitalisations Control arm: 8% (TOPIC) Intervention arm: 6% expected *2% reduction expected in CPR group*	
m = number of individuals per cluster *Z(alpha/2) 95.00% = 1.96; Z(beta) 90.00% = 1.28*	

Based upon the results shown above, we chose a number of 150 GPs in each arm, with 50 patients per cluster, so that the power of the study is sufficient to get a difference in paraclinical tests. We therefore need a total amount of 300 GPs, each of them recruiting 50 patients complaining of chest pain, leading us to a total amount of 15,000 patients.

Duration of inclusion is also calculated upon the TOPIC study in which chest pain occurred in 672 cases among 24,620 consultations during 300 weeks. We can therefore expect 2 to 3 patients with chest pain per week on the average, which leads us to an inclusion period of about 6 months for GPs to enrol the 50 patients needed.

N.B. This is an estimation based on the TOPIC study, which was run in the same target population of GPs as the current trial. This may eventually lead to a bias, as they were aware of chest pain as the purpose of the study. Investigators may therefore decide to run a Baseline Survey among Swiss GPs to verify true proportions before starting with the proper implementation study.

10.2 Data analysis

a) Sampling and characteristics of GPs recruited (+/- Baseline Survey)

b) Patients characteristics in usual practice group versus CPR group (age, sex, personal history of cardiovascular disease, cardiovascular risk factors, emergency consultation, telephonic interview, home visit, chest pain as main or secondary complaint)

c) Patients characteristics within CPR group: low-risk versus high-risk of cardiogenic chest pain

d) Impact of the CPR within CPR group

	CPR < 5 points (low risk)	CPR 5 to 7 points (intermediate risk)	CPR > 7 points (high risk)
Extra investigations Referral Patient's outcome			

e) CPR calculated *a posteriori* in usual practice group, endpoints values and comparison of endpoints in low risk patients of usual practice group versus CPR group

f) CPR group versus usual practice group

	CPR	Usual practice
Extra investigations Referral Patient's outcome		

g) Implementation: use/non use rate of the CPR, acceptability and satisfaction.

10.3 Dropouts and missing data management

Every case of dropout will undergo a complete analysis to avoid any bias. In case of missing data, the following procedure will be attempted:

1) Complete missing data by contacting GP/patient if feasible
2) Extrapolation if feasible
3) Exclusion of patient

10.4 Criteria for the termination of the trial

Termination is scheduled at most 9 months after index visit of the last patient included in the trial.

11. Ethics

11.1 Relation to primary care practice

The current study only aims to provide GPs an assistive tool to assess risk of cardiogenic chest pain. Moreover, each item of the CPR is known and already used in everyday practice to manage chest pain. We therefore believe that giving a defined weight to each of those items in order to help GPs' assessment should not alter in an unfavourable way GPs' behaviour and final decision regarding patient's complaint. It is important to note that the current CPR is not a decision rule and that it only incites GPs to take care of well-known and validated assessment criteria regarding chest pain.

11.2 Ethical committee

The current protocol will be submitted to the cantonal ethical committee of Vaud, Lausanne, Switzerland.

11.3 Information and consent

Each patient eligible for the study will be asked to participate at index visit. Patients agreeing to participate will get an information form to explain the purpose of the study and the modalities of follow up (see Annex 4, in French). They will be asked to sign a consent form and will be informed of their right to withdraw at any time of the study.

11.4 Confidentiality

Confidentiality is guaranteed for each patient and GP taking part of the study. All the data collected are made anonymous by attributing a single code to each patient and GP so that it will not be possible to link medical information to patient's name and details. Patients agreeing to give a mobile phone number are informed that the number will not be kept after intermediate analysis.

12. Financing

Financing will be requested at the RRMA commission of the Swiss Academy of Medical Sciences. Other sponsors may be contacted later on according to financial needs.

13. Registration

This study will be properly registered to competent regulatory authorities in expectation of an eventual publication.

14. References

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16. Appendices

Annex 1: General practitioners' intensive training
Annex 2: Case report form (in French)
Annex 3: Questionnaire for intermediate analysis and end of follow-up (in French)
Annex 4: Information form for subjects enrolled (in French)

General practitioners' intensive training

Two members of research team will provide GPs' training. One trainer will meet every GP selected to use the cardiovascular CPR while the other will meet every participating GP of the usual care group. Training at GP's office allows investigators to adapt to GP's schedule while a mandatory common training period at a defined date might have compromised participation.

We remember that in case of real implementation of the CPR, a personal training at the GP's office would not be feasible, but the content of the training would perfectly fit into seminars or congresses, within the context of the presentation of the current study for instance. We therefore believe that there is no major bias to expect and that meeting GPs at their own offices will only insure a higher participating rate.

Content of intensive training

CPR group:

- The cardiovascular CPR is a new, simple and safe tool to rule out CHD in primary care patients complaining of chest pain when it is used in the proper way.
- The cardiovascular CPR has been especially developed for primary care and is only based upon patient's history and physical examination.
- Initial management of patient's complaint should not be modified. After first clinical evaluation, calculating the CPR provides extra information regarding the risk of cardiac origin to chest pain.
- Sensitivity, specificity, negative predictive value and negative likelihood ratio of the CPR.
- GPs should use the CPR to calculate the risk of cardiogenic chest pain, and only after that, decide whether they need to run complementary exams or not, depending on how the CPR reinforces their clinical impression.
- Decision to run further investigation remains to GP's judgment. The cardiovascular CPR is not a decision rule.
- In case of contradiction between clinical impression and CPR's result, GPs must pursue investigations. The cardiovascular CPR is derived from logistic regression and cannot identify unusual presentation (consider young patient who abuses cocaine for instance).

Usual care group:

- Investigators are running a new study about patients complaining of chest pain in primary care settings.
- The current study is a cluster-randomized trial.
- Some of the GPs get an intensive training before the trial while the others get the formation after the trial. They belong to the second group.
- The final purpose is to improve and facilitate the management of chest pain at GP's office.

Première consultation

No patient :	No médecin :	Date :

Patient : connu ☐ / nouveau patient ☐ sexe : F ☐ / H ☐ âge : _____ ans

Consultation: planifiée ☐ urgence ☐

Lieu: cabinet ☐ à domicile ☐ par téléphone ☐
autre ☐ (préciser) : _____

<u>Douleur thoracique:</u>

Contexte : nouvelle ☐ / connue ☐ plainte principale ☐ / plainte secondaire ☐

Intensité: faible ☐ modérée ☐ forte ☐

Installation: soudaine ☐ progressive ☐

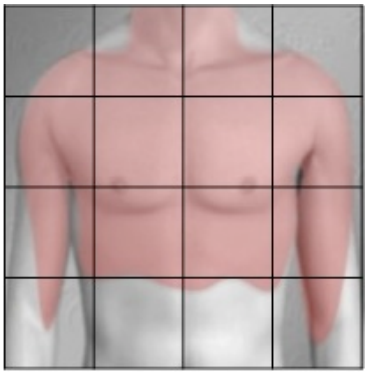
Evolution: en augmentation ☐ en diminution ☐ intermittente ☐
constante avec exacerbations ☐

Durée: <1 minute ☐ <15 minutes ☐ <1 heure ☐ heures ☐
jours ☐ mal défini ☐

Type: superficielle ☐ profonde ☐ oppressante ☐ en lancées ☐
brûlure ☐

Localisation : rétrosternale ☐ transfixiante ☐ localisée ☐ étendue ☐

Préciser (avec irradiation si présente) :



Facteur déclenchant: effort ☐ mouvement ☐ décubitus ☐ repas ☐
anxiété ☐ palpation ☐

Facteur aggravant: toux ☐ respiration ☐ position ☐ déglutition ☐
effort ☐

Autre(s) caractéristique(s) (préciser) : _____

Symptômes d'accompagnement :

Général : fièvre ☐ frissons ☐ sudations ☐ altération conscience ☐

Cardiovasculaire : palpitation ☐ syncope ☐ tachycardie ☐ arythmie ☐
instabilité hémodynamique ☐
autre ☐ (préciser) : _____

Respiratoire : dyspnée ☐ toux ☐ expectorations ☐
autre ☐ (préciser) : _____

Digestif : dysphagie ☐ reflux ☐ épigastralgies ☐
autre ☐ (préciser) : _____

Articulaire : préciser si présent(s) : _____

Facteurs de risque :

HTA ☐ diabète ☐ dyslipidémie ☐

Tabagisme ☐ : _____ UPA OH ☐ : _____ dl/semaine

Anamnèse familiale positive ☐

Antécédents personnels cardiovasculaires (maladie coronarienne, maladie cérébrovasculaire, artériopathie périphérique) ☐

Antécédent personnel maladie thromboembolique veineuse ☐

Score clinique cardiovasculaire (uniquement pour les médecins du « groupe CPR ») :

Swiss Heart Score	
Men over 55 years, women over 65 years	2 points
Known cardiovascular risk	2 points
Personal history of cardiovascular disease	2 points
Substernal pain	2 points
Duration of pain from 1 to 60 minutes	1 point
Increasing with effort	1 point
No tenderness at palpation	1 point
Total < 5 points: low risk of cardiogenic chest pain Total 5 to 7 points: intermediate risk of cardiogenic chest pain Total > 7 points: high risk of cardiogenic chest pai	
- *Sensitivity 97.6%, specificity 71.3%, negative likelihood ratio 0.033, negative predictive value 99,5% (derivation cohort)* - *Sensitivity 85.6%, specificity 47.2%, negative likelihood ratio 0.305, negative predictive value 94.8% (validation cohort)*	

Total : _____ points

Alternativement :

Marburg Heart Score	
Men over 55 years, women over 65 years	1 point
Known clinical vascular disease*	1 point
Pain worse during exercise	1 point
Pain not reproducible by palpation	1 point
Patient assumes pain is of cardiac origin	1 point
Total ≤ 2 points: low risk of cardiogenic chest pain * Coronary artery disease, occlusive vascular disease or cerebrovascular disease	
Sensitivity 89.1%, specificity 63.5%, negative likelihood ratio 0.17, negative predictive value 97.9% (results to be published)	

Impression diagnostique :

Suspicion maladie coronarienne : oui ☐ / non ☐

Degré de certitude : faible 0 – 1 – 2 – 3 – 4 fort

Examens en urgence (effectués au moment de la consultation) :

Aucune ☐ ECG ☐ Radiographie thorax ☐ Test d'effort ☐

Laboratoire: FSC ☐ CRP ☐ Troponines ☐ CK ☐
BNP ☐ D-dimères ☐

Autre(s) ☐ (préciser) : _____

Suite de prise en charge :

Aucune ☐ Hôpital/Urgences ☐

Consultation par cardiologue : délai <6 heures ☐ <1 semaine ☐ >1 semaine ☐
avis téléphonique ☐

Consultation de contrôle au cabinet ☐

Autre(s) ☐ (préciser) : _____

Appréciation du score clinique cardiovasculaire (uniquement pour les médecins du « groupe CPR ») :

Utilisation *au cours* de la consultation : oui ☐ / non ☐

Sinon, pourquoi ? Oubli ☐ inadapté ☐ autre ☐ (préciser) : _____

Si le résultat du score a indiqué un *risque faible* d'origine cardiaque à la douleur thoracique :

Aucun impact 0 – 1 – 2 – 3 – 4 Rassurant

Degré de satisfaction : insatisfaisant 0 – 1 – 2 – 3 – 4 très satisfaisant

Suivi à 3 et 9 mois

Questionnaire rempli par : infirmière de recherche (analyse intermédiaire à **3 mois**) ☐
médecin (terme du suivi à **9 mois**) ☐

No patient :	No médecin :	Date :

Suivi du patient :

Le patient a-t-il été revu *en raison de la douleur thoracique* **APRES** la consultation initiale :
oui ☐ / non ☐

Si oui, nombre de consultations ultérieures en lien avec la douleur thoracique : _____

Investigations complémentaires de la douleur thoracique (réalisées APRES l'inclusion dans l'étude) :

Aucune ☐

ECG de contrôle ☐ *Si oui*, nombre : _____

Laboratoire ☐ *Si oui*, nombre : _____

Radiographie thorax ☐ *Si oui*, nombre : _____

Test d'effort ☐

Autre ☐ (préciser examen et nombre) : _____

Référence au spécialiste dans le cadre de la douleur thoracique :

Aucune ☐

Cardiologue ☐ *Si oui*, nombre de consultation(s) : _____

Autre spécialiste ☐ (préciser) : _____ nombre de consultation(s) : _____

Hospitalisations en lien avec la douleur thoracique durant la période de suivi :
oui ☐ / non ☐
Si oui, durée : _____ jour(s)

Diagnostic retenu pour la douleur thoracique :

Maladie coronarienne : oui ☐ / non ☐

Degré de certitude : faible 0 – 1 – 2 – 3 – 4 fort

Etude TOPIC (Thoracic Pain In Community), 2e partie

Information à l'attention des patients

Madame, Monsieur,

Vous avez évoqué ce jour une douleur dans la poitrine. Les douleurs localisées dans la région thoracique peuvent avoir différentes origines et plusieurs études ont déjà été menées afin de mieux les connaître et les caractériser. L'objet de la présente étude est de se pencher sur l'étape suivante, à savoir la prise en charge de la douleur thoracique dans le contexte particulier de la médecine générale. Cette étude est menée par le groupe de recherche de l'Institut Universitaire de Médecine Générale à Lausanne.

Dans le cadre de cette étude, nous collectons diverses données concernant les patients de médecine générale présentant des douleurs thoraciques. Il s'agit en particulier de la manière dont la douleur se présente, des antécédents médicaux d'ordre cardiovasculaire, de l'âge et du sexe des patients ainsi que des moyens diagnostiques mis en œuvre par votre médecin. Nous nous intéressons également au devenir de cette douleur et au diagnostic retenu à terme. C'est pourquoi, avec votre accord, vous serez contacté(e) par téléphone dans 3 mois afin d'effectuer un bilan intermédiaire de l'évolution et des mesures entreprises concernant cette douleur. En cas de nouvelle consultation chez votre médecin entre 6 et 9 mois à dater de ce jour, la présente douleur sera à nouveau évoquée afin d'effectuer un bilan final. Si tel n'est pas le cas, vous serez à nouveau contacté(e) par téléphone par votre médecin traitant.

Le fait de récolter ces différentes données ne va en aucun cas modifier la prise en charge de votre problème. Il s'agit surtout d'examiner comment les médecins procèdent et les ressources qu'ils utilisent dans le cadre de la prise en charge des douleurs thoraciques. Les données médicales vous concernant seront rendues anonymes pour être analysées et la confidentialité tout comme le secret médical sont garantis. La seule information transmise au groupe de recherche est votre numéro de téléphone mobile, qui sera détruit une fois l'analyse intermédiaire des données effectuée. Vous êtes par ailleurs libre de quitter l'étude à tout moment sur simple appel à l'institut de recherche ou en en informant directement votre médecin. Nous restons évidemment à votre disposition pour toute information complémentaire.

En vous remerciant pour votre précieuse collaboration, veuillez recevoir, Madame, Monsieur, l'assurance de toute notre considération.

L'équipe TOPIC 2, Institut Universitaire
de Médecine Générale, Lausanne

Contact : _____

Formulaire de consentement

Je, sous-signé(e), déclare avoir pris connaissance de la page d'information concernant l'étude TOPIC 2.

Par ma signature, j'accepte de participer à la présente étude et serai donc contacté(e) par téléphone dans 3 mois à compter de ce jour et reverrai mon médecin dans un délai de 6 à 9 mois. La prise en charge de mon problème ne sera pas modifiée et je reste libre de quitter l'étude à tout moment.

Date : _____

Signature : _____