UNIVERSITEIT TWENTE.

August 2018

Study to the clinical outcomes and compliance of Fast Track Poli 'chest pain' patients on the long term

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August 15, 2018

Study to the clinical outcomes and compliance of Fast Track Poli 'chest pain' patients on the long term.

A retrospective, cross-sectional study to long-term results of the Fast Track Poli 'chest pain'.

Thesis MSc Health Sciences
Track Optimization of Healthcare Processes
February 2018 – August 2018

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ACKNOWLEDGEMENTS

I proudly present this thesis entitled “study to the clinical outcomes and compliance of Fast Track Poli ‘chest pain’ patients on the long term”. This thesis is the final product of the Master Health Sciences at the University of Twente with a focus on Optimization of Healthcare Processes. The study started at Zorggroep Twente (ZGT) in Hengelo and is carried out from February 2017 till August 2018. This study would not have been possible without the effort and support of several people. First of all, I would like to thank my supervisors of the University of Twente, Janine van Til and Karin Groothuis-Oudshoorn for providing my thesis of feedback. Furthermore, I would like to thank Marieke Weernink for providing some tools for digital questionnaires and Kelly de Ligt for her feedback on my study design. Next to that, I am grateful for the support of my supervisor of the ZGT hospital, Rogier Nijhuis. I would also like to thank all employees of the FTP (in particular Marion Lubbers, Marissa Bultje-Peters, Maudy Hesselink-van de Wetering, and Marije Kamphuis) for their help during my study. Besides these persons, I would like to thank Marloes Vermeer of the ZGT academy, Kim Brokelman of the Repro service and Annelieke Lankamp of the Communication department for their input in this study. I am also grateful to the secretariat of the cardiology policlinic, the ICT department, and the unit-head policlinic cardiology (Barbara Koenis) for their efforts. At last, I would like to thank all respondents, because this study could not have been successfully conducted without their participation.

I hope you will enjoy reading this thesis.

Melanie Kok

Enschede, 15 august, 2018

ABSTRACT

Background – Ziekenhuisgroep Twente (ZGT)'s cardiology department started with the Fast Track Poli "chest pain" (FTP) in September 2009. Although the FTP delivers outstanding results regarding to the speed of diagnosing and assessing patients with chest pain with mild to moderate suspicion of coronary heart diseases, clinical utility of the FTP department is not investigated. Therefore this study aims to map long-term clinical outcomes and differences in these clinical outcomes between patients with different FTP outcomes; FTP related tests and scores which best predict long-term clinical outcomes; and long-term compliance.

Methods – This retrospective, cross-sectional study used questionnaires and was performed in 1000 Dutch patients who visited the FTP between 2009 and 2015. Descriptive analyses were performed to study long-term clinical outcomes and to which extent they differed for patients with different FTP outcomes; and long-term compliance to stop smoking and diet advice. Univariate and multivariate Cox Proportional Hazard analyses were performed to find the diagnostic- and/or prognostic test(s) and/or score(s) within the FTP pathway which best predicted long-term clinical outcomes.

Results – Mean patient age was 54.8±10.5 years and 61.9% was male (n=519) at baseline. Of the 505 respondents (60.3%), 0.6% (n=3) had a cardiac related death; 0.4% (n=2) had a myocardial infarction (MI); 5.1% (n=26) had a coronary artery bypass grafting (CABG); 7.3% (n=37) had a percutaneous coronary intervention (PCI); 0.4% (n=2) had a heart valve surgery; 3.0% (n=15) had a cardiac related rehospitalisation; and 6.3% (n=32) had a cardiac related referral after their FTP visit. Significantly higher rates were found in respondents with diagnosed high-grade stenosis on the FTP ($p<0.001$). The Framingham score ($p=0.030$) and the CTCA ($p<0.001$) were the most accurate predictors of cardiac related death, MI, CABG, PCI, and heart valve surgery. The pre-test probability of CHD ($p=0.049$), the coronary artery calcium score ($p=0.037$), and the CTCA ($p<0.001$) were the best predictors when cardiac related rehospitalisation and -referral were also included as endpoints. 32.8% (22/67) of the respondents stopped smoking as a result of FTP lifestyle advice. Compliance to diet advice was much better with 93.3% (125/134).

Discussion – The results suggest clinical utility of the FTP as it showed (1) low CHD risk after FTP visit; (2) predictive accuracy of the Framingham score, the pre-test probability of CHD, and the coronary artery calcium score in combination with the CTCA; and (3) relative good compliance on the long term. It should be mentioned that respondents appeared to be not representative for non-respondents within this study. Future studies should focus on patient satisfaction and long-term results of regular diagnostics in the Netherlands to prove clinical utility of the FTP in Dutch patients with chest pain.

SAMENVATTING

Achtergrond – De cardiologieafdeling van Ziekenhuisgroep Twente (ZGT) is gestart met de Fast Track Poli “pijn op de borst” (FTP) in 2009. Ondanks de uitzonderlijke snelheid van diagnostiek van patiënten met pijn op de borst waarbij milde tot matige verdenking van coronaire hartziekten, is klinische meerwaarde van de FTP nog niet bewezen. Deze studie heeft als doel de lange termijnuitkomsten en verschillen hierbij tussen patiënten met verschillende FTP diagnoses; FTP gerelateerde testen en scores die het best lange termijnuitkomsten voorspellen; en lange termijn therapietrouw te onderzoeken.

Methode – Dit retrospectieve, dwarsdoorsnedenonderzoek gebruikte vragenlijsten en werd uitgevoerd bij 1000 Nederlandse patiënten die de FTP bezochten tussen 2009 en 2015. Descriptieve analyses werden uitgevoerd om klinische uitkomsten op de lange termijn en verschillen hierbij tussen patiënten met verschillende FTP diagnoses, en therapietrouw op de lange termijn te onderzoeken. Om de diagnostische- en/of prognostische test(en) en/of score(s) binnen het FTP traject in kaart te brengen die het best klinische uitkomsten op de lange termijn voorspelden, werden univariate en multivariate Cox Proportional Hazard analyses uitgevoerd.

Resultaten – Gemiddelde patiëntenleeftijd was 54,8±10,5 jaar en 61,9% was man (n=519) op moment van FTP bezoek. Van de 505 respondenten (60,3%), 0,6% (n=3) had een cardiaal gerelateerde dood; 0,4% (n=2) had een myocardiaal infarct (MI); 5,1% (n=26) had een bypassoperatie (CABG); 7,3% (n=37) had een dotterbehandeling (PCI); 0,4% (n=2) had een hartklepoperatie; 3,0% (n=15) had een cardiaal gerelateerde opname; en 6,3% (n=32) had een cardiale verwijzing na FTP bezoek. Significant hogere proporties werden gezien bij respondenten met gediagnosticeerde hooggradige stenose op de FTP ($p<0,001$). De Framingham score ($p=0,030$) en de CTCA ($p<0,001$) bleken de beste voorspellers van cardiaal gerelateerde dood, MI, CABG, PCI, en hartklepoperatie. De pretest waarschijnlijkheid van CHD ($p=0,049$), de coronaire calciumscore ($p=0,037$), en de CTCA ($p<0,001$) bleken de beste voorspellers wanneer ook cardiaal gerelateerde opname en -verwijzing werden geïncludeerd als eindpunten. 32,8% (22/67) van de respondenten stopte met roken en 93,3% (125/134) volgde dieetadviezen op na de FTP.

Discussie – De resultaten suggereren klinische meerwaarde van de FTP op basis van aangetoond (1) laag risico op CHD na FTP bezoek; (2) accurate voorspelling van lange termijnuitkomsten van de Framingham score, de pretest waarschijnlijkheid van CHD, de coronaire calciumscore en de CTCA; en (3) relatief goede compliance op de lange termijn. Kanttekening bij de resultaten is dat respondenten niet representatief voor non-respondenten bleken te zijn binnen deze studie. Toekomstige studies zullen zich moeten focussen op patiënttevredenheid en vergelijking met lange termijn resultaten van reguliere diagnostiek in Nederland om klinische meerwaarde van de FTP te bewijzen bij Nederlandse patiënten met pijn op de borst.

TABLE OF CONTENT

1. INTRODUCTION

Cardiovascular disease is a group of diseases of the heart and the blood vessels. Cardiovascular disease includes coronary heart disease, cerebrovascular disease, and peripheral artery disease. Coronary heart disease (CHD) is characterized by atherosclerosis in coronary arteries and can be asymptomatic, or symptoms like exercise- and stress related chest pain can occur.[1,2] The Framingham Heart Study, a long-term ongoing cardiovascular study to the common factors that contribute to CHD in regional inhabitants of the town of Framingham (USA), has defined the major risk factors of CHD. These major risk factors are hypertension (140/90 mmHg), hyperlipidaemia (6.5 mmol/L), smoking, obesity (30 kg/m2), Diabetes Mellitus, and physical inactivity.[3,4] CHD is responsible for approximately one-third of all deaths in people older than 35 years.[1,5] This disease is still the most common cause of death in developed countries, even though the incidence has already decreased due to better cardiovascular risk management.[6]

The diagnosis of CHD as the cause of chest pain symptoms requires a careful assessment of clinical history with the patient as well as physical examination and accurately diagnostic tests to confirm the diagnosis; exclude alternative diagnoses; and assess the severity of the underlying disease.[2] In the regular diagnostic procedure, a patient has to visit the hospital several times over a long period of time (sometimes months), because often multiple diagnostic tests are needed to determine the cause of chest pain symptoms which can not be performed at the same moment. Moreover, it is insufficiently known which diagnostic test or scores should be used.[7] To be able to offer the patient the correct treatment plan immediately after assessment and diagnosis, the Ziekenhuisgroep Twente (ZGT)'s cardiology department (location Hengelo) started with the Fast Track Poli 'chest pain' (FTP) in September 2009. Patients who visit the general practitioner with chest pain with mild to moderate suspicion of CHD, can be referred to the FTP. The logistical possibility of allowing cardiology and radiology to work together in such a way that the diagnosis can be made within four hours, makes the FTP so unique.

Coronary angiography is considered as the gold standard for the diagnosis of CHD, but its invasiveness and costs, make it less appropriate for use in clinical settings.[8] The regular diagnostic tests used in patients with suspected CHD in the hospital are standard laboratory biochemical testing (haemoglobin, thyroid hormone levels, plasma glucose, glycated haemoglobin, lipid profiles, troponin levels, renal function, and levels of c-reactive protein); a resting electrocardiogram (ECG); and a resting hand-held echocardiography (to test cardiac structure and function).[2] Other accurate and non-invasive diagnostic tests performed within the FTP pathway are the 64-detector CT Coronary Angiography (CTCA) and the exercise ECG or bicycle test.[8-13] In addition to the diagnostic tests, the Duke Treadmill Score; the pre- and post-test probabilities of CHD; and the HEART score are calculated based on diagnostic test outcomes and patient characteristics.[14-16] Besides the performed diagnostic tests and -scores, some additional prognostic scores are calculated in the FTP pathway to assess cardiovascular risk on the long term. These prognostic scores are the coronary artery calcium score; the Framingham score; and the European SCORE risk estimation.[17,18] After performing the diagnostic tests and calculating the diagnostic- and prognostic scores, there are generally three possible FTP outcomes: (1) no abnormalities, the patient will be reassured; (2) cardiovascular risk

management (cholesterol-restricted diet; anti-smoking intervention; medication; and follow-up) by the general practitioner in patients with mild, medium or intermediate stenosis; and (3) invasive testing or treatment in patients with high-grade stenosis.

It is important to closely and critically monitor the efficiency of the care delivered by clinical departments since hospital management is increasingly asking for this because of increasing costs of health care.[13] For the FTP, it is important to demonstrate clinical utility. Clinical utility is the extent to which FTP diagnostics improves health outcomes relative to regular diagnostics of chest pain.[19] To demonstrate clinical utility of the FTP, long-term clinical outcomes and the best predictive tests, scores and/or patient characteristics of these outcomes are needed because of no literary evidence for the clinical added value of FTP related test and scores, which are not standard applied in regular diagnostics of chest pain, in the Netherlands.[7] In addition, compliance to lifestyle advice has to be studied because of its contribution to long-term clinical outcomes as both smoking and diet are known as major risk factors of CHD in literature.[2,3,20,21] In the study of Stefanovska, et al. (2014) is mentioned that patient satisfaction is important when evaluating clinical utility, as patient satisfaction is directly correlated with compliance to lifestyle advice and therefore indirectly influences clinical outcomes.[20]

At this moment, approximately ten patients a week are visiting the FTP. Although the FTP delivers outstanding results with regard to the speed of diagnosing patients with chest pain and the more accurate and patient-friendly diagnostics, clinical utility of the FTP department is not investigated.[8-10,12,13] Only data of 1000 patients who have visited the FTP between 2009 and 2015 has been gathered and includes the date of consultation; background characteristics of the patients, performed diagnostic and prognostic tests and scores including outcomes; diagnosis; treatment policy; and treatment.

The main purpose of this study is mapping the long-term clinical outcomes of the FTP to demonstrate the clinical utility of the care delivered by this clinical department in the 1000 patients who visited the FTP between 2009 and 2015. Second, the predictive accuracy of long-term clinical outcomes by performed tests, calculated scores, and determined patient characteristics within the FTP pathway are studied. Third, compliance to lifestyle advice is investigated to study the clinical utility of the FTP. Based on these three aims, there are three research questions defined for this study.

1. What are the long-term clinical outcomes of the patients who visited the FTP between 2009 and 2015, and to which extent are they different for patients with different FTP outcomes at baseline?

2. Which diagnostic test(s) and/or prognostic score(s) and/or patient characteristics within the FTP pathway are the best predictors of long-term clinical outcomes?

3. What is the degree of compliance to lifestyle advice of patients after their FTP visit between 2009 and 2015?

These three research questions are PICO formulated and more explained in appendix I – PICO formulated research questions.

2. THEORETICAL FRAMEWORK

The theoretical framework describes the FTP pathway in more detail with regard to what is known in literature about the performed diagnostic tests; the calculated diagnostic- and prognostic scores; and the outcomes of the FTP pathway. This theoretical framework is useful to clarify the FTP pathway; in creating the research proposal; as well as in interpreting the results.

2.1. Referral of FTP patients

A patient is eligible for the FTP pathway when the following inclusion criteria are met:

- chest pain with mild to moderate suspicion of CHD;
- no cardiac history;
- not familiar with contraindications for a CTCA.

Contraindications for a CTCA are defined as renal impairment (glomerular filtration rate < 45% or glomerular filtration rate < 60% with Diabetes Mellitus); a contrast allergy or iodine allergy; atrial fibrillation; a heart rate above 75/min despite use of metoprolol/ivabradine and/or oxazepam; pregnancy; morbid adiposity (BMI above 40 kg / m2); inability to hold breath longer than fifteen seconds; severe chronic obstructive pulmonary disease; seriously calcified vessels/coronaries; and/or coronary stents.[22]

2.2. Patient characteristics

Prior to the FTP pathway, to indicate the likelihood of CHD, some background characteristics of the patients are mapped based on the known major risk factors of CHD in literature.[3] The mapped background characteristics prior to the FTP pathway are age, sex, body mass index (BMI), systolic and diastolic blood pressure, heart frequency, typical; atypical; or non-anginal chest pain symptoms, familiarity with Diabetes Mellitus, smoking, coronary related diseases in first-degree family members, and cholesterol levels (total cholesterol and High Density Lipoprotein (HDL)). Chest pain symptoms can be classified as typical angina; atypical angina; and non-anginal chest pain.[2] Degree of typical; atypical or non-anginal chest pain symptoms is determined by the following criteria: (I) substernal chest pain or discomfort experienced at least once a week, and if so, (II) whether these symptoms arise with exercise and/or cold and/or emotion, and (III) whether the chest pain disappeared at rest or within five minutes after taking Nitro glycerine. Atypical chest pain is defined within the FTP pathway as fulfilling two of these criteria. Typical chest pain is diagnosed when fulfilling three criteria, see table 1.[2,23,24]

Table 1 Classification of chest pain in the FTP pathway[2]

Typical angina (definite)	Meets all three of the following characteristics: • substernal chest discomfort of characteristic quality and duration; • provoked by exertion or emotional stress; • relieved by rest and/or nitrates within minutes.
Atypical angina (probable)	Meets two of these characteristics.
Non-anginal chest pain	Lacks or meets only one or none of the characteristics.

2.3. Diagnostic tests and -scores within the FTP pathway

The 64-detector CT Coronary Angiography (CTCA) and the exercise ECG or bicycle test are non-invasive diagnostic tests that are performed in the FTP pathway to assess whether there is CHD. In addition, the Duke Treadmill Score; the pre- and post-test probabilities of CHD; and the HEART score are calculated. These diagnostic tests and -scores will be further explained below.

Implementation of the CTCA is widely recommended to diagnose and screen patients with a low to intermediate risk of CHD because of the high negative predictive value in ruling out relevant plaques and stenosis in coronary arteries. The CTCA is a cost-effective (in the UK), accurate, reliable, and safe non-invasive imaging test for guiding management in patients with symptoms concerning for CHD in clinical practice.[8-10,12,13] The average sensitivity and specificity of the 64-slice CTCA for the determination of clinically relevant coronary stenosis are 91% and 96% respectively.[25-34] A more recently published systematic review about the 64-slice CTCA showed a diagnostic sensitivity, specificity, positive predictive value, and negative predictive value of 94%, 97%, 87%, and 99% respectively.[35] The CTCA is proved to be profitable and cost-saving because of the more effective use of national health services; improved prognosis for adults with chest pain because of the accurate and appropriate diagnostics; and reduced adverse events.[12,13] Another article of Genders, et al. (2015) concluded that the CTCA is cost-effective for 60-year-old patients who have stable chest pain and a low to intermediate CHD-risk.[36] The recently published and updated National Institute for Health and Care Excellence (NICE) guideline (2016) recommends the CTCA as the first-line diagnostic test for the evaluation of stable coronary artery disease in chest pain pathways.[12,13] A major limitation of the CTCA is that the extent of stenosis tends to be overestimated due to reduced ability to quantify the degree of stenosis and imaging artefacts in comparison with invasive angiography.[17]

The exercise ECG or bicycle test is a non-invasive tool which is used within the regular diagnostic procedure to detect clinically significant coronary artery stenosis. The sensitivity and specificity of the exercise ECG test for the determination of clinically relevant coronary stenosis are 68% and 77% respectively.[11] Due to the lower sensitivity and specificity of this test compared to the CTCA, the exercise ECG test is assumed to be less suitable in diagnostics of FTP patients with chest pain.[11,26-35] Therefore, an exercise ECG test is only performed within the FTP pathway when the patient suffers from exercise related symptoms and/or when the CTCA has diagnosed intermediate stenosis. Standard endpoints of the exercise ECG test (and dismissed as "positive") are fatigue, severe ischemia (severe angina > 2 mm ST depression), hypertension (systolic blood pressure > 220 mmHg), hypotension (decrease of systolic blood pressure > 20 mmHg), or arrhythmias.[14] The Duke Treadmill Score is also used to predict cardiovascular risk based on treadmill ECG stress testing in patients without known CHD and is therefore only calculated in FTP patients who performed an exercise ECG test.[11,14] The Duke Treadmill Score is calculated based on the exercise capacity, the maximum ST-segment deviation, and the presence of (non-)limiting chest pain. A Duke Treadmill Score of -10 or lower is considered as high CHD risk and of +5 or higher as low CHD risk.[14]

Furthermore, the pre-test- and post-test probability of CHD are calculated within the FTP pathway, which are the probabilities that CHD will occur. The pre-test probability of CHD is determined by age, sex, and type of chest pain, and the post-exercise test probability of CHD is determined by the pre-test probability of CHD and the degree of ST-segment depression on exercise testing. Type of chest pain is defined in the FTP pathway by following the traditional and valid clinical classification of chest pain symptoms, shown in table 1. The pre-test probability of CHD is determined prior to the FTP pathway based on the referral of the general practitioner. The post-test probability of CHD can only be calculated when an exercise ECG is performed. The pre-test- and post-test probabilities of CHD vary from 0.1% (asymptomatic females in the age from 30 till 39 years with no or minimal ST changes) to 99.8% (typical angina in men aged from 60 till 69 years with >2.5 mm ST depression).[15]

The last diagnostic score calculated within the FTP pathway is the HEART score. The HEART score estimates the risk of a major adverse cardiac event. The HEART score is calculated based on history, ECG result, age, risk factors, and troponin value in the blood, see table 2. As shown in table 2, a HEART score of ten points represents the highest possible risk.[16]

Table 2 Heart score[16]

History (=anamnesis)	
Highly suspicious*	2
Moderately suspicious	1
Slightly or nonsuspicious	0
ECG	
Significant ST depression	2
Nonspecific repolarization disturbance	1
Normal	0
Age	
≥65 years	2
45–65 years	1
≤45 years	0
Risk factors	
≥3 risk factors† or history of atherosclerotic disease‡	2
1 or 2 risk factors	1
No risk factors known	0
Troponin	
≥3× normal limit	2
1–3× normal limit	1
≤normal limit	0
Total	

*Suspicious elements are middle- or left-sided chest pain, initiated by exercise of emotion, radiation, relief of symptoms by sublingual nitrates, nausea, vomiting, and sweating.

†Classical risk factors are hypertension, hypercholesterolemia, diabetes, smoking, obesity, and positive family history.

‡History of atherosclerotic disease is myocardial infarction, percutaneous coronary intervention, coronary artery bypass graft, significant stenosis on coronary angiogram, cerebrovascular event, and peripheral arterial disease.

2.4. Prognostic scores within the FTP pathway

Additional prognostic scores calculated within the FTP pathway are the coronary artery calcium score; the Framingham score; and the European SCORE risk estimation. The coronary artery calcium score, a strong and independent predictor of future CHD, is correlated with the extent of atherosclerotic plaque burden in the coronary arteries. A CTCA is capable to quantify calcification after which the coronary artery calcium score can be calculated.[37] The coronary artery calcium score improves CHD risk prediction in addition to the Framingham score and the SCORE in patients at intermediate risk of CHD (a 10-year absolute risk of 10% to 20%).[17,37] Coronary artery calcification scoring is considered as less relevant in low- or high Framingham scores.[17] The Framingham risk score is a gender-specific 10-year cardiovascular risk score that is determined in advance based on the additional information about the patient in the referral of the general practitioner. The European Society of Cardiology developed the SCORE risk estimation. This risk estimation predicts the risk of fatal CHD within ten years separately for countries with a low or high CHD-risk in the EU. Both the Framingham risk score and the SCORE risk estimation include age, gender, smoking, blood pressure (including anti-hypertensive medication), and cholesterol levels (total cholesterol and high-density cholesterol) to calculate the final score.[18]

2.5. Outcomes of the FTP pathway

There are three treatment policies possible after the FTP pathway: (1) no intervention at all, reassurance of the patient; (2) cardiovascular risk management (cholesterol-restricted diet; anti-smoking intervention; and follow-up) by the general practitioner with or without prescribed medication; and (3) invasive testing as coronary angiography, and fractional flow reserve or treatment as coronary artery bypass grafting, percutaneous coronary intervention, heart valve surgery, or replacement. Option 1 is applied when no abnormalities are found and there are no risk factors; option 2 in mild, medium or intermediate stenosis and/or presence of risk factors; and option 3 in patients with high-grade stenosis. A high-grade stenosis is diagnosed when there is a stenosis of 50% or more in the left main coronary artery and/or a stenosis of 70% or more in one or more major coronary arteries.[2] Invasive tests mentioned in option 3 will now be briefly explained. Invasive coronary angiography is more explained above. The other mentioned invasive test, fractional flow reserve, is a relatively new technique in which the fractional flow reserve is calculated from standard CTCA acquisitions using computational fluid dynamics.[8] Coronary artery bypass grafting and percutaneous coronary intervention are revascularization procedures.[38] In high-risk patients or patients in whom a CTCA was not possible due to too high heart frequencies or coronary artery calcium scores above 400, a Myocardial Perfusion Scan (MIBI) can be performed. A MIBI is also known as a D-SPECT. The main disadvantage of this D-SPECT is the high radiation exposure for the patient.[39] Therefore, this D-SPECT is only performed in FTP patients when clinically indicated. At last, the type of eventually diagnosed plaque is determined to make a risk estimation of CHD in the future. In the FTP the following categories of plaque are distinguished: no plaque; soft plaque; calcium; or mixed (soft plaque and calcium).

2.6. The FTP pathway in a scheme

Concluding, the Framingham score and the SCORE are calculated prior to the FTP pathway to predict the future risk of CHD. Within the FTP pathway, first the HEART score and pre-test probability of CHD are calculated based on the intake and physical examination to assess the likelihood of CHD. The coronary artery calcium score is calculated in all patients. A coronary artery calcium score of zero is considered within the FTP pathway as sufficient evidence that there are no abnormalities and therefore no additional CTCA is performed.[40] Besides coronary artery calcium scores of zero, a CTCA is not performed in coronary artery calcium scores above 400 because of clinical irrelevance as the calcifications cause unjudgeable CTCA's and a D-SPECT or invasive coronary angiography is indicated.[13,40] It has to be mentioned that the coronary artery calcium score is more used as a diagnostic tool instead of a prognostic score within the FTP pathway.

Only when the patient suffers from exercise related symptoms and/or when the CTCA has diagnosed intermediate stenosis, an exercise ECG test, Duke Treadmill score and post-test probability of CHD are performed. The FTP pathway is summarized by creating a scheme of the performed diagnostic tests; the calculated diagnostic- and prognostic scores; the possible clinical outcomes; and the treatment options, see figure 1. The sequence of tests and scores is also shown in figure 1.

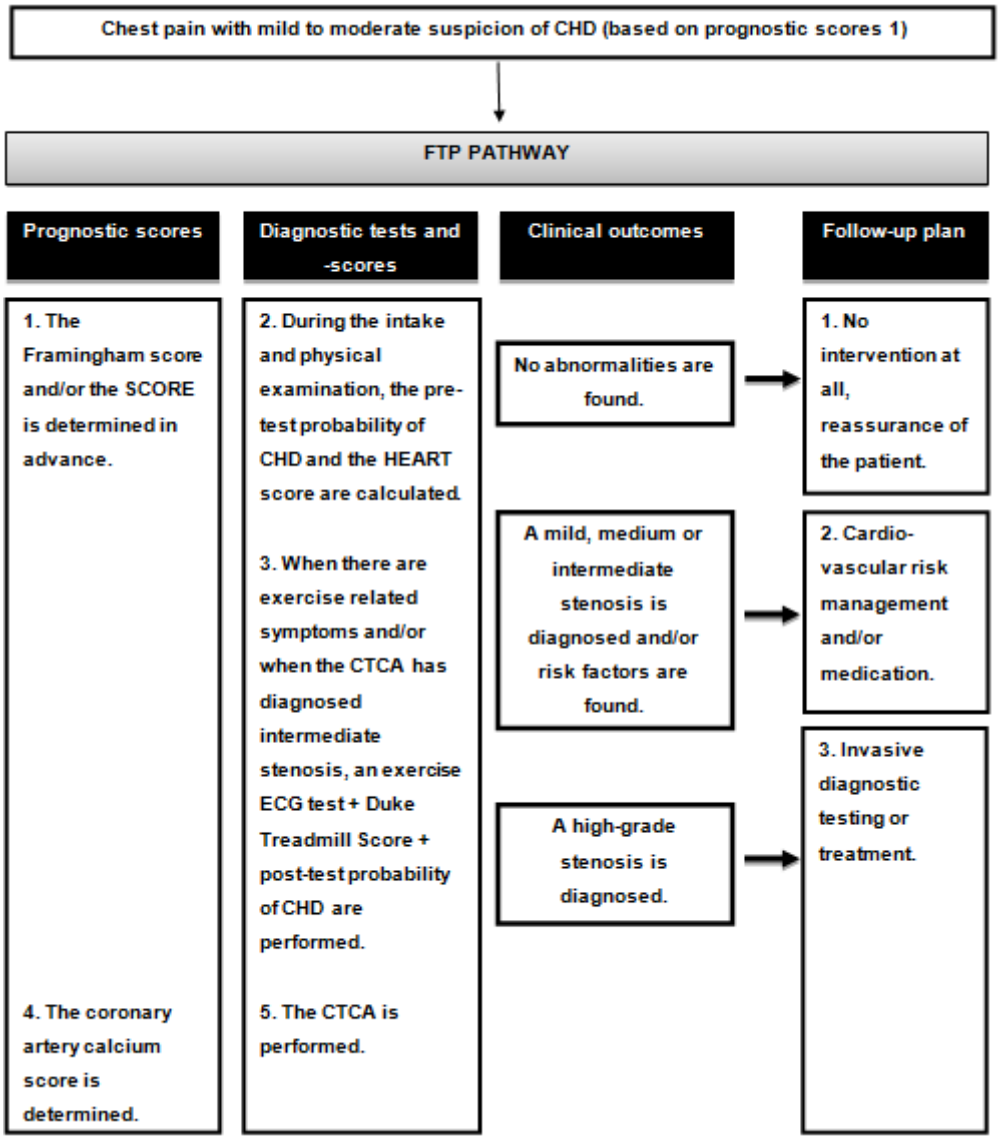

Figure 1 FTP pathway

3. METHODS

A study to long-term results of the FTP was conducted to investigate clinical utility of the care delivered by this department and will be further explained in this paragraph.

3.1. Study design

Baseline data of 1000 regional patients who visited the FTP in the ZGT hospital between 2009 and 2015, included date of consultation; background characteristics of the patients (age, sex, BMI, systolic blood pressure, diastolic blood pressure, heart frequency, total cholesterol, HDL, typical; atypical or non-anginal symptoms, coronary related diseases in first-degree family members, familiarity with Diabetes Mellitus, and smoking); performed diagnostic tests (exercise ECG test and CTCA); calculated diagnostic scores (HEART score, pre- and post-test probability of CHD, and Duke Treadmill Score); calculated prognostic scores (coronary artery calcium score, Framingham Score, and SCORE); outcome of the diagnostic and prognostic tests and scores; diagnosis; treatment policy; and treatment within the FTP pathway. This retrospective, cross-sectional study used questionnaires to gather data on the long-term clinical outcomes and compliance to lifestyle advice in these patients.[41-43]

3.2. Study population

This study was conducted in the same 1000 Dutch, competent men and women from the region Hengelo who visited the FTP between 2009 and 2015 and who gave their permission to participate in FTP research. Patients from the original database were excluded if:

- they followed only a part of the FTP pathway.
- they visited the FTP twice between 2009 and 2015. In that case only data of their first FTP visit was included in this study.
- they had a myocardial infarction, coronary artery bypass grafting, percutaneous coronary intervention, or heart valve surgery in advance of the FTP pathway.
- they had no valid address and/or phone number.

3.3. Ethics

Ethical approval was obtained from the Ethics Committee of the faculty of Behavioural, Management and Social sciences of the University of Twente. It was assumed by this Committee that this study did not have to be registered at the METC (Medical Ethical Test Commission), because it did not expose included patients to interventions or invasive procedures. Included patients had given permission for processing of collected data in research when visiting the FTP. Data was processed anonymously.[41,44]

3.4. Questionnaire

A questionnaire was designed to collect quantitative data about (1) clinical outcomes and (2) compliance to lifestyle advice of FTP patients on the long term. First, long-term clinical outcomes and long-term compliance to lifestyle advice were defined, and are described in paragraph 3.4.1. and paragraph 3.4.2. respectively. Next, a systematic approach is described in paragraph 3.4.3. which was followed to obtain a validated questionnaire. The paragraphs below only refer to long-term clinical outcomes and long-term compliance. Appendix II – Flow diagram selection articles and appendix III – Paper version of the questionnaire (in Dutch) refer to the full questionnaire, with topics included for future FTP studies. These topics were patient satisfaction, current CHD related medication use, and current state of chest pain symptoms.

3.4.1. Definition of long-term clinical outcomes

Long-term clinical outcomes were evaluated by mapping primary and secondary endpoints defined by literature and expert opinion. Primary endpoints were defined as the occurrence of one of the following events after FTP diagnostics between 2009 and 2015: cardiac related death, myocardial infarction (MI), coronary artery bypass grafting (CABG), percutaneous coronary intervention (PCI), or heart valve surgery on April 01, 2018.[38]

Because of the interest in the long-term guarantee of FTP diagnostics and sufficiency of reassurance of patients without diagnosed abnormalities, but also because of the expected low incidence of CHD, a composite endpoint was defined.[12,13,38,40] Secondary endpoints were defined as the occurrence of primary events including cardiac related rehospitalisation or -referral on April 01, 2018 after visiting the FTP.[38]

3.4.2. Definition of long-term compliance to lifestyle advice

Based on expert opinion, it was determined that only lifestyle advice with regard to smoking and diet was given within the FTP pathway. Therefore, long-term compliance to lifestyle advice was defined as stop smoking and/or change of diet in response to the FTP pathway on April 01, 2018.

3.4.3. Development of the questionnaire

The systematic review of Nse, et al. (2015) was used to develop a validated questionnaire.[45] The following steps were performed: (1) a systematic review to identify existing questionnaires which could be used in constructing a new questionnaire; (2) selecting and generating questionnaire items; (3) input of experts in the field on the selected items; (4) input for the questionnaire of the study population; (5) experts reached consensus to validate the questionnaire; and (6) pretesting the questionnaire.[45] This process is described below in which step 2 and 3 were merged because relevant questionnaire items were identified by combining literature and expert opinion. Step 4 was not performed as the entire study population participated in this study.

3.4.3.1. Systematic review

A systematic review was conducted to questionnaires about CHD related disease or treatment or secondary coronary prevention. No existing systematic review was found about questionnaires related to these topics, so a literature study was conducted using Pubmed, Cochrane Library and Scope. The following search key words were used: (questionnaire OR survey) AND ("chest pain" OR angina OR cardio* OR coronary*). The search deadline was March 08, 2018. Articles were included when reported in English; a free full-text was available; and the text was about humans. An initial screening was conducted based on respectively: (1) titles; (2) abstracts; and (3) full-text articles. Articles were excluded when they described studies with youth or children; were not related to FTP questionnaire topics; data was not collected by a valid or standardized questionnaire or survey in patients; or data was collected by a questionnaire developed or adjusted for one specific country (with the exception of the Netherlands). Articles were considered as eligible if they met the inclusion criteria. Data was extracted and checked by one reviewer. The quality of each included article was guaranteed by checking the validation of the included questionnaire in that article for FTP patients. In appendix II – Flow diagram selection articles, a flow diagram was constructed showing details of the literature study. In the end, three articles were included which met the inclusion criteria. These articles all described the Rose angina questionnaire.[23,46,47] The Rose angina questionnaire was developed in 1962 and was widely used to detect CHD in epidemiological research.[23,46,47] However, the clinical use of the Rose angina questionnaire in individual patients was determined as limited.[23]

3.4.3.2. Selecting questionnaire items

Relevant items were identified by combining literature and expert opinion for the two different domains. Several considerations were made based on the performed literature search to existing questionnaires and the previously mentioned definitions of long-term clinical outcomes and long-term compliance. These are further explained below.

No existing, validated questionnaires were found related to CHD related disease or treatment as the clinical use of the Rose angina questionnaire in individual patients was determined as limited.[23] Based on the determined individual components from which the questionnaire had to exist, the questionnaire included questions which inquired the occurrence of CHD (MI, CABG, PCI or heart valve surgery) after visiting the FTP between 2009 and 2015, and any (cardiac related) deaths were registered before.[38] Furthermore, cardiac related rehospitalisation or -referral were questioned.[38]

Taking into consideration the given lifestyle advices in the FTP pathway regarding to smoking and diet, but none found existing, validated questionnaire related to secondary coronary prevention, compliance to smoking and diet related advice was included in the questionnaire.

3.4.3.3. Generating the questionnaire

After selecting the relevant items for the questionnaire, the questionnaire was developed. Questions, answer categories and lay-out of the questionnaire were formulated based on the book written by Nederhoed (2007).[43] A questionnaire was developed by using Qualtrics.[48]

The questionnaire consisted of multiple choice questions to increase reliability.[43] It was assumed that two or three answer categories were easy to interpret, so the strain on a respondent was kept to a minimum and made it more likely that respondents finish the questionnaire.[43] Completion of the questionnaire took about five minutes. The questionnaire was written in Dutch based on the inclusion criteria. A status-quo option was not included because this was considered as not plausible.[43] An opt-out link was included in the digital version of the questionnaire.[48]

The questionnaire started with a short introduction into the aim of this study, and the content and duration of the questionnaire. The patients were also thanked for participation in this study and it was mentioned that data was processed anonymously. After that, there was a short instruction with regard to filling in the answers to ensure clarity.[43] Own interpretation of FTP diagnostics between 2009 and 2015 was questioned. Based on baseline FTP outcomes, there were four answers possible: (1) no intervention at all, reassurance of the patient; (2) cardiovascular risk management (cholesterol-restricted diet and follow-up) by the general practitioner with or without medication; (3) invasive testing as coronary angiography, and fractional flow reserve or treatment as CABG, PCI, and heart valve surgery or replacement; or (4) otherwise, in which respondents were asked to give an explanation.

The patients were asked if they had a CHD related primary event (MI, CABG, PCI or heart valve surgery) after diagnostics and treatment within the FTP pathway between 2009 and 2015 (true or untrue) and if so, when this was (month and year of occurrence) and where they were treated (place of specific hospital). Furthermore, in this part was asked if the patients received cardiac related rehospitalisation and/or -referral after FTP diagnostics and treatment. When this was the case, also place of rehospitalisation and/or referral was asked for checking this. It was assumed by expert opinion that patients remembered date and place of their event because of the impact.

Regarding to compliance, patients were asked if they received diet advice during the FTP pathway where they could answer with yes or no. If they answered positively, the patients were asked if they changed their diet in response to this diet advice (true or untrue). Furthermore, it was asked if patients smoked prior to the FTP pathway (yes or no) and whether they stopped smoking in response to the FTP pathway (true or untrue). At the end, it was asked whether patients were still quit smoking (yes or no).

There was space for additional remarks at the end of the questionnaire. At last, patients (not) allowed the researchers to contact them for additional explanation when needed and to verify events at the specified hospitals to increase the validity of the self-reported answers. Furthermore, patients were thanked for their participation again, the deadline of May 01, 2018 was mentioned, and it was explained how to return the paper version of the questionnaire. The final version of the questionnaire is shown in appendix III – Paper version of the questionnaire (in Dutch).

3.4.3.4. Validating the questionnaire

Experts within this study domain, staff of the FTP and supervisors of the University of Twente, reached consensus about the final version of the questionnaire.

3.4.3.5. Pre-testing the questionnaire

It was not possible to pre-test the questionnaire in the study population as they were all included in this study. In total, the questionnaire was pre-tested by eight employees of the FTP and random known people without a medical background who checked clarity, plausibility and eventually overlapping questions in the questionnaire.[42] Based on the pre-test outcomes, inaccuracies with regard to formulation were adjusted before the questionnaire was sent to the included FTP patients.

3.5. Data collection

Questionnaire administration took place between April, 2018 and June, 2018. There was checked on deceased patients on March 01, 2018 and these patients did not receive a questionnaire. An information brochure was developed to inform patients about the questionnaire prior to the study and was sent to all included patients by post. This brochure mentioned study aim, procedure of data collection, time indication and deadline for completing the questionnaire. It was clearly stated that patients were not obliged to participate in this study; could always and without consequences terminate their participation; and that collected data was processed anonymously. At last, contact information of the FTP secretariat was included when patients need more information or explanation of the questionnaire.[43] The information brochure was checked and styled by the communication department of ZGT and the final version is shown in appendix IV – Information brochure (in Dutch). If no e-mail from the included patients was known, a questionnaire was sent by post. However, the digital version of the questionnaire was preferred for the following reasons:

- More reliable and timesaving for respondents as only relevant questions, based on previous answers, were shown to respondents.[43,49]
- More complete and valid as drop-down lists were possible with pre-programmed answer options; response was forced; and only one answer was possible.[43]
- Decreased workflow because data could automatically recoded and easily copied from Qualtrics to SPSS.[48]
- Less administrative costs.[49]

Therefore, when an e-mail was known, a link for the digital questionnaire was sent to the included patients. In the information brochure was mentioned that patients could send an e-mail when they preferred the digital or the paper version of the questionnaire to prevent responder bias. The patients received a reminder by e-mail or phone when they had not responded on May 14, 2018. May 14 was taken as “reminder date” to prevent non-response due to the holidays. In the reminder per phone primary and secondary endpoints were questioned by phone, because of the importance of that part in this study. After that, patients were asked to answer the other parts of the questionnaire by themselves (in which the option of the digital version of the questionnaire again was presented to the patients). A limit of at least 60-80% response was assumed to guarantee validity by preventing non-response bias with this high response rate.[41]

3.6. Data analysis

All analyses were carried out using IBM SPSS Statistics, version 24 and Microsoft Office Excel 2010. First, the original database was cleaned by applying the inclusion- and exclusion criteria. Second, respondents were contacted when questionnaire results were incomplete or implausible if they gave permission for this. Third, CHD related events were checked by contacting the specific hospital when respondents agreed with this. Furthermore, cardiac related deaths and date of death were checked in decedent patients. Fourth, it was decided that the first CHD related event after FTP visit was included as primary endpoint and that only coronary or chest pain related hospitalisations and referrals were included as secondary endpoint. However, in the questionnaire were primary and secondary endpoints requested after FTP visit and treatment. Therefore, registered events at baseline (CABG and PCI in response to the FTP pathway) were compared to reported CABG's and PCI's by respondents in the questionnaire and were also included as primary and secondary endpoints after checking. Moreover, self-reported absence of CHD related events was checked in 10% of the respondents to measure validity of self-reported absence of primary- and secondary endpoints. Incorrectly self-reported absence of events were included as primary or secondary endpoints. Fifth, time to follow-up in days was calculated (the follow-up date or date of event minus the date of visiting the FTP). As follow-up date, 01 March 2018 was taken in all patients with no CHD related events. At last, the coronary artery calcium score was dichotomized (0 and >0) because of the major difference in clinical consequences between a coronary artery calcium score of zero and a coronary artery calcium score above zero within the FTP pathway.[2,40] Results at baseline were defined as the results measured at time of FTP visit between 2009 and 2015.

3.6.1. Patient characteristics and diagnostics at baseline

The descriptive statistic function and the explore function in SPSS were used to measure patient characteristics, test outcomes and scores at time of FTP visit of all included patients in this study. Results were expressed as numbers and percentages in categorical variables. A mean (± standard deviation) was reported in normal distributed continuous variables (assessed by using a histogram), and otherwise a median [interquartile range].[50]

3.6.2. Representativeness of the respondent population

Representativeness of respondents was assessed by performing an analysis in which patient characteristics, test outcomes and scores at baseline of respondents were compared to that of non-respondents. Significant differences ($p<0.05$) were tested by performing an independent samples T-test in normally distributed continuous variables and a Mann-Whitney test in skewed distributed continuous variables. Based on the Levene's test, the p-value of equal variances assumed or -not assumed was reported in performed independent samples T-tests. The p-value of the Pearson chi-square independence test was reported in categorical variables.[50]

3.6.3. Validity of self-administration of FTP outcomes by patients

Percentage (dis)agreement between registered treatment policy at baseline and self-reported FTP outcome by the respondent in this study was calculated. Validity of the questionnaire was checked by calculating the Cohen's Kappa in which agreement was measured between treatment policy at baseline and reported FTP outcome.[50] Reassurance, cardiovascular risk management, and further invasive testing or treatment were the possible FTP outcomes and first three answers options in the questionnaire. In the questionnaire a fourth answer option was included, own interpretation, which was attempted to trace to one of the three corresponding categories.

3.6.4. Long-term clinical outcomes

Trends in primary and secondary endpoints were analysed and to which extent they differed for patients with different FTP outcomes at baseline.

3.6.4.1. Trend analyses of primary and secondary endpoints in respondents on the long term

Trends in primary and secondary endpoints in respondents within nine years after FTP diagnostics were analysed by performing a Kaplan-Meier survival analysis in which censored data referred to the end of follow-up.[50] Cumulative proportions of respondents without primary and secondary endpoints after nine years of follow-up (maximum possible follow-up period in this study) were analysed by survival tables. 95% confidence intervals (CI) were calculated by using the following formula: $s(t) \pm 1.96 * SE(s(t))$ in which s(t) was the cumulative proportion of respondents who had no primary or secondary endpoint after nine years and SE(s(t)) was the standard error of s(t).[50]

3.6.4.2. Trend analyses of differences between patients with different FTP outcomes at baseline in primary and secondary endpoints on the long term

Similarly to the procedure described in paragraph 3.6.4.1., cumulative proportions of respondents without diagnosed abnormalities (code "0", no intervention at all); respondents with mild, medium or intermediate stenosis (code "1", cardiovascular risk management); and respondents with high-grade stenosis (code "2", invasive testing and/or treatment) without primary and secondary endpoints within nine years after FTP diagnostics were analysed and compared by using a log-rank test.[50] Furthermore, primary and secondary endpoints were linked to one diagnostic score (pre-test probability of CHD), one diagnostic test outcome (degree of stenosis diagnosed by the CTCA), and one prognostic score (coronary artery calcium score), selected based on literature, to determine to what extent the correct treatment policy was implemented in FTP patients.[40]

3.6.5. The best predictive FTP related tests, scores and characteristics of long-term clinical outcomes

An univariate Cox Proportional Hazard analysis was performed to select relevant variables for the multivariate Cox Proportional Hazard analysis. The multivariate analysis was performed to study the patient characteristics and/or diagnostic tests and/or diagnostic- and/or prognostic score(s) within the FTP pathway which best predicted the long-term clinical outcomes. At last, the predictive accuracy of each test or score performed within the FTP pathway was studied.

3.6.5.1. Univariate analyses in primary and secondary endpoints

The following variables were included in the univariate Cox Proportional Hazard analysis: age, sex, BMI, systolic blood pressure, diastolic blood pressure, heart frequency, total cholesterol, HDL, typical; atypical or non-anginal symptoms, coronary related diseases in first-degree family members, familiarity with Diabetes Mellitus, smoking, performed diagnostic tests (exercise ECG test and CTCA), calculated diagnostic scores (HEART score; pre- and post-test probability of CHD; and Duke Treadmill Score), calculated prognostic scores (coronary artery calcium score; Framingham Score; and SCORE), eventually diagnosed calcium and/or plaque, and degree of stenosis. A two-tailed alpha level of $p<0.15$ was used in this statistical test as criterion for the selection.[50,51] The results were reported as hazard ratios (HR), 95% CI and p-values.[50]

3.6.5.2. Multivariate analyses in primary and secondary endpoints

The selected variables by performing the univariate analysis were evaluated on relevance by expert opinion and literature as only four variables could be included in the multivariate analyses regarding to the small numbers of primary and secondary endpoints in respondents.[50] The Framingham score, the pre-test probability of CHD, the coronary artery calcium score, and the CTCA were selected as determinants for the multivariate analysis in both primary and secondary endpoints in which the following considerations were made:

- Age, gender and type of symptoms were represented by the pre-test probability of CHD as these were used to calculate this probability.[15]
- Age, gender, systolic blood pressure and HDL were represented by the Framingham score as these were needed for calculating this score.[18]
- Influence of height and heart frequency were considered as not relevant when evaluating long-term results based on literature and expert opinion.[2-4]
- The exercise ECG test, the post-test probability of CHD, and the Duke Treadmill Score, only performed in patients with exercise related symptoms and/or diagnosed intermediate stenosis by the CTCA, were not plausible to include because of the selected group respondents in whom these test and scores were performed.
- Degree of stenosis and diagnosed plaque and/or calcium were not included because these were not risk factors, tests, or scores, but FTP outcomes.
- The Framingham score and SCORE calculated both future cardiovascular risk. The Framingham score was preferred in literature in combination with the coronary artery calcium score and the CTCA, and was therefore included.[18,40]
- The pre-test probability of CHD and the HEART score calculated both CHD risk. The pre-test probability of CHD was selected as this score was preferred in literature.[16,40]
- Weight was not included as it was not known as risk factor of CHD in literature.[2-4]

A multivariate Cox Proportional Hazard analysis was performed with time to follow-up; whether or not occurrence of a primary and/or secondary endpoint; and as determinants the selected tests and scores. The backward stepwise multivariate Cox Proportional Hazard analysis was first performed manually, after which it was checked by automatically performing the analysis in SPSS. In the multivariate analysis, only patients with no missing values on the selected relevant determinants were included by using the SPSS NMIS function. Categorial variables were converted into dummy variables.[50] A two-tailed alpha level of $p<0.05$ and the log likelihood ratio test were used for constructing the best predictive model of long-term clinical outcomes.[50,51] The best predictors were reported including HR, 95% CI, and p-values. The predictive accuracy of the models was presented by the Harrel's C-index.[50]

3.6.5.3. Predictive accuracy of tests and scores performed within the FTP pathway

Predictive accuracy of primary and secondary endpoints by tests and scores performed within the FTP were evaluated and compared based on the Harrel's C-index.[50] The SPSS NMIS function was not applied in this analysis as some tests and scores were not performed in all respondents because of clinical irrelevance and therefore caused missing data.

3.6.6. Long-term compliance

Compliance to dietary and anti-smoking intervention was measured by performing a descriptive analysis in SPSS. The number of respondents who smoked prior to the FTP pathway was compared to the number of respondents who indicated that they stopped smoking in response to the FTP and the number of respondents who were still smoking. Furthermore, the number of respondents that received diet advice within the FTP pathway was compared to the number of respondents that changed their diet in response to the FTP.

4. RESULTS

In this paragraph, the results of the questionnaires are presented for long-term clinical outcomes and compliance. Furthermore, representativeness of the study is described and the validity of self-administration within this study is shown. But first, the process of data collection and patient characteristics are explained.

4.1. Data collection

A flow diagram was made to demonstrate the details of the data collection process, see appendix V – Flow diagram data collection. After applying the exclusion criteria, 838 out of 1000 FTP patients left. The response rate to the questionnaire was 60.3% (n=505). 142 self-reported primary and secondary endpoints (28.1%) were checked. Furthermore, reported absence of primary and secondary endpoints was checked in 9.9% (n=50) of the respondents. Of these 50 respondents, four turned out to have had a cardiac related rehospitalisation or -referral. At last, 18 primary endpoints (seven CABG's and 11 PCI's) registered at baseline, but not reported by respondents, were verified.

4.2. Patient characteristics and diagnostics at baseline

Table 3 presents a complete overview of the patient characteristics at baseline and the percentage (n), mean (± SD), and median [IQR] test outcomes and scores at baseline of all included patients (n=838). The mean ± SD age of all included patients was 54.8 ± 10.5 years in which ages ranged from 17 years to 81 years. The majority (61.9%) was men (n=519). Out of 838 included FTP patients, 9.7% (n=81) was familiar with Diabetes Mellitus and 14.6% (n=122) smoked. Furthermore, 11.3% (n=95) had a body mass index above 30 kg/m2; 14.7% (n=123) had a blood pressure above 140/90 mmHg; and 7.8% (n=65) was diagnosed with a total cholesterol above 6.5 mmol/L. The majority of the included FTP patients had atypical symptoms prior to the FTP (64.9% (n=544)) and were familiar with coronary related diseases in first-degree family members (54.7% (n=458)). A form of coronary arterial plaque was diagnosed in 36.5% (n=306) within the FTP. Moreover, 11.3% (n=95) was diagnosed with high-grade stenosis by performing the CTCA. Invasive tests or treatment, coronary angiography, CABG, PCI, heart valve surgery, and fractional flow reserve, were performed in respectively 12.4% (n=104), 3.5% (n=29), 4.7% (n=39), 0.4% (n=3), and 1.7% (n=14).

Table 3 Patient characteristics, diagnostic test outcomes, and diagnostic- and prognostic scores at baseline of all included patients; respondents; and non-respondents including p-values of baseline differences between respondents and non-respondents

Baseline screening at time of FTP visit	**All included patients** ***(n=838)***	**Respondents** ***(n=505)***	**Non-respondents** ***(n=333)***	**P-value[a]**
Age, years, mean (± SD)	54.8 ± 10.5 (n=838)	56.2 ± 9.8 (n=505)	52.6 ± 11.1 (n=333)	*<0.001*
Gender, male, % (n)	61.9 (519) (n=838)	62.2 (314) (n=505)	61.6 (205) (n=333)	0.857
Body mass index, kg/m2, mean (± SD)	27.0 ± 3.9 (n=838)	27.0 ± 4.0 (n=505)	27.1 ± 3.9 (n=333)	0.690
Systolic blood pressure, mmHg, mean (± SD)	148.5 ± 18.2 (n=838)	148.7 ± 17.9 (n=505)	148.1 ± 18.6 (n=333)	0.645
Diastolic blood pressure, mmHg, mean (± SD)	83.0 ± 10.8 (n=838)	82.9 ± 10.8 (n=505)	83.2 ± 10.7 (n=333)	0.759
Total cholesterol, mmol/L, mean (± SD)	5.4 ± 1.0 (n=834)	5.5 ± 1.0 (n=501)	5.4 ± 1.0 (n=333)	0.082
High-density lipoprotein, mmol/L, median [IQR]	1.3 [1.1-1.6] (n=831)	1.3 [1.1-1.6] (n=499)	1.3 [1.1-1.6] (n=332)	0.695
Typical symptoms, % (n)	22.2 (186) (n=838)	26.5 (134) (n=505)	15.6 (52) (n=333)	*0.001*
Coronary related diseases in first-degree family members, % (n)	55.0 (458) (n=833)	55.7 (279) (n=501)	53.9 (179) (n=332)	0.423
Diabetes Mellitus, % (n)	9.7 (81) (n=835)	9.7 (49) (n=503)	9.6 (32) (n=332)	0.961
Smoking, % (n)	14.6 (122) (n=835)	12.5 (63) (n=502)	17.7 (59) (n=333)	*0.038*
HEART score, mean (± SD)	3.6 ± 1.2 (n=634)	3.7 ± 1.2 (n=387)	3.5 ± 1.2 (n=247)	0.162
Pre-test probability of CHD, median [IQR]	54.0 [32.0-67.0] (n=807)	54.0 [32.0-79.0] (n=487)	46.0 [22.0-59.0] (n=320)	*<0.001*

Positive exercise ECG test, % (n)	12.9 (78) (n=604)	16.4 (62) (n=378)	7.1 (16) (n=226)	*0.003*
Post-test probability of CHD, median [IQR]	5.0 [4.0-8.0] (n=420)	6.0 [4.0-16.0] (n=275)	4.0 [2.0-6.0] (n=145)	*<0.001*
Duke Treadmill Score, median [IQR]	8.0 [6.0-9.0] (n=412)	8.0 [5.5-9.0] (n=268)	8.0 [6.1-9.5] (n=144)	*0.012*
A form of coronary arterial plaque (soft plaque/calcium/mixed), % (n)	54.5 (306) (n=561)	57.1 (202) (n=354)	50.2 (104) (n=207)	0.306
Diagnosed high-grade stenosis (by performing the CTCA), % (n)	16.7 (95) (n=568)	18.6 (67) (n=361)	13.5 (28) (n=207)	0.131
Coronary artery calcium score above zero, % (n)	61.7 (400) (n=648)	65.7 (264) (n=402)	55.3 (136) (n=246)	*0.008*
Framingham score, median [IQR]	7.4 [3.9-12.6] (n=650)	8.3 [4.2-13.4] (n=404)	6.5 [3.4-11.9] (n=246)	*0.001*
SCORE, median [IQR]	4.0 [1.5-8.0] (n=575)	4.0 [2.0-9.0] (n=351)	3.0 [1.0-7.0] (n=224)	*0.004*

Abbreviations explained:
SD – Standard Deviation
% – Cumulative percentage
n – Number of patients
IQR – Interquartile range: Q1 (Quartile 1 (25%)) - Q3 (Quartile 3 (75%))
[a] *Significance level is set on p < 0.05*

4.3. Representativeness of the respondent population

There was a lower rate of typical symptoms and a higher rate of smoking in non-respondents compared to respondents, respectively 15.6% (n=52) and 17.7% (n=59) in non-respondents and 26.5% (n=134) and 12.5% (n=63) in respondents. Furthermore, non-respondents scored lower on tests and scores at baseline. In table 3 is shown that non-respondents were significantly younger (p<0.001); had less often typical symptoms (p=0.001); smoked more often (p=0.038); scored lower on pre- and post-test probabilities of CHD (p<0.001), Framingham score (p=0.001), and SCORE (p=0.004); and had less often a coronary artery calcium score above zero (p=0.008). The median Duke Treadmill Score for non-respondents was similar to the median Duke Treadmill Score for respondents (p=0.012). The percentage non-respondents with a positive exercise ECG test was lower than in respondents (p=0.003). Concluding, respondents were not representative for non-respondents.

4.4. Validity of self-administration of FTP outcomes by patients

Agreement between registered outcome of the FTP in the patient files by the ZGT hospital and self-reported FTP outcome of the respondents was 69.5% (269/387) (table 4). 28 self-reported FTP outcomes (otherwise) could not be traced to the three corresponding categories and therefore they were not included in the calculation of the Cohen's kappa. The validity of self-administration as assessed by Cohen's kappa between registered FTP outcome and self-reported FTP outcome, showed fair agreement (k=0.60). Disagreements were most frequently observed in respondents without diagnosed abnormalities who reported to have received lifestyle advices and/or medication and in respondents with mild, medium or intermediate stenosis who reported to have received invasive tests or to be reassured.

Table 4 Registered outcome of the FTP in the patient files by the ZGT hospital and self-reported FTP outcome of the respondents

Self-reported / ***FTP diagnosis***	**No action**	**Prevention/ medication**	**Invasive tests**	**Otherwise**	**Total**
No action	142	33	11	17	**203**
Prevention/ medication	19	81	24	9	**133**
Invasive tests	2	1	46	2	**51**
Total	**163**	**115**	**81**	**28**	**387**

4.5. Long-term clinical outcomes

Of all patients who responded to this questionnaire part (n=505), 0.6% (n=3) had a cardiac related death; 0.4% (n=2) had a MI; 5.1% (n=26) had a CABG; 7.3% (n=37) had a PCI; 0.4% (n=2) had a heart valve surgery; 3.0% (n=15) had a cardiac related rehospitalisation; and 6.3% (n=32) had a cardiac related referral.

4.5.1. Trend analyses of primary and secondary endpoints in respondents on the long term

Primary endpoints (first cardiac related death, MI, CABG, PCI, or heart valve surgery after FTP visit) were observed in 13.3% (n=67) and secondary endpoints (primary endpoints including cardiac related rehospitalisation or -referral) in 20.2% (n=102) of all respondents.

The Kaplan-Meier curve of trends in primary endpoints showed a drop at the beginning of a further horizontal curve (figure 2). This suggested that most cardiac related deaths, MI's, CABG's, PCI's, and heart valve surgeries occurred immediately after FTP visit and only a few within the remaining follow-up period. With regard to the longest possible follow-up time within this study, the cumulative proportion of respondents without cardiac related deaths, MI's, CABG's, PCI's, and heart valve surgeries after nine years was 86% (CI: 82–90%). Concluding, the majority of the respondents did not have any CHD related events after FTP diagnostics and treatment.

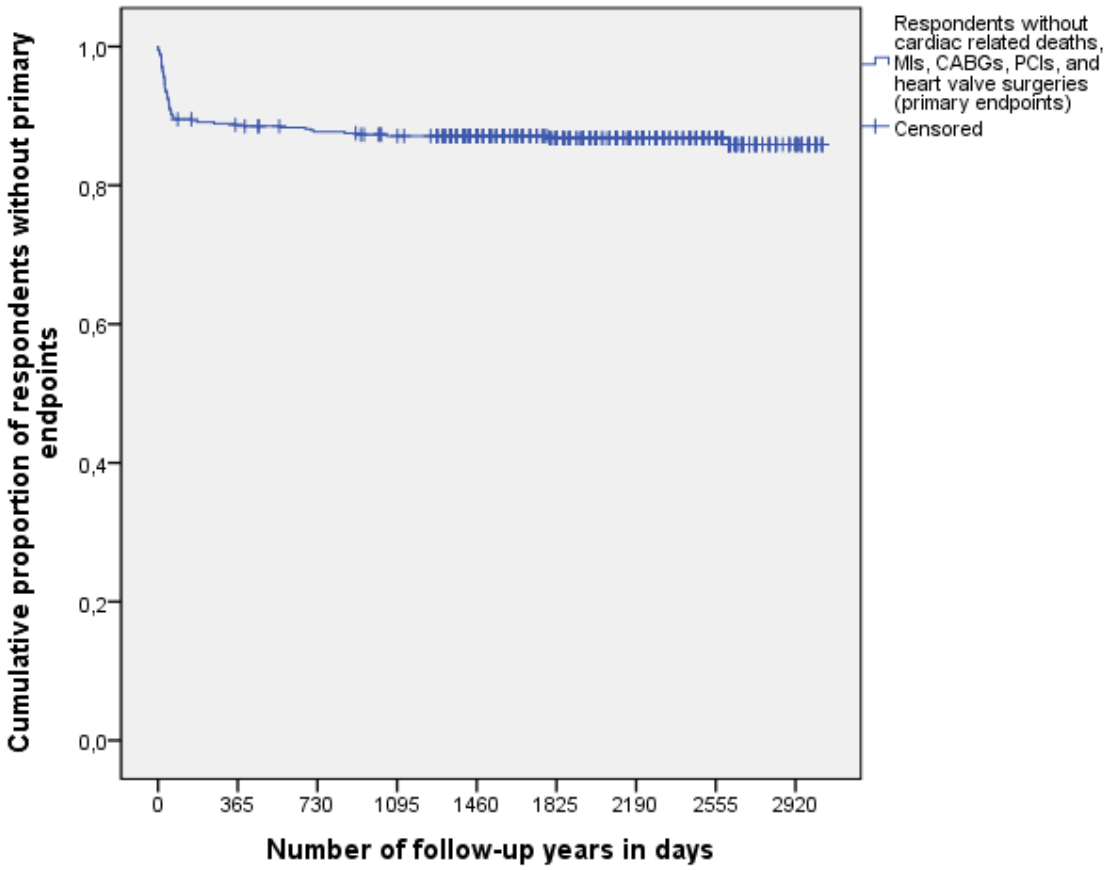

Figure 2 Kaplan-Meier curve of trends in CHD related primary endpoints in respondents

The cumulative proportion of respondents without cardiac related deaths, MI's, CABG's, PCI's, heart valve surgeries, cardiac related rehospitalizations and -referrals after nine years was 75% (CI: 69–81%). The Kaplan-Meier curve regarding to trends in secondary endpoints (figure 3) shows a similar drop as the Kaplan-Meier curve in primary endpoints. This was not surprising given that cardiac related deaths, MI's, CABG's, PCI's, and heart valve surgeries were also included in secondary endpoints. However, a more declining curve is shown in figure 3, which indicated that cardiac related rehospitalizations and -referrals occurred more widespread during the follow-up period.

After three years (1095 days) of follow-up, both the curves in primary endpoints and in secondary endpoints showed much censored data due to the different follow-up times of respondents with a minimum of three years and a maximum of nine years (2920 days).

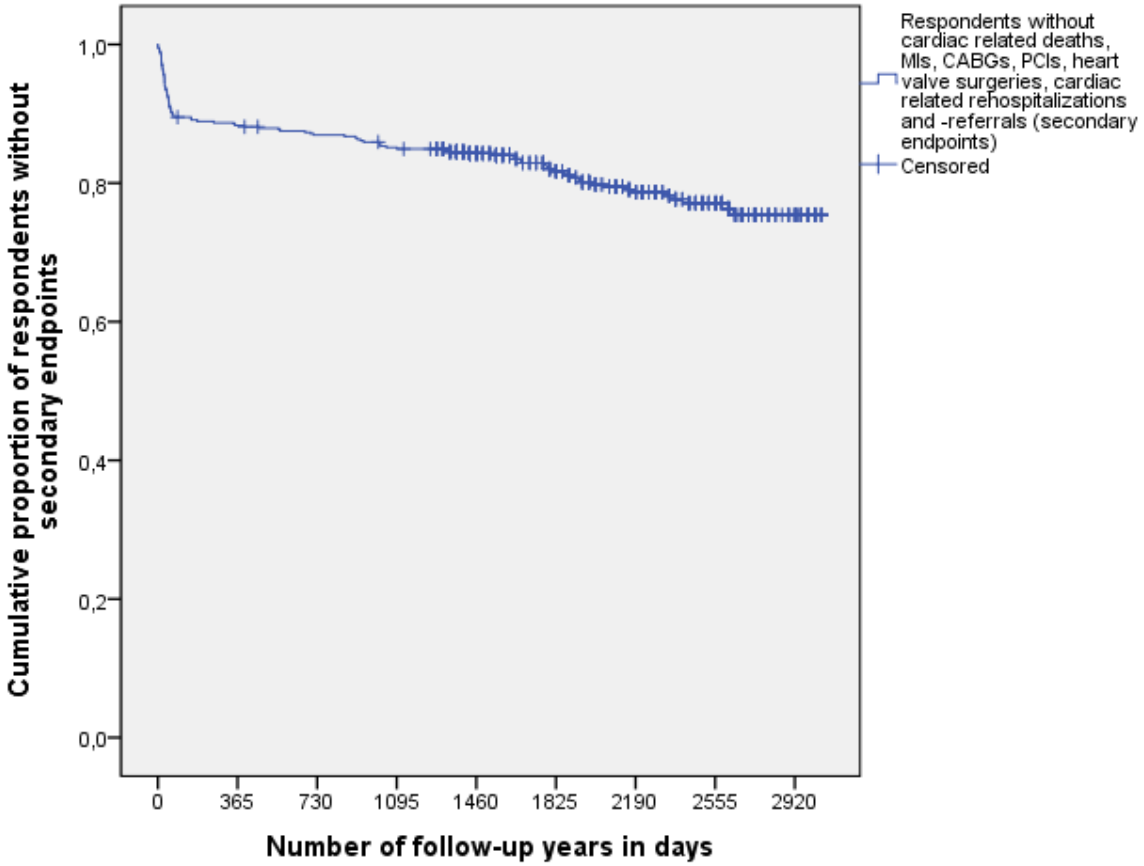

Figure 3 Kaplan-Meier curve of trends in CHD related secondary endpoints in respondents

4.5.2. Trend analyses of differences between patients with different FTP outcomes at baseline in primary and secondary endpoints on the long term

In respondents without diagnosed abnormalities (n=278), there were 0.7% (n=2) cardiac related deaths, MI's, CABG's, PCI's, and heart valve surgeries and 6.5% (n=18) cardiac related deaths, MI's, CABG's, PCI's, heart valve surgeries, cardiac related rehospitalizations and -referrals. This was respectively 4.8% (n=8) and 15.2% (n=25) in respondents with mild, medium, or intermediate stenosis (n=165) and respectively 91.9% (n=57) and 95.2% (n=59) in respondents with high-grade stenosis (n=62). The median follow-up time of respondents in this study was 1916 days (IQR: 1400–2496 days) with major differences between respondents with different FTP outcomes. The median follow-up time of reassured respondents was 2099 days (IQR: 1551–2557 days). For respondents who received lifestyle advice and/or medication the median follow-up time was 1885 days (IQR: 1430–2496 days) and for respondents who received invasive tests and/or treatment, this was 34 days (IQR: 20–58 days). The relatively short follow-up period of the latter group was due to invasive treatments (PCI's and CABG's) performed as a result of diagnosed high-grade stenosis within the FTP pathway and included as primary endpoints in this study. Significant differences in time to follow-up between the treatment policy groups were demonstrated by the log-rank test ($p<0.001$) and are further mapped below.

The cumulative proportion respondents without abnormalities and without cardiac related deaths, MI's, CABG's, PCI's, and heart valve surgeries after nine years was 99% (CI: 97–101%). 90% (CI: 86–94%) of these respondents had no cardiac related deaths, MI's, CABG's, PCI's, heart valve surgeries, cardiac related rehospitalizations and -referrals after nine years and were rightly reassured on the FTP. With regard to respondents without primary endpoints after nine years who received lifestyle advice and/or medication, the cumulative percentage was 92% (CI: 84–100%). Regarding to secondary endpoints this was 79% (CI: 69–89%). The log-rank test showed a significant difference between these respondents compared to reassured respondents in occurrence of both primary endpoints (p=0.004) and secondary endpoints (p=0.001) over follow-up time. Despite cardiovascular risk management, these respondents had a less good prognosis in the long term than reassured respondents. In respondents with high-grade stenosis, the cumulative proportion without a primary endpoint after nine years was 8% (CI: 2–14%). 3% (CI: -3–9%) of these respondents had no cardiac related deaths, MI's, CABG's, PCI's, heart valve surgeries, cardiac related rehospitalizations and -referrals. Based on these results, high-grade stenosis diagnosed within the FTP pathway seemed to be correct as most were treated with CABG's or PCI's.

Correct diagnostics by the FTP is supported by table 5 in which the link is shown between FTP outcome based on the pre-test probability of CHD and the coronary artery calcium score combined with the CTCA and occurrence of cardiac related death, MI, CABG, PCI, heart valve surgery, cardiac related rehospitalisation and -referral within nine years after visiting the FTP. A pre-test probability of CHD was not calculated in 3.6% (n=18) of the respondents. In these respondents only one primary endpoints and only three secondary endpoints were observed. 12.4% (n=12) cardiac related deaths, MI's, CABG's, PCI's, and heart valve surgeries and 15.5% (n=15) cardiac related deaths, MI's, CABG's, PCI's, heart valve surgeries, cardiac related rehospitalizations and -referrals were observed in respondents with missing data regarding to performed coronary artery calcium scores and CTCA outcomes at baseline (n=97). There were four respondents in which the coronary artery calcium score was not performed and the CTCA had diagnosed no, mild, medium, intermediate or high-grade stenosis. In these respondents was only one secondary endpoint observed. As shown in table 5, FTP diagnostics seem to predict primary endpoints correctly as no cardiac related deaths, MI's, CABG's, PCI's, and heart valve surgeries were observed in pre-test probabilities of CHD below 10% and in coronary artery calcium scores of zero. This suggested that patients without abnormalities were rightly reassured. Furthermore, they had the lowest number of secondary endpoints in which also cardiac related rehospitalisation and -referral were included and therefore FTP diagnostics seem to guarantee long-term reassurance in patients without abnormalities. Most primary endpoints were observed in respondents with a pre-test probability of 60% or higher and in respondents with high-grade stenosis diagnosed by the CTCA, probably due to further invasive testing or treatment.

Table 5 The pre-test probability of CHD, the coronary artery calcium score and the CTCA outcome at baseline linked to the primary and secondary endpoints in respondents on the long term

	Primary endpoints, % (n)	**Secondary endpoints, % (n)**	**Total number of respondents (n)**
PTP < 10	0 (0.0)	0 (0.0)	13
PTP 10-30	4.6 (4)	12.6 (11)	87
PTP 30-60	6.8 (14)	12.6 (26)	207
PTP > 60	26.7 (48)	34.4 (62)	180
CAC=0	0.0 (0)	5.9 (8)	135
CAC 1- 400 & CTCA=0[a]	3.1 (5)	11.8 (19)	161
CAC > 400	39.0 (16)	41.5 (17)	41
CTCA=1[b]	50.7 (34)	62.7 (42)	67

Abbreviations list:

PTP – Pre-test probability of CHD

CAC – Coronary artery calcium score

CTCA – CT Coronary Angiography

% – Cumulative percentage

n – Number of participants

Primary endpoints – cardiac related deaths, MI's, CABG's, PCI's, or heart valve surgeries

Secondary endpoints – cardiac related deaths, MI's, CABG's, PCI's, heart valve surgeries, cardiac related rehospitalizations or -referrals

[a] *No, mild, medium, intermediate or high-grade stenosis was diagnosed by the CTCA*

[b] *High-grade stenosis was diagnosed by the CTCA*

4.6 The best predictive FTP related tests, scores and characteristics of long-term clinical outcomes

4.6.1. Univariate and multivariate analyses in primary endpoints

In table 6, univariate analyses of cardiac related death, MI, CABG, PCI, and heart valve surgery related to FTP related patient characteristics, tests and scores are shown. In older (p<0.001), longer (p=0.002) and heavier (p=0.112) men (p<0.001) with a higher systolic blood pressure (<0.001), a lower heart frequency (p=0.144), a lower HDL level (p=0.001), typical symptoms (p=0.001), a positive exercise ECG test (p<0.001), a lower Duke Treadmill Score (p<0.001), a higher HEART score (p<0.001); pre-test probability of CHD (p<0.001); post-test probability of CHD (p<0.001); and Framingham score (p<0.001), a coronary artery calcium score above zero (p=0.001), and high-grade diagnosed CHD by the CTCA (p<0.001) occurred significantly more primary endpoints.

The multivariate analysis was performed in 329 respondents with no missing values on the pre-test probability of CHD, the coronary artery calcium score, the Framingham score, and the CTCA which were included as determinants. First the coronary artery calcium score was removed (p=0.230) and second the pre-test probability of CHD (p=0.205). In table 6 is shown that the best predictors of cardiac related death, MI, CABG, PCI, and heart valve surgery within nine years after FTP diagnostics were the Framingham score (p=0.030) and the CTCA (p<0.001). The Harrell's C-index of this model was 0.91, which indicated a strong model.

Table 6 Univariate and multivariate Cox Proportional Hazard analyses for primary endpoints

Univariate analysis	**HR**	**95% CI**	**p-value[a]**	**Multivariate analysis**	**HR**	**95% CI**	**p-value[b]**
Age, years	1.05	1.02-1.08	*<0.001*				
Gender, male	4.28	2.12-8.64	*<0.001*				
Height, cm	1.04	1.02-1.07	*0.002*				
Weight, kg	1.01	1.00-1.03	*0.112*				
BMI, kg/m2	0.99	0.93-1.05	0.707				
Systolic blood pressure, mmHg	1.02	1.01-1.04	*<0.001*				
Diastolic blood pressure, mmHg	1.01	0.99-1.03	0.450				
Heart frequency per minute	0.98	0.96-1.01	*0.144*				
Total cholesterol, mmol/L	1.12	0.89-1.42	0.345				

High-density lipoprotein (HDL), mmol/L	0.27	0.13-0.56	*0.001*			
Symptoms			*<0.001*[c]			
Atypical symptoms*	2.75	0.65-11.55	0.168			
Typical symptoms*	10.21	2.46-42.35	*0.001*			
**reference category is 'non-anginal symptoms'*						
Coronary related diseases in first-degree family members	0.85	0.53-1.38	0.514			
Diabetes Mellitus	1.08	0.49-2.37	0.845			
Smoking	1.57	0.84-2.94	0.155			
HEART score	1.63	1.30-2.03	*<0.001*			
Pre-test probability of CHD	1.04	1.03-1.05	*<0.001*			
Exercise ECG test			*<0.001*[c]			
Positive*	11.60	5.56-24.18	*<0.001*			
Inconclusive*	4.49	2.10-9.60	*<0.001*			
**reference category is negative*						
Post-test probability of CHD	1.03	1.02-1.04	*<0.001*			
Duke Treadmill Score	0.95	0.94-0.96	*<0.001*			
Diagnosed high-grade stenosis (by performing the CTCA)	42.21	16.47-108.17	*<0.001*	32.95	12.52-86.73	*<0.001*
Coronary artery	31.53	4.36-	*0.001*			

calcium score > 0		227.95				
Framingham score	1.10	1.07-1.13	*<0.001*	1.05	1.01-1.10	*0.030*
SCORE	1.01	0.99-1.04	0.400			

Abbreviations explained:

HR – Hazard Ratio

95% CI – 95% Confidence Interval

Primary endpoints – cardiac related deaths, MI's, CABG's, PCI's, or heart valve surgeries

[a] *Significance level is set on p < 0.15*

[b] *Significance level is set on p < 0.05*

[c] *Overall p-value*

4.6.2. Univariate and multivariate analyses in secondary endpoints

The univariate analyses of cardiac related death, MI, CABG, PCI, heart valve surgery, cardiac related rehospitalisation and -referral related to FTP related patient characteristics, tests, and scores are presented in table 7. Older (p=0.003) and longer (p=0.007) men (p<0.001) with a higher systolic blood pressure (p=0.001), a lower HDL (p<0.001), typical symptoms (p=0.001), a positive exercise ECG test (p<0.001), a lower Duke Treadmill Score (p<0.001), a higher HEART score (p<0.001); pre-test probability of CHD (p<0.001); post-test probability of CHD (p<0.001); Framingham score (p<0.001); and SCORE (p=0.118), a calcium artery coronary score above zero (p<0.001), with plaque; calcium; or both plaque and calcium (p<0.001), in who was diagnosed mild stenosis; intermediary stenosis; or high-grade stenosis (p<0.001), and with high-grade diagnosed CHD by the CTCA (p<0.001) had significantly higher risk of cardiac related death, MI, CABG, PCI, heart valve surgery, cardiac related rehospitalisation and -referral.

In the multivariate analysis (n=329), the Framingham score (p=0.134) was removed. In table 7 is shown the that the pre-test probability of CHD (p=0.049), the coronary artery calcium score (p=0.037), and the CTCA (p<0.001) appeared to be the best predictors of secondary endpoints within nine years after visiting the FTP. The predictive accuracy of this model was strong (C-index=0.83).

Table 7 Univariate and multivariate Cox Proportional Hazard analyses for secondary endpoints

Univariate analysis	**HR**	**95% CI**	**p-value[a]**	**Multivariate analysis**	**HR**	**95% CI**	**p-value[b]**
Age, years	1.03	1.01-1.06	*0.003*				
Gender, male	2.64	1.63-4.26	*<0.001*				
Height, cm	1.03	1.01-1.05	*0.007*				
Weight, kg	1.00	0.99-1.02	0.579				
BMI, kg/m2	0.97	0.92-1.02	0.201				
Systolic blood pressure, mmHg	1.02	1.01-1.03	*0.001*				
Diastolic blood pressure, mmHg	1.01	0.99-1.03	0.376				
Heart frequency per minute	0.99	0.98-1.01	0.505				
Total cholesterol, mmol/L	1.08	0.89-1.31	0.420				
High-density lipoprotein (HDL), mmol/L	0.31	0.18-0.56	*<0.001*				
Symptoms			*<0.001[c]*				
Atypical symptoms*	1.55	0.66-3.62	0.315				
Typical symptoms*	4.36	1.87-10.18	*0.001*				
**reference category is 'non-anginal symptoms'*							
Coronary related diseases in first-degree family members	1.01	0.68-1.50	0.951				

Diabetes Mellitus	0.91	0.46-1.80	0.786			
Smoking	1.07	0.60-1.91	0.823			
HEART score	1.50	1.26-1.80	*<0.001*			
Pre-test probability of CHD	1.03	1.02-1.04	*<0.001*	1.01	1.00-1.02	*0.049*
Exercise ECG test			*<0.001*[c]			
Positive*	5.42	3.19-9.21	*<0.001*			
Inconclusive*	2.90	1.73-4.86	*<0.001*			
**reference category is negative*						
Post-test probability of CHD	1.02	1.02-1.03	*<0.001*			
Duke Treadmill Score	0.95	0.94-0.96	*<0.001*			
A form of coronary arterial plaque			*<0.001*[c]			
Soft plaque*	9.59	3.72-24.71	*<0.001*			
Calcium*	4.05	1.40-11.67	*0.010*			
Mixed*	11.64	4.91-27.59	*<0.001*			
**reference category is none*						
Degree of stenosis			*<0.001*[c]			
Mild*	4.04	1.59-10.25	*0.003*			
Intermediary*	5.68	2.27-14.25	*<0.001*			
High-grade*	25.44	11.27-57.43	*<0.001*			
**reference category is*						

none						
Diagnosed high-grade stenosis (by performing the CTCA)	11.47	7.01-18.77	*<0.001*	7.63	4.34-13.41	*<0.001*
Coronary artery calcium score > 0	5.28	2.65-10.53	*<0.001*	2.62	1.06-6.47	*0.037*
Framingham score	1.07	1.05-1.10	*<0.001*			
SCORE	1.02	1.00-1.04	*0.118*			

Abbreviations explained:

HR – Hazard Ratio

95% CI – 95% Confidence Interval

Secondary endpoints – cardiac related deaths, MI's, CABG's, PCI's, heart valve surgeries, cardiac related rehospitalizations or -referrals

[a] *Significance level is set on p < 0.15*

[b] *Significance level is set on p < 0.05*

[c] *Overall p-value*

4.6.3. Predictive accuracy of tests and scores performed within the FTP pathway

The predictive accuracies of FTP related diagnostic tests, diagnostic- and prognostic scores of cardiac related deaths, MI's, CABG's, PCI's, and heart valve surgeries in respondents is shown in table 8. The CTCA appeared to be the best predictor of cardiac related deaths, MI's, CABG's, PCI's, and heart valve surgeries (C-index=0.87). SCORE was found to be the worst predictor of primary endpoints (C-index=0.50).

Table 8 Predictive accuracy of FTP related diagnostic tests, diagnostic- and prognostic scores of primary endpoints

	Harrell's C-index*
HEART score	0.67
Pre-test probability of CHD	0.76
Exercise ECG test[a]	0.76
Post-test probability of CHD	0.82
Duke Treadmill Score	0.75
CTCA[a]	0.87
Coronary artery calcium score[a]	0.68
Framingham score	0.76
SCORE	0.50

**The Harrell's C-index was calculated to determine the predictive accuracy of the specific test or score for primary endpoints (cardiac related deaths, MI's, CABG's, PCI's, or heart valve surgeries).*

[a] In these categorial variables, the first category was used as reference category.

In table 9 is shown the Harrell's C-index of FTP related tests and scores regarding to the predictive accuracy of cardiac related deaths, MI's, CABG's, PCI's, heart valve surgeries, cardiac related rehospitalizations and -referrals. The best and worst predictors of secondary endpoints based on the Harrell's C-index were again the CTCA (C-index=0.76) and the SCORE (C-index=0.50).

The predictive accuracy of all tests and scores was lower in secondary endpoints, with the exception of SCORE which was similar, due to more included outcomes in secondary endpoints. Regarding to cardiac related deaths, MI's, CABG's, PCI's, heart valve surgeries, cardiac related rehospitalizations and -referrals, the best predicting diagnostic test was the CTCA; the best predicting diagnostic score was the pre-test probability; and the best predicting prognostic score was the Framingham score. The exercise ECG test, the post-test probability of CHD, and the Duke Treadmill Score, which are clinical indicated in FTP patients with exercise related symptoms and/or with diagnosed intermediate stenosis by the CTCA, appeared to be good predictors of primary and secondary endpoints in respondents with this clinical indication.

Table 9 Predictive accuracy of FTP related diagnostic tests, diagnostic- and prognostic scores of secondary endpoints

	Harrell's C-index*
HEART score	0.64
Pre-test probability of CHD	0.71
Exercise ECG test[a]	0.70
Post-test probability of CHD	0.73
Duke Treadmill Score	0.66
CTCA[a]	0.76
Coronary artery calcium score[a]	0.65
Framingham score	0.69
SCORE	0.50

**The Harrell's C-index was calculated to determine the predictive accuracy of the specific test or score for secondary endpoints (cardiac related deaths, MI's, CABG's, PCI's, heart valve surgeries, cardiac related rehospitalizations or -referrals).*

[a] In these categorial variables, the first category was used as reference category.

4.7. Long-term compliance

48.6% (n=407) responded to the questionnaire part about smoking and 48.3% (n=405) to the questionnaire part about diet. 13.3% of the respondents (n=67) reported that they smoked prior to the FTP. A total of 22 out of these 67 respondents (32.8%) reported that they stopped smoking as a consequence of the FTP pathway. Another 30 respondents (44.8%) were still smoking at the moment of responding. Compliance to diet advice in respondents was much better. 134 respondents (26.5% of the respondents) reported that they received the advice to change diet of whom 93.3% (n=125) reported that they had done this in response to the FTP advice.

5. DISCUSSION

Main results, strengths and limitations of this study will be discussed in this paragraph. Furthermore, some recommendations for further research and clinical practice will be given.

5.1. Main results

This study aimed to provide insight in the clinical utility of the FTP. The results indicate that the overall risk of cardiac related death, MI, CABG, PCI, heart valve surgery, cardiac related rehospitalisation and -referral after visiting the FTP is low. Therefore, FTP diagnostics and prognostics seem to predict accurately long-term clinical outcomes and seem to provide long-term guarantees. Despite of significant differences in long-term outcomes between patients with different FTP outcomes at baseline, patients have a good prognosis after FTP diagnostics and treatment. The Framingham score and the CTCA were the best predictors of cardiac related death, MI, CABG, PCI, and heart valve surgery within the FTP pathway. With regard to cardiac related death, MI, CABG, PCI, heart valve surgery, cardiac related rehospitalisation and -referral, the pre-test probability of CHD, the coronary artery calcium score, and the CTCA appeared to be the best predictors. In addition, the exercise ECG test, post-test probability of CHD, and Duke Treadmill Score seem accurate predictors of long-term clinical outcomes in patients with exercise related symptoms and/or with diagnosed intermediate stenosis by the CTCA. Long-term compliance to diet advice was much better than compliance to stop smoking advice.

This study hypothesized that FTP diagnostics improved long-term clinical outcomes, long-term compliance to lifestyle advice, and patient satisfaction relative to regular diagnostics of chest pain in the Netherlands because of the higher level of diagnostic accuracy, the ability to better risk stratify individuals into different treatment regimens, and the speed of diagnostics. This hypothesis is supported by literature.[7,12,13,19,20,40]

Low risk of cardiac related death, MI, CABG, PCI, heart valve surgery, cardiac related rehospitalisation and -referral is consistent with literature. The article of Fordyce, et al. (2016) and the updated NICE guidelines discussed the SCOT-HEART trial and the PROMISE trial, the two largest cardiovascular imaging outcome trials in patients with stable chest pain which compared CTCA diagnostics with diagnostics by exercise ECG testing. All-cause death, nonfatal MI, hospitalization for unstable angina, and major procedural complications were in both trials low and it was suggested that the CTCA may lead to lower MI rates.[12,13,52] Lowest occurrence of cardiac related death, MI, CABG, PCI, heart valve surgery, cardiac related rehospitalisation and -referral in patients without abnormalities is in line with the high negative predictive value of the CTCA in ruling out relevant plaques and stenosis in coronary arteries mentioned in literature.[8-10,35] The significant difference in prognosis between patients without abnormalities and patients with mild, medium or intermediate stenosis is supported by literature. The presence and extent of non-obstructive CHD is associated with a worse prognosis compared with patients with no abnormalities.[1] In the study of Wald and Law (2003) is stated that only 80% risk reduction is possible by cardiovascular risk management and therefore, patients with mild, medium or intermediate stenosis always have a higher CHD risk than patients

without abnormalities.[53] The significant increase in cardiac related death, MI, CABG, PCI, and heart valve surgery, in particular CABG's and PCI's performed at baseline, in patients with high-grade stenosis is consistent with the SCOT-HEART and PROMISE trials. In these trials is the CTCA associated with increased use of PCI's and CABG's at baseline, but less unjustified PCI's and CABG's.[52]

Age, gender, smoking, blood pressure, and cholesterol levels are considered as best predictors of gender-specific 10-year cardiovascular risk in the Framingham HEART study.[3] In our study population, the Framingham score seems to have a lower predictive value as it was only included in prediction of primary endpoints. Diagnostic tests and scores, respectively the pre-test probability of CHD, the coronary artery calcium score, and the CTCA, appeared to be the best predictors of secondary endpoints in FTP patients. This finding is supported by the NICE guidelines.[40] In these guidelines a pre-test probability of < 10% on CHD and a coronary artery calcium score of zero are considered to effectively rule out CHD which is consistent with our study results. Furthermore, they recommend, in mild to moderate suspicion of CHD or pre-test probabilities of 10-29% on CHD, to calculate coronary artery calcium scores with an additional CTCA in calcium scores of 1– 400.[40] The NICE guidelines also mention the added value of exercise ECG testing after diagnosed intermediate stenosis by the CTCA.[40] These recommendations are in line with the diagnostic procedure of the FTP. The CTCA as most accurate predictor of both primary and secondary endpoints is supported by the updated version of the NICE guidelines.[12,13,36] In this update the CTCA is recommended as first-line diagnostic test in all patients with atypical or typical chest pain symptoms, because of the high level of diagnostic accuracy; the ability to better risk stratify individuals into different treatment regimens; and the proven cost-effectiveness in the UK due to low costs of the CTCA, high sensitivity, and low probability of complications.[12,13,36] However, the systematic review of van Waardhuizen, et al. (2016) contradicts cost-effectiveness of the CTCA in all patients with chest pain by emphasizing that the CTCA is preferred in low-risk patients; the SPECT in intermediate risks of CHD; and the CAG in high risks.[54] At last, the European Society of Cardiology recommends the CAD Consortium pre-test probability score, besides the CTCA, which is the pre-test probability of CHD defined by Diamond & Forrester including Diabetes Mellitus, smoking, hypertension and hyperlipidemia.[15,55,58] The last three are included in the Framingham score within our study. In contrast to our study results, the coronary artery calcium score was not included in the European Society of Cardiology study because a CTCA was performed in all patients to investigate predictive accurateness of the CAD Consortium pre-test probability score.[55]

Long-term compliance to lifestyle advice appears to be above average in comparison with literature.[56] Willemsen, et al. (2003) gave an overview of 20 Cochrane reviews which showed that the percentage of smokers who stop after an intervention varies from 3 to 24%.[57] Compliance to diet advice within this study was more than 90%. This is not directly supported by literature in which compliance of CHD patients is generally considered as poor as a consequence of lack of knowledge among CHD patients.[58]

5.2. Strengths and limitations

A strong point of this study is that, to our knowledge, this was the first study investigating the clinical utility of the FTP. This study is supported by Zorginstituut Nederland which emphasizes that the diagnosis and treatment of patients with chest pain should be improved in the Netherlands.[7] Furthermore, a scientifically based method is used to validate the questionnaire.[45] Third, to increase the response rate, completion time was minimized; anonymity was guaranteed; and the questionnaire was set-up professional and familiar by applying ZGT style.[43] The response rate to long-term clinical outcomes was 60.3% with which the previously set limit was just met. At last, reported primary and secondary endpoints by respondents were checked on validity.

This study has also some limitations that need to be addressed. First of all, the reliability of the study results is limited because of its reliance on a retrospective, self-reported questionnaire which could have caused recall bias.[43] The Cohen's kappa to test recall of respondents, could not be estimated purely as some observations were untraceable to corresponding categories. Furthermore, reported absence of primary and secondary endpoints was only checked in 10% of the respondents and reported compliance to lifestyle advice was not verified. This might have led to cognitive bias.[43] Second, the retrospective questionnaire was considered as inappropriate to study patient satisfaction. Recall is strongly correlated to health status and therefore long-term patient satisfaction with regard to the FTP pathway will be influenced by FTP outcomes.[59] Third, respondents appeared to be not representative for non-respondents. It is notable that non-respondents seem to had lower CHD risk based on test results and scores at baseline, but the percentage smokers was significantly higher in non-respondents. Study results from non-respondents could therefore have led to different findings.[3,11-18,60] Fourth, the majority received the paper questionnaire due to unknown emails and no response to the offered opportunity to fill in the questionnaire digitally, while the digital version is more reliable.[43] The higher response rate to the digital questionnaire compared to the paper questionnaire (65.6% versus 43.0%) is supported by Nederhoed (2007) and Uhlig (2014).[43,49] Fifth, the univariate analyses in diagnosed calcium and/or plaque and degree of stenosis were not possible in primary endpoints because of the limited number of cardiac related deaths, MI's, CABG's, PCI's, and heart valve surgeries in respondents during this study. Selected variables by performing the univariate analyses could not be included in the multivariate analyses for the same reason. Sixth, it is plausible that lifestyle of Dutch men and women from the region Hengelo in whom this study is performed, differs from populations from other regions in the Netherlands.[3] Therefore, it is expected that the extern validity of the study results is limited.[61] Seventh, eventually socio-demographic differences must be taken into account when evaluating the study results as the follow-up period within this study varied from three to nine years. Eight, the previously set limit of 60% response was not met in long-term compliance to lifestyle advice. Ninth, it was not possible in this study to link long-term compliance to long-term clinical outcomes to analyse if compliance to lifestyle advice could possibly explain the occurrence of primary and secondary endpoints in respondents, due to relative small groups of respondents who have received lifestyle advice within the FTP pathway. At last, health outcomes of the FTP could not be linked to health outcomes of regular chest pain diagnostics in this study nor in literature.[19]

5.3. Recommendations for clinical practice

The NICE guidelines show that diagnostics in every patient with chest pain is important to exclude CHD. Based on our study results and literature, it can be concluded that risk stratification is recommended by applying the pre-test probability of CHD after which no further testing is needed in pre-test probabilities of CHD lower than 10% or coronary artery calcium scores of zero; coronary artery calcium scoring is recommended in pre-test probabilities of 10-29% on CHD, with an additional CTCA in coronary artery calcium scores of 1– 400 or an additional SPECT in coronary artery calcium scores above 400; coronary artery calcium scoring is indicated in Framingham scores of 10-20% on CHD; a SPECT is advised in pre-test probabilities of 30-59% on CHD; and an invasive coronary angiography in pre-test probabilities of 60% or more on CHD.[40] Pre-test probabilities of CHD should be calculated based on the adapted Diamond & Forrester model.[24,55] The HEART score and the SCORE appeared to be irrelevant in this study and the exercise ECG test, post-test probability of CHD, and Duke Treadmill Score were considered to be only useful in evaluating treatment in patients with exercise related symptoms and/or diagnosed intermediate stenosis by the CTCA.[40] A workflow is made for the Netherlands to help in clinical decision making regarding to diagnostics of patients with chest pain and it is recommended to further imply this in Dutch clinical practice.[24,36,40,62] This workflow is shown in appendix VI – Recommended workflow chest pain for the Netherlands (in Dutch). The workflow connects to the recently published improvement report on chest pain, in which Zorginstituut Nederland (ZIN) recommends better risk stratification and evident guidelines with respect to diagnostics and treatment.[7] It has to be mentioned that the updated NICE guidelines, in which the CTCA is recommended as first-line diagnostic test in all patients with chest pain, have not been used to design this workflow because of insufficiently proved cost-effectiveness for the Netherlands.[12,13,54]

5.4. Recommendations for further research

There are some recommendations for further research to chest pain fast track pathways. First of all, long-term compliance and absence of long-term clinical outcomes have to be checked in all respondents. Second, further research to the long-term clinical outcomes by checking primary and secondary endpoints within the ZGT hospital and surrounding hospitals for non-respondents is recommended as respondents were not representative for non-respondents. METC approval is advised in this. Third, as patient satisfaction is an important outcome when evaluating clinical utility, it is recommended to study patient satisfaction in further studies with shorter follow-up periods. Fourth, to map the added value of the FTP, cost-effectiveness has to be demonstrated.[24] With regard to the limited time and possibilities to map the costs of the whole FTP pathway and to compare long-term clinical outcomes of the FTP pathway to long-term clinical outcomes of the regular chest pain pathways in the Netherlands, this was not possible in this study. It has to be mentioned that comparison with regular diagnostics of chest pain is difficult due to lack of consistency in diagnostics of chest pain within the Netherlands. At last, known risk factors as obesity, Diabetes Mellitus, and physical inactivity may contribute to the onset of CHD on the long-term and will therefore have to be included in follow-up studies to can explain long-term clinical outcomes, thus to prevent confounding.

6. CONCLUSION

This study suggests clinical utility of the FTP as it showed that (1) patients had a low risk of cardiac related death, MI, CABG, PCI, heart valve surgery, cardiac related rehospitalisation and -referral after their FTP visit, even though significant differences in long-term outcomes were found between patients with no abnormalities; patients with mild, medium or intermediate stenosis; and patients with high-grade stenosis at baseline; (2) the Framingham score, the pre-test probability of CHD, the coronary artery calcium score, and the CTCA were the best predictors of long-term clinical outcomes in FTP patients; and (3) long-term compliance of FTP patients to lifestyle advice was relative good. A workflow is made in this study for the Netherlands to implement in clinical practice for fast and accurate diagnostics and treatment after applied risk stratification. Further research is needed to can compare long-term clinical outcomes and compliance to lifestyle advice with regular diagnostics in the Netherlands. Furthermore, patient satisfaction has to be studied to prove clinical utility of the FTP.

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APPENDIX I – PICO FORMULATED RESEARCH QUESTIONS

1. What are the long-term clinical outcomes of the patients who visited the FTP between 2009 and 2015, and to which extent are they different for patients with different FTP outcomes at baseline?

P: Regional patients without a cardiac history and contraindications for a CT Coronary Angiography with chest pain with mild to moderate suspicion of coronary heart disease who are referred by the general practitioner to the Fast Track Poli “chest pain” (FTP) between 2009 and 2015.

I: The performed FTP diagnostics between 2009 and 2015 (in which the following three FTP outcomes are possible: no diagnosed abnormalities; diagnosed mild, medium or intermediate stenosis; and diagnosed high-grade stenosis).

C: Compared with the primary endpoints (cardiac related death, myocardial infarct, coronary artery bypass grafting, percutaneous coronary intervention, or heart valve surgery) and secondary endpoints (cardiac related death, myocardial infarct, coronary artery bypass grafting, percutaneous coronary intervention, heart valve surgery, cardiac related rehospitalisation or -referral) on April, 1, 2018.

O: The long-term clinical outcomes of the FTP pathway and to which extent they are different for patients with different outcomes at time of FTP visit (at baseline).

2. Which diagnostic test(s) and/or prognostic score(s) and/or patient characteristics within the FTP pathway predict(s) best long-term clinical outcomes?

P: Regional patients without a cardiac history and contraindications for a CT Coronary Angiography with chest pain with mild to moderate suspicion of coronary heart disease who are referred by the general practitioner to the Fast Track Poli “chest pain” (FTP) between 2009 and 2015.

I: The performed diagnostic tests (CT Coronary Angiography, and exercise ECG test); the calculated diagnostic scores (pre- and post-probability of CHD, HEART score, Duke Treadmill Score); the calculated prognostic scores (coronary artery calcium score, Framingham Score, and SCORE); and the registered patient characteristics (age, sex, body mass index, systolic and diastolic blood pressure, heart frequency, degree of typical; atypical or non-anginal symptoms, familiarity with Diabetes Mellitus, smoking, coronary related diseases in first-degree family members, and cholesterol levels (total cholesterol and high density lipoprotein)) within the FTP pathway.

C: Compared with the primary endpoints (cardiac related death, myocardial infarct, coronary artery bypass grafting, percutaneous coronary intervention, or heart valve surgery) and secondary endpoints (cardiac related death, myocardial infarct, coronary artery bypass grafting, percutaneous coronary intervention, heart valve surgery, cardiac related rehospitalisation or -referral) on April, 1, 2018.

O: The combination of diagnostic- and/or prognostic test(s) and/or patient characteristics within the FTP pathway which predicts best the primary and secondary endpoints.

3. What is the degree of compliance of patients who received lifestyle advice during their FTP visit between 2009 and 2015?

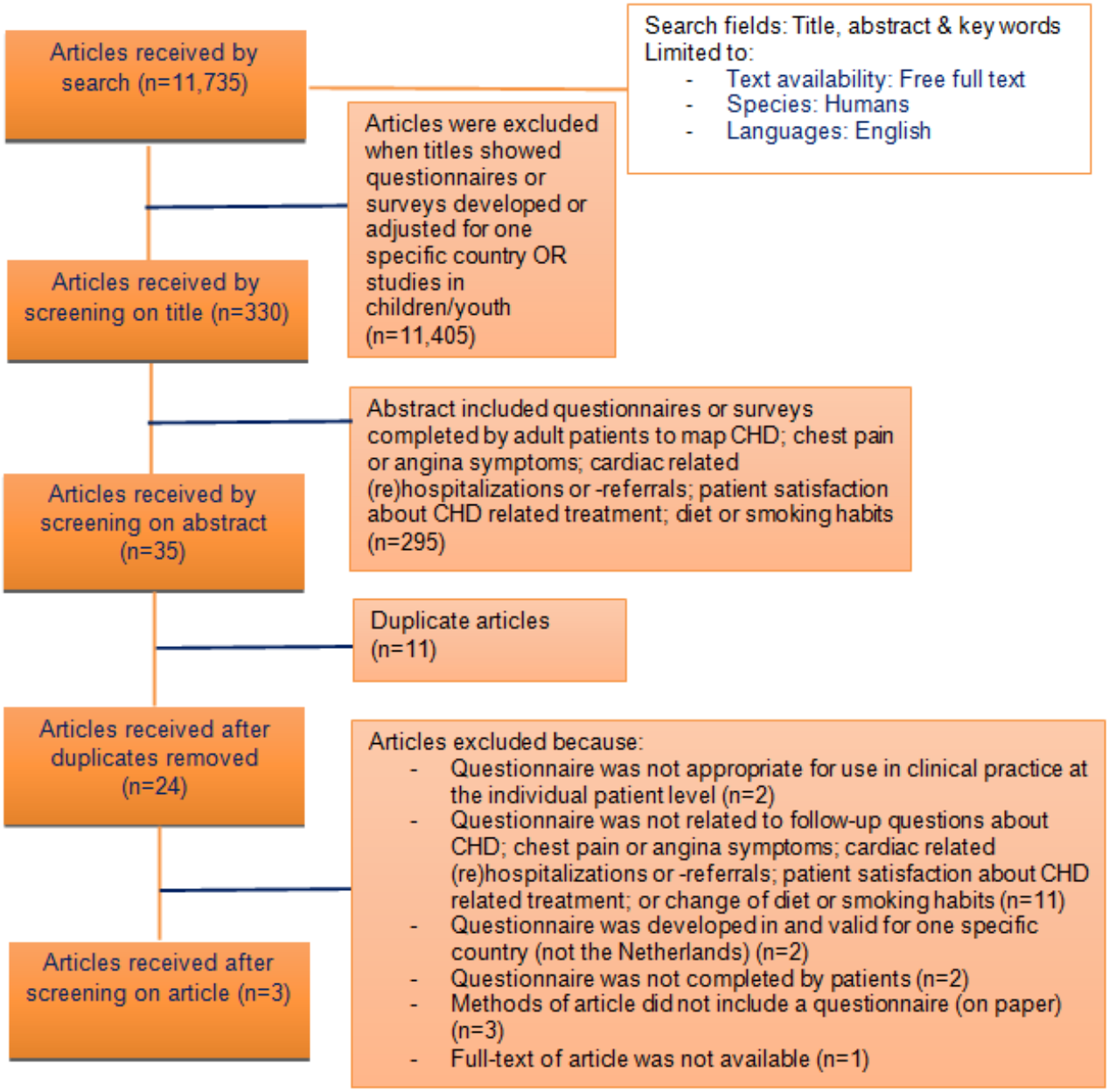
P: Regional patients without a cardiac history and contraindications for a CT Coronary Angiography with chest pain with mild to moderate suspicion of coronary heart disease who are referred by the general practitioner to the Fast Track Poli "chest pain" (FTP) between 2009 and 2015.

I: Received lifestyle advice (regarding to smoking and diet) in response to FTP diagnostics between 2009 and 2015.

C: Compared with the degree of compliance to this lifestyle advice on April, 1, 2018.

O: The long-term compliance to lifestyle advice of patients within the FTP pathway.

APPENDIX II – FLOW DIAGRAM SELECTION ARTICLES



APPENDIX III – PAPER VERSION OF THE QUESTIONNAIRE (IN DUTCH)

Fast Track Poli ‘pijn op de borst’ vragenlijst

17-04-2018

VOORWOORD

Hartelijk dank voor uw deelname aan ons onderzoek.
Wij vinden het belangrijk te weten hoe het nu gaat met de mensen die in het verleden de Fast Track Poli ‘pijn op de borst’ in Hengelo hebben bezocht.
Daarnaast zijn we benieuwd naar uw ervaringen met de Fast Track Poli ‘pijn op de borst’. De vragenlijst bestaat veelal uit meerkeuzevragen en zal ongeveer vijf minuten van uw tijd in beslag nemen.
Wij zullen uw antwoorden uitsluitend anoniem verwerken.

INSTRUCTIE

In de vragenlijst is de Fast Track Poli ‘pijn op de borst’ afgekort tot “FTP”.
De vragenlijst is opgebouwd uit de delen A t/m E en gaat over de volgende deelonderwerpen:

Deel A - Diagnostiek
Deel B - Ervaringen
Deel C - Klachten
Deel D - Klinische uitkomsten
Deel E - Leefstijlaanpassingen.

Elk deel begint met een korte introductie waarna de bijbehorende vragen worden gesteld.
Hieronder volgt een korte instructie met betrekking tot het invullen van de meerkeuzevragen.

- Geef één antwoord per vraag.
- Zet een kruisje in het vakje van uw keuze.

Voorbeeld:
☐ Waar ☐ Weet ik niet ☐ Onwaar

Als u het verkeerde antwoord heeft aangekruist, kunt u dit verbeteren door het goede antwoord helemaal in te kleuren.

Voorbeeld:
☐ Waar ☐ Weet ik niet ☐ Onwaar

DEEL A - DIAGNOSTIEK

U heeft de FTP bezocht. Hierbij onderging u een aantal onderzoeken. Vervolgens had u een gesprek met de arts. In dit gesprek zijn de uitkomsten van de onderzoeken besproken. Ook is een eventueel vervolgplan gemaakt. Onderstaande vragen gaan over dit traject.

A.1. Wat was de conclusie in uw geval? U kunt hieronder het juiste antwoord aanvinken.

☐ Optie 1: Er zijn geen afwijkingen gevonden. Er is daarom geen vervolgplan gemaakt.

☐ Optie 2: Ik kreeg leefstijladviezen (bijvoorbeeld het advies te stoppen met roken en/of cholesterolbeperkt te eten) en/of medicatie.

☐ Optie 3: Ik kreeg aanvullend onderzoek en/of behandeling (zoals een hartkatheterisatie, een dotterbehandeling, een bypassoperatie, een hartklepoperatie, een MRI-scan etc.)

☐ Optie 4: Anders, namelijk

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

LET OP:
Ga door naar STELLING A.1.1. indien u VRAAG A.1. met OPTIE 1 OF OPTIE 2 beantwoord heeft. Ga anders door naar STELLING A.1.2.

A.1.1. Geef aan in hoeverre u het eens of oneens bent met de volgende stelling: “Ik ben gerustgesteld door mijn bezoek aan de FTP.”

☐ Sterk mee eens

☐ Mee eens

☐ Niet mee eens, maar ook niet mee oneens

☐ Mee oneens

☐ Sterk mee oneens

A.1.1.1. Geef alstublieft een korte toelichting op uw antwoord.

_____

_____

_____

_____

_____

LET OP:
Ga door naar STELLING A.1.2. indien u VRAAG A.1. met OPTIE 2 OF
OPTIE 3 beantwoord heeft.
Ga anders door naar DEEL B – KLACHTEN.

A.1.2. Geef aan in hoeverre de volgende stelling klopt: “Op dit moment gebruik ik dagelijks medicatie voor mijn hart.” Met ‘dit moment’
bedoelen we het moment van het invullen van de vragenlijst.

☐
Waar

☐
Niet waar

DEEL B - KLACHTEN

Wij vinden het belangrijk te weten hoe het nu gaat met de mensen die in het verleden de FTP hebben bezocht. Daarom worden eventuele klachten uitgevraagd in deel B. Deze vragen zijn geformuleerd als stellingen. Geef hierbij aan in hoeverre de stellingen kloppen in uw geval op dit moment. Met 'dit moment' bedoelen we het moment van het invullen van de vragenlijst.

B.1. "Op dit moment ervaar ik nog minimaal 1 keer per week pijn of druk op de borst."

☐ Waar

☐ Niet waar

☐ Anders, namelijk _____

LET OP:
Ga door naar de STELLINGEN B.1.1. EN B.1.2. indien u VRAAG B.1. met WAAR beantwoord heeft.
Ga anders door naar DEEL C - KLINISCHE UITKOMSTEN.

B.1.1. "De pijn of druk op de borst die ik ervaar, ontstaat bij inspanning en/of kou en/of emotie."

☐ Waar

☐ Niet waar

☐ Ik weet het niet

B.1.2. "De pijn of druk op de borst die ik ervaar, verdwijnt in rust en/of binnen 5 minuten na het nemen van Nitrospray." Nitrospray omvat hierbij een Nitrospray of Nitrotablet onder de tong.

☐ Waar

☐ Niet waar

☐ Ik weet het niet

DEEL C - KLINISCHE UITKOMSTEN

Deel C gaat over nieuwe behandelingen aan het hart of ziekte van het hart. Het gaat hierbij om behandeling of hartziekte NA diagnostiek en behandeling op en naar aanleiding van de FTP. De vragen zijn geformuleerd als stellingen. Twee aanvullende vragen volgen indien een stelling als waar beantwoord is.

LET OP:
Het kan voorkomen dat u meerdere, dezelfde behandelingen en/of hartziektes heeft gehad. Ga in dat geval uit van de EERSTE behandeling of hartziekte NA diagnostiek en behandeling op en naar aanleiding van de FTP.

C.1. “Na mijn bezoek aan de FTP en de daaropvolgende behandeling, heb ik een hartinfarct gehad.”

☐ Waar

☐ Niet waar

LET OP:
Ga door naar de VRAGEN C.1.1. EN C.1.2. indien u VRAAG C.1. met WAAR beantwoord heeft. Ga anders door naar VRAAG C.2.

C.1.1. Geef hieronder alstublieft aan in welk ziekenhuis (plaats van betreffende ziekenhuis) u voor dit EERSTE hartinfarct bent behandeld.

_____

C.1.2. Geef hieronder alstublieft aan wanneer u dit EERSTE hartinfarct heeft gehad (in welk jaar en welke maand). Probeer een schatting te doen indien u dit niet precies weet.

Maand: _____ Jaartal: _____

C.2. “Na mijn bezoek aan de FTP en de daaropvolgende behandeling,
heb ik (opnieuw) een dotterbehandeling gehad.”

☐ Waar

☐ Niet waar

LET OP:
Ga door naar de VRAGEN C.2.1. EN C.2.2. indien u VRAAG C.2. met WAAR beantwoord heeft.
Ga anders door naar VRAAG C.3.

C.2.1. Geef hieronder alstublieft aan in welk ziekenhuis (plaats van betreffende ziekenhuis) u deze EERSTE dotterbehandeling heeft gehad.

_____

C.2.2. Geef hieronder alstublieft aan wanneer deze EERSTE dotterbehandeling heeft plaatsgevonden (in welk jaar en welke maand).
Probeer een schatting te doen indien u dit niet precies weet.

Maand: _____ Jaartal: _____

C.3. “Na mijn bezoek aan de FTP en de daaropvolgende behandeling,
heb ik (opnieuw) een bypassoperatie gehad.”

☐ Waar

☐ Niet waar

LET OP:
Ga door naar de VRAGEN C.3.1. EN C.3.2. indien u VRAAG C.3. met WAAR beantwoord heeft.
Ga anders door naar VRAAG C.4.

C.3.1. Geef hieronder alstublieft aan in welk ziekenhuis (plaats van betreffende ziekenhuis) u deze EERSTE bypassoperatie heeft gehad.

_____

C.3.2. Geef hieronder alstublieft aan wanneer deze EERSTE bypassoperatie heeft plaatsgevonden (in welk jaar en welke maand). Probeer een schatting te doen indien u dit niet precies weet.

Maand: _____ Jaartal: _____

C.4. “Na mijn bezoek aan de FTP en de daaropvolgende behandeling, heb ik (opnieuw) een hartklepoperatie gehad.”

☐ Waar

☐ Niet waar

LET OP:
Ga door naar de VRAGEN C.4.1. EN C.4.2. indien u VRAAG C.4. met WAAR beantwoord heeft. Ga anders door naar VRAAG C.5.

C.4.1. Geef hieronder alstublieft aan in welk ziekenhuis (plaats van betreffende ziekenhuis) u deze EERSTE hartklepoperatie heeft gehad.

_____

C.4.2. Geef hieronder alstublieft aan wanneer deze EERSTE hartklepoperatie heeft plaatsgevonden (in welk jaar en welke maand). Probeer een schatting te doen indien u dit niet precies weet.

Maand: _____ Jaartal: _____

C.5. “Na mijn bezoek aan de FTP en de daaropvolgende behandeling, ben ik opgenomen geweest op de afdeling cardiologie in een (willekeurig) ziekenhuis.”

☐ Waar

☐ Niet waar

LET OP:
Ga door naar VRAAG C.5.1. indien u VRAAG C.5. met WAAR beantwoord heeft. Ga anders door naar VRAAG C.6.

C.5.1. Geef hieronder alstublieft aan in welk ziekenhuis (plaats van betreffende ziekenhuis) u bent opgenomen geweest.

_____

C.6. “Na mijn bezoek aan de FTP en de daaropvolgende behandeling,
heb ik van de huisarts (opnieuw) een verwijzing naar de cardioloog gekregen en/of ben ik met hartklachten op de eerste hulp geweest.”

☐ Waar

☐ Niet waar

LET OP:
Ga door naar VRAAG C.6.1. indien u VRAAG C.6. met WAAR beantwoord heeft. Ga anders door naar DEEL D – LEEFSTIJLAANPASSINGEN.

C.6.1. Geef hieronder alstublieft aan in welk ziekenhuis (plaats van betreffende ziekenhuis) u bent gezien op de eerste hulp of naar welk ziekenhuis u bent verwezen door de huisarts.

_____

DEEL D - LEEFSTIJLAANPASSINGEN

Onderstaande vragen in deel D gaan over gekregen leefstijladviezen op de FTP. Deze leefstijladviezen hebben betrekking op roken en voeding.

D.1. Rookte u voorafgaand aan uw bezoek van de FTP?
☐ Ja
☐ Nee

LET OP:
Ga door naar de VRAGEN D.1.1. EN D.1.2. indien u VRAAG D.1. met JA beantwoord heeft. Ga anders door naar VRAAG D.2.

D.1.1. Geef hieronder aan in hoeverre de volgende stelling klopt:
“Ik ben gestopt met roken naar aanleiding van het advies dat ik heb gekregen tijdens mijn bezoek aan de FTP.”
☐ Waar
☐ Niet waar

D.1.2. Rookt u op dit moment nog? Met ‘dit moment’ bedoelen we het moment van het invullen van de vragenlijst.
☐ Ja
☐ Nee

D.2. Heeft u het advies gekregen op de FTP om uw voeding aan te passen (zoals een cholesterolbeperking)?

☐ Ja

☐ Nee

LET OP:
Ga door naar de VRAAG D.2.1. indien u VRAAG D.2. met JA beantwoord heeft. Ga anders door naar DEEL E – ERVARINGEN.

D.2.1. Geef hieronder aan in hoeverre de volgende stelling klopt:
“Ik heb mijn voeding aangepast (bijvoorbeeld minder cholesterolrijke producten, meer groente en fruit, slechte vetten vervangen door goede vetten etc.) naar aanleiding van mijn bezoek aan de FTP.”

☐ Waar

☐ Niet waar

DEEL E - ERVARINGEN

De stellingen in deel E gaan over uw ervaringen met de FTP.

E.1. Geef bij elke stelling aan in hoeverre u het hiermee oneens of eens bent.

	Sterk mee oneens	Mee oneens	Niet mee oneens, maar ook niet mee eens	Mee eens	Sterk mee eens
1. Ik ben tevreden over mijn bezoek aan de FTP.	☐	☐	☐	☐	☐
2. De volgorde van onderzoeken en gesprekken op de FTP heb ik als prettig ervaren.	☐	☐	☐	☐	☐
3. Het contact met de artsen, verpleegkundigen en andere medewerkers van de FTP heb ik als prettig ervaren.	☐	☐	☐	☐	☐
4. Het contact met de andere mensen die dezelfde ochtend als ik het FTP traject doorliepen, heb ik als prettig ervaren.	☐	☐	☐	☐	☐
5. Tijdens mijn verblijf op de FTP had ik voldoende privacy.	☐	☐	☐	☐	☐
6. Voor, tijdens en na mijn verblijf op de FTP ben ik voldoende geïnformeerd.	☐	☐	☐	☐	☐

LET OP:
Geef een korte toelichting op uw antwoord indien u STERK MEE ONEENS of STERK MEE EENS ingevuld heeft bij één of meerdere van bovenstaande stellingen. Hiervoor is onderstaand ruimte gereserveerd
per stelling.

E.1.Stelling 1:

_____
_____
_____
_____

E.1.Stelling 2:

_____
_____
_____
_____

E.1.Stelling 3:

_____
_____
_____
_____

E.1.Stelling 4:

_____
_____
_____
_____

E.1.Stelling 5:

_____
_____
_____
_____

E.1.Stelling 6:

_____
_____
_____
_____

OVERIG

Hierna volgen nog drie aanvullende vragen. Beantwoord alstublieft ook de laatste twee vragen. Deze vragen hebben betrekking op het geven van toestemming voor telefonisch contact en het verifiëren van antwoorden. Dit wordt ALLEEN gedaan indien noodzakelijk voor een goede verwerking van de gegevens.

Heeft u nog tips of opmerkingen? Noteer deze alstublieft hieronder.

_____
_____
_____
_____
_____
_____
_____
_____
_____
_____

Ik geef toestemming aan de onderzoekers om telefonisch contact met mij op te nemen indien nodig.

☐ Ja, dit mag op het volgende telefoonnummer (graag hieronder noteren)

_____

☐ Nee

Ik geef toestemming aan de onderzoekers om contact op te nemen met het ziekenhuis waar ik behandeld ben om de gegeven antwoorden in deel C te verifiëren.

- ☐ Ja
- ☐ Nee

U kunt deze vragenlijst door middel van de bijgaande en reeds gefrankeerde retourenvelop naar ons terug sturen.

Neem gerust contact met ons op via de contactgegevens in de brochure indien u nog vragen heeft.

Wij willen u heel hartelijk danken voor het invullen van deze vragenlijst!

cardiologie

Topzorg voor uw levenskwaliteit

Onderzoek naar langetermijnuitkomsten van Fast Track polikliniek 'Pijn op de borst'

In september 2009 startte de Fast Track polikliniek 'Pijn op de borst' in ZGT, ziekenhuislocatie Hengelo. In de periode van september 2009 tot oktober 2014 heeft u het Fast Track traject doorlopen. Hoe gaat het nu met de mensen die in het verleden de Fast Track polikliniek bezochten? Het doel van dit onderzoek is om dit in kaart te brengen. De uitkomsten van het onderzoek gebruikt ZGT voor het verbeteren van de kwaliteit van de polikliniek.

Het onderzoek
Het onderzoek bestaat uit het invullen van een digitale vragenlijst.

Deelnemen
Vul de vragenlijst in over uw ervaringen met de Fast Track polikliniek en hoe het na het traject met u ging. De vragenlijst is opgedeeld in vijf blokken waarbij elk blok kort wordt geïntroduceerd. Aan het begin van de vragenlijst staat een korte instructie over het invullen.

Hoeveel tijd vraagt deelname?
Het invullen van deze vragenlijst duurt ongeveer vijf minuten.

Hoe doet u mee?
Vul de vragenlijst in via de link die u binnenkort ontvangt per e-mail. Geen e-mailadres bekend? U ontvangt de vragenlijst per post. Deze papieren vragenlijst kunt u in de retourenvelop sturen naar de onderzoekers. Wenst u alsnog de vragenlijst digitaal in te vullen? Stuur een e-mail naar [redacted]

Wat is de deadline voor het invullen van de vragenlijst?
U kunt de vragenlijst invullen tot 1 mei 2018.

Overige belangrijke mededelingen
- U bent niet verplicht deel te nemen aan het onderzoek.
- U kunt altijd en zonder consequenties uw deelname beëindigen.
- De verzamelde gegevens worden uitsluitend anoniem verwerkt.

Samenwerkingsproject
Dit onderzoek is een samenwerkingsproject van ZGT, Universiteit Twente en Cardion.

Vragen
Heeft u vragen? Neem contact op met de afdeling cardiologie, telefoonnummer [redacted]

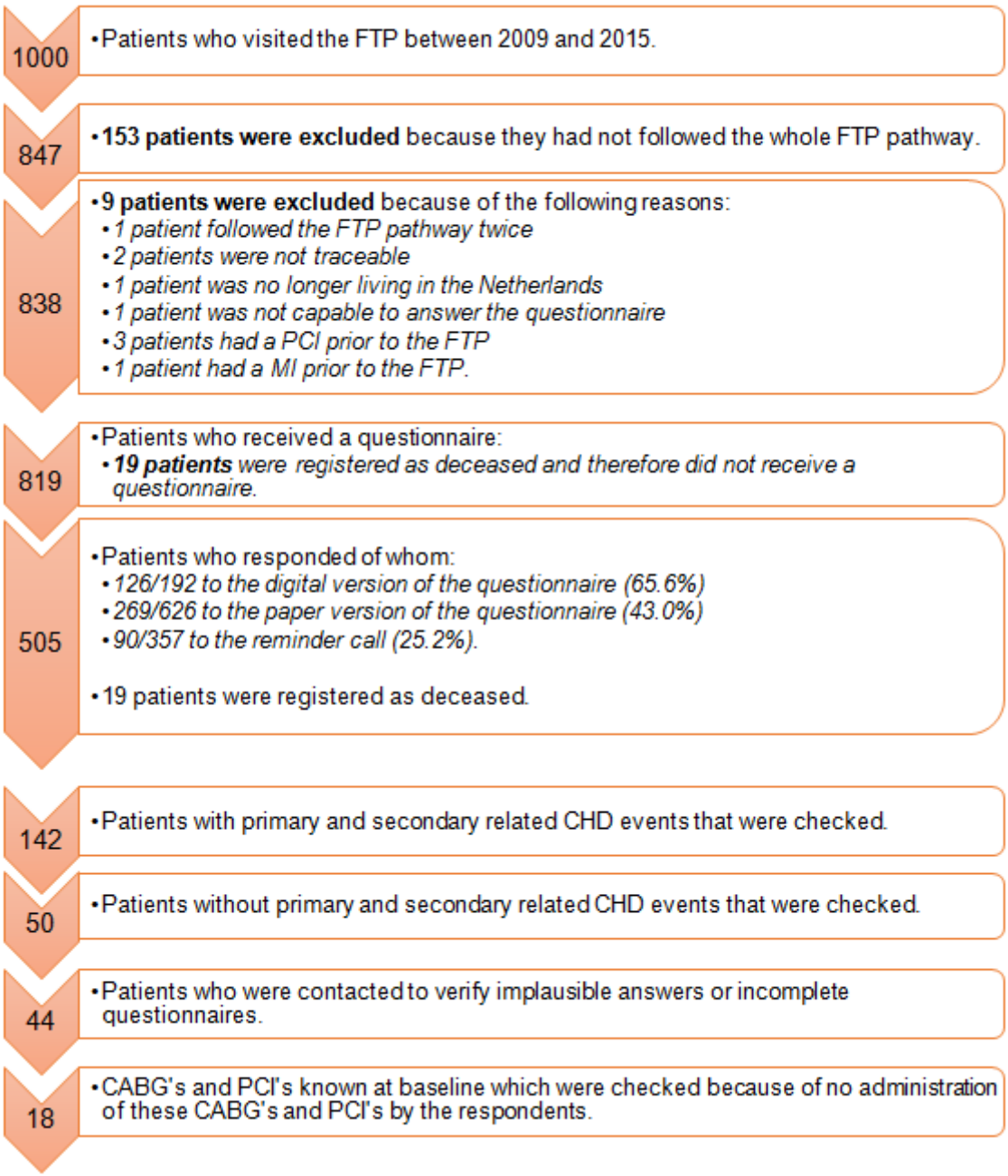
Almelo
Zilvermeeuw 1
Postbus 7600
7600 SZ Almelo

Hengelo
Geerdinksweg 141
Postbus 546
7550 AM Hengelo

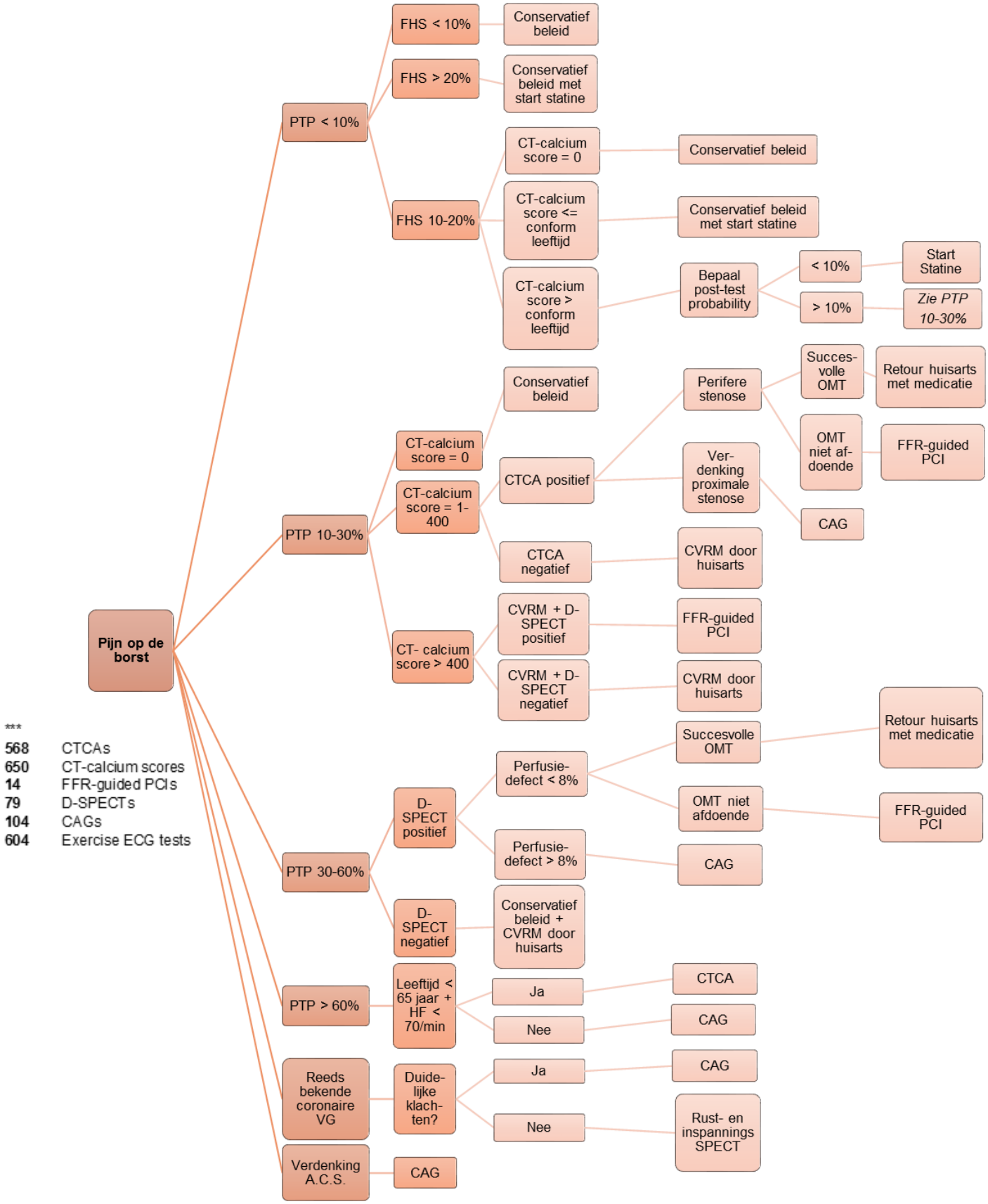
zgt.nl/mijnzgt
http://bit.ly/1y7WjbP
facebook.com/zgtinfo

linkedin.com/company/zgt
twitter.com/zgt_info
youtube.com/user/zgtinfo

APPENDIX V – FLOW DIAGRAM DATA COLLECTION



APPENDIX VI – RECOMMENDED WORKFLOW CHEST PAIN FOR THE NETHERLANDS (IN DUTCH)



Afkortingenlijst (in het Nederlands)

PTP	Pre-test probability op CHD berekend op basis van het aangepaste Diamond&Forrester model
FHS	Framingham score op cardiovasculair risico in 10 jaar
CTCA	64-detector CT Coronaire Angiografie
CVRM	Cardiovasculair Risico Management
OMT	Optimale Medicamenteuze Therapie
FFR-guided PCI	Fractional Flow Reserve (FFR)–gerichte Percutane Coronaire Interventie (PCI)
CAG	Coronaire Angiografie
(D-)SPECT	Myocardperfusiescan
HF	Hartfrequentie
VG	Voorgeschiedenis
A.C.S.	Acuut Coronair Syndroom/NSTEMI (geen totale afsluiting van de coronairarterie)
	**Indien STEMI (volledige afsluiting coronairarterie): direct naar meest dichtbij gelegen PCI-centrum ten behoeve van primaire PCI*
***	Aantal verrichtingen van die specifieke test in de 838 geïncludeerde FTP patiënten binnen deze studie

Abbreviations list (in English)

PTP	Pre-test probability of CHD based on adapted Diamond&Forrester model
FHS	Framingham score of cardiovascular risk in 10 years
CTCA	64-detector CT Coronary Angiography
CVRM	Cardiovascular Risk Management
OMT	Optimal Medicamental Therapy
FFR-guided PCI	Fractional Flow Reserve (FFR)–guided Percutaneous Coronary Intervention (PCI)
CAG	Coronary Angiography
(D-)SPECT	Myocardial perfusion scan
HF	Heart frequency
VG	Medical history
A.C.S.	Acute Coronary Syndrome/NSTEMI (no complete occlusion of the coronary artery) **In the case of a STEMI (complete occlusion of the coronary artery): directly referred to nearest PCI center for primary PCI.*
***	Number of that test performed within the 838 included FTP patients within this study