

Telephone triage of patients with chest discomfort



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Colofon

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Telephone triage of patients with chest discomfort

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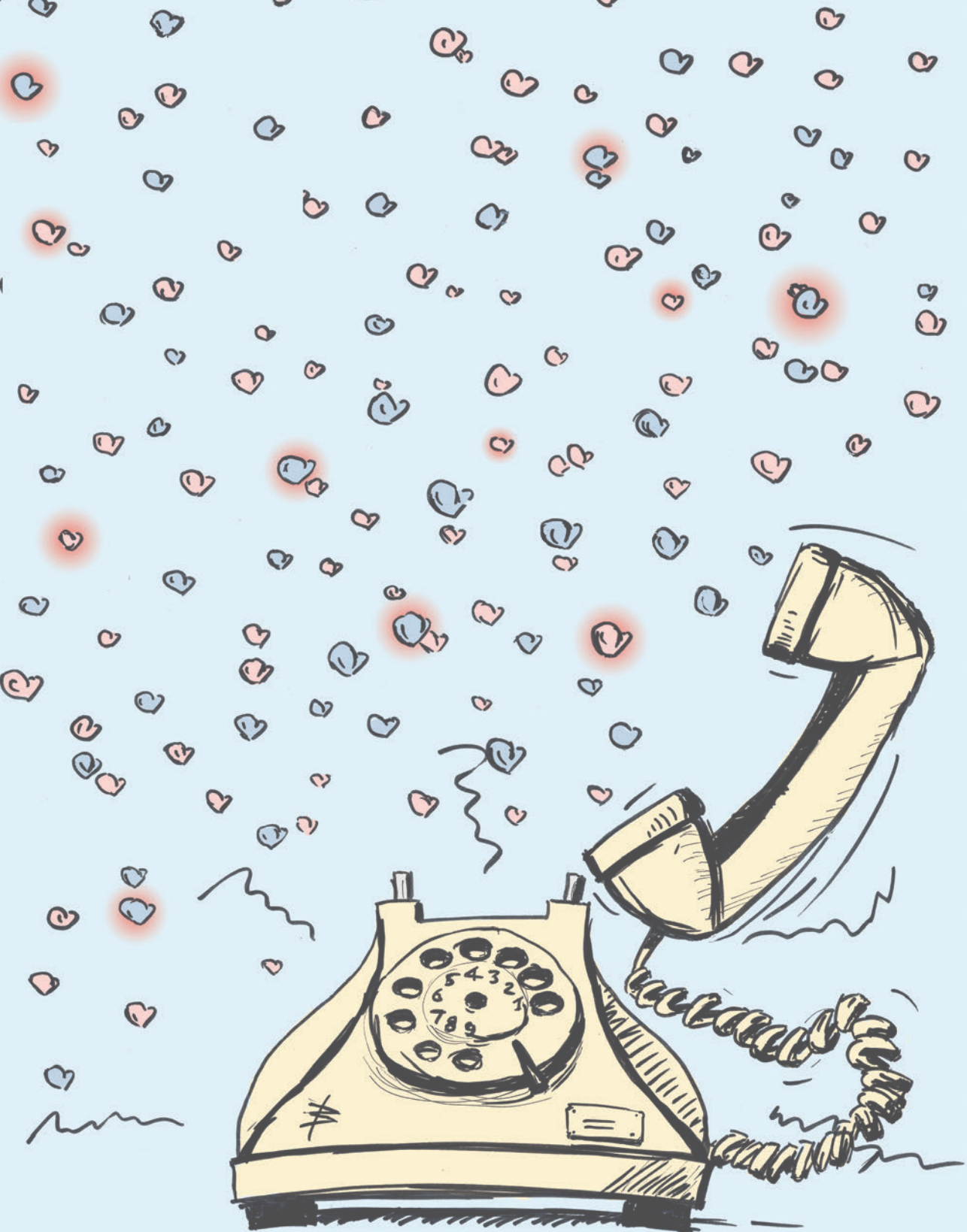
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1

CHAPTER

General introduction

The following case concerns a true case that was judged by the Medical Disciplinary Court on the charge of insufficient medical actions by the general practitioner.¹ On the basis of this case we introduce the problems with telephone triage of patients with chest discomfort in out-of-hours services for primary care (OHS-PC, in Dutch 'Huisartsenpost').

"A woman with acute chest discomfort at the OHS-PC"¹

Mrs. Brown, a 65-year-old woman, contacted the OHS-PC because of symptoms of chest discomfort. The telephone triage nurse assessed the urgency of her condition with the help of a decision support tool, the Netherlands Triage Standard (NTS). In the electronic medical file (EMF), the nurse noted that Mrs. Brown had been experiencing for two hours (i) a tightening chest pain, (ii) which radiated to her back, (iii) with vomiting (without blood) and (iv) sweating. Mrs. Brown experienced similar symptoms before, but then during exercise, and subsiding in rest (how long such periods usually lasted was not notified). The triage nurse allocated an urgency U2 (patient should be seen within one hour) with a consultation at the OHS-PC."*

**Fictional name*

Had the triage nurse chosen, within the NTS, 'chest pain' (in Dutch 'thoracale pijn') as the 'main complaint' (in Dutch 'ingangsklacht') among the 56 available options, then the very first pop-up question of the 'chest pain' hierarchically ordered algorithm would have been 'what is the severity of chest pain?' on a numeric rating scale (NRS) ranging from 0-10.² If Mrs. Brown had answered with a pain severity score of eight or higher and answered 'yes' to the second question 'Does the pain last for less than 12 hours?', the NTS would have immediately recommended an urgency U1, which means that the patient should be seen at home within 15 minutes by an ambulance (see table 1 for all NTS urgency levels, response times and recommended help).³ The NTS algorithm behind the main complaint 'chest pain' is programmed as such that in that case no additional questions need to be asked. If the triage nurse classifies the severity of pain as moderate (NRS 5 to 7) or light (NRS 4 or less), additional questions pop-up to gather further information on symptoms. The triage nurse should have answered 'yes' to at least one of the linked pop-up questions about (i) tightening or pressing chest pain, (ii) radiation of pain and (iii) autonomous nervous system related symptoms (nausea, vomiting, sweating, feeling of fainting), which would also result in the NTS generating an U1 urgency level. Appendix-Figures 1-6 show the combinations of Mrs. Brown's symptoms if filled out in the pop-up questions of the main complaint 'chest pain' and which corresponding urgencies would automatically have been generated by the NTS.

Appendix-Table 1 and 2 give an overview of the 'chest pain' related questions, and of more NTS main complaints that are commonly used for telephone triage of patients with chest discomfort.

Table 1. NTS levels of urgency

NTS Urgency level	Definition	Response time	Medical help
U0 – Resuscitation	Loss of vital functions	Immediately	Ambulance
U1 – Life threatening	Unstable vital functions	Immediately, within 15 minutes	Ambulance
U2 – Emergent	Vital functions in danger or organ damage	As soon as possible, within 1 hour	Home visit by GP or consultation at OHS-PC
U3 – Urgent	Possible risk of damage, human reasons	A few hours (<3 hours)	Home visit by GP or consultation at OHS-PC
U4 – Non-urgent	Marginal risk of damage	24 hours	Consultation at OHS-PC or telephone advice
U5 – Advice	No risk of damage	Advice, no time related	Telephone advice

GP: General practitioner

NTS: Netherlands Triage Standard

OHS-PC: Out-of-hours services for primary care

We do, however, not know what main complaint the triage nurse used for Mrs. Brown. We also do not know what the nurse exactly filled out in the NTS system. Moreover, the triage nurse may have overruled and downscaled the NTS-generated urgency, on her own or after consultation of the supervising general practitioner (GP). ⁴ Still, in the case of Mrs. Brown, an ambulance should have been sent directly (U1 according to the NTS) aimed at initiating treatment at the patient's home within 15 minutes. An urgency level U2 (patient seen within one hour) is the second best option in her case, because this still implies high urgency with a fast response. Importantly, Mrs. Brown should have been seen at her home, and not at the OHS-PC. Probably unwillingly, the triage nurse took a major risk because an acute coronary syndrome (ACS) could be the underlying cause, with the risk of life-threatening ventricular arrhythmias during the first hours. ^{5 6} Moreover, patients with ACS gain much by early treatment which can only be delivered in the hospital after safe transportation by an ambulance. ⁷

Continuation of case:

"When Mrs. Brown arrived at the OHS- PC, she vomited in the waiting room, and the triage nurse asks the GP to see the patient with priority.

The GP immediately sees the patient and includes her findings in the EMF which was already partly filled out by the triage nurse. She notified that Mrs. Brown was anxious. The tightening chest pain was located on both the left and right side of the thorax and radiated to the back. She had vomited, but had no shortness of breath. She had gone beyond her limits during exercise the previous day. Her medical history reported asthma, hypertension and a stoma, and she used antihypertensive drugs and a proton pump inhibitor. On physical examination, Mrs. Brown was not short of breath (breaths per minute not notified) and neither clammy nor sweaty, which was in contrast to what the triage nurse had notified in the EMF. Her blood pressure was 150/90 mmHg, the pulse rate 74 beats per minute and her temperature 36.8 °C. Lung auscultation and abdominal examination did not reveal abnormalities, and palpation of the chest wall was painful. The GP concluded that Mrs. Brown had musculoskeletal thoracic pain and advised her to take pain killers.

Mrs. Brown's chest discomfort continued for the next days, and after one week she ended in a resuscitation setting and died in the hospital. Autopsy revealed cardiac insufficiency due to an anteroseptal myocardial infarction with anterior wall rupture and cardiac tamponade. It was estimated that the myocardial infarction was 1 to 1.5 weeks old.

The family mentioned that a few days before her death, the patient had written an e-mail (but had not sent it) in which she notified that she felt she was not taken seriously by the GP at the OHS-PC.

The GP received an official warning (In Dutch 'waarschuwing') from the Medical Disciplinary Court. The court judged that the GP should have paid more attention to the nurse's triage report. From that report in the EMF suspicion of an ACS should have arisen. The GP answered "I read the report, but relied more on my own observations." The court also judged that the distress of Mrs. Brown should have been taken more seriously. The GP indicated that she has learned from this case that women often have 'atypical' cardiac symptoms and that distress is an important symptom to recognize and act upon. Furthermore, she had learned that she needed to explain her findings and chosen therapy more

clearly to the patient and to check whether this was understood and agreed upon by the patient.”

This true story of Mrs. Brown shows that telephone triage of patients with chest discomfort may be the starting point of a serious adverse event. We do not exactly know how the triage nurse filled out the NTS, but if she had answered a 'yes' in the NTS to the symptoms she notified in the EMF, it certainly would have generated an U1 urgency, which might have triggered more sense of urgency for the next care providers in line. In this case the GP's assessment of the patient's physical condition together with the nurse's notes unfortunately did not lead to the adequate interpretation of presenting symptoms, resulting in the fatal outcome for Mrs. Brown.

Interestingly, both the GP and female journalist who wrote down the court case wrote that Mrs. Brown had 'atypical' cardiac symptoms. Yet, what is 'atypical' about 'tightening chest pain, radiating to the back, and experiencing sweating and vomiting'? Has the dominating medical and lay opinion that women are more likely to have 'atypical' cardiac symptoms resulted in an underestimation of the value of classical symptomatology of ACS? Notably, the poor telephone triage in this case of Mrs. Brown was not taken into consideration by the court.

This thesis focuses on the first part of the case; on how telephone triage of patients with chest discomfort at the OHS-PC is done and how it could be improved. But first I will provide some background knowledge on ACS and the history of triage that is relevant for the telephone triage of patients with chest discomfort at the OHS-PC.

Acute coronary syndrome

Definitions and pathophysiology

ACS is an umbrella term for myocardial infarction (MI) and unstable angina pectoris (UAP). In the domain of patients with acute symptoms suggestive of cardiac ischemia, e.g. chest discomfort, MI is defined as cardiomyocyte necrosis, which can be detected with elevated cardiac biomarkers of (high sensitivity) troponin I or T.⁸ When there are repolarization abnormalities (ST and/or T wave) on the 12-lead electrocardiogram (ECG), the MI is called ST-elevated myocardial infarction (STEMI) and without these ECG abnormalities, non-ST-elevated myocardial infarction (NSTEMI).^{7,8} Patients in the same domain are classified as UAP if troponin levels are not elevated and thus cardiomyocyte necrosis is lacking.⁹ Currently, such an assessment with troponin and ECG is done in the hospital, although, point-of-care tests of high sensitivity troponin are being developed for use in primary care.¹⁰

The pathophysiology of most MIs is characterized by atherosclerotic plaque rupture, ulceration, fissure, erosion or dissection resulting in intraluminal thrombus in one or more of the epicardial coronary arteries leading to decreased myocardial blood flow and/or distal embolization and subsequent myocardial necrosis (type 1 MI).¹¹ Most of these patients have underlying coronary artery disease (CAD) visible with imaging, but occasionally (5-20% of cases), there may be an MI with non-obstructive epicardial coronary atherosclerosis (MINOCA) or no angiographic evidence of CAD (NOCAD) in the epicardial vessels. These two latter types are more common in women than men.¹² ¹³ Type 2 MI is caused by myocardial necrosis due to an imbalance between myocardial oxygen supply and demand. Mechanisms include coronary artery spasm, coronary microvascular dysfunction, tachyarrhythmias, bradycardia, anemia, respiratory failure, hypotension and severe hypertension.¹¹ Type 3 concerns MI without available biomarker investigation (acute cardiac death), and type 4 and 5 MI are related to coronary interventions and are out of the scope of this thesis.¹¹

Clinical presentation of patients with ACS

The main symptom caused by myocardial ischemia is acute chest discomfort (i.e. chest pain, tightness, or pressure), which usually lasts more than 20 minutes and often the discomfort radiates to the arms, neck or jaws.^{8,14,15} Additionally shortness of breath and autonomous nervous system (ANS) related symptoms may be present, e.g. sweating, nausea, pale face and (near) collapse.⁸ Life-threatening ventricular arrhythmias may occur in up to 6% of patients with ACS within the first hours after the onset of symptoms, most often before arrival at the hospital.⁵

Incidence and prevalence of ACS

In 2018 in the Netherlands, 49,200 men and 21,110 women were newly diagnosed with an acute MI, and MI is in the top five causes of death.^{16,17} Worldwide, ACS was ranked as the leading cause of death in 2017 for both sexes.¹⁸ The prevalence of ACS among patients with chest discomfort who call OHS-PC or emergency medical service (EMS or ambulance dispatch center) is about 10%, and at the emergency department (ED) visits between 10 to 30%.¹⁹⁻²¹

Management of ACS

Early diagnosis of ACS is of vital importance to initiate lifesaving interventions in order to prevent or reduce myocardial necrosis ('time is muscle').²² Patients with ACS should as soon as possible be treated, to restore cardiac blood flow. Treatment options include (rescue) percutaneous coronary intervention (PCI), coronary artery bypass surgery (CABG) and/or pharmacological treatment.⁸ The role of the GP in this process is to adequately assess which chest discomfort patients have a high risk of ACS and therefore should immediately be referred to the hospital and in which patients ACS can be safely excluded and thus do not require referral. This is a difficult task.

The history of triage

The word triage is derived from the French verb 'trier', which means to sort, separate, and select.²³ The original concept was developed around 1800 for use in warfare, where in mass casualty situations the need for medical attention exceeds the availability of resources. Patients who needed surgery and had a chance to survive needed to be sorted out at the battlefield.²⁴ In modern healthcare systems there are three stages of triage (i) pre-hospital telephone triage by OHS-PC or EMS (ii) physical triage at the scene by the first clinician attending the patient and (iii) physical triage at the ED.³

²⁴ Most commonly used digital triage systems automatically generate five levels of urgency, which are linked to a certain time period within which the patient should be seen by a physician.²⁵ Worldwide, different triage systems are used, with ED triage systems being the most studied (stage 3, physical triage). Most used and studied in the ED are the Manchester Triage Standard (MTS), the Canadian Triage and Acuity Scale (CTAS), the Emergency Severity Index (ESI), and the Australasian Triage System (ATS).^{23,25} In the pre-hospital setting there is more diversity in telephone triage systems, and these are less studied.²⁶

The Netherlands Triage Standard

Since 2011, most Dutch OHS-PC and half of the EMS have been using the NTS for urgency assessment.³ In EDs, both the NTS and MTS are used.²⁷ The aim of the NTS

and other triage systems is to establish both efficient and safe care, by standardizing urgency decision.^{26 28 29} The NTS is constructed with lists of hierarchically ordered questions related to main complaints, and the answers filled out in the system automatically generate an urgency level linked to a certain time frame within which the patient should be seen by a physician or ambulance personnel.³ Triage nurses are supervised by GPs in the OHS-PC who have the final responsibility for the urgency allocation.⁴

The NTS was implemented straightaway in the OHS-PC setting, although, the system has never been validated against clinical outcomes.³ Therefore, the NTS' accuracy of urgency allocation is unknown. The NTS was developed by an expert panel who integrated knowledge from (i) the MTS, (ii) the Dutch national clinical guidelines for general practice ('NHG triage index') and (iii) the Dutch national standard for ambulance dispatch centers ('LSMA').³ A national report showed an increase in high urgency allocations after the implementation of the NTS at the OHS-PC, which was not related to a change in distribution of diseases, and thus suggests a more defensive triage strategy by the introduction of the NTS.³⁰ Also, a survey among 428 GPs reported that the majority (83.9%) was convinced that telephone triage with NTS had resulted in (i) increase in unnecessary consultations and home visits in patients with non-urgent problems, and (ii) a higher workload at the OHS-PC.⁴

Triage nurses are trained to 'reason in urgencies' (and not consider diagnoses!), which would, according to experts, increase the NTS guided safety of urgency allocations.³¹⁻³³ Focusing on urgency originates from the 'ABCD-approach', taught in Advanced Trauma Life Support (ATLS®) courses for the initial assessment and treatment of critical ill patients in amongst others ED-setting.³⁴ When the triage nurse starts the telephone triage with the NTS, the system requires a mandatory 'ABCD-check'; i.e. the triage nurse has to ask questions to assess whether the patient has life-threatening problems concerning the Airway, Breathing, Circulation and Disability for which an ambulance should be sent immediately.^{34 35} The argumentation for 'reasoning in urgencies' is that clinical signs and symptoms of critical conditions are similar for all underlying causes of life-threatening situations, and this renders knowledge of the underlying cause redundant for the initial assessment and treatment.³⁴ This may be true for the initial assessment of critically ill patients in the ED setting, but the usefulness of applying the 'reasoning in urgencies' to anybody calling the OHS-PC is at least questionable, simply because only 2.3% of all callers is ABCD-unstable.³⁶

When the triage nurse has assessed the patient as ABCD-stable, the triage nurse has to choose out of 56 main complaints and follow the hierarchically ordered pop-up questions generated by the NTS that often require a 'yes' or 'no' answer. Triage nurses must choose an option, while often patients answer with 'a little bit' or 'doubtful', or patients describe their chest pain as 'burning' or 'uncomfortable' which are no answer options in the NTS. This rigidity of the NTS seems to prevent personalized patient assessment and easily results in 'interactional workability dilemmas'; i.e. difficulties for the triage nurse caused by applying a rigid system structure in the wider context of the patients' narrative.^{37 38} In conclusion, general triage rules may hamper tailored management of a specific case.^{38 39} Understanding how triage nurses are reasoning while working with the NTS and what interactional workability dilemmas they might experience may help to develop adequate education material for telephone triage of patients with chest discomfort and improve patient management.

Current telephone triage of patients with chest discomfort at the OHS-PC

Chest discomfort accounts for 2.1% of all telephone consultations at the OHS PC, and is included in the top five reasons for telephone contact in this setting.^{40 41} In the Netherlands, the majority (80%) of patient who seek medical help for chest discomfort call their own general practitioner (GP) or OHS-PC, the other 20% either directly calls the ambulance (112) or are self-referrals to the ED.⁴²

Telephone triage of patients with chest discomfort at OHS-PC is notoriously challenging, because it is difficult to differentiate ACS from other causes of chest discomfort based on symptoms only.^{43 44} Chest discomfort may also be caused by a wide range of non-life-threatening conditions such as musculoskeletal, gastrointestinal and psychological conditions that together account for the majority of underlying causes.⁴⁵ Diagnostic predictions models for acute chest discomfort and applicable for telephone triage at the OHS-PC are scarce, and are at best characterized by a moderate predictive performance.^{46 47}

There are indications that both efficiency and safety need improvement for telephone triage of patients with chest discomfort at the OHS-PC. Efficiency is limited, because chest discomfort is the most common reason (60.7%) for allocating ambulances to patients calling OHS-PC, but only 1 out of 10 patients has an ACS or other life-threatening event.^{45 48} Moreover, a missed ACS with as a result death or severe impairment is the most common cause (30.4%) for a serious adverse event at the OHS-PC setting with an incidence of approximately 2 per 100.000 consultations.^{49 50}

Thus, there is an urgent need to improve both efficiency and safety of the telephone triage of patients with chest discomfort in the OHS-PC setting.

Should telephone triage be different in men compared to women with chest discomfort?

In the last decade, much scientific and public attention was paid to possible differences between men and women with ACS.^{51 52} Hospital based studies showed a delayed recognition of ACS in woman compared to men and it was suggested this delay was related to a less specific presentation in women.^{53 54} The 'atypical-symptoms' message gained much dominance, despite that most studies had methodological limitations, due to recall- and hindsight bias, and several other studies found no gender differences.^{55 56} More importantly, nearly all studies evaluated the wrong comparison; comparing women with confirmed ACS to men with confirmed ACS. However, for clinically relevant information, one should compare diagnostic predictors of ACS in men and women. This should ideally be done by comparing symptom presentation of ACS-suspected women that are eventually diagnosed with ACS to suspected women without ACS, and compare suspected men with ACS with those without ACS.^{57 58} Just one study performed such an analysis in patients with chest discomfort seen at the ED, and one additional study in the OHS-PC setting.^{59 60} Both studies stressed that there were more similarities than differences in symptom predictors of ACS for women and men.^{59 60} Unbalanced attention to differences, neglecting the much larger overlap may even introduce new blind spots in recognizing ACS in women.⁶¹

In conclusion, telephone triage of patients with acute chest discomfort comes with many challenges. Yet, it is currently still unknown how the NTS really performs because it was never validated on clinical outcomes. In addition, knowledge is needed about how triage nurses use the NTS tool and how they reason during telephone triage of patients with chest discomfort. Furthermore, much is unknown about sex differences in symptoms predictive for ACS and whether triage assessment should be different for women and men. The studies published in this thesis were carried out to fill some of these knowledge gaps.

Objectives and outline of this thesis

This thesis focuses on:

- (i) Gaining insights into how the telephone triage of patients with chest discomfort in OHS-PC is currently done.
- (ii) Discovering leads for improvement of triage, both in terms of patient safety and efficiency.

- (iii) Assessing whether triage of patients with chest discomfort should be different in women and in men.

In **Chapter 2**, we present the design and study protocol of the mixed-method Safety First project, which consists of multiple quantitative and qualitative studies, each with their own design. The aim of the Safety First project is to describe, understand and improve the diagnostic process and urgency allocation of telephone triage of patients suspected for acute cardiovascular diseases calling the OHS-PC.

In **Chapter 3**, we describe how we assessed the accuracy of telephone triage in patients with chest discomfort with as the reference the combined outcome ACS or other life-threatening events. We calculate the accuracy of both the NTS tool and the 'final' urgency allocation, including the overruled urgency allocations and discuss the clinical implications of these findings.

Chapter 4 describes the results of an interview study among 24 triage nurses, who were asked to reflect on their reasoning while using the NTS for patients suspected of ACS. Recent audiotapes (<14 days old) of each of the nurse's triage conversations were used to stimulate the reflection.

In **Chapter 5**, we investigate whether the time of calling is associated with the risk of ACS in patients suspected of ACS who call the OHS-PC. Are there certain time periods in which the risk is higher? If so, this knowledge could be helpful in improving the telephone triage.

In **Chapter 6**, we assess whether there are gender-specific differences in symptoms predictive of ACS by comparing symptom presentation of women and men with ACS to women and men without ACS, in the domain of patients with chest discomfort who call the OHS-PC.

In **Chapter 7** we developed novel sex-specific symptom-based prediction models for diagnosing ACS in patients with chest discomfort who call the OHS-PC.

Finally, in **Chapter 8**, the main findings and conclusions of this thesis are presented and we will discuss about the relevance of considering the patient's eventual diagnosis in triage system research and telephone triage in clinical practice. At the end, we reflect on the clinical case presented in the introduction of the thesis.

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Appendix- Figure 1. NTS fragment of triage criteria within main complaint 'chest pain' with combination of symptoms of Mrs. Brown.

Urgentie

Vervolgactie AMBU

1 Ernst pijn/druk thorax: Nee, geen pijn/druk Licht (<4) Matig (5-7) Hevig (8-10)

1 Tijdsduur pijn/druk thorax: Langer dan 12 uur Korter dan 12 uur

1 Karakter pijn thorax: Stekend/scherp Vastzittend aan de ademhaling Onduidelijk Beklemmend/drukkend

English translation; The combination of moderate intensity pain (NRS 5-7), lasting for less than 12 hours and a tightening or pressing character generates an urgency U1.

Appendix-Figure 2. NTS information pop-up about triage criterion character of pain.

Karakter pijn thorax

? Kunt u de pijn beschrijven (beklemmend, scherp/stekend, vastzittend aan de ademhaling, onduidelijk)?

i Beklemmende pijn is verdacht voor cardiale pijn. Typische cardiale pijn is krampende, beklemmende of drukkende pijn op het midden van de thorax, dat vooral optreedt bij inspanning. Het kan aanvoelen als een druk op de borst of knijpen in de borstkas.

English translation; when the patient describes the character of pain as cramping, tightening, pressing or feels as squeezing of the chest wall, the triage nurse should be aware the pain may be caused by a cardiac problem.

Appendix-Figure 3. NTS fragment of triage criteria within main complaint 'chest pain' with combination of symptoms of Mrs. Brown.

Urgentie: 0 1 2 3 4 5

Vervolgactie: AMBU

1 Ernst pijn/druk thorax: Nee, geen pijn/druk Licht (<4) **Matig (5-7)** Hevig (8-10)

1 Tijdsduur pijn/druk thorax: Langer dan 12 uur **Korter dan 12 uur**

1 Uitstraling pijn thorax: Geen Niet Typisch **Typisch cardiaal**

English translation; the combination of moderate intensity pain (NRS 5-7), lasting for less than 12 hours and 'typical' cardiac radiation generates an urgency U1.

Appendix-Figure 4. NTS information pop-up about triage criterion radiation.

Uitstraling pijn/druk thorax

? Straalt de pijn of druk uit? Waarheen?

i Typisch is passend bij cardiale pijn zoals uitstraling naar de kaak, arm of rug. Zie afbeelding



English translation; When the patient describes the chest pain radiates to the jaws, arm or the back, the triage nurse should consider the radiation to be 'typically' cardiac.

Appendix- Figure 5. NTS fragment of triage criteria within main complaint 'chest pain' with combination of symptoms of Mrs. Brown.

Urgentie Vervolgactie AMBU

1	1 Ernst pijn/druk thorax:	Nee, geen pijn/druk	Licht (<4)	Matig (5-7)	Hevig (8-10)
1	1 Tijdsduur pijn/druk thorax:	Langer dan 12 uur	Korter dan 12 uur		
1	1 Vegetatieve verschijnselen:	Nee	Voorbij	ja	

English translation; the combination of moderate intensity pain (NRS 5-7), lasting for less than 12 hours and present or past (not shown in this figure) autonomous nervous system-related symptoms generates an urgency U1.

Appendix-Figure 6. NTS information pop-up about triage criterion autonomous nervous system-related symptoms.

Vegetatieve verschijnselen

? | Heeft u het gevoel flauw te vallen? Transpireert u? Bent u bleek, misselijk of duizelig?

i | Vegetatieve verschijnselen zijn misselijkheid, transpireren, klam en/of gevoel flauw te vallen, bij een verdenking op een cardiovasculair event dreigende shock. Niet bij hevige pijn door een trauma.
Voorbij is vegetatieve verschijnselen in de afgelopen uren (max. 6).

English translation; When the patient reports nausea, sweating, clamminess or feels like fainting the triage nurse should be aware about the possibility of a cardiovascular event or shock. Past autonomous nervous system-related symptoms are defined as the presence of these symptoms within the last 6 hours.

Appendix-Table 1: NTS main complaints with triage criteria that generate an urgency U1 level, within the domain chest discomfort.

→ ABCD unstable (no main complaint is selected)			Urgency level U1: ambulance within 15 minutes
Main complaint 'Chest pain'			
→ ABCD stable	AND severe chest pain (Numeric Rating Scale ² (NRS)-score ≥ 8) lasting less than 12 hours		
→ ABCD stable	AND mild (NRS ≤ 4) to moderate (NRS 5-7) chest pain lasting for less than 12 hours	AND one of the following: <ul style="list-style-type: none">• retrosternal located pain• tightening or pressing• radiation to jaw, arm or upper back• progressive pain intensity in short time• past or present autonomous nervous system-related symptoms• dizziness	
Main complaint 'Collapse'			
→ ABCD stable	AND collapse	AND chest pain of any severity	
Main complaint 'Back complaints'			
→ ABCD stable	AND severe upper back pain (NRS ≥8)	AND past or present autonomous nervous system-related symptoms	

Appendix-Table 2: NTS main complaints with triage criteria that generate an urgency U2 level, within the domain chest discomfort.

Main complaint 'Chest pain'		
→ ABCD stable	AND severe chest pain (Numeric Rating Scale (NRS)-score ≥ 8) lasting longer than 12 hours	
→ ABCD stable	AND mild (NRS ≤ 4) to moderate (VRS 5-7) chest lasting longer than 12 hours	AND one of the following: <ul style="list-style-type: none">• retrosternal located• oppressive or tight• radiation to jaw, arm or upper back• pain intensity being quickly progressive• past or present autonomous nervous system-related symptoms• dizziness
Main complaint 'Arm complaints'		
→ ABCD stable	AND severe arm pain (NRS ≥8)	AND past or present autonomous nervous system-related symptoms
Main complaint 'Abdominal complaints'		
→ ABCD stable	AND severe abdominal pain (NRS ≥8)	AND past or present autonomous nervous system-related symptoms

Urgency level U2: GP visit or consultation within one hour



2

CHAPTER

Optimisation of telephone triage of callers with symptoms suggestive of acute cardiovascular disease in out of hours primary care: observational design of the Safety First study

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ABSTRACT

Introduction In the Netherlands, the “Netherlands Triage Standard” (NTS) is frequently used as digital decision support system for telephone triage at out-of-hours primary care services (OHS-PC). Aim of NTS is to guarantee accessible, efficient and safe care. However, there are indications that current triage is inefficient, with overestimation of urgency, notably in suspected acute cardiovascular disease. In addition, in primary care setting the NTS has only been validated against surrogate markers, and diagnostic accuracy with clinical outcomes as the reference is unknown. In the Safety First study, we address this gap in knowledge by describing, understanding and improving the diagnostic process and urgency allocation in callers with symptoms suggestive of acute cardiovascular disease, in order to improve both efficiency and safety of telephone triage in this domain.

Methods and analysis An observational study in which 3,000 telephone triage recordings (period 2014-2016) will be analysed. Information is collected from the recordings including caller- and symptom characteristics and urgency allocation. The callers’ own general practitioners are contacted for the final diagnosis of each contact. We included recordings of callers with symptoms suggestive of acute coronary syndrome (ACS) or transient ischemic attack (TIA)/stroke. With univariable and multivariable logistic regression analyses the diagnostic accuracy of caller- and symptom characteristics will be analysed in terms of predictive values with urgency level, and ACS and TIA/stroke as outcomes, respectively. To further improve our understanding of the triage process at OHS-PC, we will carry out additional studies applying both quantitative and qualitative methods; (i) case-control study on calamities, (ii) conversation analysis study, and (iii) interview study with triage nurses.

Ethics and dissemination The Medical Ethics Committee of the University Medical Centre Utrecht, the Netherlands endorsed this study (National Trial Register identification: NTR7331). Results will be disseminated at scientific conferences, regional educational sessions, and publication in peer-reviewed journals.

INTRODUCTION

Digital decision support systems for telephone triage are widely used, also in primary care out of hours settings. For these settings, telephone triage systems were derived from triage systems applied in emergency department (ED) settings. An important difference, however, is that telephone triage systems do not include items related to face-to-face contact and physical examination.¹ In the Netherlands, a digital decision support system for telephone triage called the “Netherlands Triage Standard” (NTS) was introduced in 2011.² The NTS was constructed by an expert panel using (i) the Dutch national telephone guidelines for office hours in family practice (‘NHG triage index’) and (ii) a modified version of the Manchester Triage System (MTS) developed in the ED setting.³ Since its introduction in 2011, the NTS has been used by most out-of-hours services in primary care (OHS-PC), and by approximately half of the ambulance dispatch centres in the Netherlands.⁴ An important argument for using the same system within the ‘critical care chain’ was that it would facilitate communication during care transitions, and potentially improve transitional safety.⁵

Many studies assessed the diagnostic accuracy of triage systems in the ED setting.⁶⁻⁹ Yet, comparable studies on validity of telephone triage systems in primary care settings are limited.⁵ The validity of the five-level triage system for physical triage in the ED setting was evaluated in a systematic review of 57 studies.¹ Various reference standards for the assessment of validity were used; researchers’ own creation of a reference standard or combining severity with resource measures, e.g. hospital admissions.¹ Only one of the included studies in this review assessed the validity of the NTS, for both physical triage in the ED and for telephone triage in the OHS-PC.⁵ For the assessment of telephone triage in OHS-PC, 6,668 patients were evaluated. Referrals to the ED and self-care advices were the two surrogate markers used as best proxies for adequate urgency allocation. Consequently, patients referred to the ED were considered as being correctly labelled as high urgency and those receiving a self-care advice as correctly low urgency, independent of the final diagnosis related to the episode. Not surprisingly, the researchers found an association between high urgencies and ED referrals and between low urgency level allocation by the triage nurse and self-care advices. Information on whether the urgency allocation was in line with the clinical outcomes is lacking.⁵ There are no other studies available that assessed the validity of the NTS for telephone triage in the OHS-PC setting or validated the NTS to the final diagnosis instead of to surrogate markers.^{5,10} Our study addresses this current knowledge gap.

Over the last decade, out of hours primary care in the Netherlands has been reorganised from small practices into larger OHS-PC. ⁴ Patients primarily contact the OHS-PC when they need medical help outside office hours. In case of life-threatening symptoms, however, patients can also directly contact the emergency number of the ambulance dispatch centres or directly visit the ED. At the OHS-PC, triage nurses trained in using the NTS handle all incoming calls, under supervision of a general practitioner (GP). ⁴ The goal of this telephone triage is to identify callers with the most urgent need of care. ¹¹ With urgent clinical situations in mind the experts formulated the NTS questions in a hierarchically ordered algorithm; questions focusing on the symptoms and circumstances considered most critical first, followed by questions about less critical symptoms. ² The triage nurse fills out the caller's responses in the semi-automatic NTS system, which then automatically generates urgency allocations. Within the NTS six possible urgency levels can be distinguished that are linked to the response time within which a caller should receive medical help (see table 1). The urgency level generated by the NTS can be adjusted by the triage nurse if the nurse disagrees with the NTS allocation (upgrading or downgrading). ¹¹ Most often such adjustments are preceded by consultation of the supervising GP, who has the final responsibility for the urgency level allocation.

Table 1. NTS urgency levels

NTS Urgency level	Definition	Response time	Medical help
U0 – Resuscitation	Loss of vital functions	Immediately	Ambulance
U1 – Life threatening	Unstable vital functions	Immediately, within 15 minutes	Ambulance
U2 – Emergent	Vital functions in danger or organ damage	As soon as possible, within 1 hour	Home visit by GP or consultation at OHS-PC
U3 – Urgent	Possible risk of damage, human reasons	A few hours (<3 hours)	Home visit by GP or consultation at OHS-PC
U4 – Non-urgent	Marginal risk of damage	24 hours	Consultation at OHS-PC or telephone advice
U5 – Advice	No risk of damage	Advice, no time related	Telephone advice

GP: General practitioner

NTS: Netherlands Triage Standard

OHS-PC: Out-of-hours services for primary care

The aim of the NTS is to guarantee both efficient and safe care. Questions have been raised, however, about the current efficiency. ⁴ A national report showed an increase in high urgency allocations after the implementation of the NTS at the Dutch OHS-PC,

notably U2 urgencies.¹² This is in contrast to the unchanged distribution of diseases, and suggests an increase of a more defensive triage strategy. In addition, a survey in 2016 among GPs revealed that the large majority (83.9%) believed that telephone triage with NTS resulted in (i) many unnecessary consultations and home visits in patients with non-urgent problems, and (ii) a high workload at the OHS-PC.¹³ The authors of this survey speculated that overconsumption of care at the OHS-PC was attributable to certain characteristics of the users of the NTS. Previous studies on OHS-PC telephone triage in the United Kingdom described that the clinical background of triage nurses, the range of their experience, their gender and their attitudes to risk did not affect the triage decisions made.¹⁴⁻¹⁵ More insight in the users of the NTS (triage nurse) could help improve the system. Yet, it is currently unknown how triage nurses actually use the NTS in their clinical reasoning process and how this affects the performance of the triage system. Also, media coverage of (fatal) adverse events has grown, and adverse event reports and investigation by the Dutch Health and Youth Care Inspectorate have been made publically available.¹⁶ The increasing attention for (fatal) adverse events might possibly be related to more defensive triage to avoid such (fatal) adverse events, which could potentially worsen efficiency. Thus, thorough research on the accuracy and use of the NTS is needed in order to assess whether improvements in the balance between efficiency and safety are required.

Callers with symptoms suggestive of acute cardiovascular diseases, e.g. acute coronary syndrome (ACS), or transient ischemic attack (TIA)/stroke generally receive high urgency allocations.¹⁷ Chest pain is the most common reason for dispatching an ambulance (U1) with 60.7% of all ambulance rides deployed from the OHS-PC.¹⁸ However, the incidence of ACS among patients experiencing chest discomfort in the Dutch primary care setting and referred to the hospital is low with around 10%.¹⁹⁻²¹ The trade-off between efficiency and patient safety of telephone triage is particularly challenging in these cases. On the one hand, prompt detection of ACS or TIA/stroke is crucial to initiate interventions as early as possible and prevent myocardial or brain necrosis, and improve prognosis.²²⁻²⁴ On the other hand, overestimation of urgency results in unnecessary high workload, high referral rates, high costs, and potentially in iatrogenic damage of the caller.²⁵ The discussion about balancing efficiency and safety is especially complicated because missing an acute myocardial infarction is the most common reason for malpractice claims worldwide.²⁶⁻²⁸

Our ultimate goal is to improve the efficiency and safety of the triage of callers with symptoms suggestive of ACS or TIA/stroke who contact the OHS-PC, and to improve diagnosis. In the SafetyFirst study we will evaluate real-life telephone triage recordings

with corresponding urgency allocations, and patients' final clinical outcomes. Our research questions are (i) what is the diagnostic accuracy of the urgency allocation in callers with symptoms suggestive of ACS or TIA/stroke, (ii) which (clinical) determinants are predictive of an ACS or TIA/stroke diagnosis, and (iii) how is the NTS triage system used and how can it be improved in view of balancing efficiency and safety.

METHODS AND ANALYSIS

Design

An observational study in which telephone triage recordings from nine OHS-PC will be evaluated against the clinical outcomes. The researchers will listen to 3,000 real-life recordings, and collect information on the medical history (e.g. history of heart failure, hypertension, ACS, TIA/stroke, diabetes, etc.), caller and symptom characteristics (e.g. onset, duration and severity of symptom(s), additional symptoms (e.g. transpiration, nausea, vomiting, pale skin), pain score in case of chest discomfort, etc.) discussed between the caller and triage nurse during the telephone triage conversations. We will also collect call characteristics (i.e. time of calling, duration of the call, and who calls) and triage information such as the urgency allocation, available from the registered notes of the OHS-PC (i.e. notes from both triage nurses and the supervising GP). All information will be collected on an electronic case record form. Because there is no national Dutch database containing information about diagnoses, we will ask the callers' own GPs to provide the final diagnosis related to the OHS-PC contact, which is based on the patient's medical record, and includes medical specialists' and hospital discharge letters.

Setting

The foundation 'Primair Huisartsenposten' is a collaboration of six different OHS-PC locations in the central part of the Netherlands that provides out-of-hours primary care for approximately 1,5 million residents. It is one of the largest OHS-PC collaborations in the Netherlands and it covers both rural and urban areas. Every OHS-PC location has its own telephone triage centre.

Data collection

All telephone calls are routinely recorded and archived for training, quality control, and research purposes in a computer program called 'Callmanager' (i.e. electronic patient record of the OHS-PC). Archiving is based on the International Classification of Primary Care (ICPC) code.²⁹ ICPC codes allow for classification of symptoms and diagnoses in the electronic patient records. The standardisation of the coding facilitates (inter)national

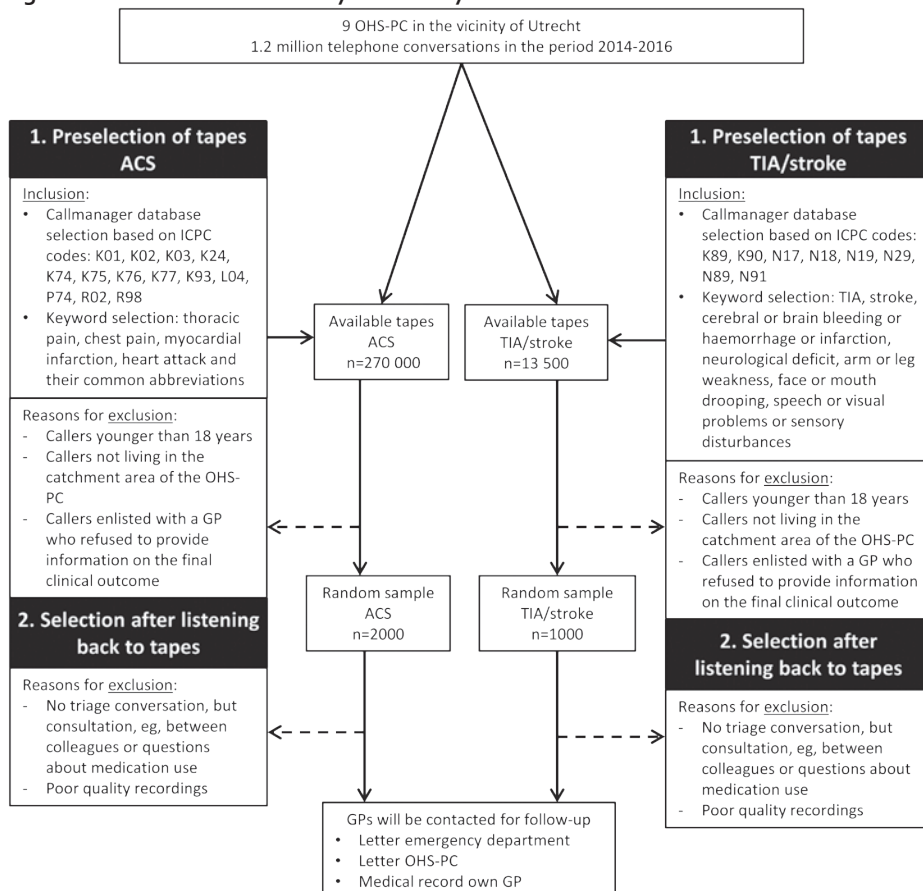
comparison of primary care diagnoses. At Dutch OHS-PC both triage nurses and GPs assign ICPC codes to patient contacts manually. The study sample will be derived retrospectively from all triage recordings in the years 2014 to 2016 and will contain calls linked to the ICPC codes reflecting our study domain: symptoms suggestive of ACS (i.e. K01, K02, K03, K24, K74, K75, K76, K77, K93, L04, P74, R02, R98) and symptoms suggestive of TIA/stroke (i.e. K89, K90, N17, N18, N19, N29, N89, N91). The distribution of sampling of ICPC codes within our study was based on the actual distribution of ICPC codes at the OHS-PC in 2014, and thus best reflects current practice. Per ICPC code a random sample will be taken.

Inclusion and exclusion criteria

Telephone triage recordings of callers of the OHS-PC with complaints that lead to suspicion of ACS or TIA/stroke will be included. The selection of recordings is based on (i) specific ICPC codes and (ii) a selection of keywords used in Callmanager (figure 1). As the specific ICPC codes may not cover all eligible callers due to inter-rater variability as a result of ICPC coding by different triage nurses and GPs^{30,31}, we choose to select cases not only on ICPC codes, but also on keywords in the free text, in order to include a broad but nevertheless clinically realistic' range of patients with possibly typical and less typical symptoms that could be considered to be caused by underlying ACS or TIA/stroke. A major exclusion criterion is other recordings than triage conversations, e.g. calls between colleagues. All exclusion criteria are displayed in table 2.

Table 2. Inclusion and exclusion criteria for participation in the Safety First study

Inclusion criteria	Exclusion criteria
<ul style="list-style-type: none"> Recordings of triage conversations of callers with symptoms suggestive of ACS based on (i) the following ICPC codes in 'Callmanager': K01, K02, K03, K24, K74, K75, K76, K77, K93, L04, P74, R02, R98; and (ii) key word selection: thoracic pain, chest pain, myocardial infarction, heart attack and their common abbreviations. Recordings of triage conversations of callers with symptoms suggestive of TIA or stroke based on (i) the following ICPC codes in 'Callmanager': K89, K90, N17, N18, N19, N29, N89, N91; and (ii) key word selection: TIA, stroke, cerebral or brain bleeding or haemorrhage or infarction, neurological deficit, arm or leg weakness, face or mouth drooping, speech or visual problems or sensory disturbances. 	<ul style="list-style-type: none"> No triage conversation, but consultation between colleagues or questions about medication use Poor quality recordings Callers younger than 18 years Callers not living in the catchment area of the OHS-PC Callers enlisted with a GP who refused to provide information on the final clinical outcome

Figure 1. Flowchart of the Safety First study

Data analysis

- (i) The diagnostic accuracy of the urgency allocation on two separate outcomes: ACS, or TIA/stroke, will be calculated in terms of sensitivity, specificity, positive and negative predictive values. In addition, we will perform sensitivity analyses; a) also considering other emergency cases with chest discomfort, e.g. pulmonary embolism, acute heart failure, and thoracic aortic dissection, or in the domain symptoms suggestive of TIA/stroke; b) other emergency cases with neurological symptoms, e.g. subarachnoid haemorrhage (SAH), epilepsy.
- (ii) Multivariable logistic regression analysis will be applied to identify history items or caller characteristics that independently predict either ACS or TIA/stroke. In addition, multivariable models will be developed that predict the

presence of respectively ACS, or TIA/stroke, and the C-statistic with the 95% confidence interval will be calculated after bootstrapping to correct for over-optimism.³² Before multivariable analysis, multiple imputation techniques will be applied for missing values. Variables with more than 50% missings will not be considered. Variable selection will be based on literature review (known diagnostic predictors in both domains) and on univariable analysis (inclusion of variables with $p < 0.15$). Special attention will be paid to gender and age, either as interaction term or by calculating gender and/or age-specific prediction models. All data analyses will be performed using SPSS statistical software program version 25.0.

Blinding of researchers

All researchers listening to the recordings, and filling out the electronic case record forms or who are otherwise involved in the Safety First study, e.g. the expert panel of one of our additional studies, will be blinded to the callers' clinical outcomes.

Power calculation

For the power calculation we used the recommendations that apply to diagnostic studies. Records of 2014-2016 were used and after application of the exclusion criteria two random samples of 2,000 recordings with 'symptoms suggestive of ACS' and 1,000 recordings with 'symptoms suggestive of TIA/stroke' will be drawn. A prior pilot study showed that 1 out of 9 callers symptoms suggestive of ACS is, after diagnostic work-up, diagnosed with ACS and 1 out of 2 callers symptoms suggestive for TIA-stroke is diagnosed with TIA or stroke. Based on Harrell's rule of thumb, for ACS 2,000 audio-tapes allow for the analysis of 22 variables and for TIA-stroke 1,000 audio tapes allow for the analysis of 50 diagnostic items. We speculated that more variables would be needed to evaluate suspected TIA/stroke cases than patients in the domain 'suspicion of ACS' because the former patients may present themselves with a larger variety of symptoms.³³

ADDITIONAL STUDIES

We explicitly chose to describe the observational cross-sectional study in more detail and not the other three studies because it is the largest study within the Safety First project, and for readability. As part of the Safety First project, three additional but smaller studies will be carried out to further expand the knowledge about the triage process at OHS-PC.

(i) A case-control study on calamities

A calamity is defined as an adverse event with serious permanent patient harm or death as a consequence.³⁴ By Dutch law, root cause analysis (RCA) of every single calamity is required. RCA often points at flaws in the triage process as root causes for such calamities³⁵, resulting in an array of improvement measures for daily practice. However, it is unknown whether cases that result in a calamity really differ from those not evolving into a calamity, as all only have been evaluated as individual cases by experts knowing they evaluated a calamity and their assessment is thus prone to hindsight bias.^{36 37} In the OHS-PC setting calamities are very rare (0.006%) and the majority is of cardiovascular origin, e.g. missed acute myocardial infarction (AMI).³⁵ The aim of this additional study is to provide a more thorough view on missed or too late diagnosed AMIs that resulted in calamities by comparing these cases with matched controls in the domain of callers with chest pain, either due to ACS or not. The main question is whether the calamity cases actually differ from controls with respect to call and patient characteristics. For this additional study we will collect new data (calamity cases) and use data from the larger observational study described earlier for sampling our controls. Archived triage conversations from the period January 2013 – December 2017 of the calamity cases (defined as a missed diagnosis of AMI) will be compared with triage conversations of controls not meeting the calamity definition but also contacting the OHS-PC with symptoms suggestive of ACS. Per calamity case 8 controls will be matched to the case according to age, gender and symptom presentation. A researcher blinded to the outcome will extract information regarding call characteristics, caller and symptom characteristics (including medical history) and urgency allocation, by re-listening the archived triage calls and by using the registered information. All data will be inserted in a database. An expert panel of experienced GPs blinded to the final outcome (calamity or no calamity), thus without case specific hindsight bias, will evaluate the quality and safety of triage conversations, and the diagnostic accuracy (sensitivity, specificity, predictive values) of safe triage handling according to the expert panel will be calculated against the final outcome (calamity or no calamity).

(ii) Conversation analysis study

In this additional study we will assess how conversation aspects may affect the urgency allocation during telephone triage. The ways in which obligatory NTS questions and other questions are formulated by the triage nurse (i.e. suggestive questions), and responded to by the conversation partner may provide more thorough insight into question-answer sequences at the OHS-PC that can be helpful to improve the (use of) the NTS. We will transcribe a sample of the conversations from the case-control

study following the Jefferson conventions. These transcripts that can be considered as new data will then be qualitatively analysed with established conversation analysis techniques.³⁸⁻⁴⁰ We will specifically focus on either/or questions and their various formats (e.g. two-choice, multiple choice, open-ended or tag format) in the urgency decision phase of the triage calls.

(iii) Interview study with triage nurses

Finally, we will perform a qualitative interview study of triage nurses with the aim to gain more knowledge on triage nurses' reasoning during telephone triage of callers with symptoms suggestive of ACS or TIA/stroke, and how they use the NTS for decision making in these two domains. We will conduct semi-structured audio-stimulated recall interviews.⁴¹ Per interview one or two recordings from a recent shift at the OHS-PC will be used to stimulate triage nurses' reflections. The interviews will be transcribed and the transcripts will be qualitatively analysed according to the principles of the grounded theory approach.⁴²

Patient and public involvement

Patients were not directly involved in the design of this study, but representatives participate in the stakeholders meetings every 6 months together with other representatives, i.e. of the local and national OHS-PC organization and the Dutch Health and Youth Care Inspectorate. They provide crucial input that helps us with formulating additional, clinically relevant research questions.

Ethics and dissemination

The Medical Ethics Committee of the University Medical Centre Utrecht, the Netherlands endorsed this study (National Trial Register (NTR) identification number: NTR7331). All personal data, as well as all research data were stored anonymized according to the European General Data Protection Regulation. Data collection started in January 2016 and will last until December 2020. Communications and publications on the results will not enable identification of individual callers. Results will be disseminated to relevant primary care communities in peer-reviewed journals, and at scientific conferences. In addition, this research project will also result in two PhD theses.

DISCUSSION

The Safety First study will provide diagnostic accuracy data on ACS and TIA/stroke in the primary care setting. The efficiency and safety of the NTS in the out-of-hours primary care setting will be evaluated for callers with symptoms suggestive of ACS or TIA/stroke. In a case-control study we will explore calamities (missed acute myocardial infarctions) and assess whether they differ from controls (other patients with symptoms suggestive of ACS but not fulfilling the calamity criteria) with respect to call and patient characteristics. With qualitative studies we will generate more thorough knowledge on how triage nurses work and how the NTS is used.

Efficiency and patient safety

A systematic review about patient safety in the OHS-PC setting concluded that 10% of all OHS-PC calls could be considered as 'unsafe'.⁴³ However, the claim of 'unsafe' calls was based on surrogate markers, and not on patients' clinical outcomes, and clearly contrasts with the very low incidence of calamities (0.006%).³⁵ By using the patients' final clinical outcomes as the reference, the Safety First study will address an important knowledge gap on diagnostic accuracy of telephone triage. In addition, our study will provide a more complete view on the patient safety of the NTS than can be achieved with root cause analysis of individual cases only, often resulting in the conclusion that the urgency level is underestimated.^{35 44} It is difficult to define when telephone triage at the OHS-PC is safe. Our case-control study will provide deeper knowledge on telephone conversations that resulted in calamities and their matched controls. This knowledge might put the general view on (i) analysing calamities, and (ii) the weight that is assigned to improvement measures in a different perspective.

Users of the NTS

A questionnaire among Dutch GPs working at the OHS-PCs reported that a majority of GPs (83.9%) believe that nowadays telephone triage contributes to overconsumption of care at OHS-PC. About 85% of responders consider this to be at least partly attributable to the level of experience and education, and the attitude and personality of the triage nurses.⁴³ As the performance of the NTS is inextricably linked to its users, we want to include conversation analysis and interview studies with triage nurses. The quality of telephone triage is highly dependent on the quality of communication between the triage nurse and the caller, and therefore the communication skills of triage nurses.^{27 45} Moreover, they have to deal with callers who greatly vary in their ability to communicate effectively and coherently.^{46 47} Additionally, the telephone triage is necessarily only based on oral information provided by the caller, lacking

any visual cues or diagnostic information from physical examination. Our additional study on conversation analysis will add knowledge on the ways in which questions and answers are formulated by triage nurses and callers, and how this affects the triage conversation.

Secondly, we will also focus on the obligatory question structure within the NTS, and how this affects the users. The NTS is a semi-automatic support system that is heavily dependent on the input of the triage nurses themselves; which 'main presenting problem' he/she chooses is based on the initial information from the caller, and each of the in total 57 'presenting problems' are linked to a separate algorithm of hierarchically organized, pre-specified questions. These questions need to be filled out before the NTS generates an urgency allocation.⁴⁸ Previous studies suggested that triage nurses may experience interactional dilemmas while working with a computer decision support.⁴⁹ Our interview study will provide more insight into triage nurses' clinical reasoning process during telephone triage, and how they use the NTS for decision making within the domains of callers with symptoms suggestive of ACS or TIA/stroke. This information can help improve the workability of NTS in daily practice. Furthermore, in these domains the knowledge that 'time is muscle' or 'time is brain' puts extra strain on the triage nurse, because unnecessary delays directly affect morbidity and mortality of patients who actually show to have ACS or TIA/stroke.^{22 23} Beside this stress factor, other factors such as shift work, fatigue, multitasking and understaffing can attribute to the risk of errors during the triage process.²⁷ In our interview study we want to include these risk factors, and their possible influence on the reasoning process of triage nurses.

CONCLUSION

Our Safety First study will provide diagnostic accuracy data on ACS and TIA/stroke, and new insights on efficiency, patient safety and the use of the NTS by triage nurses during telephone triage of callers with symptoms suggestive of ACS or TIA/stroke at the OHS-PC. Results from our study will help to improve the telephone triage in these important domains and improve both efficiency and safety for callers.

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3

CHAPTER

Accuracy of telephone triage in primary care patients with chest discomfort: a cross-sectional study

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ABSTRACT

Objectives To assess the accuracy of semi-automatic assisted telephone triage in patients with acute chest discomfort against the diagnosis acute coronary syndrome (ACS) or other life threatening events (LTEs).

Methods Cross-sectional study with telephone conversations of 2,023 patients with acute chest discomfort (pain, pressure, tightness, or discomfort) who called out-of-hours services for primary care (OHS-PC) between 2014 and 2016. Sensitivity, specificity, positive and negative predicted values were calculated for a high urgency (patient seen within one hour) against the diagnoses ACS and other LTEs. Diagnoses were retrieved from the patient's medical records in general practice, including hospital specialists discharge letters.

Results Of 2,023 patients who called for chest discomfort, 227 (11.2%) had an ACS (men 14.9%, women 8.2%) and 58 (2.9%) had another LTE (men 3.6%, women 2.3%). The sensitivity and specificity of a high Netherlands Triage Standard (NTS) urgency allocation against ACS/other LTEs were 0.73 (95% CI 0.68-0.78) and 0.43 (95% CI 0.40-0.45). In 13.2% of the calls, the triage nurse overruled the NTS urgency, mostly by upscaling (11.0%). The sensitivity and specificity of the final urgency allocation were 0.86 (95% CI 0.81-0.90) and 0.34 (95% CI 0.32-0.37). The positive and negative predictive values of the final urgency were 0.18 (95% CI 0.17-0.19) and 0.94 (95% CI 0.92-0.95).

Conclusions The semi-automatic triage NTS tool underestimated the urgency in 27% of patients with ACS/other LTEs. Overruling by triage nurses improved safety, but still 14% of men and women with ACS/other LTEs received a too low urgency, while efficiency remained poor.

INTRODUCTION

Adequate triage followed by early diagnosis is vital in patients with acute chest discomfort. They might have an acute coronary syndrome (ACS) or other life-threatening event (LTE), e.g. pulmonary embolism. Telephone triage of such patients as done in out-of-hours services primary care (OHS-PC) and emergency medical services (EMS or ambulance dispatch centres) is however challenging, because based on symptoms only it is difficult to differentiate ACS/other LTEs from other causes of chest pain. ¹ In the Netherlands 80% of people with chest discomfort first calls the general practitioner (GP) or OHS-PC and 20% directly calls EMS (call 112) for an ambulance or are self-referrals to the emergency department (ED).²

In most Western countries, semi-automatic computer triage systems are used to support telephone decision making. ³ Triage nurses fill out a standard list of hierarchically ordered questions that pops up after the triage nurse choose the patient's main complaint in the computer system, and herewith the computer automatically generates a recommended urgency (one out of six urgency levels). ^{3,4} These triage systems have never been validated in the OHS-PC setting against clinical outcomes as the reference. ⁴

Since 2011, most OHS-PC in the Netherlands and half of the EMS use the Netherlands Triage Standard (NTS). ⁵ In Dutch EDs, both the NTS and the Manchester Triage Standard (MTS) are used. ⁶ The NTS was developed by an expert panel who integrated knowledge from (i) the MTS, (ii) the Dutch national guidelines for general practice ('NHG triage index') and (iii) the Dutch national standard for ambulance dispatch centres ('LSMA'). ⁴ The aim of the NTS was similar to other triage systems to guarantee efficient and safe care. ⁷ The NTS seems safe with 0.006% serious adverse events (SAEs) a year at OHS-PCs (SAE is an unintended or unexpected event resulting in death or a severe harmful event). ⁸ Still, most SAEs are of cardiovascular origin (46.2%), most often missed myocardial infarctions and sudden cardiac death. ^{9,10} More questions are asked about the NTS' efficiency for patients with chest pain. It is the most common reason for allocating an ambulance within 15 minutes (U1) to patients calling OHS-PC (60.7% of all dispatches), but only around 10% actually has an ACS. ¹¹⁻¹³

The aim of our study was to assess the accuracy of telephone triage for patients with chest discomfort who call the OHS-PC with the clinical outcome ACS/other LTE as the reference. Both the accuracy of the NTS tool, and the 'final' urgency including overruling of the triage nurses were evaluated.

METHODS

The study design and data collection have been published in our study design paper.

¹⁴ In short, we performed a cross-sectional study in 2,023 patients who contacted one of nine OHS-PCs in the Netherlands with acute chest discomfort (pain, pressure, tightness, or discomfort) between 2014 and 2016. We selected calls on the basis of International Classification of Primary Care (ICPC; a WHO world-wide code system for primary care) codes (K01, K02, K03, K24, K74, K75, K76, K77, K93, L04, P74, R02, R98) and keywords (thoracic pain, chest pain, myocardial infarction, heart attack and their common abbreviations).^{15 16} On purpose, we sampled broadly to capture the entire domain of patients that could be suspected of ACS.

We used electronic health record (EHR) data of OHS-PC ('Callmanager') and re-listened telephone triage recordings in order to collect information about symptoms, patient and conversation characteristics of patients, and urgency allocation. The final diagnoses were retrieved from the patients' GP, and these were based on hospital specialist discharge letters or GP's diagnoses. For the diagnosis of ACS we used the cardiologist's diagnosis. Patient without elevated levels of (high-sensitivity) troponin were classified as unstable angina pectoris (UAP), and those with elevated levels as myocardial infarction, divided in STEMI (ST-elevation MI) and NSTEMI (non-ST elevation myocardial infarction). Other life-threatening diagnoses were classified by an expert panel of experienced GPs (DZ, FR, RD) based on medical specialist letters (majority of votes).

Context

Triage assessment with the NTS starts with a mandatory 'ABCD-check' (Airway, Breathing, Circulation and Disability); this check determines whether there are direct life-threatening problems for which an ambulance must be sent straight away.¹⁷ When the patient is 'ABCD-stable', the triage nurse has to choose one out of 56 main complaints to continue the urgency assessment. Based on the triage nurses' input, the NTS automatically generates an urgency allocation ranging from U0 (reanimation) to U5 (telephone self-care advice) (Appendix - table 1). The triage nurse can overrule this recommendation and up- or downscale the urgency allocation, often after consulting the supervising GP.⁵ For clarification of the work process in the OHS-PC see an adapted SEIPS (Systems Engineering Initiative for Patient Safety) framework (Appendix - figure 1).¹⁸ In the Netherlands there is a strong primary care, and general practitioners (GPs) take care of 93% of all health care problems for 3% of the total health care budget.¹⁹

The GP has a gatekeeper's role to hospital care, although, people may call EMS (112) in case they suspect is a life-threatening situation.¹⁹

The NTS and final urgency

The NTS urgency was the automatically NTS generated urgency based on the input of the triage nurse. The final urgency was the 'overruled' urgency or the NTS urgency, when not adjusted. In around 15% the final urgency allocation was unclear because of incomplete registration of overruled urgencies. For these cases, an expert panel of three experienced GPs (DZ, FR, IK) independently decided on the final urgency blinded for the outcome (majority of votes) (See also Appendix - figure 2).

Data analyses

We dichotomized urgency allocation in high (U1 and U2) and low (U3, U4 and U5) urgency, and calculated the accuracy of the (i) NTS and (ii) final urgency for allocating a high urgency to patients with the outcome ACS/other LTEs in terms of sensitivity, specificity, positive and negative predictive values. For patient and call characteristics we used the Chi² test for comparison of dichotomous variables and the independent sample t-test or Mann-Whitney U test for continuous variables. We compared baseline characteristics between patients in whom the eventual diagnosis was retrieved to those in whom the GP did not provide these outcomes, to get an impression on whether selection bias could have occurred. Sample size was calculated using Harrell's rule of thumb, which can be found our study design paper.¹⁴ All data analyses were performed using SPSS statistical software program version 25.0.

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, or in developing plans for design, however, they were involved in the implementation of the study. In addition, they were asked to advise on interpretation and writing up of results. Results will be shared and discussed with the national patient community of cardiovascular diseases ('Harteraad').

Ethical approval

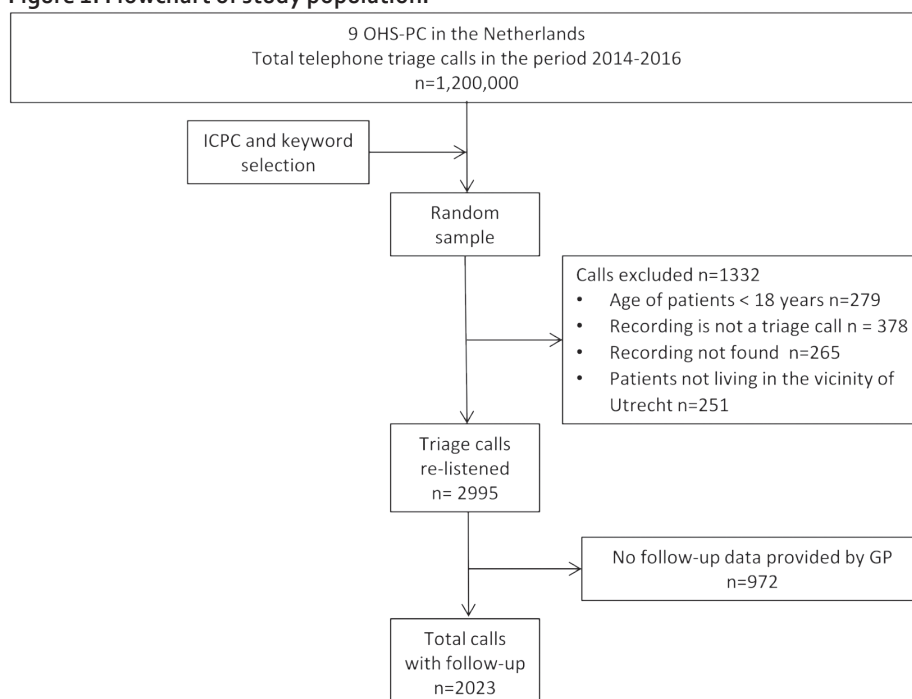
The Medical Ethics Committee Utrecht, the Netherlands (reference number WAG/mb/16/003208; National Trial Register identification number: NTR7331) approved this study. In addition, a waiver of informed consent was given as our study involves no more than minimal risk to subjects and this study could not be carried out practicably without the waiver. All personal and research data were handled and stored according to the European General Data Protection Regulation (GDPR).

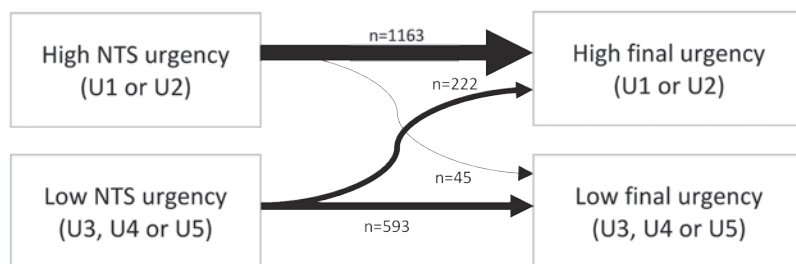
RESULTS

Baseline characteristics

Of the 2,023 patients with acute chest discomfort and a retrieved diagnosis, 227 (11.2%) had an ACS (women 8.2%, men 14.9%), and 57 (2.8%) had another LTE (women 2.3%, and men 3.5%) (Figure 1). The mean age was 58.9 (SD 19.5) years, and 54.9% were women. The NTS allocated 59.7% (men 57.6%, women 61.5%) to a high urgency (U1/U2) and this was 68.5% (men 68.2%, women 68.7%) for the final urgency. Triage nurses overruled in 13.2% of patients the NTS urgency, mostly upscaling (11.0% of all calls) (Figure 2).

Figure 1. Flowchart of study population.





Patients allocated a high urgency were significantly older (62.7 (SD 18.2) years vs. 53.1 (SD 19.9) years, $p < 0.001$), had a shorter mean duration of calls (6:57 min vs. 8:30 min, $p < 0.001$), and more often someone else called on behalf of the patient (58.9% vs. 38.9%, $p < 0.001$) than those allocated a low urgency. Nearly all callers expressed concerns (92.1% vs. 86.4%, $p = 0.003$). In 2.1% of the patients labelled as 'ABCD-unstable' the NTS urgency allocation was downgraded by the triage nurse/GP. When the triage nurse chose for 'shortness of breath' as the main complaint, relatively more patients received a high urgency than when 'chest pain' was the main complaint (73.8% vs. 56.5%, $p < 0.001$).

Patients classified as high urgent had more often acute shortness of breath (71.0% vs. 53.9%, $p < 0.001$), chest pain lasting for less than 12 hours (81.3% vs. 62.5%, $p < 0.001$), heavier chest pain (Numeric Rating Scale > 7 , 46.7% vs. 22.1%, $p < 0.001$) and sweating (47.7% vs. 31.5%, $p < 0.001$). They also more often recognized their symptoms from a previous cardiac event than those who received a low urgency (30.9% vs. 21.5%, $p = 0.002$). Patients with stabbing pain (33.8% vs. 15.0%, $p < 0.001$) or pain located on either the left or right side of the thorax (53.4% vs. 28.6%, $p < 0.001$) were more often classified as low urgent.

There were no clinically meaningful differences in patient or call characteristics between the 2,023 patients with a retrieved diagnosis and 972 patients without a diagnosis (Appendix-table 2).

Table 1. Baseline characteristics of 2,023 patients with chest discomfort (chest pain, pressure, tightness, discomfort) calling OHS-PC, divided in high (U1-U2) and low (U3-U5) NTS urgency.

Characteristics	NTS High urgency n= 1208 (59.7%)	NTS Low urgency n= 815 (40.3%)	p-value
Patient characteristics			
Mean age in years (SD)	62.7 (18.2)	53.1 (19.9)	<0.001
Female sex	683 (56.5)	428 (52.5)	0.074
Call characteristics			
Mean total call duration in min (SD)	6:57 (3:42)	8:30 (3:48)	<0.001
Mean patients' introduction duration in min (SD)	0:18 (0:12)	0:21 (0:14)	<0.001
Triage nurse consulted the GP	643 (53.2)	418 (51.3)	0.391
Someone else called on behalf of patient	711 (58.9)	317 (38.9)	<0.001
Caller has expressed concerns	500 (92.1)	413 (86.4)	0.003
NTS main complaints			
ABCD –unstable	93 (7.7)	2 (0.2)	<0.001
Chest pain	867 (71.8)	668 (82.0)	<0.001
Shortness of breath	121 (10.0)	43 (5.3)	<0.001
Palpitations	33 (2.7)	27 (3.3)	0.450
Back pain	19 (1.6)	7 (0.9)	0.162
Dizziness	11 (0.9)	8 (1.0)	0.871
Arm problems	2 (0.2)	8 (1.0)	0.010
Other	62 (5.1)	52 (6.4)	0.233
NTS triage criteria			
Chest pain	1088 (93.5)	738 (93.5)	0.954
Shortness of breath	664 (71.0)	337 (53.9)	<0.001
Chest pain duration <12 hours	843 (81.3)	453 (62.5)	<0.001
Pain intensity severe (NRS >7, range 1-10)	224 (46.7)	83 (22.1)	<0.001
Pressing heavy chest pain*	623 (73.4)	309 (47.5)	<0.001
Stabbing chest pain*	127 (15.0)	220 (33.8)	<0.001
Chest pain located retrosternal**	401 (51.2)	196 (30.0)	<0.001
Chest pain located left or right on thorax**	224 (28.6)	349 (53.4)	<0.001
Radiation of chest pain to any location	662 (71.5)	341 (54.3)	<0.001
Radiation to the arm	273 (50.8)	151 (34.5)	<0.001
Radiation to the shoulder blades	206 (43.8)	102 (26.2)	<0.001
Radiation to the jaws	93 (26.1)	22 (7.1)	<0.001
Sweating	363 (47.7)	159 (31.5)	<0.001
Nausea or vomiting	308 (55.3)	137 (39.4)	<0.001
Pallor	187 (39.0)	55 (22.8)	<0.001
Dizziness or (feelings of nearly) fainting	274 (26.6)	113 (14.8)	<0.001
History of coronary artery disease	234 (38.6)	127 (27.1)	<0.001
Diabetes mellitus	98 (23.1)	62 (14.8)	0.002

Table 1. (Continued)

Characteristics	NTS High urgency n= 1208 (59.7%)	NTS Low urgency n= 815 (40.3%)	p-value
Other than NTS items, if they were discussed in triage call			
Coin size area of chest pain	77 (45.3)	154 (48.0)	0.571
Tingling sensations on chest, hands or elsewhere	112 (86.8)	97 (79.5)	0.121
Patient recognized symptoms from previous cardiac event	152 (30.9)	76 (21.5)	0.002
CVD risk factors other than diabetes			
Hypertension	190 (43.0)	116 (28.6)	<0.001
Hypercholesterolemia/statin use	103 (28.0)	89 (22.0)	0.056

*Pain described by patient. Pressing heavy pain: pressing, heavy or tightening pain vs. other types of pain (stabbing, burning, cramping, tearing) Stabbing pain: stabbing vs. other types of pain (pressing, heavy, tightening, burning, cramping, tearing)

** P-value comparing retrosternal or left/right side thorax vs. others locations of pain together (retrosternal, left/right side thorax, back/shoulder, epigastric region)

Coronary artery disease: History of MI, PCI, CABG, stable or unstable angina pectoris (patient reported)

Diagnoses

Of the 227 patients with an ACS (91 women, 136 men), 67 (29.5%) patients had a STEMI (women 22.1%, men 33.8%), 93 (40.0%) a NSTEMI (women 46.2%, men 37.5%), 52 (22.9%) unstable angina pectoris (UAP) (women 20.9%, men 24.3%) and 15 (6.6%) unspecified ACS, including three sudden cardiac deaths in women (women 9.9%, men 4.4%) (Table 2). In nearly all cases (97.0%) the ACS diagnosis was from the cardiologist and based on symptom presentation, troponin levels and electrocardiography. Three patients died before arrival of the ambulance (they were classified as acute cardiac death), one patient died after resuscitation at the ED. Three patients were classified as ACS by the GP, while not referred because of short life expectancy due to cancer. Of the 58 patients with other LTEs (2.9%), 13 had a pulmonary embolism, five an acute abdominal aneurysm, five a thoracic aortic dissection and 35 other diagnoses (amongst others diabetic ketoacidosis, sepsis). The majority of patients had non-urgent medical conditions (85.9%); non-urgent cardiovascular diseases (18.7%), non-cardiac chest pain (not further specified) (17.3%), musculoskeletal pain (17.9%), psychogenic disorder (11.2%), gastrointestinal disorders (7.1%), respiratory disorders (5.5%) and other non-urgent diagnoses (8.4%).

Table 2. Diagnosis of 2,023 patients who contacted the OHS-PC for chest discomfort (pain, pressure, tightness, or discomfort), divided in NTS high (U1-U2) and low urgency (U3-U5).

Diagnosis, n (%)	NTS High urgency n= 1208 (59.7%)	NTS Low urgency n= 815 (40.3%)	p-value
Acute coronary syndrome	171 (14.2)	56 (5.6)	<0.001
STEMI	51 (29.8)	16 (28.6)	0.858
NSTEMI	71 (41.5)	22 (39.3)	0.768
UAP	38 (22.2)	14 (25.0)	0.668
Non-classified ACS	11 (6.4)	4 (7.1)	0.853
Other life threatening events (LTEs)	38 (3.1)	20 (2.5)	0.361
Pulmonary embolism	6 (15.8)	7 (35.0)	0.095
Acute abdominal aneurysm	5 (13.2)	0 (0.0)	0.151
Thoracic aortic dissection	3 (7.9)	2 (10.0)	0.786
Other*	24 (63.2)	11 (55.0)	0.546
Non-urgent cardiovascular diseases**	257 (21.3)	121 (14.8)	<0.001
Non-cardiac chest pain, not further specified ***	180 (14.9)	169 (20.7)	0.001
Musculoskeletal pain	173 (14.3)	189 (23.2)	<0.001
Psychogenic disorders	116 (9.6)	110 (13.5)	0.006
Gastrointestinal tract disorders	97 (8.0)	46 (5.6)	0.040
Respiratory tract disorders	66 (5.5)	45 (5.5)	0.955
Other non-urgent diagnoses****	110 (9.1)	59 (7.2)	0.137

* Stroke, severe COPD exacerbation, acute severe heart failure, sepsis, coronary spasm caused by hypokalaemia, diabetic ketoacidosis, epileptic insult, bleeding from oesophageal varices, ovarian torsion, ventricular fibrillation.

** Stable angina pectoris (including atypical chest pain), stable heart failure, arrhythmias, hypertension

*** Cardiac pathology unlikely after cardiologist's or GP's diagnostic work-up, but without differential diagnosis

**** Amongst others: anaemia, carcinoma, vasovagal collapse, side effects medication, dermatologic diseases

Relation diagnosis and urgency allocation

Patients with an ACS had received a NTS high urgency in 75.3% (women 74.7%, men 75.7%), and final high urgency in 88.5% (women 89.0%, men 88.2%). Patients with another LTE received a NTS high urgency in 65.5% (women 76.0%, men 57.6%), and a final high urgency in 74.1% (women 84.0%, men 66.7%). Of the 41 ACS/other LTE patients who had received a final low urgency most were categorized as U₃ (87.8%), and a minority as U₄ (7.3%) or U₅ (4.9%) (Table 3).

Patients with non-urgent cardiovascular diseases were more often classified as high-urgent (21.3% vs. 14.8%, $p < 0.001$) and patients with psychogenic disorder as low-urgent (9.6% vs. 13.5%, $p = 0.006$).

Table 3. Overview of the NTS and final urgency allocation of 285 patients with ACS or LTEs

	Final U ₁	Final U ₂	Final U ₃	Final U ₄	Final U ₅	Total
NTS U ₁	153	14	1	0	0	168
NTS U ₂	16	24	0	0	1	41
NTS U ₃	20	9	34	0	0	63
NTS U ₄	0	0	0	0	0	0
NTS U ₅	4	4	1	3	1	13
Total	193	51	36	3	2	285

NTS urgency: NTS urgency allocation, retrieved from electronic health record

Final urgency: the overruled urgency, retrieved from re-listening calls

Black: the NTS urgency and final urgency were the same

Blue: the user (triage nurse in coordination with the GP) has scaled up the urgency

Red: the user (triage nurse in coordination with the GP) has scaled down the urgency

Accuracy NTS and final urgency

The NTS high urgency had a sensitivity of 0.73 (95% CI 0.68-0.78), specificity of 0.43 (95% CI 0.40-0.45), positive predictive value of 0.17 (95% CI 0.16-0.19), and negative predictive value of 0.91 (95% CI 0.89-0.92) for the outcome ACS/other LTE (Table 4). For the final urgency this was: sensitivity 0.86 (95% CI 0.81-0.90), specificity 0.34 (95% CI 0.32-0.37), positive predictive value 0.18 (95% CI 0.17-0.19) and negative predictive value 0.94 (95% CI 0.92-0.95).

Table 4. Accuracy outcomes of the NTS and final high urgency allocation (U₁/U₂) against ACS or other LTEs.

Accuracy outcomes Value (95% CI)	NTS high urgency	Final high urgency
ACS -LTE prevalence 14.1%		
Sensitivity	0.73 (0.68-0.78)	0.86 (0.81-0.90)
Specificity	0.43 (0.40-0.45)	0.34 (0.32-0.37)
Positive predictive value	0.17 (0.16-0.19)	0.18 (0.17-0.19)
Negative predictive value	0.91 (0.89-0.92)	0.94 (0.92-0.95)

DISCUSSION

The safety and efficiency of the Dutch NTS decision support tool were rather poor for telephone triage at OHS-PC in patients with acute chest discomfort, given the sensitivity (0.73) and specificity (0.43) for high urgency allocation of patients who had an ACS/other LTE. Safety improved after intervening of the triage nurse; the final high urgency had a sensitivity of 0.86 and specificity of 0.34.²⁰ Women and men with ACS/other LTE received equally high urgencies. At a prevalence of ACS/other LTE of 14.1% (11.2% and 2.9%, respectively), the positive predictive value for both the NTS and final urgency was low (0.17 and 0.18, respectively) and the high negative predictive value high (0.91 and 0.94, respectively).

Clearly, the triage system is calibrated on the safe side. Most GPs highlight the over triage, but in our opinion, in the critical domain of patients with chest discomfort under triage should receive more attention.^{19,5,21} It is evident that patients with an ACS and those classified with other LTEs should receive a high urgency allocation, but the NTS classified 27% of the ACS/LTE patients as low urgent, and this was still rather high for the final urgency (14%).

We were able to analyse the original and very first conversation with patients, and these conversations were assessed without knowledge of the diagnosis; the assessment of symptoms was not affected by recall or hindsight bias. Moreover, we were able to include a large sample of patients and missing outcome data did not lead to patient or call selection. We therefore are confident our results are well generalizable, not only to Dutch settings but also to similar OHS-PC settings, e.g. UK and Scandinavian countries.¹ Our results may also be generalizable to EMS settings, because the prior chance of having an ACS among those calling for chest discomfort is rather similar in the EMS setting as in the OHS-PC setting.^{13,22}

A limitation is that in 15% of calls the overruled urgency was unclear. In these cases, an expert panel (blinded to the clinical outcome) decided on all available information to be heard in the calls.

We could not find studies evaluating the accuracy of telephone triage in the OHS-PC among patients with chest discomfort against clinical outcomes. A systematic review of six studies evaluating the Manchester Triage Standard (MTS) in the ED setting reported that the MTS had allocated a high urgency in patients who showed to have an ACS with a sensitivity of 0.70-0.80.²³ One of these six studies also reported specificity

(0.59) among patients with chest pain referred to a Portuguese ED.²⁴ Thus, the MTS, with the advantage of face-to-face contact seems to have a similar sensitivity and somewhat higher specificity as seen in our study. Interestingly, the prevalence of ACS among the 233 patients with chest pain in the Portuguese study was lower than in our study (9.4% vs. 11.2%).²⁴ None of the studies reported positive and negative predictive values, which prevented us from comparing these to ours. The prior risk of ACS and LTEs of 14.1% changed only marginally with 17% and 18%, for the NTS and final high urgency, respectively, and to 9% and 6% for the NTS and final low urgency allocation. To the best of our knowledge, there are no accuracy studies performed in the EMS-setting in which urgency allocation with EMS (112 or 911) telephone triage was compared to presence or absence of ACS. In an observational Swedish study among 14,454 patients calling EMS for chest discomfort, 63.5% received an urgency 1 ambulance and 11.5% turned out to have an ACS (women 9% and men 14%).²² An EMS study from USA with 3,007 calls of patients with acute chest pain to the Medical Priority Dispatch System (MPDS) for decision support reported a prevalence of 8.7% of acute myocardial infarction.²⁵

In a primary care study, the GP's clinical gestalt was more accurate in predicting ACS than a prediction rule (c-statistic 0.75 vs. 0.66) in patient with acute chest discomfort.²⁰ This is in line with our finding that the sensitivity of the final urgency (including over-ruled cases) was higher than that of the NTS alone (0.86 vs. 0.73). Previous studies reported that the risk of ACS in women was underestimated, a finding in contrast to our result in which women and men with ACS received similarly high urgency allocation.^{26 27} One of the former mentioned EMS studies also found women and men received similarly high urgency allocation, the other EMS study did not report sex-stratified analyses.^{22 25}

Missing an ACS is the most common reason for malpractice claims worldwide.^{9 28} There are no generally accepted guidelines that define what rate of missed ACS is considered acceptable, and this threshold will likely differ among different health care providers. A survey performed among 1,029 ED doctors in the US, New Zealand and Australia showed that they considered on average a missing rate between 0.1-1% (range 0-10%) as acceptable.²⁹ We do not have such information from GPs or lay people, but we suspect that this will be rather similar in the Netherlands. Alarming, this number is not in line with our finding that 27% of patients with ACS/other LTEs received a NTS' low urgency allocation and a 14% final low urgency allocation. Indeed, a low urgency allocation does not necessarily mean the ACS is being missed, yet still an undesirable patient safety risk has been taken for the hazard of life-threatening

ventricular arrhythmias and sudden death due to severe pumping failure of the heart in those with AMI.^{30 31} On the other hand, triage nurses and their supervising GPs increased triage safety by overruling the decision support system adequately, though with significantly increasing over triage. Apparently, the 'human factor' remains conducive for safety in the current telephone triage process.^{18 32} Nonetheless, potential room for improvement should be studied, both of the decision support tool itself by developing better diagnostic prediction rules as well as by improving its use by triage nurses and management.³³

CONCLUSION

The semi-automatic triage NTS tool underestimated the urgency in 27% of patients with ACS/other LTEs. Overruling by triage nurses improved safety, but still 14% of men and women with ACS/other LTEs received a too low urgency, while efficiency remained poor.

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APPENDICES

Appendix – table 1. NTS urgency levels

NTS Urgency level	Definition	Response time	Medical help
U ₀ – Resuscitation	Loss of vital functions	Immediately	Ambulance
U ₁ – Life threatening	Unstable vital functions	Immediately, within 15 minutes	Ambulance
U ₂ – Emergent	Vital functions in danger or organ damage	As soon as possible, within 1 hour	Home visit by GP or consultation at OHS-PC
U ₃ – Urgent	Possible risk of damage, human reasons	A few hours (<3 hours)	Home visit by GP or consultation at OHS-PC
U ₄ – Non-urgent	Marginal risk of damage	24 hours	Consultation at OHS-PC or telephone advice
U ₅ – Advice	No risk of damage	Advice, no time related	Telephone advice

GP: General practitioner

NTS: Netherlands Triage Standard

OHS-PC: Out-of-hours services for primary care

Appendix – Table 2. Patient and call characteristics of 2,995 patients with chest discomfort calling OHS-PC, comparing patients with and without follow-up information on diagnosis

Characteristics	Follow-up n= 2023 (%)	No follow-up n= 972(%)	P-value
Patient characteristics			
Mean age in years (SD)	58.9 (19.5)	57.4 (20.2)	0.055
Female sex	1111 (54.9)	533 (54.8)	0.966
Urgency			
NTS urgency high	1208 (59.7)	540 (55.6)	0.031
Final urgency high	1384 (68.5)	625 (64.7)	0.038
Call characteristics			
Mean total call duration in min (SD)	7:34 (3:49)	7:31 (3:37)	0.093
Mean patients' introduction duration in min (SD)	0:19 (0:13)	0:19 (0:14)	0.370
Triage nurse consulted the GP	1061 (52.4)	509 (52.4)	0.967
Someone else called on behalf of patient	1028 (50.8)	458 (47.1)	0.058
The person who calls expressed concerns	913 (89.4)	402 (89.3)	0.959
NTS entry complaints			
Breathing	58 (2.9)	32 (3.3)	0.523
Circulation	37 (1.8)	11 (1.1)	0.155
Chest pain	1535 (75.9)	731 (75.2)	0.688

Appendix – Table 2. (Continued)

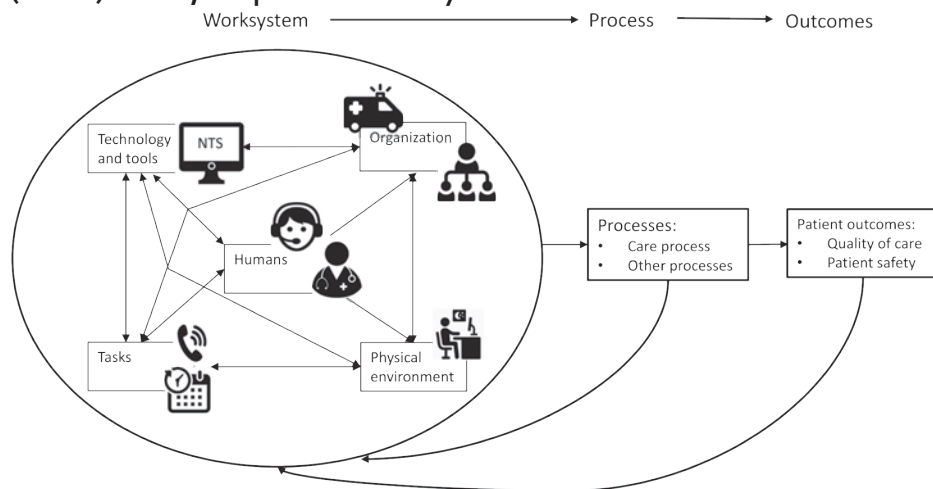
Characteristics	Follow-up n= 2023 (%)	No follow- up n= 972(%)	P-value
Shortness of breath	164 (8.1)	95 (9.8)	0.129
Palpitations	60 (3.0)	29 (3.0)	0.979
Back pain	26 (1.3)	6 (0.6)	0.096
Dizziness	19 (0.9)	8 (0.8)	0.753
Arm complaints	10 (0.5)	6 (0.6)	0.666
Other	114 (5.6)	54 (5.6)	0.929
NTS triage criteria			
Chest pain	1826 (93.5)	856 (92.3)	0.252
Shortness of breath	1001 (64.2)	509 (65.7)	0.472
Chest pain duration <12 hours	1296 (73.6)	569 (68.7)	0.011
Pain intensity severe (NRS >7)	307 (35.9)	172 (42.5)	0.024
Pressing chest pain*	771 (51.4)	354 (50.9)	0.828
Stabbing chest pain*	347 (23.1)	167 (24.0)	0.651
Chest pain located retrosternal**	597 (41.6)	283 (40.7)	0.688
Chest pain located left or right on thorax**	573 (39.9)	265 (38.1)	0.418
Radiation of chest pain to any location	1003 (64.5)	439 (59.6)	0.021
Radiation to the arm	424 (43.5)	175 (37.0)	0.019
Radiation to the shoulder blades	308 (35.9)	124 (29.4)	0.021
Radiation to the jaws	115 (17.3)	45 (13.1)	0.088
Sweating	522 (41.2)	239 (40.7)	0.833
Nausea or vomiting	445 (49.2)	211 (47.6)	0.595
Pallor	242 (33.6)	107 (29.2)	0.137
Dizziness or (feelings of nearly) fainting	387 (21.6)	211 (23.5)	0.260
Coronary artery disease	361 (33.6)	157 (32.0)	0.531
Diabetes mellitus	160 (19.0)	72 (18.8)	0.933
Other than NTS items, if they were discussed in triage call			
Point or coin size area of chest pain	231 (47.0)	99 (41.9)	0.196
Tingling sensations on chest, arm or else	209 (83.3)	71 (78.9)	0.352
Patient recognized symptoms from previous cardiac events	228 (27.0)	86 (24.3)	0.340
CVD risk factors other than diabetes			
Hypertension	306 (36.1)	117 (31.7)	0.140
Hypercholesterolemia/statin use	192 (24.9)	87 (24.9)	0.996

* P-value comparing pressing or stabbing vs. the others types of pain together (pressing, stabbing, burning, cramping, gnawing)

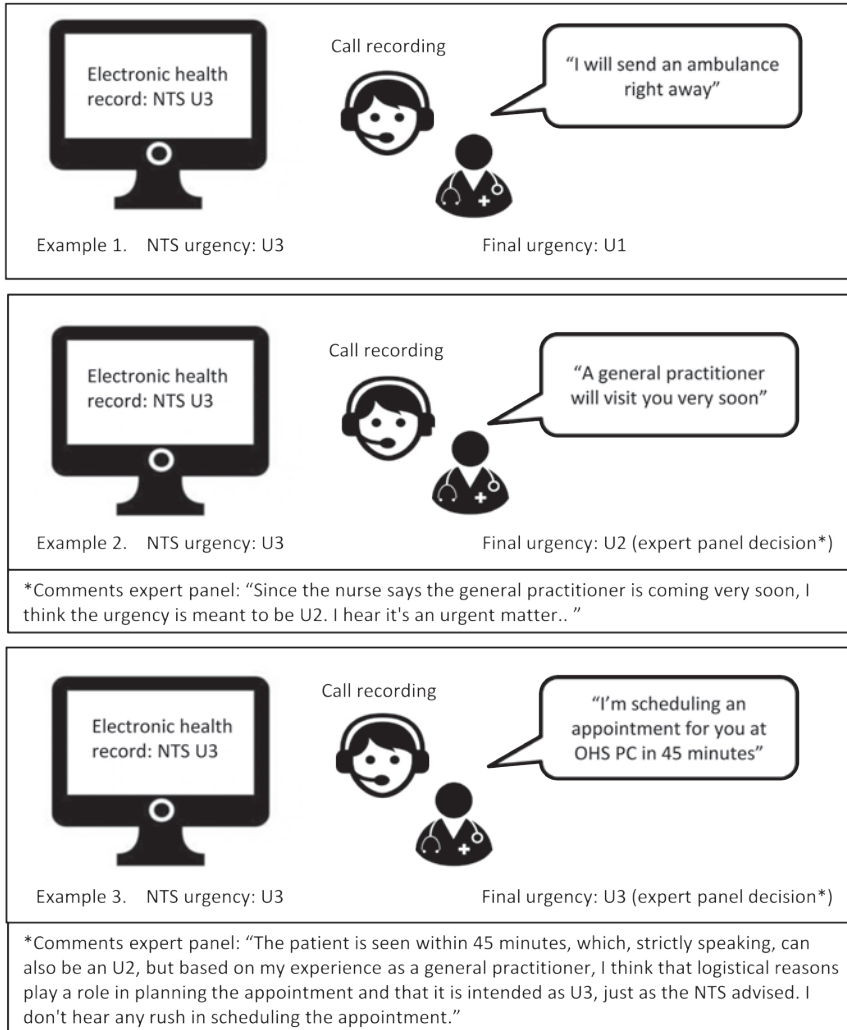
** P-value comparing retrosternal or left/right side thorax vs. others locations of pain together (retrosternal, left/right side thorax, back/shoulder, epigastric region)

Coronary artery disease: patient reported history of myocardial infarction, stable or unstable angina pectoris

Appendix-Figure 1. The Systems Engineering Initiative for Patient Safety (SEIPS) model, adapted from Carayon ¹⁸



Appendix-Figure 2. Examples of urgency adjustments and process of expert panel defining the final urgency.





4

CHAPTER

Tinkering and overruling the computer decision support system: working strategies of telephone triage-nurses who assess the urgency of callers suspected of having an acute cardiac event

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ABSTRACT

Aims and objectives Our aim is to understand clinical reasoning and decision making of triage-nurses during telephone conversations with callers suspected of having acute cardiac events, and support from a computer decision support system (CDSS) herewith.

Background In telephone triage, nurses assess the urgency of callers' conditions with clinical reasoning, often supported by CDSS. The use of CDSS may trigger interactional workability dilemmas.

Design Qualitative study using principles of a grounded theory approach following COREQ-criteria for qualitative research.

Methods Audio-stimulated recall interviews were conducted amongst twenty-four telephone triage-nurses at nine out-of-hours primary care centers (OHS-PC).

Results Telephone triage-nurses use clinical reasoning elements for urgency assessment. Typically in telephone triage, they interpret the vocal – but not worded-elements in communication (paralanguage) such as tone of voice and shortness of breath and create a mental image in order to compensate for lack of visual information. We confirmed that interactional workability dilemmas occur. Congruence, established when the CDSS supports the triage-nurses' decision making, is essential for the CDSS' value. If congruence is absent, triage-nurses may apply four working strategies: (i) tinker to make CDSS final recommendation align with their own assessment, (ii) overrule the CDSS recommendation, (iii) comply with the CDSS recommendation or (iv) transfer responsibility to the GP.

Conclusion Triage-nurses who assess urgency may experience absence of congruence between the CDSS and their decision making. Awareness how triage-nurses reason and make decisions about urgency and what aspects influence their working strategies can help in achieving optimal triage of callers suspected of acute cardiac events at OHS-PC.

Relevance to clinical practice Triage-nurses' reasoning and their working strategies are vital for outcome of triage decisions. Understanding these processes is essential for CDSS developers and OHS-PC managers, who should value how triage-nurses interact with the CDSS, while they have the benefit of callers in mind.

INTRODUCTION

Telephone triage is the gateway to medical help for patients in primary care in the Netherlands¹. Accurate triage is of vital importance, specifically for the identification of highly urgent cases, such as patients who are suspected of having an acute cardiac event.^{2,3} Triage-nurses assess the urgency of the patient's health problem; should an ambulance be sent right away or is consultation at the out-of-hours service sufficient? Urgency assessment may be seen as a clinical reasoning process of triage-nurses.⁴ Clinical reasoning has been studied in physical triage.^{5,6} However, clinical reasoning during telephone triage, a situation where triage-nurses have limited clinical information, is not well investigated.^{7,8}

In most Western countries, computer decision support systems (CDSS) are used to support telephone triage decision making.⁹ Commonly used CDSS are constructed as a list of questions; starting with questions that ask for an immediate medical response, and gradually questions come up about symptoms which allow for a longer response time.¹⁰ The use of CDSS in telephone triage has a complex dynamic which can induce many, so-called, 'interactional workability dilemmas'.^{11,12} Interactional workability dilemmas may be described as difficulties between the rigid CDSS structure and the wider context of the patients' narrative.¹² The use of CDSS in telephone triage has been investigated during day practice of general practitioners and in a study about telenurses handling calls patients with chronic obstructive pulmonary disease (COPD).^{12,13} These situations differ from the triage of patients suspected of acute cardiac events³ because urgency and time pressures may specifically trigger interactional dilemmas with CDSS in the triage assessment.

Out-of-hours primary care (OHS-PC) are general practice cooperatives which were set up for urgent help requests that could not wait until the daytime consulting hours of the patient's general practitioner (GP).¹⁴ In the Netherlands, triage-nurses handle calls independently with a GP stand-by to consult in difficult situations. In the OHS-PC, the GP stand-by and the triage-nurses are not familiar with the callers and their medical history. In the Netherlands, the triage system is overall safe, with only 0.006% serious adverse events a year.¹⁵ A serious adverse event is defined as an unintended or unexpected event related to the quality of care and resulting in death or a severe harmful event for the patient.¹⁶ The majority of serious adverse events is of cardiovascular origin, such as missed myocardial infarction.¹⁵

It is unknown how triage-nurses reason during their out-of-office hour's telephone conversations. These conversations are under time-pressure when callers are suspected of having acute cardiac events.

Rationale and research questions

Our aim is to understand clinical reasoning and decision making of triage-nurses during telephone conversations, under time-pressure with callers suspected of having acute cardiac events, and support of these processes from a CDSS. Such understanding is necessary to improve the workability of the CDSS and to optimize support for triage-nurses.

Our research questions are:

1. How do triage-nurses reflect on their reasoning elements and decisions which took place during their telephone conversations for triage of callers suspected of having acute cardiac events?
2. How do triage-nurses use a CDSS to support their clinical reasoning and decision making during these telephone conversations?

Given our interest in clinical reasoning, relevant theories were the hypothetico-deductive approach, the intuitive humanistic approach and the dual-process theory.^{4 17} For the use of the CDSS and interactional aspects, we employ the interactional workability theory.^{11 12}

Clinical reasoning

The hypothetico-deductive approach aims to understand how clinicians make decisions and hypotheses as if they are logical, rational decision-makers.¹⁸ It assumes that reasoning starts with gathering information, from which cues are used to generate preliminary hypotheses about a specific diagnosis or list of differential diagnoses. The professional interprets and classifies cues as confirmatory, negative or non-contributory to the hypotheses. The professional weighs each alternative hypothesis and then chooses the one supported by evidence.^{19 20} Knowledge and experience are required to process information into reliable hypotheses successfully.

The hypothetico-deductive approach was found to be abstract and difficult to apply in real-life decisions, and hence, the importance of intuition was recognized.²¹ The intuition-humanistic approach was defined in six key aspects: pattern recognition, similarity recognition, common sense understanding, skilled know-how, sense of salience, and deliberate rationality.⁴ Intuitive judgments are said to be unaware and

intrinsic, often referred to as a 'gut-feeling', 'hunch' or 'sixth –sense'.²² However, intuition was never seen as in opposition to traditional analytical reasoning. Although one is considered to be unaware of intuitive judgments, the process involves rational elements of knowledge.^{23 24} For example, the assessment of the vital sign pain, an indicator of a patient's acuity, entails both intuitive and rational elements.²⁵

The concurrent use of rational and intuitive decision elements comes together in the dual-process theory.¹⁷ The dual-process theory consists of system one reasoning, which is automatic, fast and intuitive, and system two reasoning, which is deliberate, reliable and analytical.²⁶ Croskerry suggested that these reasoning systems work separate from one another, in stages.²⁶ In contrast, Norman said the systems work together in a continuum, and the reasoning processes are parallel and complementary.^{20 27} Furthermore, Croskerry argued that system one reasoning is more susceptible to cognitive biases, because it heavily relies on heuristics, and he suggested that cognitive biases may be reduced by slowing down the reasoning.²⁸ The evidence for the effect of slowing down strategies is scarce: in contrast, several studies show that faster response times are more often associated with a correct diagnosis.²⁴ Norman proposed that prior experience and knowledge is more important to reduce cognitive biases.^{24 27}

Reasoning during triage

In assessing the urgency, the triage-nurse uses the caller's response to the CDSS questions and the CDSS recommendation, which consists of one out of six possible urgency levels (Appendix-Table 1).¹⁰ Previous studies assessing physical triage by nurses identified that decisions were based both on analytical and non-analytical reasoning strategies.^{6 29} With an increase in experience, triage-nurses' decisions became more based on intuition.⁴ Experienced nurses relied more on behavioural cues, time factors and medical, social and contextual factors to judge the patients' complaints.^{30 31} During telephone triage, nurses have to deal with the absence of physical parameters and compensate for this lack of information, by creating a mental image of the patient and the situation from which the call is made.^{7 32}

Interactional workability

The aim of using a CDSS is to standardize and thereby presumably increase the accuracy and reliability of nurses' urgency decisions.^{4 31} However, there are limits to standardization because general rules may underdetermine what should be done in a specific case.³³ Interactional workability is the way that a complex intervention, such as a CDSS, affects interactions between people and their work processes.¹¹ During telephone triage, the interaction is between the patient, the triage-nurse and

the CDSS.¹² Interactional workability is characterized by the dimensions *congruence* and *disposal of work*.¹¹ *Congruence* in the interactions between the intervention, the users' role, and the context is key to promote the ease of use and efficiency of the intervention. *Disposal of work* considers how the interactions with (technical) interventions, such as the CDSS, contribute to the fulfilment of the purpose of the intervention (e.g. following a guideline).¹¹ Congruence in the interactions gives rise to disposal of work. The introduction of a CDSS for triage systems seems to reduce the nurses' opportunities for making their own judgments.³¹ In practice, triage-nurses rarely use the recommendations from the CDSS in isolation. Instead, they combine and compare digital, clinical and subjective patient information to identify any conflicts.¹³
³⁴ The level of experience influences how nurses use decision support. Novice nurses said they carefully followed the guidelines, whereas more senior triage-nurses said they have internalized the guidelines and use these alongside their own judgment.⁶

METHODOLOGY

We designed a qualitative study using the principles of a grounded theory approach.
³⁵ ³⁶ Twenty-four triage-nurses from nine OHS-PC locations were invited for semi-structured audio stimulated recall interviews.³⁷ The Consolidated criteria for Reporting Qualitative Research (COREQ) were used to report the findings of this study (see supplementary file 1).

Context

The study was conducted at nine OHS-PC locations in the Netherlands, who collaborate in the foundation 'Primair Huisartsenposten'.³⁸ This foundation provides care for approximately 1.5 million residents in the Netherlands, covering both rural and urban areas. The triage-nurses working at the OHS-PC are required to have a 3-year education for certified primary care nursing assistant and a specific training for telephone triage about how to use the CDSS the Netherlands Triage Standard (NTS, a modified version of the Manchester Triage Standard).³⁹ ⁴⁰ Since the introduction of the NTS in 2011 in the Netherlands, this system has been used by most OHS-PC, by approximately half of the ambulance dispatch centers and by an increasing number of emergency departments.¹ The triage-nurse fills out the caller's responses in the semi-automatic NTS system, which then automatically generates urgency allocations. The urgency level generated by the NTS can be adjusted by the triage-nurse if the nurse disagrees with the NTS advice. Most often, adjustments are preceded by consultation of the supervising GP, who has the final responsibility for the urgency level decision.

¹⁴ All telephone calls to the OHS-PC locations are routinely recorded and archived for training and quality control purposes.

Recruitment procedures

Recruitment of participants was done by the research team members, who initially contacted the triage-nurses managers. The manager asked the triage-nurses in their team who was interested in reflecting on their clinical reasoning during telephone triage. We encouraged the managers to maximise variation of sampling, to gather triage-nurses with varying levels of experience in telephone triage and experience in health care elsewhere. We have no insight in how many triage-nurses refused to participate, but as the triage-nurses were enabled to participate within working hours, we assume there were no other than practical reasons to refuse. Triage-nurses who expressed themselves as senior in general had at least six years of working experience in telephone triage in the OHS-PC. When a triage-nurse was recruited by the manager, the research team members made an appointment for an interview of one hour at their OHS-PC. Before the interview, the triage-nurses were asked to focus on triage conversations in which they suspected that the caller had an acute cardiac event, during telephone shifts in the two weeks before the interview. We encouraged them specifically to bring forward not only conversations of 'clear' cases, but also cases in which the triage-nurse was uncertain about his or her urgency assessment. The research team members retrieved the recordings of these conversations from the recording archive. All interviews were conducted between July 2016 and July 2018 by three researchers (LW, MH, DE). The researchers introduced themselves to the triage-nurses as GP-trainees and researchers in the field of telephone triage of acute cardiac events.

Design

We performed face-to-face semi-structured interviews, using audio stimulated recall technique. Every interview, we started with listening to an audio tape of a telephone triage conversation. This technique helps the participant to give meaning to and reflect on their behavior in a real life situation. ⁴¹ A topic list comprised of open questions about clinical reasoning and working with the CDSS was used as a framework (appendix 2). All interviews were audio-taped and subsequently transcribed verbatim for analysis. In addition, triage-nurses completed a 6-question questionnaire about their education, working experience at the OHS-PC and whether they had working experience in patient care elsewhere.

Research team

Our research included three female GPs in training (LW, MH, DE), of which two clinician-scientists who combine the GP specialty training with a PhD-project (LW, DE) about telephone triage. Since these researchers were in training and had limited clinical experience, they had no assumptions beforehand about clinical reasoning and workability with the NTS. Four members of the team were experienced researchers in primary care clinical research (female DZ and males FR, AH, RD) of which one a practicing GP who has a special interest in mixed methods studies on quality and patient safety (DZ) and two with a special interest in cardiovascular diseases (FR, AH). RD is a practicing GP and the director of the GP specialty training. Finally, in the team was one female researcher qualified in the learning sciences and qualitative research (EdG).

Ethical approval

This interview study is part of a mixed-method study about telephone triage in patients suspected of having acute cardiac events³⁸; the study was approved by the Ethical Review Board of the UMC Utrecht. Anonymity was guaranteed and participation was voluntary. Informed consent of the participants was obtained at the beginning of each interview.

Data-analysis

Data were analyzed with constant comparison within and between cases, using both deductive and inductive approaches.^{35,36} We took an approach according to the principles of a grounded theory (iterative and focused on theory development) for the inductive analysis of the data about the CDSS use, and we took a deductive approach for the analysis of reasoning strategies. Coding was done using NVivo version 11, qualitative data analysis software. Two researchers (LW, MH) studied independently in iterative cycles of four transcripts and started with open coding. They discussed their findings with a third researcher (EdG) until consensus was achieved. The codes were identified through active interaction with the data by carefully reading each line and memo writing. The initial codebook was developed through reading and coding the first nine transcripts and discussed with a third and fourth researcher (EdG, DZ). The codes were categorized, and each theme was compared across all participants, in order to investigate, clinical reasoning strategies and working with the CDSS. Sixteen interviews were independently coded by two researchers (LW, MH) and five interviews were coded by one researcher (LW). From then on, a framework was developed and improved through axial and thematic coding. The final coding was then applied to the last three transcripts by three researchers to confirm the emergent theory (EdG,

DZ, DE). The remaining research team members discussed and approved the analysis during the development of the final manuscript (FR, AH, RD). Researcher triangulation was achieved through discussions about our findings with a research team with diverse research and working backgrounds. In addition, we discussed our results with members of the national association of primary care organizations, and with GPs with additional training and skills in acute care; the attending triage-nurses and GPs in these meetings recognized our findings as relevant and representative for daily practice at OHS-PC.

RESULTS

Baseline characteristics of the participants are presented in Table 1. Variety was achieved in all the relevant characteristics such as education level, telephone triage working experience and other working experience in health care with direct patient observations. Most of the respondents were women (91.6%).

Table 1. Baseline characteristics of triage-nurse participants (n=24)

Median age (IQR) in years	46 (36.5-53.5)
Gender	22 women, 2 men
Education level	20 nursing assistants, 2 nurses, 1 medical student and 1 nurse practitioner
Education for telephone triage assessment	17 triage-nurses have completed the formal education for telephone triage assessment, 7 are in training
Working experience as telephone triage-nurse in the OHS-PC	1 < one year, 9 one-three years, 5 four-six years, 9 > six years
Previous working experience elsewhere with direct patient observations	14 triage-nurses have worked or currently work with direct patient observations, 10 have never worked with direct patient observations
Present working experience elsewhere with direct patient observations	12 triage-nurses currently work with direct patient observations, at the following settings: <ul style="list-style-type: none"> • 8 in GP daycare practice • 3 in hospital • 1 in homecare

Clinical reasoning

The analyses showed that triage-nurses combined elements of the hypothetico-deductive approach with elements of the humanistic-intuitive approach in their clinical reasoning. Triage-nurses gathered information, use their knowledge about diseases and test hypotheses about the disease(s) of concern. Within the humanistic-intuitive approach, triage-nurses used pattern recognition, intuition, and they created a mental

image of the patient to compensate for the lack of visuals during telephone triage. The more senior triage-nurses tended to ask more questions beyond the required CDSS' questions during the telephone conversations. They aimed to gather in-depth information about the symptoms and the patient's context and wishes. In our analyses, there were no remarkable differences in clinical reasoning between nurses who work or have worked elsewhere in health care with direct patient contact. Furthermore, we found triage-nurses were aware of potential cognitive biases in their reasoning, described in the literature about the dual-process theory.³⁷

"She said straight off that she was sweating because of the heat and the menopause, but I don't agree with her explanation, though it could be, of course. It can be a real pitfall, getting distracted. You stop having a clear view of the situation." (T8)

"Yesterday the ECG was okay. The E.R. doctor thought the symptoms were stomach-related but I don't want to be influenced by that. I want to know why this patient is phoning now. What has changed?" (T18)

Triage-nurses strongly included the patient's sound of voice in their clinical reasoning. They used the non-verbal, paralinguistic, aspects of the conversations, such as talking and breathing speed, gasping and tone of the voice. The vocal elements in communication, such as the intensity of voice or volume were in previous studies defined as paralanguage.⁴² Interpreting paralanguage was particularly adapted to judge the credibility of the degree of pain and dyspnea that the patients communicate. Both senior and novice triage-nurses interpreted paralanguage, but senior nurses were more confident, they said it is a skill that improved with experience.

"I can tell by the sound of her voice that she's anxious. She's breathing fast and she can't hear or answer my questions. There's a certain haste in her voice." (T13)

"Experience teaches you when someone sounds sick. You can really hear if someone's in pain, or feeling worried, or that it's serious.... It's also a gut feeling." (T18)

Interpreting paralanguage is combined with other reasoning processes to create a mental image of the patient, with the aim to judge the clinical status of the patient.

"I make a mental image of the patient's physical state: how is she doing at the moment, what's the color of her skin, how is her breathing..." (T6)

Interactional workability with the CDSS

The support that the CDSS provides for the urgency decision making was dependent on whether the CDSS's recommendation is congruent to the triage-nurses' based on their assessment of the caller's narrative. Triage-nurses considered the CDSS supportive for the registration of patient's name, date of birth, location and the gathering of clinical information.

"It was quite clear what to do for this patient. He'd had pain in the middle of his chest for under twelve hours and vegetative symptoms. The NTS advice was a U1, so I sent for the ambulance." (T14)

Interactional workability dilemmas occurred when the CDSS does not support the triage-nurse's clinical reasoning or decision making: then the CDSS constrains the decision-making process. This occurred, for example, when in the CDSS there is a mandatory choice for a main presenting symptom which misaligns with the clinical situation. As a result of the CDSS' construction, the triage-nurse is forced to continue with the list of questions to be able to complete the triage assessment in the CDSS.

"If you have a patient who is breastfeeding and has chest pain, the main presenting symptom 'chest pain' doesn't fit the clinical condition. It's an inflammation of the breast, nothing cardiac is happening. But you have to tick all the boxes in the list of questions to complete the triage assessment." (T4)

Another example of an interactional dilemma is when the answer options within the CDSS are too restrictive in conjunction with the caller's narrative.

"You have to choose between oppressive, stabbing or unclear pain, but some people have both pressing and stabbing pain. In that case I go for unclear, but actually I don't think that's appropriate." (T13)

Strategies of triage-nurses

To deal with absence of congruence of the CDSS with the triage-nurses' decision making, triage-nurse applied four working strategies. These strategies were labeled by us as tinkering, overruling, complying and transferring responsibility to the GP. Tinkering was often practiced when the CDSS does not support the decision making

of the triage-nurse. With tinkering the triage-nurse strived for a certain CDSS urgency recommendation which fitted her own decision through, amongst others, switching between main presenting symptoms and up- or downgrading pain or dyspnea scores.

"She'd had oppressive pain for under twelve hours... but I needed more to get U1 urgency, so I looked for symptoms that could increase the urgency. Finally I set the pain score to 'severe'. Then the NTS advice is U1 so I don't have to explain why to the GP." (T10)

In overruling, the triage-nurse entered the symptoms according to how the patient responds, but the triage-nurse did not comply with the CDSS recommended urgency, because she thought a higher or lower urgency was appropriate for the patient. In overruling, the triage-nurse involved the supervising GP as is required according to the triage protocol of the OHS-PC.

"Some patients say they're having severe dyspnea. Then the NTS advises immediate U1. But if the patient doesn't sound dyspneic on the phone ... then I'll go to the GP and ask if I can give it less urgency." (T13)

Complying was the third strategy of triage-nurses. In complying, the triage-nurse complied with the urgency recommendation given by the CDSS despite the fact that the CDSS recommendation was not in line with his or her own decision making. Some triage-nurses indicated that management demands make them decide as such. Managers audit the triage-nurses' telephone conversation recordings on a regular basis to establish whether the triage-nurses complies with a certain conversation format, based on the CDSS structure. Triage-nurses expressed that they feel the tension between performing triage assessment which is accurate according to their professional convictions, and what is expected from them to meet the audit demands.

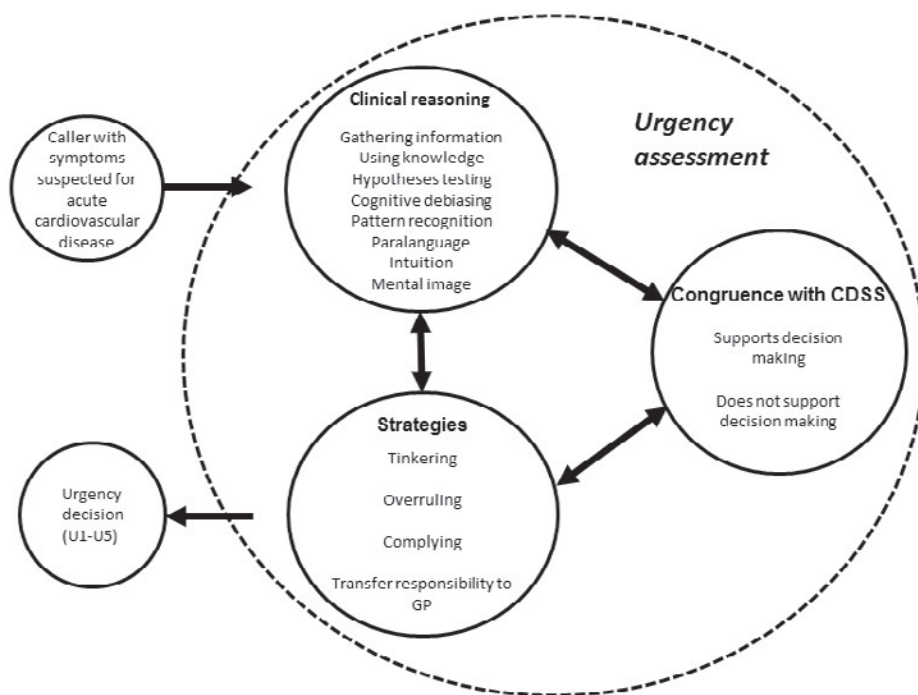
"But then they say you don't perform well... that your conversations should be different, that you should comply more to the NTS and you should change your way of questioning.. " (T3)

The fourth working strategy was to transfer the responsibility to the supervising GP of duty. The triage-nurse asked the supervising GP to take over and let him or her take the decision.

"This elderly patient had so much going on. It began with dizziness and falling over, which led to a head wound of uncertain size. He had a long medical history, including diabetes, and besides that lived alone. Every question I asked seemed to turn up more problems. It got so confusing for me that I decided the GP should take over." (T1)

In figure 1, a full model is presented with the clinical reasoning elements, centrally the congruence with the CDSS and the four working strategies.

Figure 1. Model of telephone triage nurses' urgency assessment while working with the CDSS



Results indicate that the triage-nurses' experience, the patient's context, feelings of uncertainty and management demands influenced their choice for the strategies. In general, novice nurses may experience more feelings of uncertainty and be more likely to comply or ask the GP to take over responsibility. Senior triage-nurses expressed to feel more confident about their decision making and therefore they tended more to overrule and tinker.

"I didn't know what effect a pacemaker has on chest pain... so that's why I asked the GP. In general I tend to consult the GP fairly quickly, just to be sure, since I'm still in training." (T17)

Senior triage-nurses told that they used the context to support their decision making. Context may be about patient characteristics, cultural background, caller history or behavior on the telephone.

"People in this area code rarely call for help. They don't have medical insurance, so if they do call, you know it's serious." (T12)

Uncertainty was mentioned by all triage-nurses, meaning they perceived the patient to be giving too limited or too much information or conflicting information. Conversations with callers who had limited language skills or showed strong emotions were also mentioned to trigger uncertainty. Triage-nurses mentioned that their uncertainty was sometimes enhanced by the CDSS, which constrains them because the CDSS necessitates them to reduce the patient's problem to one or more individual measurable symptoms that can be administrated within the CDSS structure. For patients with potentially urgent conditions triage-nurses tended to go for the safest strategy.

"I asked five or six times if he was unconscious, but the son didn't seem to understand what I meant. I thought it was serious because the patient had a history of stroke and cardiac bypasses. Meanwhile the call had already gone on for five minutes, so I decided not to wait for more clarity and just sent an ambulance." (T16)

DISCUSSION

With the principles of a grounded theory approach we analyzed the reflections of telephone triage-nurses and we identified that triage-nurses use diverse known reasoning elements for their urgency assessment. In combining elements of the hypothetico-deductive approach with elements of the humanistic-intuitive approach, they adjust to the patient's narrative. Triage-nurses assess the urgency by creating a mental image and interpreting the callers' paralanguage. Whether the CDSS supports the decision making of the triage-nurse is important in choosing the triage-nurses' working strategies. We distinguished four working strategies triage-nurses apply

while using CDSS: tinkering to make the final advice align with their own assessment, overruling the CDSS advice, complying with the CDSS advice and transferring responsibility to the GP. We found that the triage-nurses' work experience, the patient's context (such as patient characteristics, caller history), feelings of uncertainty and management demands influence their choice for a strategy.

Interactional dilemmas, earlier reported in the literature, are present in our study and described as the feeling of negotiating between the CDSS questions and the patient's narrative which may include diverse symptoms.¹² In the few studies about interactional workability, which are not specifically about telephone triage-nurses, the telemedicine setting both enabled and constrained the nurses' reasoning and decision making.¹²¹³ When the CDSS does not support the triage-nurses' decision making, this may lead to time delay, which worsens the patient's prognosis when having acute cardiac event.³ The technical design of the CDSS in our study supports in a certain manner the purpose of the intervention; triage-nurses consider the CDSS supportive for the registrations of patient's name, date of birth and gathering clinical information with the help of the question lists that pop-up after choosing a main presenting symptom in the CDSS. However, triage-nurses consider the CDSS only supportive for gathering clinical information when the main presenting symptom and corresponding questions align with the clinical condition. In the case of absence of congruence, triage-nurses will apply strategies which will not fulfil the purpose of the CDSS (such as following the guideline) and therefore the CDSS does not accomplish disposal of work. Studies about interactional dilemmas are scarce and knowledge is lacking on what strategies triage-nurses apply when they experience absence of congruence. In one Swedish interview study about working environment, it was briefly mentioned that some triage-nurses complied to the CDSS because they were afraid of making a wrong assessment.⁴³ We also found that management demands was one of the aspects that influenced the choice for the working strategies. Given telephone triage in the Netherlands is very safe¹⁵, it is a shortcoming when managers should limit their audits' focus on complying to the CDSS. We argue that it would be more relevant for managers to use feedback on clinical outcomes, which will be helpful for the triage-nurse to improve their urgency assessment performance, given the fact that providing feedback improves accuracy of new tasks.⁴⁴

In our study, interpreting paralinguistic showed to be important for urgency assessment. Triage-nurses combine interpreting paralinguistic with other reasoning elements and create therewith a mental image to compensate for the lack of visual information. Paralinguistic is studied within linguistics, but there is limited research

about interpreting paralinguistic cues in telephone triage conversations.⁴² In one study, senior triage-nurses used caller self-tests and listened carefully to detect physical signs.⁷ In this study, the concept interpreting paralinguistic cues was not mentioned, but 'listening for physical signs' suggests that triage-nurses use the paralinguistic aspects of the conversation. In a study performed at the emergency department, telephone triage-nurses said they judged the credibility of patient's symptoms on how they narrate their story, how they behave or speak and imagine what the patient's physical appearance looks like.³⁰ Detailed information was, however, lacking in these studies on how triage-nurses listened for physical signs and how they interpreted these for their urgency assessment. 'Knowing the patient' was the cornerstone of reasoning in the prior mentioned Swedisch study about tele-nurses who managed patients with COPD; such familiarity with the patients enabled tele-nurses to value the clinical symptoms as either normal for the patient or as a warning sign.¹³ In this way the triage-nurses of acquired in-depth knowledge that empowered them to see past the CDSS and adapt their decision to the clinical situation. In our study, triage-nurses were not familiar with the callers, which implicates that they have to rely stronger on other reasoning elements for urgency assessment. Our study indicates that interpreting paralinguistic cues and creating a mental image may be keystones for urgency assessment when triage-nurses are not familiar with and cannot see the caller. Further research in exploring how triage-nurses interpret paralinguistic cues in their urgency assessment may help to acquire additional knowledge for improving telephone triage training.

Strengths

We interviewed twenty-four triage-nurses with a variety of work experience and training. By using the audio stimulated recall interview technique, we obtained an accurate view of triage-nurses' reasoning elements. This method is considered reliable to understand participants' implicit theories and reflections on key events in a real situation of interest.⁴³ Findings were discussed with the members of the research team, who have diverse research backgrounds, to optimize transparency and researcher triangulation. Understanding how clinical reasoning takes place in telephone triage of patients suspected of potential urgent conditions while working with a CDSS is important to improve workability with the CDSS and improve the training of triage-nurses. As these interviews were performed in an open, non-judging, and confidential atmosphere, we had rich data to analyze and achieved a good understanding of triage-nurses' clinical reasoning.

Limitations

At the time of the interviews, the telephone conversations that were used for listening during the interview, were performed at a maximum of two weeks before the interview. However, because the nurses perform a large number of calls every shift, some nurses may have found it hard to remember their reasoning during these specific conversations used during the interview. The literature about audio-stimulated recall recommends that an interview should be conducted as soon as possible after the recording, but does not indicate a specific period.³⁷ For future research, a (video) observation study might give additional information on how triage-nurses use the CDSS by observing exactly how they use the options provided by the interface of the CDSS. Also, a think-a-loud study with triage-nurses during telephone conversations, although very difficult to realize in an urgency setting, could contribute to our understanding.⁴⁵

CONCLUSION

Telephone triage-nurses use clinical reasoning elements for urgency assessment of callers suspected of potentially acute cardiac events. They interpret paralanguage and create a mental image to compensate for the lack of visual information. Congruence with the CDSS is a key aspect, which in this study is established when the CDSS supports the triage-nurses' decision making. If congruence is absent, triage-nurses apply four working strategies, which are (i) tinkering to make the final recommendation align with their own assessment, (ii) overruling the CDSS recommendation, (iii) complying with the CDSS recommendation or (iv) transferring responsibility to the GP.

RELEVANCE TO CLINICAL PRACTICE

This study confirms triage-nurses have to deal with interactional dilemmas while working with CDSS, with lists of questions that may misalign to the clinical condition or have too restrictive answer options. Understanding triage-nurses' working strategies with CDSS and what influences their choices herewith, may help to develop improved education and also may add to a constructive safety culture in the workplace. Telephone triage training may benefit by sharing how interpreting paralanguage and creating a mental image is done. Awareness that triage-nurses' reasoning and their working strategies are vital for the outcome of triage decisions is important for CDSS developers and managers. CDSS developers may benefit by involving the triage-nurses' input to improve interactional workability. About implications for managers,

we argue that it would be counter-effective when managers solely focus their audits of triage-nurses on complying with the CDSS. Given that in the Netherlands, current telephone triage is very safe, managers better shift the focus of audits more to clinical outcomes of triage decisions.

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APPENDICES

Appendix- Table 1. NTS urgency levels

NTS Urgency level	Definition	Response time	Medical help
U ₀ – Resuscitation	Loss of vital functions	Immediately	Ambulance
U ₁ – Life threatening	Unstable vital functions	Immediately, within 15 minutes	Ambulance
U ₂ – Emergent	Vital functions in danger or organ damage	As soon as possible, within 1 hour	Home visit by GP or consultation at OHS-PC
U ₃ – Urgent	Possible risk of damage, human reasons	A few hours (<3 hours)	Home visit by GP or consultation at OHS-PC
U ₄ – Non-urgent	Marginal risk of damage	24 hours	Consultation at OHS-PC or telephone advice
U ₅ – Advice	No risk of damage	Advice, no time related	Telephone advice

GP: General practitioner

NTS: Netherlands Triage Standard

OHS-PC: Out-of-hours services for primary care

Appendix 2. Questionnaires

Original version questionnaire, August 2016

Topic: clinical reasoning

- Which moment or moments in the call was/were important for your reasoning? We will listen to the fragment/fragments again.
- Why was this fragment important for your reasoning?
- What did you take into consideration here?
- What made it striking for you?
- What did it mean to your reasoning process that the patient said this (.....)?
- Here you asked the following question (...?) What made you think of that question?

Topic: interactional workability

- Does the NTS support the decision (s) you made in this fragment?
- Where in this fragment did the NTS decision supporter help you? Can you say more about that?
- Are the questions you asked here based on the NTS, or did you also have questions that come from outside the NTS?

- Why did you ask those questions? And why did you ask those questions right here?
- Do you often ask questions that go beyond the NTS?
- Do you remember the main presenting symptoms that the NTS suggests?
- Which main presenting symptom did you choose? Why?
- What is / are the most important reason/s that led to this choice?
- Did you answer all the questions related to this presenting complaint? Why or why not?
- Did you switch to another main presenting symptom while asking questions? Why did you?
- Do you remember what the NTS recommended level of urgency was?
- What do you think of the urgency the NTS recommends? Why do you agree or disagree?

Topic: acute cardiac events

- Are there any special features in the triage of these patients? What makes the triage special or difficult or easy?
- Is the triage of patients with suspected acute cardiac event (compared to other types of triage phone calls) generally very clear or do you also get conversations where it is not so clear?

Topic: uncertainty

- How sure of your reasoning were you in this call?
- What were you unsure about and why?
- How did you deal with this uncertainty?
- How did this doubt / uncertainty influence your determination of urgency?
- Consultation with general practitioner: why did you or why did you not consult the GP? What did you expect from this consultation?

Topic: context

- Did anything else influence your reasoning process (other than the patient's characteristics) in this call? Things in yourself, in the environment?
- Can you imagine the circumstances to this call?
- How did that influence your reasoning during the triage call?

Supplementary topics, February 2017

Topic: interactional workability (adapted questions)

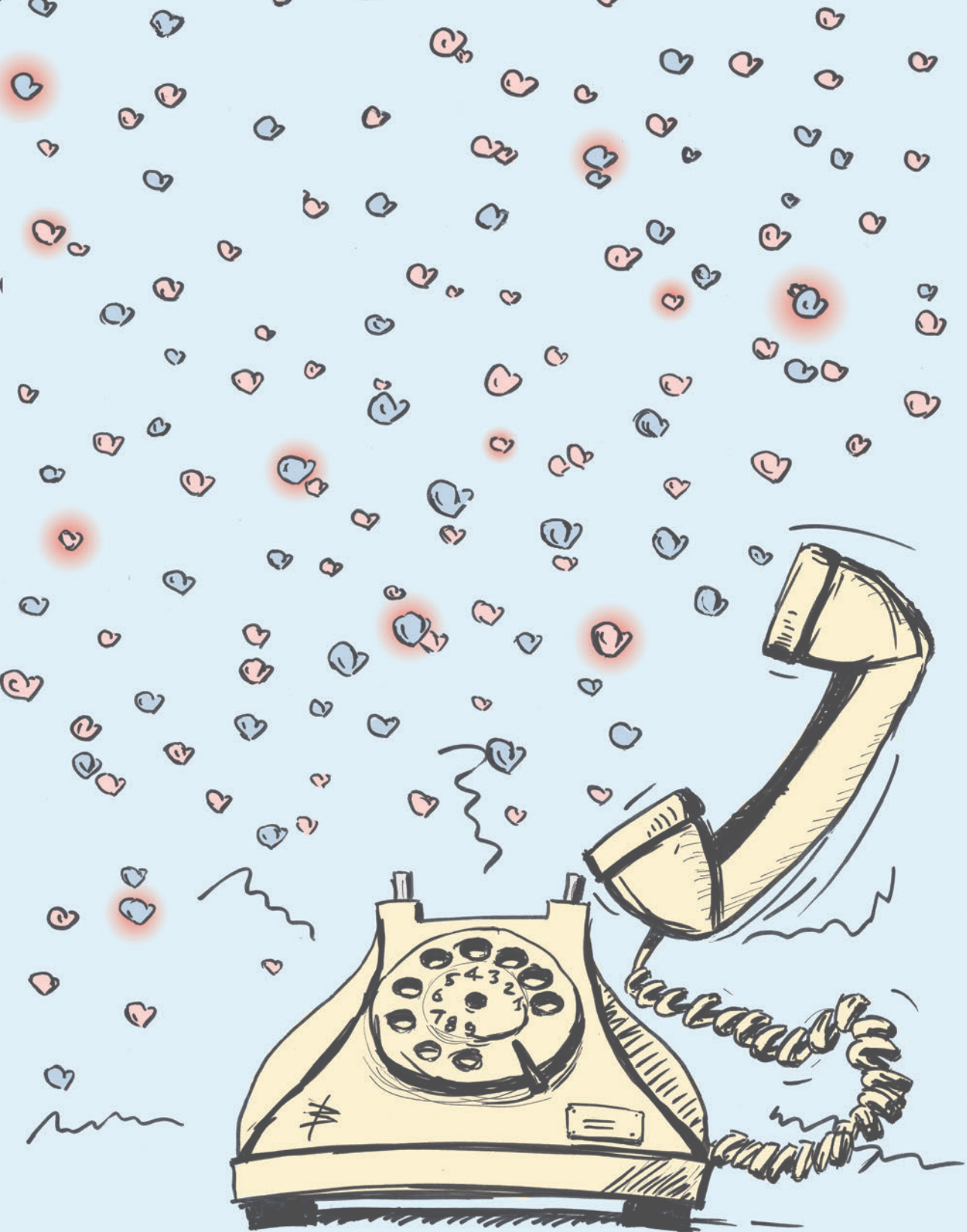
- When does the NTS work for you and when does it get in your way?
- In your opinion, when is the NTS suitable for a particular case, and when is it not?
- If the NTS is not “working” for you, how do you do the triage? What do you base your decisions on?
- Have you noticed if using the NTS has any influence on the conversation with the patient? Do the questions match, or not? Have you noticed any clashes? What do you do if the questions do not fit the patient’s story very well?
- What do you do if the patient gives unclear answers? The NTS requires a yes / no choice. Do you fill it in, or leave it open?

Topic: paralinguage

- You say the patient sounds sick ... what do you mean by that? What precisely do you base this on?
- Can you state explicitly what you hear then, in this fragment?
- How decisive for the triage is it for you, that the patient sounds like that?

Topic: patient’s personality

- You indicate that this patient is a ... type of person. What do you mean? What kind of influence does this have on your reasoning process?
- How decisive for the triage is it for you that this patient is a ... type?



5

CHAPTER

Chest discomfort at night and risk of acute coronary syndrome: cross-sectional study of telephone conversations

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ABSTRACT

Background During telephone triage it is difficult to assign the adequate urgency to patients with chest discomfort. Considering the time of calling could be helpful.

Objective To assess the risk of acute coronary syndrome (ACS) in certain time periods and whether sex influences this risk.

Methods Cross-sectional study of 1,655 recordings of telephone conversations of patients who called the out-of-hours services primary care (OHS-PC) for chest discomfort. Call time, patient characteristics, symptoms, medical history and urgency allocation of the triage conversations were collected. The final diagnosis of each call was retrieved at the patient's general practice. Absolute numbers of patients with and without ACS were plotted and risks per hour were calculated. The risk ratio of ACS at night (oam to gam) was calculated by comparing to the risk at other hours, and was adjusted for gender and age.

Results The mean age of callers was 58.9 (SD \pm 19.5) years, 55.5% were women and in total 199 (12.0%) had an ACS. The crude risk ratio for an ACS at night was 1.80 (CI 1.39-2.34, $p < 0.001$); 2.33 (1.68-3.22, $p < 0.001$) for men, and 1.29 (0.83-1.99, $p = 0.256$) for women. The adjusted risk ratio for ACS of all people at night was 1.82 (1.07-3.10, $p = 0.039$).

Conclusions Patients calling the OHS-PC for chest discomfort between o-gam have almost twice a higher risk of ACS than those calling other hours, a phenomenon more evident in men than in women. At night, dispatching ambulances more 'straightaway' could be considered for these patients with chest discomfort.

BACKGROUND

Adequate triage of patients with chest discomfort and timely diagnosis of those with ACS is crucial for initiation of lifesaving early interventions in order to prevent or reduce myocardial necrosis ('time is muscle'), and thus improve outcome and prognosis.¹ Urgency allocation of patients with chest discomfort based on telephone triage as done in out-of-hours services for primary care (OHS-PC) and emergency medical dispatch centers is, however, challenging because it is very difficult to differentiate ACS from other reasons for chest discomfort. For the diagnosis of ACS an abnormal electrocardiogram (repolarization abnormalities (ST and/or T wave)) and/or elevated blood levels of troponin I or T are needed. ACS may then be further subdivided in ST-elevated myocardial infarction (STEMI) and non-ST-elevated myocardial infarction (NSTEMI) if the troponin levels are elevated². If troponin levels are not elevated (or increased over time), it is called unstable angina pectoris (UAP)².

In the Netherlands, around 80% of patients with chest pain first call the general practitioner (GP) or OHS-PC, while 20% directly calls the ambulance (112) or are self-referrals³. In the 20% who called directly the emergency medical dispatch center, 63% received a priority 1 ambulance, and 10% had an ACS.⁴ In people who first called the OHS-PC, 70% received a priority 1 ambulance, and also 10% had an ACS.⁵⁻⁷

Previous studies in the emergency department setting showed circadian variability in the occurrence of acute coronary events, with a peak early mornings which was twice as high as in the evening.⁸⁻¹⁰ This early morning peak of acute myocardial infarction is considered related to physiological changes in these hours such as a rise in blood pressure and plasma adrenaline levels that could possibly trigger plaque rupture and thrombosis.^{8,9,11} Studies in primary care setting are lacking and studies dividing the absolute numbers of ACS by the number of patient who contacted because of chest pain are limited.¹¹ Also studies about sex differences in circadian rhythm of ACS are limited. If there were a high incidence of ACS relative to the number of callers for chest discomfort during certain hours, this would facilitate triage at the OHS-PC.

In the Netherlands, the OHS-PC is organized in large services, similar to the United Kingdom and Scandinavian countries.¹² Dutch triage nurses use the Netherlands Triage Standard (NTS) to assess the urgency and use five priority levels related to the time within which the patients should be seen. The NTS is a semi-automatic computerized decision support system that is based on the Manchester Triage Standard.¹³ Previous studies showed that chest discomfort is the most common reason (60.7%) for allocating

the highest priority (U1; ambulance dispatched, patient should be seen within 15 minutes) for those contacting the OHS-PC. On the second place came respiratory tract symptoms with just 8.1% ambulances dispatched.⁷ The Dutch triage system is overall safe with only 0.006% calamities a year, but this incidence is higher with around 0.03% in the domain of chest discomfort.^{14,15} Besides safety, also efficiency could very likely be improved in the domain chest discomfort because only one out of ten of the referred patients actually has an ACS.^{5-7,14}

For better safety and efficiency, there is an urgent need for determinants that improve prediction and thus help triage nurses in their task.⁷ If there are hours with a high incidence of ACS as compared to the total number of telephone calls, then considering the time of calling could help to improve the triage. Therefore we assessed whether there are certain time periods in which there is a higher risk ratio of ACS and whether sex differences influence this risk ratio.

METHODS

The study design and data collection are published before in our study design paper.¹⁵ In short, we performed a cross-sectional study with a random sample of 1,655 calls of people calling the OHS-PC for chest discomfort between 2014 and 2016. We selected calls on the basis of ICPC codes (K01, K02, K03, K24, K74, K75, K76, K77, K93, L04, P74, R02, R98) and keywords (thoracic pain, chest pain, myocardial infarction, heart attack and their common abbreviations). On purpose, we sampled broad to capture the entire domain of patients that could be suspected of ACS. We drew a random sample of all available calls of these patients (270,000 between 2014-2016) with the Random Number Generator (RAND) function in Microsoft Excel.

We re-listened telephone triage recordings in order to collect information about characteristics of patients and their conversation, on symptoms, medical history, urgency allocation, and whether a supervising GP was involved in the triage. Nine OHS-PC in the Netherlands participated, serving a total population of 1.5 million people. The final diagnoses were provided by the patients' GP, and this was based on the electronic medical file and cardiologist discharge letters. An ACS was based on the cardiologist's diagnosis, including information on levels of (high-sensitivity) troponin and electrocardiography.

In the OHS-PC, trained triage nurses used the NTS to generate an urgency allocation. The NTS is hierarchically ordered with key questions, and answers are linked to urgency recommendations. Linked to the nurse's urgency allocation is the time frame within which a physician should see the patient.¹⁷ Direct, within 15 minutes (by ambulance or GP (U₁)), urgently within one hour (U₂), less urgent within three hours (U₃), non-urgent the same day (U₄), or telephone advice (U₅). The GP may see the patient at the patient's home or at the OHS-PC. Triage nurses can always consult the supervising GP on call.¹⁸

Data-analyses

We plotted the absolute numbers of patients calling for chest discomfort hourly, subdivided in patients with and without a final diagnoses ACS, and we calculated the risks of ACS per hour by dividing the absolute number of ACS by the total numbers of callers with chest discomfort per hour. The risk ratio of ACS was calculated over several time periods. The aim was to find a time period in which the risk of ACS was high, and also practical in use. We performed separate analyses for men and women, and used the likelihood ratio test to assess the difference. Adjusted risk ratios for ACS were calculated after correction for gender and age below and over forty years.

We compared patient and call characteristics, and urgency allocation between callers at night and callers at others hours. For comparison of dichotomous variables we used the Chi² test, and for continuous variables the independent sample t-test. Finally, we compared the correlation between urgency allocation and the final diagnosis ACS. Data analysis was performed using SPSS, IBM version 21.

RESULTS

Of the 1,655 patients with chest discomfort the mean age was 58.9 (SD ± 19.5) years, and 919 (55.5%) were women. In total, 199 (12.0%) had an ACS; 82 (8.9%) women and 117 (15.9%) men, $p < 0.001$; in 41.7% a NSTEMI, 26.6% a STEMI, 24.1% UAP and 7.5% a non-classified ACS.

Variation was small in the absolute numbers of ACS during 24 hours, see figure 1. The incidence of ACS varied with a peak from 0-9am of 17.7% compared to 9.8% at the remaining hours. The highest risk of ACS was between 2-5am with 21.5%, and lowest between 4-7pm with 6.8%. In figure 2 the distribution of risks for ACS per hour are plotted, subdivided for men and women. The risk ratio for an ACS from 0-9am was 1.80 (CI 1.39-

2.34, $p < 0.001$) compared to other hours; for men 2.33 (CI 1.68-3.22, $p < 0.001$) and for women 1.29 (CI 0.83-1.99, $p = 0.256$). The difference in risk ratios for men and women was statistically significant ($p = 0.030$). The adjusted risk ratio for ACS from 0-9am compared to other hours was 1.82 (1.07-3.10, $p < 0.001$) after correction for both age and sex.

Figure 1. Call time of 1,655 patients with chest discomfort calling the OHS-PC between 2014-2016, subdivided in those with and without ACS.

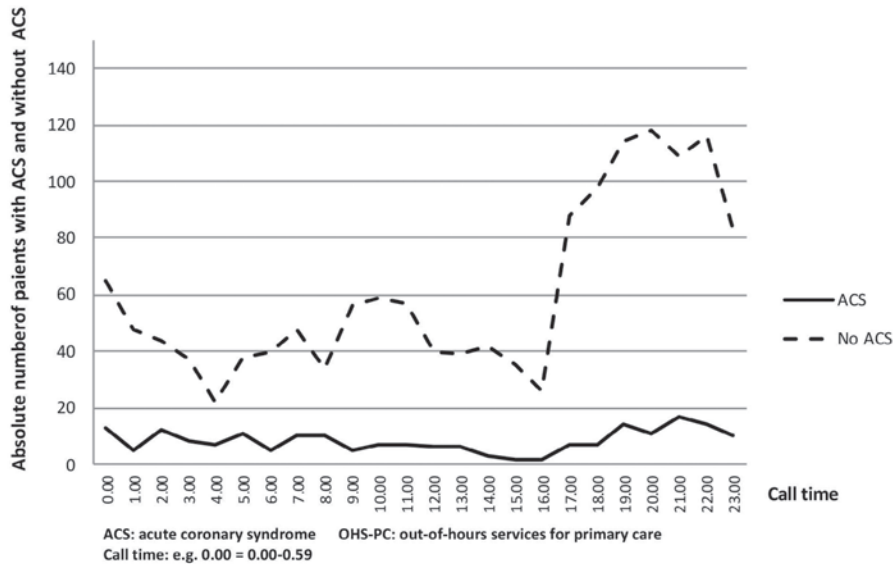


Figure 2. Risk of ACS per hour of 1,655 patients with chest discomfort calling the OHS-PC between 2014-2016, subdivided for men and women.

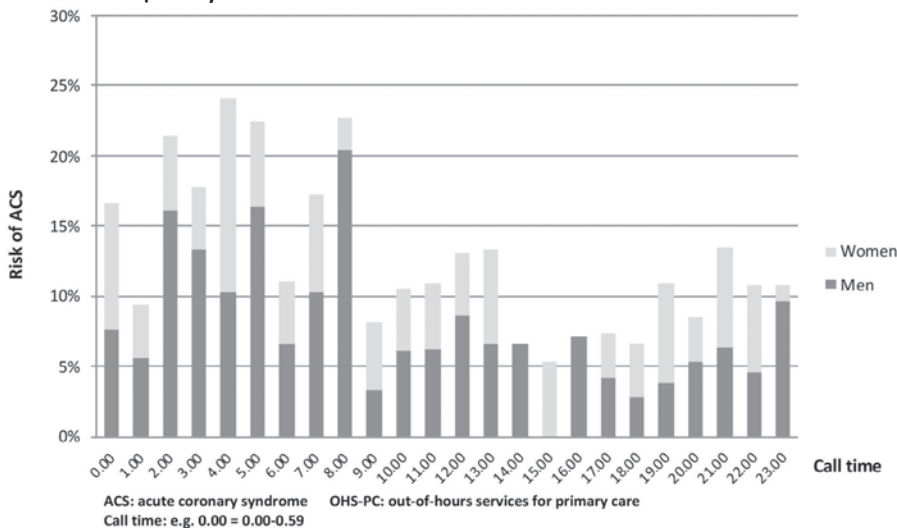


Table 1. Baseline characteristics of 1,655 patients calling the OHS-PC with chest discomfort between 2014-2016, divided into those who called between oam-gam and other hours.

Characteristics		Total 1655	oam-gam No. (%) n = 457	Other hours No. (%) n = 1198	p-value
Patient characteristics	Mean age (SD)	1655	61.4 (19.7)	57.9 (19.3)	0.001
	Male sex	736	193/457 (42.2)	543/1198 (45.3)	0.759
Call characteristics	Call duration in min:sec (SD)	1655	7:02 (3:40)	7:42 (3:47)	0.001
Medical History	Cardiovascular disease	1350*	227/365 (62.2)	592/985 (60.1)	0.485
	Coronary artery disease	902*	88/251 (35.1)	225/651 (34.6)	0.888
	Hypertension	701*	70/188 (37.2)	189/513 (36.8)	0.924
	Diabetes mellitus	686*	32/185 (17.3)	89/501 (17.8)	0.887
Symptoms	Chest pain	1601*	412/442 (93.2)	1090/1159 (94.0)	0.536
	Pain lasting < 12 hours	1438*	320/385 (83.1)	741/1053 (70.4)	<0.001
	Radiation of pain	1283*	239/348 (68.7)	593/935 (63.4)	0.080
	Autonomous nervous system related symptoms **	1599*	257/434 (59.2)	658/1165 (56.5)	0.325
	Shortness of breath	1260*	214/333 (64.3)	610/927 (65.8)	0.612
GP participated in triage	In consultation or taking over the call	1655	233/457 (51.0)	650/1198 (54.3)	0.233
Urgency allocation	U1	753	249/457 (54.5)	504/1198 (42.1)	<0.001
	U2	371	85/457 (18.6)	286/1198 (23.9)	***
	U3,U4,U5	531	123/457 (26.9)	408/1198 (34.1)	0.005 ****
Diagnosis ACS		1655	81/457(17.7)	118/1198 (9.8)	<0.001

Notes: * For these variables there were missing data.

** Autonomous nervous system (ANS) related symptoms consist of one or more of the following: nausea and/or vomiting, sweating, pallor/ashen skin, (near) collapse.

*** p-value comparing U1 vs. U2-U5

**** p-value comparing U1,U2 vs. U3,U4,U5

OHS-PC: out-of-hours services for primary care GP: general practitioner ACS: acute coronary syndrome

The baseline characteristics for those calling at night and those calling the other hours are presented in table 1. Patients calling between o-gam were significantly older (61.4 (SD \pm 19.7) years vs. 57.9 (\pm 19.3) years, $p=0.001$), had less patient decision delay (calling

<12 hours after symptom onset 83.1% vs. 70.4%, $p<0.001$), and received more often the highest urgency 1 (54.5% vs. 42.1%, $p<0.001$) than those calling other hours.

In table 2 the correlations between urgency allocation and diagnosis of ACS are presented. Triage nurses dispatched significantly more ambulances to patients who turned out to have an ACS than no ACS (70.4% vs. 42.1%, $p<0.001$) and this was more so at night (80.2% vs. 48.9%, $p<0.001$).

Table 2. Correlation between urgency allocation and final diagnosis ACS of 1,655 patients with chest discomfort calling the OHS-PC between 2014-2016.

Total calls	ACS n=199 (%)	No ACS n= 1,456 (%)	p-value 1*	p-value 2**
U1	140 (70.3)	613 (42.1)	<0.001	<0.001
U2	31 (15.6)	340 (23.4)		
U3, U4 and U5	28 (14.1)	503 (34.5)		
oam-gam	ACS n= 81 (%)	No ACS n= 376 (%)		
U1	65 (80.2)	184 (48.9)	<0.001	<0.001
U2	11 (13.6)	74 (19.7)		
U3, U4 and U5	5 (6.2)	118 (31.4)		
Other hours	ACS n= 118 (%)	No ACS n= 1,080 (%)		
U1	75 (63.6)	429 (39.7)	<0.001	<0.001
U2	20 (17.0)	266 (24.6)		
U3, U4 and U5	23 (19.4)	385 (35.7)		

* p-value 1: U1 vs. U2-U5

** p-value 2: U1/U2 vs. U3-U5

ACS: acute coronary syndrome

OHS-PC: out-of-hours services for primary care

The final diagnoses of patients without ACS (n=1,456) were in 2.6% diseases that need urgent treatment (e.g. thoracic aortic dissection, acute severe heart failure, pulmonary embolism), and in the remaining 85.4% non-urgent disorders (e.g. musculoskeletal, pulmonary, psychiatric or gastrointestinal causes).

DISCUSSION

Patients with chest discomfort who called the OHS-PC between o-gam had almost twice as high a risk of an ACS than patients calling at other hours. This effect remained after adjustment for sex and age, but the risk was highest for men and less evident for women.

An important strength of our study is that we analyzed all patients calling for chest discomfort, not selectively those with ACS. Another strength is that the original and very first conversations with patients were available, and analyzed before knowledge of the eventual diagnosis, which assures our results are not affected by recall bias, as was possibly in many of the previous studies. A limitation is missing values on some clinical variables; a phenomenon common for research with routine care data. Importantly, however, we had no missing data for the time of calling, sex category, age, or the outcome (ACS/no ACS), and thus we could perform our multivariable analysis without the need of imputing data. Finally, the less pronounced circadian effects among women compared to men should be interpreted carefully, because our study could be under-powered for this subgroup analysis.

To the best of our knowledge, this is the first study in the OHS-PC setting assessing risks of ACS over 24 hours of patients with chest discomfort. Most previous studies analyzed patients with established ACS and reported absolute numbers, not risks or risk ratios. They reported a peak of ACS early mornings if considering the time of arrival at the hospital.^{8,10,19} A Swedish study reported likelihoods for ACS among patients with chest pain seen at the emergency department (ED), and reported a peak incidence from 8-10am of 10.6% and a trough between 6-8pm of 5.6%, based on arrival time at the ED⁹. The incidence peak of ACS 0-9am in our study could at least partly be explained by the fact that we used time of calling.⁹ Interestingly, in the Swedish study the incidence peak of ACS at the ED was lower than in our study, and the contrast between peak and trough less. In another Swedish study among 2,205 patients with chest pain calling the dispatcher center, the odds ratio among patients with an ACS for calls arriving before lunch at the dispatch center was 2.02 (95% CI 1.22-3.43) compared with midnight.²¹ Possibly, differences in patient decision delay and organization of health care between Sweden and the Netherlands could have played a role.

We found a significant lower risk of ACS among women than men (8.9% vs. 15.9%, $p < 0.001$), and among women there was less difference in ACS between 0-9am and other hours; 1.29 (CI 0.83-1.99) vs. 2.33 (CI 1.68-3.22) among men. In the aforementioned Swedish study in emergency department setting, women also had a lower likelihood for ACS than men, but they did not find a sex difference in the circadian pattern of ACS.⁹

To appreciate our findings; presence of radiation of chest pain to the left arm had a likelihood ratio of ACS of 1.30 (CI 1.13-1.47), presence of sweating 1.34 (1.09-1.65) and nausea and/or vomiting 1.32 (CI 1.09-1.65) in a meta-analyses of 16 studies with

non-selected patients.²⁰ These symptoms typically are considered important items during triage of patients with chest discomfort, but their impact is fairly low. Currently, pre-hospital decision rules do not consider time of calling as a valuable triage item and there seems to be no awareness among lay people about these 'critical hours'.²¹⁻²³ Some awareness about a higher risk of ACS at night seems to be present among triage nurses and GPs working at the OHS-PC, as ACS patients received more often priority 1 with ambulance straightaway if calls arrived o-gam than during other hours (80.2% vs. 63.6%, $p < 0.001$). A previous study reported that *missed* diagnoses of ACS most often occurred at night.¹⁴ Also this study stresses the importance of considering the time of calling with triage of patients with chest discomfort; it helps improve patient safety and accuracy of pre-hospital telephone triage.

CONCLUSION

Patients calling the OHS-PC for chest discomfort between o-gam have almost twice a higher risk of ACS than those calling other hours, a phenomenon more evident in men than in women. At night, dispatching ambulances more 'straightaway' than during daytime could be considered for these patients with chest discomfort.

ACKNOWLEDGEMENTS

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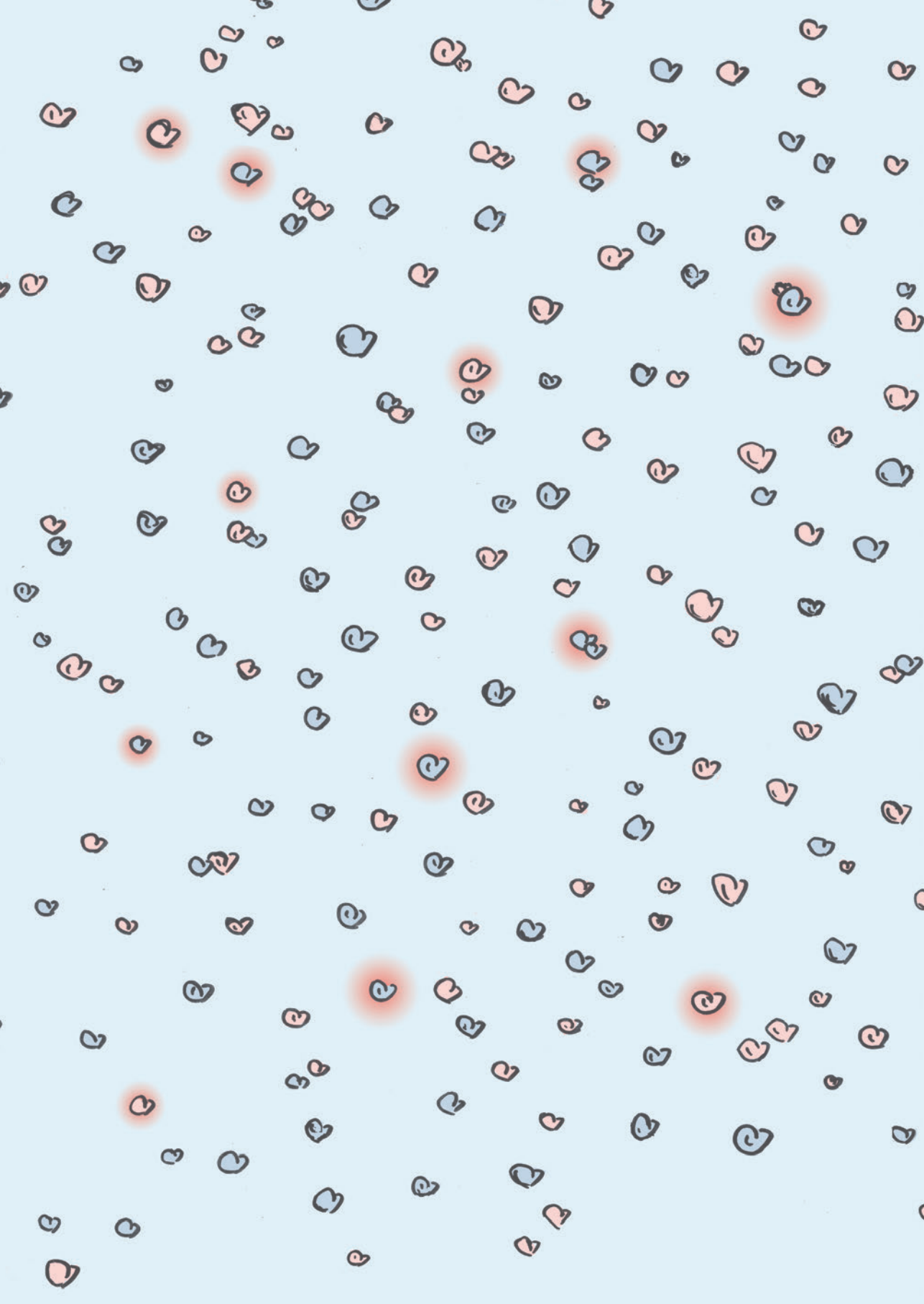
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6

CHAPTER

Gender differences in telephone triage of patients with chest discomfort in out-of-hours primary care

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Submitted

ABSTRACT

Objectives To assess differences in symptoms predictive of acute coronary syndrome (ACS) between women and men presenting with chest discomfort in out-of-hours primary care (OHS-PC).

Design Cross-sectional study.

Setting Nine OHS-PC in the Netherlands.

Participants 993 women and 802 men who called OHS-PC for acute chest discomfort (pain, pressure, tightness, or discomfort) between 2014 and 2017.

Primary outcome measure Diagnosis of acute coronary syndrome (ACS). We compared patient and call characteristics of triage call recordings between women with and without ACS, and men with and without ACS. Diagnoses were retrieved from the patient's medical record in general practice, including hospital specialists' discharge letters.

Results Among 1,795 patients (mean age 58.8 (SD 19.5) years, 55.3% women), 15.0% of men and 8.6% of women had an ACS. In both sexes, retrosternal chest pain was discriminative for ACS (women with ACS vs. without 62.3% vs. 40.3%, $p=0.002$, men with ACS vs. without 52.5% vs. 39.7%, $p=0.032$), as was pressing/tightening pain (women 78.6% vs. 61.5%, $p=0.011$, men 82.1% vs. 57.4%, $p<0.001$) and radiation to arm (women 75.6% vs. 45.9%, $p<0.001$, men 56.0% vs. 34.8%, $p<0.001$). In women, severe pain (65.4% vs. 38.1%, $p=0.006$), a pale face (50.0% vs. 22.9%, $p=0.007$) and radiation to jaw (50.0% vs. 29.8%, $p=0.017$) were also discriminative for ACS, while in men this was sweating (52.4% vs. 38.1%, $p=0.015$), and against ACS stabbing pain (8.4% vs. 26.5%, $p<0.001$).

Ambulances were dispatched equally in women (72.9%) and men with ACS (70.0%).

Conclusion Symptoms predictive of ACS were rather similar for women and men with chest discomfort, with some important exceptions, such as severity, type, and radiation of pain, and some autonomous nervous system related symptoms.

INTRODUCTION

Adequate triage and early diagnosis is key in patients with acute chest discomfort because they might have an acute coronary syndrome (ACS) for which lifesaving early interventions are available. ACS is an umbrella term including ST-elevated myocardial infarction (STEMI), non-ST-elevated myocardial infarction (NSTEMI) and unstable angina pectoris (UAP).¹ Increased preventive measures and development of (timely) effective therapeutic interventions ('time is muscle') have resulted in improved outcomes and prognosis in ACS.² Telephone triage of patients with chest discomfort, as done in out-of-hours service primary care (OHS-PC) and emergency medical services (EMS or ambulance dispatch centres) is, however, challenging because it is difficult to differentiate ACS from other causes of chest discomfort based on symptoms only.^{3,4} Importantly, the majority of patients with chest discomfort (80%) in the Netherlands first approach the general practitioner (GP) or OHS-PC, and 20% directly calls the ambulance (112) or are self-referrals to the emergency department (ED).⁵

Previous hospital-based studies reported a delayed recognition of ACS in women compared to men.^{6,7} It was suggested that this delayed recognition was related to a less specific presentation in women.^{8,9} This caused an ongoing debate on whether women with ACS, compared to men, present with less specific symptoms, and how this affects diagnosis, but also treatment, and prognosis.^{10,11} A recent meta-analysis of 27 studies showed that women with ACS, compared to men with ACS, had higher odds of presenting with pain between the shoulder blades (OR 2.15, 95% CI 1.95-2.37), nausea or vomiting (OR 1.64, 95% CI 1.48-1.82) and shortness of breath (OR 1.34 (95% CI 1.21-1.48)).¹² Women with ACS had lower odds of sweating (OR 0.84, 95% CI 0.76-0.94) and presenting with chest pain (OR 0.70, 95% CI 0.63-0.78), but in both sexes chest pain remained the most common symptom (pooled prevalence men 79% and women 74%).¹² Importantly, researchers suggested standardization in methods of symptoms assessment is needed, because of the difficulties to formulate any definitive statements about symptom presentation, as studies assessed symptoms in different ways (questionnaires or abstracting from medical records).^{9,13-15} Abstracting symptoms from medical records may dilute symptom presentation, as they are translated by the clinician in medical terminology.¹⁶ Moreover, many studies suffer from recall or hindsight bias of both patient and researcher as they know the outcome (ACS).

For the clinician or telephone triage nurse it is crucial to differentiate ACS from other causes of chest discomfort. For that, studies are needed that include female and male patients presenting with chest discomfort, in which women and men who turn out to

have ACS are compared to those who do not have ACS. Such studies are scarce. In a study performed among patients with chest discomfort seen at the ED in the USA (77 women and 244 men with ACS, and 195 women and 240 men without ACS) were compared. Women with ACS more often reported arm pain than women without ACS (47% vs. 32%, $p=0.021$), while men with ACS reported pressing heavy feelings on the chest (63% vs. 54%, $p=0.035$) and chest pain (72% vs 60%, $p=0.005$) more often than men without ACS.¹³ In a recent Dutch OHS-PC study among 23 women and 34 men with ACS, and 253 women and 208 men without ACS, differences in symptom presentation between women and men were small.¹⁷ In men, radiation of pain (89.3% vs. 64.9%, $p\text{-value}=0.011$) was discriminative for ACS, while stabbing chest pain (3.7% vs. 24.0%, $p\text{-value}=0.014$) was discriminative for the absence of ACS. Both these symptoms were not discriminative in women (90.0% vs 78.6%, $p=0.227$, and 15.8% vs. 18.8%, $p=0.743$), respectively.¹⁷

We aimed to assess symptoms predictive of ACS in women and men separately, among patients presenting with acute chest discomfort to OHS-PC based on analyses of recorded telephone triage conversations.

METHODS

We performed a cross-sectional study with a random sample of 1,795 OHS-PC calls for chest discomfort (chest pain, pressure, tightness, or discomfort) between 2014 and 2016.¹⁸ We first selected calls on the basis of International Code for Primary Care (ICPC; a WHO world-wide code system for primary care) codes (K01, K02, K03, K24, K74, K75, K76, K77, K93, L04, P74, R02, R98) and keywords (thoracic pain, chest pain, myocardial infarction, heart attack and their common abbreviations).^{19,20} On purpose, we sampled a broad variety of symptoms to capture the entire domain of patients that could be suspected of ACS. We drew a random sample of all available calls of these patients with the Random Number Generator (RAND) function in Microsoft Excel. Calls were excluded from re-listening when the patients' age was below 18 years or when the patient did not live in the surrounding area of the OHS-PCs (because we could not retrieve a diagnosis from the general practitioner of patients living outside the area of the OHS-PCs). Calls were also excluded from re-listening when it did not concerned a triage call (e.g. inter-collegial consultation) or when the recording was of poor quality.

We re-listened the telephone triage recordings and collected information about patient and conversation characteristics, on symptom presentation, medical history, urgency allocation, and involvement of a supervising general practitioner (GP) in the triage.

Nine OHS-PC in the Netherlands participated, serving a total population of 1.5 million people. The final diagnoses were provided by the patients' GP, and this was based on the electronic medical file including ED and cardiologist discharge letters, and notes from the OHS-PC. An ACS was based on the cardiologist's diagnosis, including information on levels of (high-sensitivity) troponin and electrocardiography results.

Context

In the Netherlands, OHS-PC covers primary care during 73% of week hours, and the initial contact is by telephone. In most OHS-PC and EMS, the 'Netherlands Triage Standard' (NTS) is used as a decision support to classify the urgency of the patients' conditions.²¹ Based on the patient's symptom presentation, the triage nurse needs to choose the most appropriate complaint out of 56 'main complaints'. Each NTS 'main complaint' incorporates a decision tree with hierarchically ordered questions, which are similar for men and women. Triage nurses fill out the caller's responses in the semi-automatic NTS system, which then generates urgency allocations (U0 (reanimation) to U5 (self-care advice, see also appendix-table 1). The triage nurse can overrule this recommendation and up- or downscale the urgency allocation, often after consulting the supervising GP.²² Since its introduction in 2011, the NTS system has, however, never been formally validated by correlating the generated urgencies to clinical endpoints.²¹

Data analyses

We compared patient and call characteristics between women with and without ACS, and men with and without ACS. We analysed the association between urgency allocation and the final diagnosis ACS (with or without other life threatening events (LTEs)). We considered pulmonary embolism, thoracic aortic dissection and acute abdominal aneurysm as LTEs; patients with LTEs as well as those with ACS should receive an U1-level urgency (full list in table 2).

For comparison of dichotomous variables we used the Chi² test or the Fisher exact test and for continuous variables the independent sample t-test or Mann-Whitney U test. Data analysis was performed using SPSS, IBM version 25.

Patient and public involvement

No patients were involved in setting the research question or the outcome measures, or in developing plans for design, however, they were involved in the implementation of the study. In addition, patients were asked to advise on interpretation and writing up of results. Results will be shared and discussed with the national patient community of cardiovascular diseases ('Harteraad').

Ethics

The study (National Trial Register identification number: NTR7331) was approved by the Medical Ethics Committee Utrecht, the Netherlands (reference number WAG/mb/16/003208) and complied with the Declaration of Helsinki. A waiver of informed consent was given because our study had minimal risk to subjects and could otherwise not be carried out logistically. Personal and research data were handled and stored according to the European General Data Protection Regulation (GDPR).

RESULTS

Among the 1,795 callers with chest discomfort (mean age 58.8 (SD 19.5) years, 55.3% women), 8.6% of women and 15.0% of men had an ACS. In women with an ACS, 18.8% had a STEMI, 48.2% a NSTEMI, 20.0% an UAP, and 13.0% non-classified ACS. In men with ACS, 32.5% had a STEMI, 36.7% a NSTEMI, 27.5% an UAP, and 3.3% non-classified ACS.

A total of 22 (2.2%) women and 23 men (2.9%) had another LTE than ACS (e.g. pulmonary embolism, thoracic aortic dissection, acute abdominal aneurysm, acute heart failure).

Patient and call characteristics

In table 1, patient and call characteristics are presented for women and men with and without ACS.

Men and women with ACS were older than those without ACS (mean age of women 73.6 vs. 57.8 years, $p < 0.001$, men 67.2 vs. 56.9 years, $p < 0.001$), and the mean duration of the telephone calls shorter (women 6:47 vs. 7:47 minutes, $p = 0.021$, men 6:31 vs. 7:33 minutes, $p = 0.004$).

The GP was consulted by the triage nurse in the majority of cases (52.2% in women and 55.5% in men, $p = 0.161$). However, in women with ACS, the GP was less often consulted than in women without ACS (41.2% vs. 53.2%, $p = 0.034$). In men such a difference was not observed (53.3% vs. 55.9%, $p = 0.607$). In around half of the calls, someone else called on behalf of the patient; somewhat less often in women than in men (49.5% vs. 54.7%, $p = 0.029$). In cases with ACS, for both sexes more often someone else called than in those without ACS (in women 69.4% vs. 47.7%, $p < 0.001$, in men 65.8% vs. 52.8%, $p = 0.008$). In men with ACS, most often their female partner (53.3%) called, while in women with ACS, it was either their male partner (17.6%), their daughter (20.0%) or a nurse (17.6%). See appendix-table 2.

Table 1. Baseline characteristics of 993 (55.3%) women and 802 (44.7%) men patients contacting the OHS-PC with chest discomfort (pain, pressure, tightness, or discomfort)

Characteristics	993 women		802 men	
	ACS	No ACS	ACS	No ACS
	N = 85 (8.6%) N = 908 (91.4%)		N = 120 (15.0%) N = 682 (85.0%)	
Mean age in years (SD)	73.6 (±14.1)	57.8 (±20.1)	67.2 (±13.0)	56.9 (±19.2)
Call characteristics				
Mean call duration in min (SD)	6:47 (±5:16)	7:47 (±3:48)	6:31 (±3:13)	7:33 (±3:42)
Mean patient's introduction duration in min (SD)	0:14 (± 0:08)	0:19 (±0:13)	0:16 (±0:11)	0:19 (±0:14)
Triage nurse consulted the GP	35 (41.2)	483 (53.2)	64 (53.3)	381 (55.9)
Someone else called on behalf of patient	59 (69.4)	433 (47.7)	79 (65.8)	360 (52.8)
The patient or person who called expressed concerned *	36 (97.3)	409 (88.9)	52 (96.3)	321 (86.5)
Chest pain *	81 (98.8)	817 (93.1)	110 (92.4)	624 (94.5)
Severe Pain (>7 on a scale 0-10)*	17 (65.4)	147 (38.1)	13 (23.6)	87 (30.4)
Duration *				
> 15 min	66 (100)	729 (95.8)	99 (97.1)	541 (94.6)
< 12 hrs	60 (85.7)	575 (72.7)	88 (81.5)	431 (72.6)
Location **				
Retrosternal*	33 (62.3)	263 (40.3)	42 (52.5)	191 (39.7)
Right or left side thorax *	14 (26.4)	260 (39.8)	26 (32.5)	211 (43.9)
Type of pain ***				
Pressing/heavy/tightening*	44 (78.6)	423 (61.5)	78 (82.1)	284 (57.4)
Stabbing *	8 (14.3)	155 (22.5)	8 (8.4)	131 (26.5)
Radiation of chest pain ****				
Any location*	61 (85.9)	485 (68.6)	65 (63.7)	292 (57.1)
Arm *	31 (75.6)	188 (45.9)	47 (56.0)	117 (34.8)
Between the shoulder blades *	11 (52.4)	159 (41.7)	14 (27.5)	91 (29.4)
Jaws *	10 (50.0)	66 (22.9)	1 (2.6)	28 (11.6)

Table 1. (Continued)

Characteristics	993 women			802 men		
	ACS	No ACS	p-value	ACS	No ACS	p-value
	N = 85 (8.6%) N = 908 (91.4%)			N = 120 (15.0%) N = 682 (85.0%)		
Shortness of breath *	47 (72.3)	455 (66.3)	0.328	53 (60.9)	329 (62.4)	0.788
Symptoms similar to previous cardiac events *	13 (32.5)	79 (21.4)	0.108	27 (52.9)	92 (32.1)	0.004
ANS-related symptoms						
Sweating *	28 (49.1)	234 (42.5)	0.340	43 (52.4)	168 (38.1)	0.015
Nausea or vomiting *	16 (44.4)	240 (56.2)	0.173	27 (45.8)	122 (42.7)	0.661
Pallor *	17 (50.0)	91 (29.8)	0.017	20 (40.8)	82 (33.)	0.315
Dizziness or near fainting *	13 (18.6)	197 (24.4)	0.277	17 (15.9)	127 (20.2)	0.249
Medical history						
CV disease or risk factors*	54 (78.3)	407 (57.5)	0.001	75 (72.1)	359 (61.9)	0.046
Coronary artery disease *	17 (42.5)	114 (25.1)	0.017	45 (57.0)	151 (38.4)	0.002
Hypertension *	22 (71.0)	142 (35.1)	<0.001	17 (47.2)	94 (33.0)	0.091
Diabetes mellitus *	12 (41.4)	56 (14.6)	<0.001	12 (28.6)	59 (20.3)	0.220
Hypercholesterolemia, use of statins*	8 (36.4)	81 (23.2)	0.161	19 (45.2)	62 (23.3)	0.003

*These variables had missing values

**p-value comparing retrosternal or left/right side thorax vs. others locations of pain together (retrosternal, left/right side thorax, back/shoulder, epigastric region)

*** Pressing/ heavy/tightening pain vs. other types of pain (stabbing, burning, cramping, tearing). Stabbing pain: stabbing vs. other types of pain (pressing/heavy/tightening, burning, cramping, tearing)

**** p-value comparing radiation arm or back/shoulder or jaws vs. no radiation

NRS: Numeric Rating Scale

ANS-related symptoms: Autonomous nervous system related symptoms

CV (cardiovascular) disease or risk factors; patient reported history of previous coronary artery disease, heart failure, stroke, cardiac arrhythmia, hypertension, and/or diabetes.

Coronary artery disease: patient reported history of prior myocardial infarction and interventions, stable or unstable angina pectoris

Callers expressed concerns about their symptoms in nearly all calls, also in those without an ACS; women with ACS vs. women without ACS 97.3% vs. 88.9% ($p=0.109$), and men with ACS vs. men without ACS 96.3% vs. 86.5% ($p=0.041$).

Both women and men with ACS more often had a history of cardiovascular disease or cardiovascular risk factors (e.g. hypertension and diabetes) than those without (women 78.3% vs. 57.5%, $p=0.001$, and in men these proportions were 72.1% vs. 61.9% ($p=0.046$), respectively).

Symptom presentation

Chest pain was the most common complaint, both in those with and without an ACS; in women with and without ACS 98.8% and 93.1% ($p=0.055$), and in men 92.4% and 94.5%, respectively ($p=0.364$). Retrosternal located chest pain was more common in women and men with ACS than in those without ACS (women 62.3% vs. 40.3%, $p=0.002$, and men 52.5% vs. 39.7%, $p=0.032$). Also, radiation of pain to the arms seemed indicative of ACS in both sexes (women with vs. without ACS 75.6% vs. 45.9%, $p<0.001$, and men 56.0% vs. 34.8%, $p<0.001$), as was pressing/heavy/tightening chest pain (women with vs. without ACS 78.6% vs. 61.5%, $p=0.011$ and men 82.1% vs. 57.4%, $p<0.001$). Only in women radiation to the jaw (50.0% vs. 22.9%, $p=0.007$) and severe pain (8 or more on a Numeric Rating Scale 0-10) was indicative for ACS (65.4% vs. 38.1%, $p=0.006$). Only in men, stabbing pain was discriminative in that it was very rare in those with ACS (8.4% vs. 26.5%, $p<0.001$).

Of the autonomous nervous system (ANS)-related symptoms, nausea/vomiting and dizziness/near fainting were not indicative for ACS in either sex, with the exception of a pale face that was discriminative in women (50.0% vs. 29.8%, $p=0.017$), and sweating in men (52.4% vs. 38.1%, $p=0.015$).

Recognition of symptoms being similar to a previous cardiac event was discriminative for ACS in men (52.9% vs. 32.1%, $p=0.004$), but not clearly for ACS in women (32.5% vs. 21.4%, $p=0.108$).

Diagnoses

The most common non-ACS diagnoses in both sexes were (i) non-urgent cardiovascular diseases such as stable angina pectoris, stable heart failure and arrhythmias (19.5% of all female callers with chest discomfort vs. 21.2% of male callers, $p=0.384$) and (ii) non-cardiac unspecified chest pain (women 16.4% vs. 19.8% men, $p=0.061$). Women more often than men were diagnosed with musculoskeletal problems (women 20.8% vs. men 14.1%, $p=0.001$) and psychogenic conditions (women 14.0% vs. men 8.4%, $p<0.001$).

Table 2. Diagnosis of 1,795 patients who contacted the OHS-PC for chest discomfort (pain, pressure, tightness, or discomfort), divided in women and men

Diagnosis, n (%)	Women n= 993 (55.3%)	Men n=802 (44.7%)	p-value
Acute coronary syndrome	85 (8.6)	120 (15.0)	<0.001
STEMI	16 (18.8)	39 (32.5)	0.037
NSTEMI	41 (48.2)	44 (36.7)	0.114
UAP	17 (20.0)	33 (27.5)	0.250
Non-classified ACS	11 (13.0)	4 (3.3)	0.013
Life threatening events (LTE's)	22 (2.2)	23 (2.9)	0.448
Pulmonary embolism	6 (27.3)	7 (30.4)	0.815
Thoracic aortic dissection	4 (18.2)	2 (8.7)	0.349
Acute abdominal aneurysm	3 (13.6)	2 (8.7)	0.598
Other*	9 (40.9)	12 (52.2)	0.449
Non-urgent cardiovascular diseases**	194 (19.5)	170 (21.2)	0.384
Non-cardiac chest pain, not further specified ***	163 (16.4)	159 (19.8)	0.061
Musculoskeletal pain	199 (20.0)	113 (14.1)	0.001
Psychogenic disorders	139 (14.0)	67 (8.4)	<0.001
Gastrointestinal tract disorders	76 (7.7)	62 (7.7)	0.951
Respiratory tract disorders	52 (5.2)	45 (5.6)	0.727
Other non-urgent diagnoses***	63 (6.3)	43 (5.4)	0.380

*Acute heart failure, stroke, severe COPD exacerbation, sepsis, coronary spasm probably caused by hypokalaemia, diabetic ketoacidosis, epileptic insult, bleeding from oesophageal varices, ovarian torsion, ventricular fibrillation.

** Stable angina pectoris (including atypical chest pain), stable heart failure, arrhythmias, hypertension

*** Cardiac pathology unlikely after cardiologist's diagnostic work-up, but without differential diagnosis

**** Amongst others: anemia, malignancy, vasovagal collapse, side effects medication, dermatologic diseases

Urgencies

Women and men were equally sent an ambulance; overall (43.6% vs. 46.6%, $p=0.200$). These proportions were in women compared to men with ACS or other LTEs 66.4% vs. 67.1%, $p=0.897$).

Women and men in whom ACS was diagnosed had more often ambulances dispatched than in those showed not to have an ACS (women 72.9% vs. 40.9%, $p<0.001$, and men 70.0% vs. 42.5%, $p<0.001$). See table 3.

Table 3. Association between urgency allocation, diagnose ACS and other LTEs

Women	ACS n=85 (8.6%)	No ACS n=908 (91.4%)	p-value 1*	p-value 2**
U1	62 (72.9)	371 (40.9)	<0.001	<0.001
U2	12 (14.1)	231 (25.4)		
U3-U5	11 (13.0)	306 (33.6)		
Men	ACS n=120 (15.0%)	No ACS n=682 (85.0%)		
U1	84 (70.0)	290 (42.5)	<0.001	<0.001
U2	19 (15.8)	142 (20.8)		
U3-U5	17 (14.2)	250 (36.7)		
Women	ACS or LTE n=107 (10.8%)	No ACS or LTE n=886 (89.2%)		
U1	71 (66.4)	362 (40.9)	<0.001	<0.001
U2	21 (19.6)	222 (25.1)		
U3-U5	15 (14.0)	302 (34.0)		
Men	ACS or LTE n=143 (17.8%)	No ACS or LTE n=659 (82.2%)		
U1	96 (67.1)	278 (42.2)	<0.001	<0.001
U2	24 (16.8)	137 (20.8)		
U3-U5	23 (16.1)	244 (37.0)		

* p-value 1: U1 vs. U2, U3, U4 and U5

** p-value 2: U1,U2 vs. U3,U4,U5

***LTE = life threatening event. Life threatening events consist of: ACS; pulmonary embolism; thoracic aortic dissection; acute heart failure; stroke; abdominal aortic aneurysm; severe COPD exacerbation; diabetic ketoacidosis; coronary spasm probably caused by hypokalaemia; epileptic insult; bleeding from oesophageal varices; ovarian torsion; ventricular fibrillation.

DISCUSSION

For both sexes, retrosternal pain, pain described as pressing, heavy or tightening, and radiation to the arm were indicative of ACS in patients presenting with chest discomfort to out-of-hours primary care (OHS-PC). Radiation of pain to the jaw, severe pain, and a pale face was indicative for ACS in women. In men with chest discomfort sweating was positive related to ACS and stabbing pain negatively. Women and men were equally often sent an ambulance.

Our finding that radiation of pain to the arm and chest pressure were discriminative for ACS in both sexes was not reported in the two previous studies that assessed ACS symptoms using the same methodology. The US study in ED-setting found that

radiation to the arm was indicative for ACS in women but not for men, and chest pressure was distinctive for men but not for women.¹³ The OHS-PC study reported opposite to our study that radiation to the arm was indicative for ACS in men, but not in women, and reported similar to our study that stabbing pain is very uncommon in men with ACS.¹⁷

Regarding dispatching the ambulance, the aforementioned OHS-PC study and two EMS studies showed, similar to our findings, that there was no difference in dispatch priorities between men and women with ACS.^{4,17,23} This is in contrast with studies that show delay in hospital presentation of women with ACS.^{9,24}

We need to realize that focusing on differences may blur the large overlap in symptoms. Moreover, comparing *selectively* women with ACS to men with ACS as many previous studies did, is clinically irrelevant.^{9,14,25} Clinicians, including GPs, and triage nurses need to know whether and how women with ACS differ from women without ACS, with the same question for men. Nevertheless, even guidelines stick to comparing those with established disease, and express the view that women with ACS more likely present with less specific symptoms than men with ACS.^{1,26} Unfortunately, public awareness campaigns follow this reasoning, and over-emphasize sex differences in women awareness campaigns ('Go Red for Women' in the United States and 'Invisible me' in Australia).^{7,25,27} Unbalanced attention to differences, neglecting the much larger overlap may even introduce new blind spots in recognizing ACS in women.²⁸

A likely reason behind the predominant message that women present with other ACS symptoms than men is the difference in pathophysiology of coronary artery disease. Women, compared to men, more often have elongated plaques, located on bifurcations in epicardial coronaries, coronary spasm, microvascular dysfunction, and spontaneous coronary dissection.^{27,29} These pathophysiological differences have an effect on interventional treatment and prognosis.^{2,29} However, these differences do not necessarily imply an effect on symptom presentation because the pain pathway is equal in women and men: i.e. triggered by myocardial ischemia.^{30,31} A supply and demand mismatch of the myocardial oxygen consumption triggers sensory nerve endings in the myocardium and cause ischemia symptoms, and this is irrespective of the fact whether the ischemia is caused by a plaque rupture in an epicardial artery or spasm, or any other cause.³¹ The sex differences in pathophysiology of ACS do therefore not support the belief in differences in ACS symptoms between women and men.

Another reason behind the belief of 'vague' symptom presentation in women with ACS might be that they seem to present a larger number of symptoms than men with ACS, and this may be interpreted as 'vague' by physicians.^{15, 32} The presentation of multiple symptoms may influence the prompt recognition of heart disease and initial actions on the part of health care providers.^{32, 33} In a study from 2018, 2009 women and 976 men hospitalized for myocardial infarction, healthcare providers initially thought symptoms of women (53.4%) were less often heart-related than in men (36.7%).³² Women and men had the same chest pain symptoms, but women reported more additional symptoms.³²

In our study, the call duration and the number of GP consultations by the triage nurse were similar among women and men, suggesting that triage nurses seem not to experience more difficulties in interpreting symptoms in women than men. This is in line with a prospective study with 2,795 patients with chest discomfort in ED-setting that showed the physicians' diagnostic uncertainty for the presence of ACS in women was not more common as compared to men.³⁴

Interestingly, in the majority of calls in our study someone else than the patient called the OHS-PC (women with ACS 69.4%, without ACS 47.7%, and men with ACS 65.8%, and without ACS 52.8%). This was also highlighted in an Australian study among 1,681 patients with an acute myocardial infarction; in 90.5% of the women with AMI someone else called on behalf of the patient and in 87.8% of the men with AMI.³⁵

Strengths and limitations

We analysed the very first conversations with symptom presentation of a large sample of patients calling the OHS-PC because of chest discomfort. We analysed the conversations without knowledge of the eventual diagnosis (no hindsight bias of the researcher or recall bias of the patient). Another strength is that our results are generalizable to comparable primary care settings, e.g. UK and Scandinavian countries, and some other European countries. Our results may even be generalizable to EMS settings, since the prior probability of having an ACS is comparable in EMS settings as in OHS-PC settings.⁴ We had missing values on some clinical variables, a phenomenon common in routine care data.

CONCLUSIONS

Symptoms predictive of ACS were rather similar for women and men with chest discomfort, with some important exceptions, such as severity, type, and radiation of pain, and some autonomous nervous system related symptoms.

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APPENDICES

Appendix-Table 1: NTS urgency levels

NTS Urgency level	Definition	Response time	Medical help
U ₀ – Resuscitation	Loss of vital functions	Immediately	Ambulance
U ₁ – Life threatening	Unstable vital functions	Immediately, within 15 minutes	Ambulance
U ₂ – Emergent	Vital functions in danger or organ damage	As soon as possible, within 1 hour	Home visit by GP or consultation at OHS-PC
U ₃ – Urgent	Possible risk of damage, human reasons	A few hours (<3 hours)	Home visit by GP or consultation at OHS-PC
U ₄ – Non-urgent	Marginal risk of damage	24 hours	Consultation at OHS-PC or telephone advice
U ₅ – Advice	No risk of damage	Advice, no time related	Telephone advice

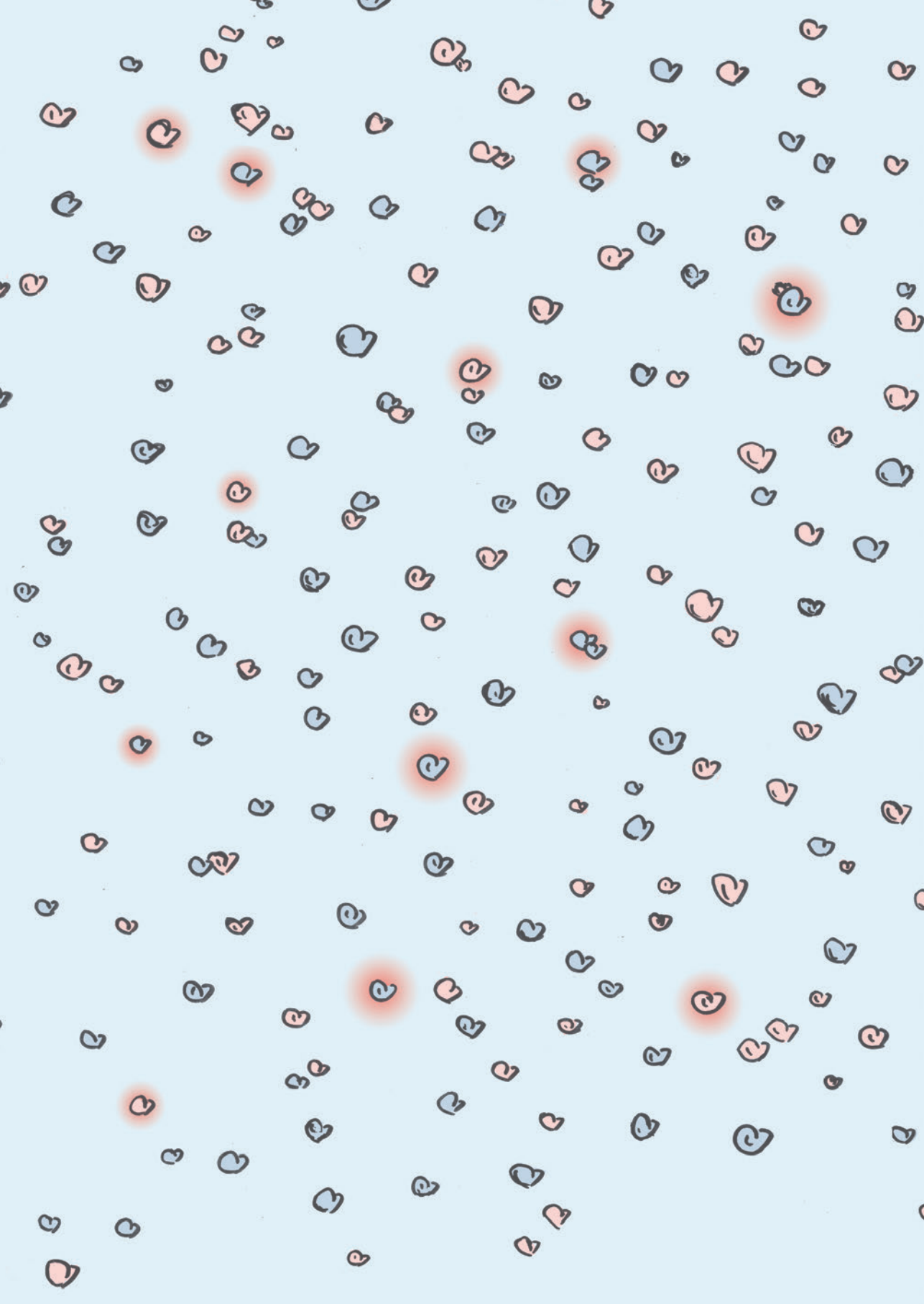
GP: General practitioner

NTS: Netherlands Triage Standard

OHS-PC: Out-of-hours services for primary care

Appendix-Table 2: Relation of caller to patient in women and men with ACS

Relationship caller	Women n = 85 (8.6%)	Men n = 120 (15.0%)	p-value
Someone else calls on behalf of patient	59 (69.4)	79 (65.8)	0.590
Partner	16 (18.8)	64 (53.3)	<0.001
Son, daughter or other family member	20 (23.5)	8 (6.7)	0.001
Nurse	15 (17.6)	4 (3.3)	<0.001
Other (neighbour, friend, colleague)	8 (9.4)	3 (2.5)	0.030



7

CHAPTER

Development of sex-specific prediction rules for early recognition of acute coronary syndrome in primary care: a cross-sectional study

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ABSTRACT

Objective To develop sex-specific symptom-based prediction rules for diagnosing acute coronary syndrome (ACS) in patients with acute chest discomfort who call out-of-hours services for primary care (OHS-PC).

Design Cross-sectional study.

Setting Nine OHS-PCs in the Netherlands.

Participants 2,192 patients who called the OHS-PC for acute chest discomfort (pain, pressure, tightness, or discomfort) between 2014 and 2017.

Main outcomes measures Diagnosis of ACS.

Methods We collected symptoms and medical history by listening to the call recordings, and obtained the age of the patient and call characteristics from the electronic medical files of the OHS-PC. We retrieved diagnoses from the patient's medical records in general practice, including hospital specialists discharge letters. Multivariable logistic regression models were used to predict ACS, for women and men separately, and we calculated c-statistics to quantify the discriminative ability of the prediction rules. The prediction rules were internally validated using bootstrapping.

Results Among the 2,192 patients (mean age 59.1 years (SD 19.5), 55.3% women) who called with complaints of acute chest discomfort, 8.3% of women and 15.3% of men had an ACS. Age, pressing heavy chest pain, sweating, and radiation of chest pain were the strongest predictors for the diagnosis ACS in both sexes. The prediction model for women included seven predictors and had a discriminative ability (c-statistic) of 0.76 (95% CI 0.71-0.80). The prediction model for men included eight predictors and had a discriminative ability (c-statistic) of 0.72 (95% CI 0.68-0.76).

Conclusion These sex-specific prediction models for ACS had moderate to good discrimination, and they could, after external validation, be applied in general practice and OHS-PC for telephone triage of patients with chest discomfort.

INTRODUCTION

Chest discomfort is among the top five reasons for telephone contact in out-of-hours services for primary care (OHS-PC) and concerns 5% of all cases at the emergency department (ED) in the USA.^{1,2} In the Netherlands, around 80% of patients with chest discomfort first calls the general practitioner (GP) or OHS-PC while 20% directly calls the emergency medical service (EMS, or ambulance dispatch centre) or are self-referrals to the ED.^{3,4} Adequate triage and early diagnosis in these patients is vital, because in case of an underlying acute coronary syndrome (ACS) early effective therapeutic interventions ('time is muscle') improve the patient's outcome and prognosis.^{5,6} For the diagnosis of ACS, a 12-lead electrocardiogram (ECG) and troponin testing is needed.^{5,6} However, before the patient is referred to an ED where these diagnostic tests can be done, patient selection is needed on the basis of symptom presentation retrieved by telephone triage.^{7,8} Symptom-based differentiating ACS from other causes of chest discomfort is notoriously difficult.⁹ In contrast to the many prediction rules developed to diagnose ACS in the hospital, symptom-based prediction rules for diagnosing ACS in general practice and other prehospital settings are needed, but scarce.^{10,11} The efficiency and safety of telephone triage in OHS-PC currently remains poor, because in this low prevalence setting a high urgency (patient seen within one hour, by ambulance or GP) is allocated to 68.7% of chest discomfort patients, but on the other hand 11% of patients diagnosed in the hospital with an ACS did not receive a high urgency.^{12,13}

Most prediction rules for diagnosing ACS were developed in the ED setting, and included results from ECG and troponin testing.^{11,14} Such prediction rules cannot be straightforward implemented for telephone triage or in general practice because in the latter setting (i) these diagnostic tests are not available, (ii) the a priori risk of ACS is lower, and (iii) disease severity is less, compared to those seen in the ED.^{15,16} The prevalence of ACS among patients with chest discomfort who call OHS-PC or EMS is about 10%, and among those seen at the ED between 10 to 30%.^{14,16,17} Only one prediction rule was developed to predict ACS in primary care (the modified Grijseels prediction rule) and included male sex, radiation of chest pain to the neck or left arm, nausea or sweating, and history of coronary artery disease (CAD), which showed a moderate discriminative ability (c-statistic of 0.66) after external validation.^{10,18} Five other primary care prediction rules were developed to predict CAD in general, not specifically for ACS, e.g. the Marburg Heart Score (MHS) and INTERCHEST prediction rule (International Working Group on Chest Pain in Primary Care).¹⁹ In these studies both patients with acute and non-acute chest discomfort were included and the

prevalence of stable CAD showed to be 10.9% to 12.6%, while that of ACS was 1.5% to 2.5%. This, of course, limits their applicability for specifically diagnosing ACS in telephone triage of patients with acute chest discomfort.¹⁹

Interestingly, many studies report that women and men differ in reporting symptoms of ACS, but never have sex-specific prediction rules been developed.^{4 20}

The aim of this study was to develop and internally validate sex-specific prediction rules for diagnosing ACS in primary care, in women and men who call OHS-PC for acute chest discomfort.

METHODS

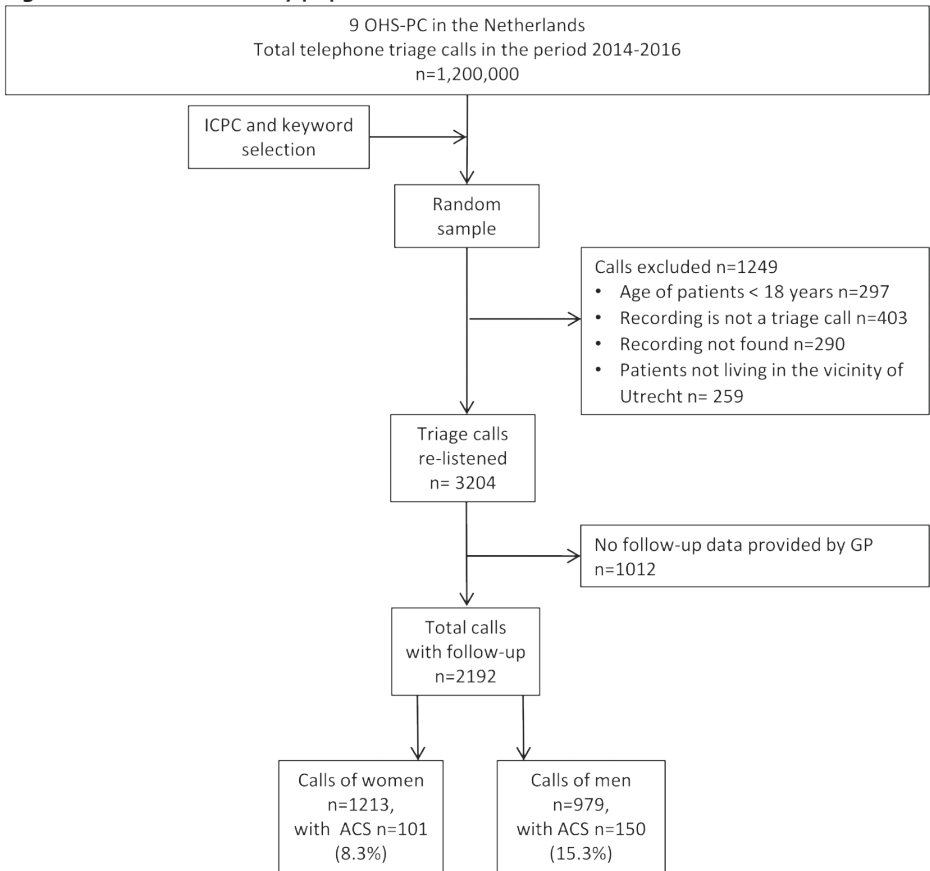
We performed a cross-sectional study among 2,192 patients who called one of nine participating OHS-PCs in the Netherlands with acute chest discomfort (pain, pressure, tightness, or discomfort) in the period 2014 and 2017.²¹ These OHS-PCs serve a total population of 1.5 million people, and cover around 300,000 calls a year. We first selected calls on the basis of the International Code for Primary Care (ICPC; a WHO world-wide code system for primary care) codes K01, K02, K03, K24, K74, K75, K76, K77, K93, L04, P74, R02, R98 and keywords thoracic pain, chest pain, myocardial infarction, heart attack and their common abbreviations (Figure 1).^{22 23} We included a broad variety of symptoms to capture the entire domain of patients that could be suspected of ACS. We drew a random sample of all available calls of these patients with the Random Number Generator (RAND) function in Microsoft Excel. Calls were excluded from re-listening when the patients' age was below 18 years or when the patient did not live in the surrounding area of the OHS-PC (because we could not retrieve a diagnosis from the general practitioner of patients living outside the area of the OHS-PCs). Calls were also excluded from re-listening when it did not concern a triage call (e.g. inter-collegial consultation) or when the recording was of poor quality (Figure 1).

Netherlands Triage Standard

In the Netherlands, OHS-PC covers primary care during 73% of week hours, and the initial contact is by telephone.²⁴ In most OHS-PCs, triage nurses use the 'Netherlands Triage Standard' (NTS) as a decision support tool to classify the urgency of the patient's condition.²⁵ The NTS is a modified version of the Manchester Triage Standard developed in ED.²⁵ Based on the patient's symptom presentation, the triage nurse

needs to select the most appropriate complaint out of 56 'main complaints' and their answers are linked to urgency recommendations. In patients with acute chest discomfort triage nurses most often choose the NTS main complaint 'chest pain', but also other main complaints could be used (Appendix-table 2 NTS main complaints with triage criteria).²³ The NTS generates urgency levels involving time frames within which a physician should see the patient: immediately, within 15 minutes by ambulance (U1); urgently, within one hour (U2); less urgent, within three hours (U3); non-urgent, the same day (U4), or telephone advice (U5) (Appendix-table 1).²⁵ The GP may see the patient at the patient's home or at the OHS-PC. At any time, triage nurses can consult the supervising GP on call.²⁶ In the Netherlands, GPs take care of 93% of all health care problems for 3% of the total health care budget.²⁷ The GP has a gatekeeper's role to hospital care, although people may call EMS (112) in case they suspect a life-threatening situation.²⁷

Figure 1. Flowchart of study population



Candidate predictors

Research team members (LW, DE) and medical students listened to the call recordings, blinded for the outcome, to collect data about symptoms, medical history and urgency allocation. Patient (age, sex) and call characteristics (call time, call duration) were collected from the OHS-PC electronic medical files of the patients. As candidate predictors we included the ACS predictors from the modified Grijseels prediction model (radiation, nausea or vomiting, sweating and history of coronary artery disease), and we added the CAD predictors from MHS and INTERCHEST prediction models (age, pain feels like pressure, CAD history or risk factors, patient assumes cardiac origin of pain), and, based on a recent study in OHS-PC, call time during the night (oam-9am).

^{10 18 19 28} Furthermore, we selected the NTS triage criteria (shortness of breath, pain severity, pain duration, pain score > seven on a Numeric Rating Scale (NRS ²⁹, range 1-10) and (near) fainting) as candidate predictors.

Outcome

The primary outcome was the diagnosis ACS. The final diagnoses were retrieved from the patient's GP, and based on the GP's electronic medical files which include ED and cardiologist discharge letters, and notes from the OHS-PC contact. An ACS was based on the cardiologist's diagnosis, and included information on levels of (high-sensitivity) troponin and electrocardiography results.

Sample size calculation

We calculated the minimally required sample sizes to test twenty candidate predictors for women and men separately, with the criteria proposed by Riley et al, using the 'pmsampsize' package in R.³⁰ Based on previous studies, we expected an ACS prevalence of 9% in women and 15% in men, and we used the modified Grijseels prediction model externally validated c-statistic of 0.66 to calculate an expected R-squared (0.169). ^{18 20 28 31} In women, the calculated minimum sample size was 962 suspected patients, including at least 87 patients diagnosed with ACS, and in men 962 suspected patients, with 145 patients with ACS. We decided to continue to include up to 100 women with ACS and 150 men with ACS.

Statistical analyses

Characteristics were compared between patients with and without information on the medical outcome - because some GPs refused diagnosis retrieval from their files - to allow for assessment of differences in characteristics between these patient groups (Appendix-table 3). There were no clinically meaningful differences in symptoms and patient or call characteristics between the 2,192 patients with information on the

outcome, and the 1,012 patients without knowledge of the medical outcome related to the OHS-PC contact because of acute chest discomfort.

We developed our sex-specific prediction model with adherence to the Transparent Reporting of a multivariable prediction rules for Individual Prognosis Or Diagnosis (TRIPOD) criteria.³² We used multivariable logistic regression analysis to predict the presence of ACS, using backward elimination with a high cut-off p-value < 0.20 for including predictors to minimize chances of overfitting.^{33,34} For missing data of predictors we carried out multiple imputation using the Multivariate Imputation via Chained Equation (MICE) package in R, with 30 imputation rounds and 30 iterations (Appendix-table 4 for missing data).³⁵ We pooled the results following Rubin's rules.³⁶ Predictors with over 60% missing were excluded from the analyses.³⁴

Internal validity of the models was assessed by means of bootstrapping, with replications of the analyses on 200 different samples in each of the 30 imputed sets, using the Regression Modelling Strategies ('rms') package in R.³⁷ Because the regression coefficients were estimated in the development set, the estimates are often too optimistic resulting in overly extreme predicted probabilities when the model is applied in a new dataset. External validation of the prediction rules was however not possible, because no similar database was available as validation sample.

Descriptive statistics were performed with SPSS version 25.0.0.2, and multiple imputation, model development and performance testing were done in R studio version 1.2.5033.

Patient and Public Involvement

No patients were involved in defining the research question or the outcome measures and neither were they involved in developing plans for design. However, patients participated in the discussion on implications and the implementation strategy. In addition, patients were asked to advise on interpretation and writing up of results. Results will be shared and discussed in more detail with the Dutch national patient community of cardiovascular diseases ('Harteraad').

Ethics

The study (National Trial Register identification number: NTR7331) was approved by the Medical Ethics Committee Utrecht, the Netherlands (reference number WAG/mb/16/003208) and complied with the Declaration of Helsinki. A waiver of informed consent was given because our study had minimal risk to subjects and could otherwise

not be carried out logistically. Personal and research data were handled and stored according to the European General Data Protection Regulation (GDPR).

RESULTS

Among the 2,192 callers (55.3% women) with acute chest discomfort and a final diagnosis, 251 (11.5%) had an ACS (women 8.3%, men 15.3%) (Table 1 and Table 2). The mean age was 59.1 (SD 19.5) years (women 59.4 (SD 20.2) years, men 58.7 (SD 18.6) years).

Women and men with ACS were significantly older than those without (mean age women with ACS 73.8 vs. women without ACS 58.1 years, $p < 0.001$ and mean age in men with ACS 67.0 vs. men without ACS 57.2 years, $p < 0.001$, respectively). The majority of patients (68.2%) were allocated a high urgency (seen within one hour; U1 or U2). For those with ACS, 88.4% had been allocated a high urgency (women 88.1%, men 88.7%) and for those without ACS 65.6% (women 66.5%, men 64.4%).

Calls of patients with ACS were shorter (median call duration 5:27 minutes for women with ACS vs. 6:59 minutes for women without ACS, $p < 0.001$ and for men 6:04 vs. 6:56 minutes, $p < 0.001$). The triage nurse consulted the GP for supervision in about half of the calls, similarly in both sexes. The majority of all patients had chest pain (94.5%), without differences between women and men, with or without ACS.

Table 1. Characteristics of 1,213 women who called OHS PC with acute chest discomfort between 2014-2017, divided between patients with and without ACS.

Characteristics	ACS n =101 (8.3%)	No ACS n =1112 (91.7%)	p-value
Patient characteristics			
Mean age in years (SD)	73.8 (13.5)	58.0 (20.2)	<0.001
Call characteristics			
Median call duration in min (IQR)	5:27 (3:57-8:24)	6:59 (5:06-9:47)	<0.001
Mean introduction time in min (IQR)	0:13 (0:09-0:18)	0:17 (0:11-0:26)	<0.001
Call during the night (oam-9am)	34 (33.7)	304 (27.3)	0.175
Triage nurse consulted the GP	43 (42.6)	580 (52.2)	0.065
Someone else called on behalf of patient	69 (68.3)	515 (46.3)	<0.001
The person who calls expressed concerns	42 (95.5)	507 (90.5)	0.275

Table 1. (Continued)

Characteristics	ACS n =101 (8.3%)	No ACS n =1112 (91.7%)	p-value
Medical history and risk factors			
Cardiovascular disease or CV risk factors	70 (81.4)	552 (61.1)	<0.001
History of coronary artery disease	23 (47.9)	131 (24.2)	<0.001
Diabetes mellitus	14 (42.4)	66 (14.3)	<0.001
Hypertension	26 (72.2)	162 (34.0)	<0.001
Hypercholesterolemia/statin use	10 (40.0)	96 (22.6)	0.047
Cardiac arrhythmia	4 (14.8)	125 (26.2)	0.189
Symptom presentation			
Chest pain	95 (96.9)	1007 (94.1)	0.246
Shortness of breath	57 (71.3)	559 (65.4)	0.290
Chest pain duration <12 hours	74 (86.0)	703 (72.3)	0.006
Pain intensity severe (NRS >7, range 1-10)	19 (61.3)	184 (39.6)	0.017
Pressing heavy chest pain*	58 (81.7)	525 (62.5)	0.001
Stabbing chest pain*	8 (11.3)	190 (22.6)	0.026
Chest pain located retrosternal**	36 (54.5)	326 (40.0)	0.020
Chest pain located left or right on thorax**	19 (28.8)	318 (39.0)	0.102
Radiation of chest pain to any location	74 (86.0)	575 (67.8)	<0.001
Radiation to the arm ***	37 (43.0)	218 (25.7)	0.001
Radiation to the shoulder blades ***	14 (16.3)	190 (22.4)	0.190
Radiation to the jaws ***	10 (11.6)	77 (9.1)	0.439
Sweating	36 (52.9)	279 (42.0)	0.083
Nausea or vomiting	24 (52.2)	295 (56.6)	0.560
Pallor or ashen skin	22 (59.5)	139 (44.3)	0.079
(Near) fainting	8 (9.5)	76 (7.7)	0.562
Palpitations	10 (100.0)	183 (84.7)	0.181
Patient recognizes symptoms from previous cardiac event	17 (35.4)	100 (22.0)	0.037
Urgency allocation			
High urgency (U1 or U2)	89 (88.1)	740 (66.5)	<0.001
U1	75 (74.3)	443 (39.8)	
U2	14 (13.9)	297 (26.7)	
Low urgency (U3 or U4 or U5)	12 (11.9)	372 (33.5)	

*Pain described by patient. Pressing heavy pain: pressing, heavy or tightening pain vs. other types of pain (stabbing, burning, cramping, tearing) Stabbing pain: stabbing vs. other types of pain (pressing, heavy, tightening, burning, cramping)

** Retrosternal location vs. other pain locations. Left or right side thorax vs. other pain locations

*** Radiation location vs. no radiation and radiation other location

Table 2. Characteristics of 979 men who called OHS PC with acute chest discomfort between 2014-2017, divided between patients with and without ACS.

Characteristics	ACS n =150 (15.3%)	No ACS n =829 (84.7%)	p-value
Patient characteristics			
Mean age in years (SD)	67.0 (12.6)	57.2 (19.2)	<0.001
Call characteristics			
Median call duration in min (IQR)	6:04 (4:03-8:17)	6:56 (5:10-9:23)	<0.001
Mean introduction time in min (IQR)	0:14 (0:09-0:21)	0:17 (0:11-0:25)	0.008
Call during the night (oam-gam)	62 (41.3)	188 (22.7)	<0.001
Triage nurse consulted the GP	75 (50.0)	449 (54.2)	0.347
Someone else called on behalf of patient	98 (65.3)	432 (52.1)	0.003
The person who calls expressed concerns	61 (96.8)	378 (87.1)	0.025
Medical history and risk factors			
Cardiovascular disease or CV risk factor	106 (78.5)	464 (64.4)	0.001
History of coronary artery disease	54 (56.3)	181 (38.8)	0.002
Diabetes	22 (39.3)	78 (22.0)	0.005
Hypertension	22 (51.2)	113 (33.3)	0.021
Hypercholesterolemia/statin use	27 (50.0)	79 (24.5)	<0.001
Cardiac arrhythmia	12 (25.0)	89 (25.2)	0.975
Symptom presentation			
Chest pain	139 (93.3)	758 (94.9)	0.433
Shortness of breath	63 (61.2)	415 (63.1)	0.710
Chest pain duration <12 hours	113 (82.5)	510 (71.3)	0.008
Severe pain intensity severe (NRS >7, range 1-10)	18 (25.4)	116 (33.0)	0.209
Pressing/heavy chest pain*	95 (81.2)	345 (57.7)	<0.001
Stabbing chest pain*	9 (7.7)	159 (26.6)	<0.001
Chest pain located retrosternal**	52 (53.1)	227 (38.7)	0.007
Chest pain located on left or right of the thorax**	28 (28.6)	262 (44.6)	0.003
Radiation of chest pain to any location	83 (65.4)	347 (56.2)	0.058
Radiation to the arm ***	54 (42.5)	143 (23.2)	<0.001
Radiation to the shoulder blades ***	19 (15.0)	103 (16.7)	0.631
Radiation to the jaws ***	4 (3.1)	33 (5.3)	0.299
Sweating	54 (51.9)	190 (35.8)	0.002
Nausea or vomiting	31 (43.1)	139 (39.9)	0.624
Pallor or ashen skin	36 (64.3)	125 (46.8)	0.017
(Near) fainting	9 (6.7)	50 (6.7)	0.996
Palpitations	8 (50.0)	83 (75.5)	0.034
Patient recognizes symptoms from previous cardiac event	30 (46.9)	103 (29.5)	0.006

Table 2. (Continued)

Characteristics	ACS n =150 (15.3%)	No ACS n =829 (84.7%)	p-value
Urgency allocation			
High urgency (U1 or U2)	133 (88.7)	534 (64.4)	<0.001
U1	106 (70.7)	350 (42.2)	
U2	27 (18.0)	184 (22.2)	
Low urgency (U3 or U4 or U5)	17 (11.3)	295 (35.6)	

*Pain described by patient. Pressing heavy pain: pressing, heavy or tightening pain vs. other types of pain (stabbing, burning, cramping, tearing) Stabbing pain: stabbing vs. other types of pain (pressing, heavy, tightening, burning, cramping)

** Retrosternal location vs. other pain locations. Left or right side thorax vs. other pain locations

*** Radiation location vs. no radiation and radiation other pain

Diagnoses

Of all women with ACS, 22.8% had a ST-segment elevation myocardial infarction (STEMI), 46.5% had a non ST-segment elevation myocardial infarction (NSTEMI), 19.8% had unstable angina pectoris (UAP), and 10.9% had non-classified ACS. In men with ACS, 33.3% had a STEMI, 36.7% had a NSTEMI, 26.0% UAP, and 4.0% non-classified ACS (Table 3). The majority (96.0%) of ACS patients was diagnosed by a cardiologist. Ten ACS patients (4.0%) were not diagnosed by a cardiologist; four died before arrival of the ambulance, one patient died after resuscitation at the ED (all five were classified as acute cardiac death due to ACS), and in five patients the ACS diagnosis was solely based on the GP's interpretation and in all five it considered patients with a short life expectancy who were not referred to the hospital.

Twenty-eight (2.3%) women and 38 men (3.9%) had another life-threatening event than ACS, e.g. pulmonary embolism, thoracic aortic dissection, acute abdominal aneurysm or acute heart failure.

All other patients (85.6%) had non-urgent medical conditions such as non-urgent cardiovascular disease (18.9%), musculoskeletal pain (17.9%), non-cardiac chest pain (not further specified) (16.9%), psychogenic disorder (11.4%), gastrointestinal disorders (7.2%), respiratory disorders (5.3%), and other non-urgent diagnoses (8.0%).

Table 3. Diagnoses of 2,192 patients who contacted the OHS-PC for acute chest discomfort between 2014-2017, by sex.

Diagnosis, n (%)	Women n= 1213	Men n= 979	p-value
Acute coronary syndrome	101 (8.3)	150 (15.3)	<0.001
STEMI	23 (22.8)	50 (33.3)	0.071
NSTEMI	47 (46.5)	55 (36.7)	0.119
UAP	20 (19.8)	39 (26.0)	0.256
Non-classified ACS	11 (10.9)	6 (4.0)	0.033
Life threatening events (LTEs)	28 (2.3)	37 (3.8)	0.043
Pulmonary embolism	8 (28.6)	10 (27.0)	0.890
Acute abdominal aneurysm	2 (7.1)	3 (8.1)	0.885
Thoracic aortic dissection	1 (3.6)	4 (10.8)	0.278
Other*	17 (60.7)	20 (54.1)	0.591
Non-urgent cardiovascular diseases**	223 (18.4)	191 (19.5)	0.069
Musculoskeletal pain	245 (20.2)	148 (15.2)	0.039
Non-cardiac chest pain, not further specified ***	191 (15.7)	179 (18.3)	0.012
Psychogenic disorders	165 (13.6)	85 (8.7)	0.005
Gastrointestinal tract disorders	89 (7.3)	68 (6.9)	0.776
Respiratory tract disorders	61 (5.2)	56 (5.7)	0.203
Other non-urgent diagnoses****	110 (9.1)	65 (6.6)	0.152

* Stroke, severe COPD exacerbation, acute severe heart failure, sepsis, coronary spasm caused by hypokalaemia, diabetic ketoacidosis, epileptic insult, bleeding from oesophageal varices, ovarian torsion, ventricular fibrillation.

** Stable angina pectoris (including atypical chest pain), stable heart failure, arrhythmias, hypertension

*** Cardiac pathology unlikely after cardiologist's or GP's diagnostic work-up, but without differential diagnosis

**** Amongst others: anemia, carcinoma, vasovagal collapse, side effects medication, dermatologic diseases

Model development, performance and internal validation

In women, seven predictors were included in the final model; 1) age, 2) sweating, 3) radiation of chest pain, 4) pressing heavy chest pain, 5) severe pain intensity on NRS > seven, 6) pain duration shorter than twelve hours and 7) history of diabetes mellitus (Table 4). The prediction model for ACS had an apparent c-statistic of 0.78 (95% CI 0.74-0.83). After bootstrapping, the optimism corrected c-statistic was 0.76 (95% CI 0.71-0.80).

Table 4. Final multivariable logistic regression model with predictors for the diagnosis ACS in women

Predictors	Beta (SE)	Odds ratio (95% CI)	p-value
Intercept	-7.297 (0.712)		
Age per year	0.043 (0.007)	1.04	<0.001
Sweating	0.434 (0.249)	1.54	0.082
Radiation	0.915 (0.312)	2.50	0.004
Pressing heavy chest pain	0.620 (0.320)	1.86	0.054
Pain intensity severe (NRS >7, range 1-10)	0.313 (0.325)	1.37	0.337
Chest pain duration < 12 hours	0.429 (0.334)	1.54	0.200
History of diabetes mellitus	0.464 (0.335)	1.59	0.170

Apparent c-statistic 0.78 (95% CI 0.74-0.83)

Adjusted c-statistic 0.76 (95% CI 0.71-0.80)

Calibration slope 0.87

SE: standard error

CI: confidence interval

In men, eight predictors were included in the final model; 1) age, 2) sweating, 3) radiation of chest pain, 4) pressing heavy chest pain, 5) history of diabetes mellitus, 6) calling during the night (oam-9am) 7) patient recognizes symptoms from previous cardiac events and 8) shortness of breath) (Table 5). The prediction model for ACS had an apparent c-statistic of 0.75 (95% CI 0.71-0.79). After bootstrapping, the optimism corrected c-statistic was 0.72 (95% CI 0.68-0.76).

Table 5. Final multivariable logistic regression model with predictors for the diagnosis ACS in men

Predictors	Beta (SE)	Odds Ratio (95% CI)	p-value
Intercept	-4.756 (0.493)		
Age	0.026 (0.007)	1.03	<0.001
Sweating	0.599 (0.238)	1.82	0.013
Radiation	0.478 (0.222)	1.61	0.032
Pressing heavy chest pain	0.911 (0.259)	2.49	<0.001
History of diabetes mellitus	0.284 (0.274)	1.33	0.303
Patient calls during the night (oam-9am)	0.770 (0.201)	2.16	<0.001
Patient recognizes symptoms from previous cardiac event	0.296 (0.260)	1.34	0.257
Shortness of breath	-0.367 (0.253)	0.69	0.148

Apparent c-statistic 0.75 (95% CI 0.71-0.79)

Adjusted c-statistic 0.72 (95% CI 0.68-0.76)

Calibration slope 0.85

SE: standard error

CI: confidence interval

DISCUSSION

This is the first study to develop symptom-based, sex-specific prediction rules for the diagnosis ACS in patients calling OHS-PC with acute chest discomfort. Our prediction rule for women includes seven predictors that had an internal validated c-statistic of 0.76 (95% CI 0.71-0.80). Our prediction rule for men includes eight predictors with an internal validated c-statistic of 0.72 (95% CI 0.68-0.76).

Strengths and limitations

The major strength of this study is that we were able to analyse the original and very first conversations with health care providers of patients with acute chest discomfort without knowledge of the diagnosis; the assessment of symptoms was therefore not affected by bias caused by knowledge of the final diagnosis. Furthermore, a large sample size of unselected patients was available which allowed us to evaluate twenty candidate predictors in both women and men. We assessed the risk of selection due to missing outcome data, and our data suggest that this missingness was unlikely to bias our findings. For missing data on clinical characteristics, we carried out multiple imputation to obtain unbiased estimates of all the parameters.³⁵ Prediction rule development was done with adherence to the universally accepted TRIPOD criteria.³² Because we used data from nine different OHS-PCs our results will be well generalizable to other OHS-PC in the Netherlands, but also to similar OHS-PC settings in for example the UK and Scandinavian countries. Our results may also be generalizable to EMS settings, because the a priori chance of having an ACS among those calling for chest discomfort is rather similar in the EMS setting as in the OHS-PC setting.^{17,38}

A limitation of our study is that we were not able to perform external validation, because no similar database was available as validation sample. Our prediction rules therefore await further validation.

Another limitation is that we did not compare the performance of the sex-specific models to the performance of a generic model, alternatively with sex as statistical interaction term. However, we have chosen on clinical grounds to develop sex-specific models because the prevalence of ACS in OHS-PC is different in women and men and there are indications of differences in the pathophysiology of ACS, as well as differences in symptoms predictive for ACS.^{20,39,40}

Comparison with other studies

Our prediction rules show a higher discriminating ability for ACS than the modified Grijseels prediction rule, and they include more predictors.¹⁰ The higher discriminating ability can be largely explained by the addition of the strongest predictor age, which is in line with the notion that the prevalence of ACS increases with age.^{11 19 41} Similar to the modified Grijseels prediction rule our prediction rules include the predictors sweating and radiation, however, the modified Grijseels rule combined nausea and sweating to a single predictor (i.e., nausea or sweating).¹⁸ We found that only sweating (OR 1.54 women, OR 1.82 men), and not nausea, was a predictor for the diagnosis ACS. Age and patient's recognition of cardiac symptoms were common predictors in our model and in the MHS and INTERCHEST prediction models.⁴²⁻⁴⁵ Of the cardiovascular diseases (CVD) or CV risk factors, we found that a history of diabetes mellitus was a predictor for the diagnosis ACS in both women and men, while a history of CAD did not contribute to ACS prediction, in contrast to the modified Grijseels prediction rule, MHS and INTERCHEST studies.^{10 42}

Our prediction rules included some new variables compared to the existing prediction rules. In women, we found that a severe pain intensity (NRS > seven) was associated with an increased risk of ACS (OR 1.37). Studies reporting on the predictive value of pain severity for the diagnosis ACS are scarce, but one ED study among 3,306 patients with potential ACS found contrasting results; a high pain score (NRS nine or ten) was not associated with an increased likelihood of ACS.⁴⁶ However, that study did not perform sex stratified analyses. In men, we found that calling at night (oam-9am) was associated with a doubled risk of ACS (OR 2.16). This finding is consistent with a previous study in OHS-PC, that analysed different time slots of calling and found that the risk ratio for ACS at night for men was 2.33 (1.68–3.22, $p < 0.001$) and for women 1.29 (0.83–1.99, $p = 0.256$).²⁸ Previous studies in the ED setting also showed circadian variability in the occurrence of acute coronary events, with an early morning peak of ACS patients.⁴⁷⁻⁴⁹

We found a large overlap in symptoms in the men's and women's prediction rules. This is in contrast with studies – including guidelines - stressing differences in symptom presentation between women and men with ACS.^{50 51} Others, however, also stress the overlap between symptoms predictive for ACS in women and men.^{42 52 53} Importantly, however, most studies compared symptoms of men and women with *confirmed* ACS and did not include an evaluation of sex-specific comparison of symptom presentation of patients with chest discomfort, suspected of ACS, in whom ACS is diagnosed or not.^{53 54} Such studies are needed to inform clinician and triage nurses about whether and how women with ACS differ from women without ACS, and similarly for men.

Moreover, many previous studies suffer from recall or hindsight bias of both patient and researcher because patient interviews or questionnaires were taken when the outcome ACS was already known.

Implications for clinical practice and future research

Some of the findings of this study can be readily applied for improving diagnosis of ACS in OHS-PC. Although we do not know how well the models perform with external validation, we anticipate that the models will do better than the current decision support tool (the NTS) that is used in Dutch OHS-PC. The NTS performs poor because it underestimates the urgency (generated an U₃ to U₅ and not a U₁/U₂) in 27% of patients with ACS (sensitivity 0.73, 95% CI 0.68-0.78) and showed also poor efficiency (specificity 0.43, 95% CI 0.40-0.45).¹³ Importantly, the NTS does not include age as a predictor and we recommend age to consider in the ACS risk assessment in OHS-PC. Furthermore, in men with acute chest discomfort who call at night (oam-gam) dispatching an ambulance right away could be considered. Future research with external validation is recommended to further optimize the prediction models before application in OHS-PC, as well as application in EMS.

CONCLUSION

These first, mainly symptom-based, sex-specific prediction models for ACS have moderate to good discrimination, and they could, after external validation, be applied in general practice and OHS-PC for telephone triage of patients with chest discomfort.

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Appendix –Table 1. NTS urgency levels

NTS Urgency level	Definition	Response time	Medical help
U0 – Resuscitation	Loss of vital functions	Immediately	Ambulance
U1 – Life threatening	Unstable vital functions	Immediately, within 15 minutes	Ambulance
U2 – Emergent	Vital functions in danger or organ damage	As soon as possible, within 1 hour	Home visit by GP or consultation at OHS-PC
U3 – Urgent	Possible risk of damage, human reasons	A few hours (<3 hours)	Home visit by GP or consultation at OHS-PC
U4 – Non-urgent	Marginal risk of damage	24 hours	Consultation at OHS-PC or telephone advice
U5 – Advice	No risk of damage	Advice, no time related	Telephone advice

GP: General practitioner

NTS: Netherlands Triage Standard

OHS-PC: Out-of-hours services for primary care

Appendix-Table 2: NTS main complaints with triage criteria that generate an urgency U1 level, within the domain chest discomfort.

→ ABCD unstable (no main complaint is selected)		
Main complaint 'Chest pain'		
→ ABCD stable	AND severe chest pain (Numeric Rating Scale ²⁹ (NRS)-score ≥ 8) lasting less than 12 hours	
→ ABCD stable	AND mild (NRS ≤ 4) to moderate (NRS 5-7) chest pain lasting for less than 12 hours	AND one of the following: <ul style="list-style-type: none">• retrosternal located pain• tightening or pressing• radiation to jaw, arm or upper back• progressive pain intensity in short time• past or present autonomous nervous system-related symptoms• dizziness
Main complaint 'Collapse'		
→ ABCD stable	AND collapse	AND chest pain of any severity
Main complaint 'Back complaints'		
→ ABCD stable	AND severe upper back pain (NRS ≥8)	AND past or present autonomous nervous system-related symptoms

Urgency level U1: ambulance within 15 minutes

ABCD: acronym for Airway, Breathing, Circulation and Disability.⁵⁵ When the triage nurse starts the telephone triage with the NTS, the system requires a mandatory 'ABCD-check'; i.e. the triage nurse has to ask questions to assess whether the patient has life-threatening problems concerning the Airway, Breathing, Circulation and Disability for which an ambulance should be sent immediately.⁵⁶

Appendix-Table 3. Patient and call characteristics of 3,204 patients with chest discomfort calling OHS-PC between 2014-2017, comparing patients with and without information on the study outcome.

Characteristics N=3204	Follow-up n= 2192 (68.4%)	No follow-up n= 1012 (31.6%)	P-value
Patient characteristics			
Median age in years (IQR)	59.1 (19.5)	57.3 (20.4)	0.020
Female sex	1213 (55.3)	565 (55.8)	0.794
Call characteristics			
Median total call duration in min (IQR)	6:51 (4:59-9:23)	6:56 (5:04-9:15)	0.836
Mean patient's introduction in min (IQR)	0:17 (0:11-0:25)	0:17 (0:11-0:26)	0.052
Triage nurse consulted the GP	1147 (52.3)	519 (51.3)	0.583
Someone else called on behalf of patient	1114 (50.8)	479 (47.3)	0.066
The person who calls expressed concerns	988 (89.7)	430 (90.1)	0.804
Medical history and risk factors			
Cardiovascular disease or risk factor combined	1192 (64.6)	515 (62.3)	0.254
History of coronary artery disease	389 (33.8)	166 (32.4)	0.573
Diabetes mellitus	180 (19.9)	68 (18.0)	0.432
Hypertension	323 (36.1)	121 (31.9)	0.150
Hypercholesterolemia/statin use	212 (25.7)	88 (25.1)	0.842
Cardiac arrhythmia	230 (25.4)	102 (24.3)	0.684
Symptoms			
Chest pain	1981 (93.6)	894 (92.8)	0.417
Shortness of breath	1094 (64.5)	520 (64.3)	0.911
Chest pain duration <12 hours	1403 (73.2)	610 (69.6)	0.052
Pain intensity severe (NRS >7, range 1-10)	337 (36.6)	185 (43.0)	0.024
Pressing heavy chest pain*	1023 (62.9)	444 (61.6)	0.538
Stabbing chest pain*	366 (22.5)	177 (24.5)	0.280
Chest pain located retrosternal**	641 (40.9)	294 (40.2)	0.736
Chest pain located left or right on thorax**	627 (40.0)	294 (40.2)	0.945
Radiation of chest pain to any location	1077 (64.3)	458 (60.1)	0.047
Radiation to the arm ***	452 (42.2)	179 (39.8)	0.373
Radiation to the shoulder blades ***	326 (30.5)	136 (30.2)	0.924
Radiation to the jaws ***	124 (11.6)	41 (9.1)	0.156
Sweating	559 (40.9)	259 (42.0)	0.638
Nausea or vomiting	489 (49.5)	229 (47.1)	0.381
Pallor or ashen skin	322 (47.8)	136 (40.8)	0.038
(Near) fainting	143 (7.4)	72 (7.8)	0.678
Palpitations	284 (80.7)	125 (83.9)	0.396
Patient recognizes symptoms from previous cardiac event	250 (27.3)	102 (26.7)	0.819

Appendix-Table 3. (Continued)

Characteristics N=3204	Follow-up n= 2192 (68.4%)	No follow-up n= 1012 (31.6%)	P-value
Urgency allocation			
High urgency (U1 or U2)	1497 (68.3)	695 (31.7)	0.095
U1	974 (44.5)	390 (38.6)	
U2	522 (23.8)	271 (26.8)	
U3,U4,U5	696 (31.8)	351 (17.4)	

Appendix – table 4. Overview of the percentages of missing predictors, divided into patients with and without diagnosis ACS.

Characteristics, missing (%)	ACS n =251 (11.5%)	No ACS n =1941 (88.5%)
Mean in years age (SD)	0	0
Female sex	0	0
Median call duration in min (IQR)	0	0
Mean patient's introduction in min (IQR)	0	0
Triage nurse consulted the GP	0	0
Someone else called on behalf of patient	0	0
The person who calls expressed concerns	57.3	48.6
Cardiovascular disease or risk factor combined	12.0	16.4
History of coronary artery disease	42.6	48.1
Diabetes mellitus	64.5	58.0
Hypertension	68.5	58.0
Hypercholesterolemia/statin use	68.5	61.6
Cardiac arrhythmia	70.1	57.2
Chest pain	1.6	3.7
Shortness of breath	27.1	22.1
Chest pain duration <12 hours	11.2	13.1
Pain intensity severe (NRS >7, range 1-10)	59.4	57.9
Pressing heavy chest pain*	25.1	25.9
Stabbing chest pain*	25.1	25.9
Chest pain located retrosternal**	34.7	27.7
Chest pain located left or right on thorax**	34.7	27.7
Radiation of chest pain to any location	15.1	24.5
Radiation to the arm ***	37.5	52.5
Radiation to the shoulder blades ***	37.5	52.5
Radiation to the jaws ***	37.5	52.5
Sweating	31.5	38.5
Nausea or vomiting	53.0	55.2
Pallor or ashen skin	62.9	70.1
(Near) fainting	13.1	11.2
Palpitations	89.6	83.2
Patient recognizes symptoms from previous cardiac event	55.4	58.6



8

CHAPTER

General discussion

This thesis focused on telephone triage and diagnosis of patients presenting with chest discomfort in out-of-hours services for primary care (OHS-PC). In this general discussion we first summarize the main findings of the thesis, followed by a discussion about the relevance of considering the patient's eventual diagnosis in triage system research and telephone triage in clinical practice. For the latter topic we will elaborate on the overarching question: "Can we really reason in terms of urgencies during telephone triage at OHS-PC"? Finally, we reflect on the clinical case presented in the introduction of the thesis.

Main findings of the studies in this thesis:

- The Netherlands Triage Standard (NTS) decision support tool performed poorly regarding both safety and efficiency. Safety, because the NTS underestimated the urgency in 27% of patients who showed to have an acute coronary syndrome (ACS) or other life threatening events (LTEs), with a sensitivity of 0.73 (95% CI 0.68-0.78). Efficiency, because the NTS overestimated the urgency in 57% of patients without ACS or other LTEs, with a specificity of 0.43 (95% CI 0.40-0.45). Triage nurses' overruling of the NTS urgency increased the safety (sensitivity of 0.86, 95% CI 0.81-0.90) of telephone triage, but not the efficiency (specificity 0.34, 95% CI 0.32-0.37). **(Chapter 3)**
- Triage nurses create a 'mental image' of the patient; "what does the patient look like at the other end of the phone?" Furthermore, they use clinical reasoning strategies and interpret paralinguistic (the vocal elements of communication such as tone of voice and breathing speed) to cope for the lack of visual information. 'Congruence' with the NTS is key for triage nurses, and if 'congruence' was absent, they applied four working strategies; i) tinkering, ii) overruling, iii) complying with the NTS urgency recommendation, or iv) transferring the responsibility of the urgency allocation by consulting the supervising general practitioner (GP). **(Chapter 4)**
- The risk of ACS among patients with chest discomfort is almost twice as high for patients calling at night (between 0.00-9.00 a.m.) as compared to patients who call at other hours, evidently in men (risk ratio 2.33 (95% CI 1.68-3.22)) and less clearly in women (risk ratio 1.29 (95% CI 0.83-1.99)). **(Chapter 5)**
- Symptoms predictive of ACS were more similar than different for women and men with acute chest discomfort who called the OHS-PC, and ambulances were equally dispatched to women and men. **(Chapter 6)**

- Age, pressing heavy chest pain, sweating, and radiation of pain were the strongest predictors for the diagnosis ACS in both sexes. The prediction model for women included also (i) severe pain > 7 on a scale from 0-10, (ii) chest discomfort duration <12 hours, and (iii) history of diabetes, with as a result a discriminative ability (c-statistic) of 0.76 (95% CI 0.71-0.80). The prediction model for men in addition included (i) history of diabetes, (ii) calling during the night, (iii) symptom recognition from a previous acute cardiac event, and (iv) shortness of breath, with as a result a discriminative ability (c-statistic) of 0.72 (95% CI 0.68-0.76). (**Chapter 7**)

Triage systems should be validated on established diagnoses

Today's decision support triage systems are developed on consensus opinion of experts, who based the triage criteria on physiological parameters, presumptive diagnoses and resource use.^{1,2} Remarkably, widely used triage systems are often not, or just partially, validated and often studies did not include the eventually established clinical diagnosis in the validation analyses.³ Only one study partially assessed the validity of the NTS for telephone triage in OHS-PC, but did not include the clinical diagnosis related to the call in the analyses. This study found that most patients with a high urgency allocation were referred to the ED (92.9% of patients with an U1 urgency allocation and 29.3% of patients with an U2 urgency) and patients allocated a low urgency received a self-care advice; on these results the authors concluded that the NTS seemed a 'feasible' triage system for use in OHS-PC.⁴ We argue that that the accuracy of triage decision support tools should always be validated against clinical diagnoses as the outcome.

To increase the accuracy of a triage decision support tool, first and foremost a proper evaluation of triage systems is required, involving assessment of validity (does the decision tool predict the 'true' urgency) and reliability (high degree of intra-observer and inter-observer variability).¹ Information on the patient's clinical outcomes should be considered to allow for establishing the urgency and thus the assessment of validity.

¹ Defining a reference standard for 'true' urgency without knowledge on the clinical diagnosis is impossible; the best surrogate reference standard of urgency is the clinical diagnosis, because based on the diagnosis, and subsequently the average of disease-related morbidity and mortality, a 'true' urgency can be defined. Delay to effective, targeted, treatment is one of the most important predictors of outcomes for patients with serious medical conditions such as sepsis, pneumonia, stroke, and ACS.^{5,6,7} We validated the NTS for the outcomes ACS or other LTEs, and found that the NTS tool underestimated the urgency in 27% of patients with ACS or other LTEs and this was

14% after triage nurses' overruling (usually upscaling) of the NTS urgency.⁸ This shows that the NTS urgency allocation in patients with acute chest discomfort is not safe enough, and triage nurses often need to correct for under-triaging by the tool. This poor safety performance we found in the important domain 'patients suspected of ACS' is in sharp contrast with the conclusion of the only previous NTS validation study, and subscribes the need of adequate validation of a decision support tool before it is widely implemented in clinical practice. Our study - around 10 years after the introduction of the NTS in the OHS-PC - shows that for patients suspected of ACS, safety of telephone triage should be improved. Importantly, we still do not know how well the NTS performs for the other domains than chest discomfort.

Triage decision support tools should be developed and validated in the setting for which they are intended.^{9 10 11} However, the NTS is a modified version of the Manchester Triage Standard (MTS), which was developed for triage at the ED, including face-to-face consultations and physical examination.^{3 4} One reason for using the same triage system in OHS-PC as at the ED is to create common situational awareness and facilitate communication among health care providers in 'the chain of emergency management'.^{4 12 13} Although we agree with the importance of effective communication among health care providers, safe patient care should have a higher priority, which means having an accurate tool validated for the setting in which it is applied. Integrating or linking several triage systems can also overcome communication problems, while creating situational awareness. For example, in the USA, UK and Australia, pre-hospital telephone triage starts with primary triage (2 minutes protocolled ABCD-check) using the Advanced Medical Priority Dispatch System (AMPDS).¹⁴ If the patient is considered ABCD-stable, the call is transferred for secondary triage with the Emergency Communication Nurse System to assess probability diagnoses and make subsequent management plans.^{14 15 16}

Summarizing, triage decision support systems should be developed and validated against established clinical diagnoses in the setting for which they are intended, and this should be done *before* implementation of a decision support tool.

Can we really 'reason in urgencies' during telephone triage at OHS-PC?

While working on this research project, the question "Can we really reason in urgencies during telephone triage at OHS-PC?" recurrently came up. Urgency assessment and establishing a diagnosis are often considered as separate entities by clinicians as well as researchers. During our studies we incrementally realized that the two go hand-in-hand.

Telephone triage nurses are currently trained to 'reason in urgencies' and not think about the potential underlying cause (diagnosis) of the patient's clinical condition.¹⁷ Indeed, the aim of triage is to *prioritize* which patients need urgent medical help and who don't, based on the clinical condition. Whereas the aim of diagnosing is to *clarify* the patient's clinical condition and increase certainty about the presence or absence of disease (with potential consequences for prognosis and targeted interventions).¹⁸ However, a patient's clinical condition is caused by a certain underlying disease or disorder. So, while knowing this, how can a triage nurse determine the patient's clinical condition based on 'reasoning in urgencies' only? We believe that the concept of 'reasoning in urgencies' creates problems for both triage nurses and supervising GPs at the OHS-PC for multiple reasons.

The concept of separating the urgency assessment from diagnosing seems useful in the very first minutes of the initial assessment and treatment of critically ill patients seen by the ambulance and in the ED. Then, first the ABCD-check (acronym for Airway, Breathing, Circulation and Disability) should be done, with stabilization of patients' vital functions.¹³ During the ABCD-check clinicians systematically assess the vital parameters of the patient in order to quickly find the most urgent life threatening unstable vital parameter. During this phase clinicians apply 'urgency reasoning', according to the rationale that the clinical signs of critical conditions are similar regardless of the underlying cause.¹³ After the ABCD-check in ED, the underlying diagnosis that can clarify the patient's clinical condition is further examined.

Firstly, we should realize that at the OHS-PC the number of contacts with *critically* ill patients is very low; in 2018, 2.5% of the OHS-PC contacts were considered in need of immediate care (urgency level U1) and only a small portion of these few patients were considered to be 'ABCD-unstable'.¹⁹ The majority of all U1 classified patients at OHS-PC were patients suspected of ACS, stroke, or having severe respiratory problems.²⁰ In our own study among all patients with acute chest discomfort around 0.25% was considered 'ABCD-unstable' by the triage nurse (9.6% in those received the highest urgency level U1). So, one may wonder on what evidence or arguments the decision was based that 'reasoning in urgencies' would be applicable in the OHS-PC, while considering the underlying cause of the patient's condition as 'redundant'.

Secondly, we think that after the ABCD check the rationale that clinical signs of critical conditions are similar regardless of the underlying cause is no longer valid. For example, the main reason for allocating a high urgency to patients with acute chest discomfort is that when an ACS is the underlying diagnosis, this inevitably carries the

risk of life-threatening ventricular arrhythmias and severe loss of pumping function.²¹

²² In addition, managing patients with ACS as early as possible improves their prognosis considerably.²³ We argue that in most cases in OHS-PC one has to *anticipate* the risk of ABCD-instability and to estimate this risk, we have to consider the consequences of the probability of the presence of a specific diagnoses that may underlie the patient's symptoms. Also their prognosis should be estimated on the probability of the specific diagnosis and consequently, one should not merely focus on determining the patient's clinical condition at that very moment of calling the OHS-PC.

Thirdly, the algorithms of each of the 56 NTS 'main complaints' consist of specific key questions that force the triage nurse to ask the patient for information about possible diagnoses and prognostic determinants anyway.¹ E.g., the questions about type of pain and radiation of pain within the NTS' main complaint 'chest pain' are more directed at estimation of the risk of ACS, than at assessment of the patient's clinical condition. Moreover, the NTS pop-ups linked to the key questions provide background information about potential critical underlying diagnoses (Figure 1). We therefore think it is nearly impossible for a triage nurse to 'reason in urgencies' without considering underlying diagnoses, while going through these questions with their pop-ups. One could even argue that most of the NTS itself is not designed for urgency reasoning!

Fourthly, we argue that forcing triage nurses to adapt a simplified reasoning method, which acquires changes in the mind-set, and which does not fit the clinical context, will easily result in interactional problems with the decision support tool and with the supervising GPs. This is underpinned by qualitative studies which showed that triage nurses' reasoning is complex, and based on a variety of clinical reasoning strategies, including analytic reasoning and the use of intuition.^{24 25} Also, for analytic reasoning, triage nurses start by gathering information, from which hypotheses are developed about probability diagnoses, which are then tested by asking confirmatory and non-confirmatory questions.^{24 26} Knowledge and experience are required to successfully process information into reliable hypotheses.²⁷ Experienced triage nurses more often use their 'intuitive knowledge' and also 'tricks' in using a decision support tool, while novice triage nurses are prone to carefully follow the guidelines.^{28 29}

Below, we further discuss this issue along with the history of the ABCD-approach, triage nurses' reflections on reasoning in telephone triage, and finally, we will return to the case description of Mrs. Brown from the introduction chapter of this thesis.

Figure 1. Information pop-ups of the NTS with references to specific diagnoses.

Information pop-ups main complaint 'Chest Pain'

Vegetatieve verschijnselen


? Heeft u het gevoel flauw te vallen? Transpireert u? Bent u bleek, misselijk of duizelig?

i Vegetatieve verschijnselen zijn **misselijkheid**, transpireren, klam en/of gevoel flauw te vallen, bij een verdenking op een **cardiovasculair event** dreigende shock. Niet bij hevige pijn door een trauma.
Voorbij is vegetatieve verschijnselen in de afgelopen uren (max. 6).

Uitstraling pijn/druk thorax

? Straalt de pijn of druk uit? Waarheen?

i Typisch is passend bij **cardiale pijn** zoals uitstraling naar de kaak, arm of rug. Zie afbeelding



Karakter pijn thorax

? Kunt u de pijn beschrijven (beklemmend, scherp/stekend, vastzittend aan de ademhaling, onduidelijk)?

i Beklemmende pijn is verdacht voor **cardiale pijn**. **Typische cardiale pijn** is krampende, beklemmende of drukkende pijn op het midden van de thorax, dat vooral optreedt bij inspanning. Het kan aanvoelen als een druk op de borst of knijpen in de borstkas.

Information pop-up main complaint 'Abdominal Pain'

Aneurysma, verdenking

? Is er een aneurysma bij u vastgesteld? Hoe is het ontstaan?

i Ja = Onbehandeld **aneurysma** in de **voorgeschiedenis**
Verdacht is plotseling ontstaan van hevige scheurende pijn

Tijdsduur pijn/druk thorax

? Wanneer zijn de klachten (pijn/druk) die u op dit moment heeft begonnen? Zijn de klachten de hele tijd in de zelfde mate/ernst aanwezig? Zijn de klachten continue hetzelfde?

i Klachten die op en af komen, die verminderen en weer terugkomen en of klachten die van aard veranderen dienen als korter dan 12 uur te worden gescand. Langer dan 12 uur wordt gescand wanneer er sprake is van continue dezelfde klachten, die niet zijn veranderd of zijn weggeweest en langer dan 12 uur bestaan.
Trombose is alleen mogelijk in de **acute fase van het infarct (<12uur)**

Information pop-up main complaint 'Collapse'

Acuut begin

? Voelde u het aankomen?

i Plotsklaps ontstaan, dus niet voelen aankomen of even niet lekker worden.
Wegkling bij inspanning past bij **cardiale oorzaak**.

History of the ABCD-approach and ‘reasoning in urgencies’

The concept of the ABCD-approach was developed in the 20th century, and the first Advanced Trauma Life Support (ATLS®) courses of teaching were held in 1978.¹³ The ABCD-approach is considered to be helpful for clinicians to systematically and completely assess the severely ill patient’s clinical condition in a short amount of time.¹³ The aim of the ABCD-approach is to provide immediate life-saving treatment, to break down complex situations into more manageable parts, to establish common situational awareness among all treatment providers, and to buy time to establish a final diagnosis, prognosis and subsequent treatment.¹³ It was developed for the very first management of severely ill patients with life-threatening underlying diseases at the ED and intensive care units (ICU).^{30,31} The ABCD approach can also be used in a first-aid pre-hospital setting for ambulance personnel and GPs when stabilizing the patient at home, and make the patient ready for transportation to the hospital.³² It was not developed for telephone triage, where inherently the assessment cannot be done completely due to lack of measurement of vital parameters. By applying the ABCD-approach, you can ‘buy time’ to establish a final diagnosis according to some authors, but how can this be done reliably with only telephone triage in the OHS-PC setting?^{13,33}

Thus, urgency reasoning, that underlies the ABCD-approach, with a focus on the very first minutes, is developed for situations when the patient is (i) seen and (ii) can be managed and (iii) is in a high casualty setting. This is completely opposite from telephone triage at in the OHS-PC setting with (i) no physical contact, (ii) no opportunity for direct management of the patient and (iii) in a domain of patients with predominantly non-urgent conditions, or in case of urgent conditions, with patients mostly (still) ABCD-stable at the time of calling.

How do triage nurses reflect on ‘reasoning in urgencies’?

Telephone triage nurses are trained to ‘reason in urgencies’, for the underlying assumption that it would increase safety of triage decision.^{17,34} However, there is no evidence to support this hypothesis. Believers in this paradigm proclaim that ‘reasoning in diagnoses’ would increase the risk of making mistakes, because asking questions intended to make a diagnose would distract the telephone triage nurses from an adequate judgement about the patients’ clinical condition.^{35,34}

In our interview study among 24 triage nurses, we asked them to reflect on their own reasoning for urgency assessment when using the NTS.²⁹ With grounded theory analysis we showed that triage nurses use clinical reasoning techniques for urgency assessment, which is the same sort of clinical reasoning that is used to come to a

diagnosis.^{28 26} Triage nurses use their knowledge about diseases, they test hypothesis of probability diagnoses, they use pattern recognition and are aware of potential cognitive biases which they try to prevent with 'cognitive debiasing strategies'. Furthermore, intuition and 'paralanguage' interpretation (use of vocal elements in conversation) were important in their reasoning, and these elements were used to make a 'mental image' of the patient. Triage nurses expressed that they felt often confused about the separation of 'urgency reasoning from diagnostic reasoning', and the fact that they had to comply with a concept that often did not fit in their working method.

"We are not allowed to reason in diagnoses, but obviously I do. I take into consideration that this woman might have a myocardial infarction, given her symptom presentation, and I would like to gather more background information that would help me decide about whether or not to accept the recommended NTS urgency U1. "

"They say we are not allowed to reason in diagnoses, but we do not get proper guidance how exactly we should reason in urgencies when applying the key questions of the NTS... they (OHS-PC management and the trainers of triage education programs) say we just should comply with the NTS."

The triage nurses indicated they had to deal with 'interactional workability dilemmas', which means difficulties in applying a rigid computer system in the wider context of the patients' narrative. They compared their own urgency considerations with the automatically generated urgency of the NTS. Based on the analysis we found that 'congruence' is key for triage nurses while working with the NTS, which is defined as whether the NTS supports their urgency decision making. If 'congruence' was absent, triage nurses applied four working strategies; (i) tinkering to make the NTS urgency align with their preferred urgency, (ii) overruling, (iii) complying with (but with 'resistance') to the NTS urgency recommendation, or (iv) transferring the responsibility about the urgency allocation to the GP. It is somewhat disturbing to realize that the training programs of triage nurses are completely based on the assumption of 'urgency reasoning'.

Even more disturbing is that Dutch OHS-PC managers use the 'core-set' to audit triage nurses for quality of their telephone triage.³⁶ The core-set consists of 29 'quality' indicators of which ten are medical items (the other items concern communication, GP supervision and documentation). The medical items involve amongst others whether

the correct 'main complaint' was chosen, and whether the urgency estimation was 'appropriate' according to the 'expert opinion' of the OHS-PC manager.³⁷ These items are assessed by just re-listening to the calls (without knowing the eventual diagnosis), and therefore essentially, this 'quality check' is only a check whether the triage nurse complies with the NTS. A Swedish qualitative study showed that telephone triage nurses often complied with the triage system because they were afraid to take the wrong decision should their performance be part of a formal 'quality' assessment.³⁸ We argue that it is counter-effective when managers solely focus their audits of triage nurses on complying with the NTS. The triage nurses in our study pointed out they were eager to receive information about the diagnosis of the patients they spoke to on the phone, to know whether they made the correct urgency decision, and we suggest this should be incorporated in future quality assessments. A study about the influence of feedback confirms this, showing that the assessments of medical doctors and students improved when they received feedback about the diagnosis in various cases.³⁹

In summary, it is clear that triage nurses, besides the ABCD-check, generally do not 'reason in urgencies', and that this concept does not fit the OHS-PC setting. Furthermore, feedback to triage nurses should also include the clinical outcome of the patient.

Return to the case of Mrs. Brown

The triage nurse allocated an urgency U2 and scheduled a consultation at the OHS-PC for Mrs. Brown. Unfortunately, however, Mrs. Brown turned out to have an ACS.

We argue that 'diagnostic reasoning' could have helped the triage nurse to allocate a higher urgency, or at least would have recommended a home visit. We do not know what the triage nurse filled out in the NTS, and neither do we know whether she downscaled the NTS urgency, which is generally only done after consultation of the supervising GP.⁴⁰ The triage nurse considered Mrs. Brown's clinical condition as 'ABCD-stable'. Thus, following the concept of urgency reasoning, indeed there was no life-threatening situation. But what about minutes to hours later? A life-threatening ventricular arrhythmia may have occurred only minutes after hanging up the telephone. When strictly applying the concept of urgency reasoning - still considered a key element of telephone triage - Mrs. Brown, as more patients with an ACS, would receive a low urgency because she passed the ABCD-check as 'stable'. Fortunately, however, Mrs. Brown would still have received a high urgency with ambulance dispatch if the triage nurse had filled out the key questions in the NTS 'main complaint chest

pain' as follows; duration of chest pain less than 12 hours, in combination with one of the following items (i) severity of pain >7/10, or (ii) pressing tightening chest pain, or (iii) radiation to arm, neck or shoulders, or (iv) sweating. Strikingly, these four items have nothing to do with urgency reasoning, but merely with diagnostic reasoning (is an ACS likely?). Every triage nurse should know that when the suspicion of ACS is high, the patient must receive the highest urgency with ambulance dispatch, given the risk of life-threatening ventricular arrhythmias, and to enable starting treatment as early as possible.^{21 23}

We conclude that not only in the case of Mrs. Brown, but in anybody with symptoms of chest discomfort who is ABCD-stable at the time of calling the OHS-PC, urgency reasoning is at the very least incomplete and usually inadequate.

Conclusions and recommendations based on the thesis

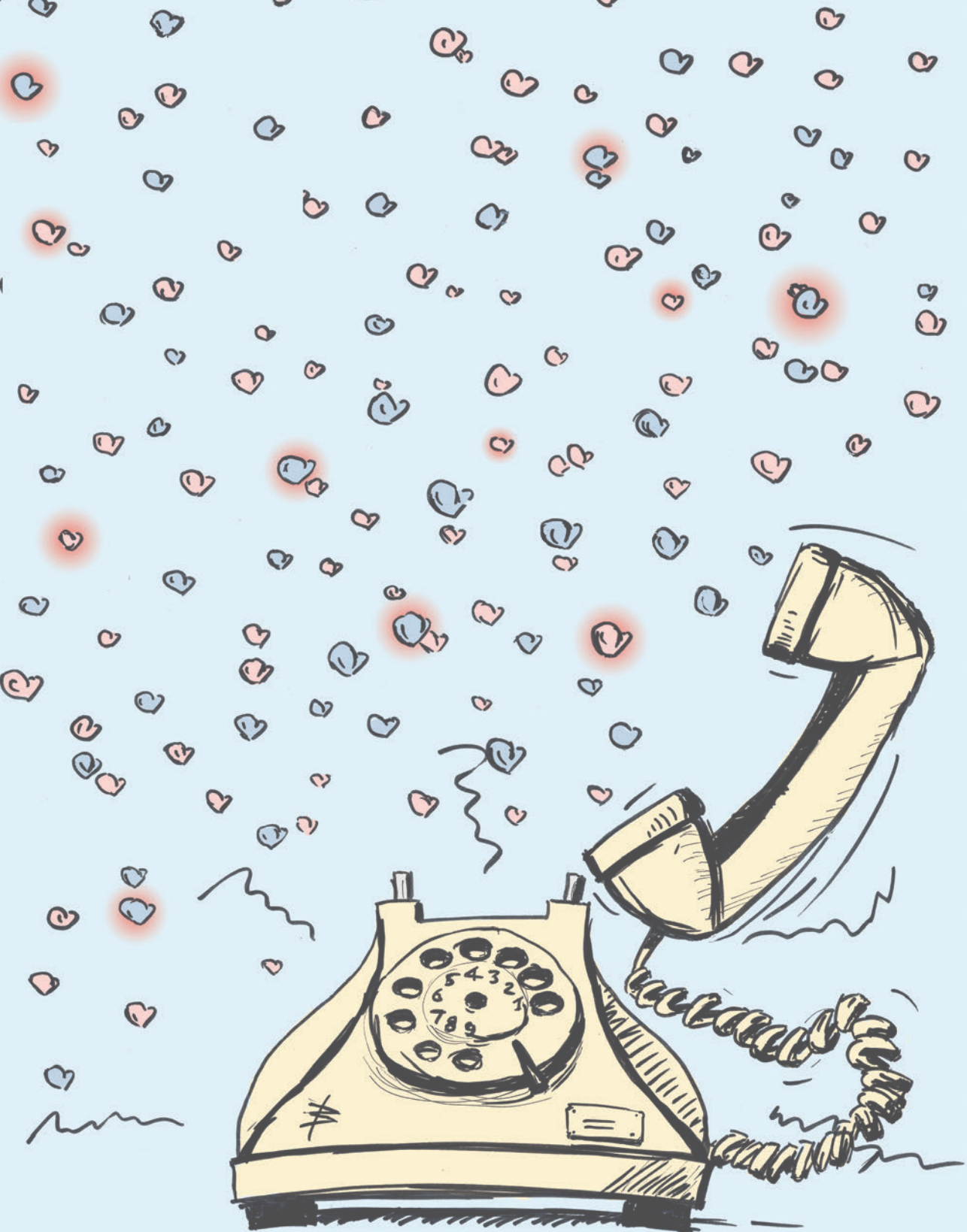
- The NTS decision support tool performs rather poor in both terms of safety and efficiency, when it comes to allocating urgencies evaluated on the outcomes ACS or other LTEs.
- Triage nurses overruling of the NTS-system improves safety in patients presenting with chest discomfort at the OHS-PC, but not efficiency.
- Understanding that triage nurses' reasoning and working strategies with the NTS are vital for triage outcomes and knowing what influences their choices may help to develop improved education.
- Auditing of triage calls should include feedback on the patient's eventual clinical diagnosis.
- When patients with chest discomfort call at night, the risk of an ACS is increased and immediate dispatch of an ambulance should be considered, notably in men.
- There are more similarities than differences in symptoms predictive for ACS in women and men.
- Our sex-specific prediction rules for patients with chest discomfort should be implemented in the OHS-PC, once they have been externally validated.
- Reasoning in urgencies without considering the diagnosis is not adequate in telephone triage in OHS-PC. Moreover, not only the actual, but much more the *anticipated* risk of ABCD-instability and prognosis of probability diagnoses should be considered.

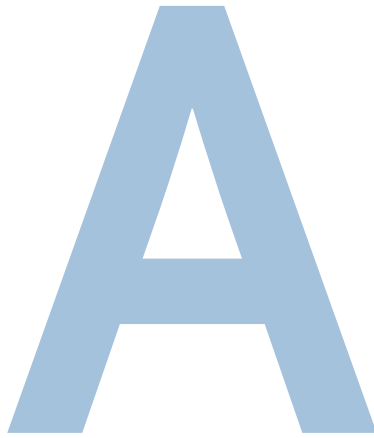
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APPENDICES

Summary

Samenvatting

List of publications

Dankwoord

About the author

SUMMARY

Introduction

The aim of telephone triage in out-of-hours services for primary care (OHS-PC) is to prioritize callers based on symptom severity. For telephone triage of patients with chest discomfort diagnostic prediction is in play, which involves assessing the risk of acute coronary syndrome (ACS).

ACS is a life-threatening condition for which early life-saving therapeutic interventions are vital to improve the patient's outcome and prognosis.¹ In the Netherlands, 80% of patients with chest discomfort first calls their general practitioner or OHS-PC, and chest discomfort is included in the top five reasons for telephone contact in the OHS-PC setting.^{2,3} The prevalence of ACS among these patients is however around 10%, while the large majority has non-life-threatening conditions such as musculoskeletal, gastrointestinal or psychological disorders.^{4,5} Telephone triage of patients with chest discomfort at OHS-PC is notoriously challenging, because it is difficult to differentiate ACS from other causes of chest discomfort based on symptoms only.⁶

In 2011, an expert-based digital decision support system called the 'Netherlands Triage Standard' (NTS) was introduced in OHS-PC with the aim to ensure safe and efficient care.⁷ The NTS is constructed with lists of hierarchically ordered questions related to 56 'main complaints', and the answers filled out in the system automatically generate six urgency levels linked to a certain time frame within which the patient should be seen by a physician or ambulance personnel (from immediate ambulance (Uo) to telephone advice (U5)).⁷ The automatically generated NTS urgency level can be scaled up or down ('overruled') by the triage nurse, which is usually done after consultation of the supervising GP, who has the final responsibility for the urgency allocation.⁸

There are indications that current efficiency, but also safety of telephone triage of patients with chest discomfort can be improved. Efficiency, because in 68.7% of patients who call the OHS-PC for chest discomfort a high urgency is allocated (patient seen within one hour, by ambulance or GP), and as already mentioned, around 10% of them has an ACS.⁵ Safety, because on the other hand missing an ACS is the most common reason for malpractice claims in the OHS-PC setting.⁹ Remarkably, the NTS was never validated against clinical outcomes and therefore its diagnostic accuracy is unknown. Furthermore, it is unknown how triage nurse actually use the NTS and how they clinically reason during triage assessment of patients with chest discomfort. Therefore insights were needed about the performance of telephone triage, to help

discover leads for improvement of safety and efficiency of triage of patients with chest discomfort.

Clinical decision rules for diagnosing ACS in the primary care setting are lacking, but very much needed. Interestingly, many studies report that women and men differ in symptoms of ACS, but never sex-specific prediction rules have been developed. Importantly, however, most studies compared symptoms of men and women with *confirmed* ACS¹⁰, and did not evaluate sex-specific symptom presentation of patients with chest discomfort; comparing patients with ACS versus those without, for men and women separately. Such studies are needed to inform general practitioners and triage nurses about whether and how women with ACS differ from women without ACS, and this similarly for men.

This thesis focused on:

- (i) Gaining insights into how the telephone triage of patients with chest discomfort in OHS-PC is currently done.
- (ii) Discovering leads for improvement of triage, both in terms of patient safety and efficiency.
- (iii) Assessing whether triage of patients with chest discomfort should be different in women than in men.

Insights into how telephone triage of patients with chest discomfort is currently done

In **Chapter 2**, we described the rationale, aims and design of the Safety First study. We wanted to evaluate telephone triage at the OHS-PC in patients suspected of (i) acute coronary syndrome (ACS), and (ii) TIA or minor/major ischaemic stroke. We targeted on these two aforementioned domains because adequate triage is crucial given the potential benefit of early treatment ('time is muscle' and 'time is brain'). We designed a mixed-method research project using both quantitative and qualitative studies, with the aim to describe, understand and improve the triage process of patients suspected for either of these two acute cardiovascular diseases at OHS-PC.

For the quantitative studies we performed a cross-sectional study with data of more than 5,000 telephone triage recordings from the period 2014-2017, coming from nine OHS-PC locations in the Utrecht area. We re-listened the recordings to collect information of (i) call characteristics, (ii) patient characteristics and (iii) symptom presentation. The researchers who carried out the data collection were blinded to the final diagnosis of the patients. Final diagnoses were requested from the patient's

own GP, and was based on information from specialists' discharge letters (i.e. the cardiologist or neurologist) or OHS-PC discharge letters. With this data we could evaluate the diagnostic accuracy of telephone triage (chapter 3), perform audio stimulated recall interviews (chapter 4), assess whether the time of calling was helpful (chapter 5), evaluate differences in symptom presentation between men and women with chest discomfort (chapter 6), and finally, develop new symptom-based diagnostic prediction rules for ACS, for men and women separately (chapter 7).

In **Chapter 3**, we assessed the accuracy of urgency allocation during telephone triage in 2,023 patients with chest discomfort who called the OHS-PC. We compared the patient's urgency allocation, categorized in high urgency level (U1 and U2) and a low urgency level (U3, U4 and U5), to the outcomes acute ACS or other life threatening events (LTEs), separately for the NTS tool and after overruling by the triage nurse. The NTS urgency was of poor safety; it underestimated the urgency in 27% of patients who showed to have an ACS or other LTEs (sensitivity of 0.73 (95% CI 0.68-0.78)). In 13.2% of the 2,023 calls, the triage nurse overruled the NTS urgency, mostly upscaling (in 11.0%). The final urgency, that is including the overruled urgencies, was safer than the urgency generated by the NTS, but still in 14% of patients with ACS or other LTEs the urgency was underestimated (sensitivity 0.86 (95% CI 0.81-0.90)). For both situations, efficiency was low; a too high urgency was allocated by the NTS in 57% (specificity 0.43 (95% CI 0.40-0.45) and final urgency in 67% (specificity 0.34 (95% CI 0.32-0.37) of patients. These patients had non-urgent conditions, e.g. gastro esophageal reflux or musculoskeletal disorders.

In **Chapter 4**, we describe the results of an audio stimulated recall interview study among 24 triage nurses, who were asked to reflect on their reasoning while using the NTS for triage assessment for patients suspected of ACS. Recent audio-tapes (<14 days old) of each of the nurse's triage conversations were used to stimulate the reflection. It became clear that triage nurses create a 'mental image' of the patient; "How does the patient look like at the other end of the phone?" They use clinical reasoning strategies and interpret paralanguage (the vocal elements of communication such as tone of voice and breathing speed) to create this mental image, which helps them in coping for the lack of visual information. They compared their own urgency considerations with the automatically generated urgency of the NTS. Using the grounded theory analysis we found that 'congruence' is key for triage nurses while working with the NTS, which is defined as whether the NTS supports their urgency decision making. If 'congruence' was absent, triage nurses applied four working strategies; i) tinkering, ii) overruling, iii) complying with the NTS urgency recommendation, or iv) transferring the responsibility

of the urgency allocation to the consulted supervising general practitioner (GP). It became evident that triage nurses have to deal with interactional dilemmas while working with the NTS. Understanding triage nurses' working strategies and what affects their choices may help to improve education material, and NTS developers may benefit by involving the triage nurses' input for adjustment in the triage system in such a way that it improves interactional workability.

Leads for improvement of telephone triage of patients with chest discomfort

In **Chapter 5**, we analyzed whether considering the time of calling could be helpful for improving telephone triage of patients with chest discomfort. Previous studies in the emergency department showed circadian variability in the occurrence of ACS, with an early morning peak incidence.¹¹⁻¹³ We found that the risk of ACS among 1,655 patients with chest discomfort is almost twice as high for patients calling at night (between 0.00-9.00am) compared to those who called outside those hours. This was clearly shown in men (risk ratio 2.33 (95% CI 1.68–3.22)), but not in women (risk ratio 1.29 (95% CI 0.83-1.99)). The age and gender adjusted risk ratio for ACS of all patients contacting the OHS-PC at night was 1.82 (95% CI 1.07–3.10). Therefore, at night, dispatching ambulances more 'straightaway' could be considered for patients with chest discomfort, notably in men.

Should triage be different in men and women who present with chest discomfort?

In **Chapter 6**, we compared patient and call characteristics of triage call recordings of women with ACS (n=85, 8.6%) versus 908 women without ACS. We did similarly in men; with ACS (n=120, 15.0%) versus 682 men without ACS. Symptoms predictive of ACS were more similar than different among women and men with chest discomfort who called the OHS-PC. In both sexes, retrosternal chest pain was discriminative for ACS (women with ACS vs. without 62.3% vs. 40.3%, $p=0.002$, men with ACS vs. without 52.5% vs. 39.7%, $p=0.032$), as was pressing/tightening pain (women 78.6% vs. 61.5%, $p=0.011$, men 82.1% vs. 57.4%, $p<0.001$) and radiation to arm (women 75.6% vs. 45.9%, $p<0.001$, men 56.0% vs. 34.8%, $p<0.001$). In women, severe pain (65.4% vs. 38.1%, $p=0.006$), a pale face (50.0% vs. 22.9%, $p=0.007$) and radiation to jaw (50.0% vs. 29.8%, $p=0.017$) were also discriminative for ACS, while in men this was sweating (52.4% vs. 38.1%, $p=0.015$), and against ACS stabbing pain (8.4% vs. 26.5%, $p<0.001$). Ambulances were dispatched equally in women (72.9%) and men with ACS (70.0%).

In **Chapter 7**, we developed the first sex-specific prediction models for diagnosing ACS. Our prediction rule for women included seven predictors (age, sweating, radiation, pressing heavy chest pain, severe pain, chest pain duration <12 hours, and a history of diabetes mellitus) and had an internally validated c-statistic of 0.76 (95% CI 0.71-0.80). Our prediction rule for men included eight predictors (age, sweating, radiation, pressing heavy chest pain, history of diabetes mellitus, calling at night, recognizing symptoms from previous cardiac event, and shortness of breath) and had an internally validated c-statistic of 0.72 (95% CI 0.68-0.76). After external validation these models are applicable for telephone triage of patients with chest discomfort calling OHS-PC.

Recommendations for future research and clinical practice

In **Chapter 8**, we summarize the main finding of this thesis and discuss the relevance of considering the patient's eventual diagnosis in triage system research and telephone triage in clinical practice. Finally, we reflect on the clinical case presented in the introduction of the thesis.

We recommend that triage decision support systems should always be validated against clinical diagnoses in the setting for which they are intended, and this should be done *before* implementation of a decision support tool. Furthermore, involvement of the users (triage nurses) in the development and implementation of such a tool is important to improve congruence, and decrease the risk of interactional workability problems. Triage nurses' input can also help to improve education, and we recommend to include feedback on the patient's eventual clinical diagnosis when auditing triage calls. Furthermore, we recommend to include age in the hierarchically ordered questions behind the NTS main complaint 'chest discomfort', and when patients call at night an immediate dispatch of an ambulance should be considered, notably in men. In addition, we expect that our sex-specific prediction models can also be used in emergency medical service setting (EMS, ambulance dispatch center, '112') because the prevalence of ACS among those with chest discomfort is similar to the OHS-PC setting.¹⁴

We clearly showed that the overlap in symptom presentation between women and men with chest discomfort is greater than the difference. This is in contrast with international guidelines and public awareness campaigns which focus on the differences, and therefore risking unbalanced attention. This may lead to the unintentional believe that women think that they *need* to have atypical symptoms for an ACS, neglecting typical symptoms. It is time for a change.

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SAMENVATTING

Introductie

Met telefonische triage op de huisartsenpost maken triagisten een inschatting van de ernst van de klachten van de patiënt, met als doel te bepalen wie het snelst medische hulp nodig heeft. Voor patiënten met acute borstkasklachten is deze inschatting voornamelijk gebaseerd op hoe groot de kans is dat zij een acuut coronair syndroom (ACS) hebben. ACS, ook wel hartinfarct genoemd, is een acute levensbedreigende aandoening van het hart waarbij zuurstoftekort van de hartspier optreedt door een afsluiting of vernauwing in de kransslagaderen. Snelle behandeling door een cardioloog om de bloeddorstrooming te herstellen verbetert de overlevingskansen van de patiënt en beperkt eventuele restschade. ¹ In Nederland belt 80% van de patiënten met acute borstkasklachten als eerste de eigen huisarts of huisartsenpost, en staat borstkasklachten in de top vijf van redenen voor telefonisch contact met de huisartsenpost. ^{2,3} Ongeveer 10% van deze patiënten heeft een ACS en de meerderheid van patiënten heeft een niet-levensbedreigende aandoening, zoals spierklachten, maagklachten of psychische klachten. ^{4,5} Telefonische triage van deze patiënten is een enorme uitdaging omdat het erg moeilijk is op basis van symptomen onderscheid te maken heeft wie een ACS heeft en wie niet. ⁶

In 2011 werd de 'Nederlandse Triage Standaard' (NTS), een door experts ontwikkelde digitale beslisondersteuning, geïntroduceerd op huisartsenposten met als doel de veiligheid en efficiëntie van triage te bevorderen. ⁷ De NTS is opgebouwd uit 56 'ingangsklachten' met gekoppelde lijstjes van hiërarchisch geordende vragen (triagecriteria), waarbij de antwoorden automatisch leiden tot een urgentiebepaling. Er bestaan zes verschillende urgentie levels die een tijdsindicatie aangeven hoe snel de patiënt gezien moet worden door een huisarts of ambulance, van U0 (reanimatie setting, directe ambulance sturen) tot U5 (telefonisch advies door de triagist). ⁷ De triagist kan de NTS urgentie op- of afschalen ('overrulen') en dat gaat meestal in samenspraak met een superviserende huisarts, die de eindverantwoordelijkheid draagt voor de urgentiebepaling. ⁸

Er zijn aanwijzingen dat de huidige efficiëntie en veiligheid van telefonische triage van patiënten met acute borstkasklachten verbetering nodig heeft. Efficiëntie, omdat 68.7% van alle patiënten met borstkasklachten een hoge urgentie krijgt toegewezen (ambulance of spoed huisartsenbezoek), en zoals eerder genoemd slechts 10% een ACS heeft. ⁵ Veiligheid, omdat aan de andere kant een gemist ACS de meest voorkomende redenen is van een calamiteit op de huisartsenpost. ⁹ Opmerkelijk

is dat de NTS nooit is gevalideerd op klinische uitkomsten en dat daardoor de diagnostische betrouwbaarheid onbekend is. Verder is ook niet bekend hoe triagisten klinisch redeneren tijdens telefonische triage en hoe ze de NTS gebruiken voor de urgentiebepaling. Daarom zijn inzichten nodig over hoe de triage momenteel verloopt om daarmee aanknopingspunten te ontdekken voor verbetering.

Er bestaan geen gevalideerde klinische beslisregels om de diagnose ACS te stellen onder patiënten die de huisartsenpost bellen met acute borstkasklachten en deze zijn hard nodig. Opvallend daarbij is dat meerdere studies verschillen in klachten beschrijven bij mannen en vrouwen met een ACS, maar dat nooit geslachtsspecifieke beslisregels zijn ontwikkeld. Een belangrijke beperking van veel van deze studies is echter dat ze verschillen hebben onderzocht tussen mannen en vrouwen met een *bevestigde* diagnose ACS en dat patiënten die wel borstkasklachten hadden maar geen ACS niet zijn meegenomen in de analyses.¹⁰ De vergelijking is nodig waarbij symptomen van patiënten met ACS worden vergeleken met symptomen van patiënten zonder ACS, voor mannen en vrouwen apart. Dergelijke studies zijn nodig om huisartsen en triagisten te informeren over de vraag of en hoe vrouwen met ACS verschillen van vrouwen zonder ACS, en idem voor mannen.

De doelstellingen van dit proefschrift waren:

- (i) Inzicht krijgen in hoe de telefonische triage van patiënten met acute borstkasklachten die de huisartsenpost bellen momenteel verloopt.
- (ii) Aanknopingspunten ontdekken voor verbetering, zowel in patiëntveiligheid als efficiëntie van triage.
- (iii) Onderzoeken of telefonische triage van patiënten met borstkasklachten anders zou moeten zijn voor mannen en vrouwen.

Inzichten in hoe de telefonische triage van patiënten met borstkasklachten die de huisartsenpost bellen momenteel verloopt.

In **Hoofdstuk 2**, beschrijven we de doelstellingen en studie opzet van het Safety First onderzoeksproject. We richten ons op de telefonische triage van patiënten met verdenking op acute cardiovasculaire ziektes, namelijk (i) patiënten die verdacht worden van een ACS en (ii) patiënten die verdacht worden van een 'transient ischemic attack' (TIA) of beroerte. De reden deze groep patiënten te onderzoeken is omdat snelle adequate triage hier van levensbelang is. We hebben een 'mixed-method' studie opzet ontworpen, bestaande uit kwantitatieve en kwalitatieve studies, met als doel de telefonische triage te beschrijven, begrijpen en te verbeteren voor patiënten met klachten verdacht voor acute cardiovasculaire ziektes die de huisartsenpost bellen.

Voor de kwantitatieve studies hebben we een cross-sectionele studie uitgevoerd met gegevens van meer dan 5000 opgenomen telefoongesprekken uit de periode 2014-2017 van negen huisartsenposten in de regio Utrecht. We hebben deze gesprekken teruggeluisterd voor informatie over (i) gesprekskenmerken, (ii) patiëntkenmerken en (iii) symptomen. De onderzoekers luisterden de gesprekken terug zonder op dat moment de diagnose van de patiënt te weten. De diagnoses van de patiënten werden opgevraagd bij de eigen huisartsenpost van de patiënt, gebaseerd op ontslagbrieven van de cardioloog, neuroloog of huisartsenpost. Met deze gegevens konden we de diagnostische accuratesse van de triage beoordelen (hoofdstuk 3), 'audio gestimuleerde recall' interviews houden onder triagisten (hoofdstuk 4), onderzoeken of het tijdstip van bellen kan helpen voor de urgentiebepaling (hoofdstuk 5), evalueren of er verschillen zijn in klachtenpresentatie tussen mannen en vrouwen (hoofdstuk 6) en, als laatste, klinische beslisregels ontwikkelen voor de diagnose ACS, voor mannen en vrouwen apart (hoofdstuk 7).

In **Hoofdstuk 3**, hebben we de diagnostische accuratesse van de urgentiebepaling onderzocht bij 2023 patiënten die de huisartsenpost belden met acute borstkasklachten. Voor de analyses hebben we de urgentie gecategoriseerd in hoog (U₁ en U₂) en laag urgent (U₃, U₄ en U₅) en beoordeeld ten opzichte van de diagnose ACS en andere levensbedreigende aandoeningen (LBA), apart voor de NTS urgentiebepaling en de definitieve urgentiebepaling (inclusief aanpassingen van de triagist). De veiligheid van de NTS urgentie bleek slecht; in 27% van de patiënten die een ACS of andere LBA bleken te hebben werd een te lage urgentie toegekend (sensitiviteit van 0.73, 95% BI 0.68-0.78). In 13.2% van de gesprekken heeft de triagist de NTS urgentie aangepast en dit betrof meestal op een opschaling (11.0%). De definitieve urgentie was veiliger dan de NTS urgentie, maar nog steeds kreeg dan 14% van de patiënten met een ACS of een andere LBA een te lage urgentie (sensitiviteit 0.86, 95% BI 0.81-0.90). Ook de efficiëntie van de NTS en definitieve urgentie was laag; de NTS urgentiebepaling was te hoog in 57% van de patiënten (specificiteit van 0.43, 95% BI 0.40-0.45) en definitief in 67% (specificiteit van 0.34, 95% BI 0.32-0.37) van de patiënten. Deze patiënten bleken niet-urgente aandoeningen te hebben, zoals reflux of spierklachten.

In **Hoofdstuk 4**, beschrijven we de resultaten van een 'audio gestimuleerde recall' interviewstudie onder 24 triagisten, die werden gevraagd hoe ze klinisch redeneren tijdens het gebruik van de NTS voor de triage van patiënten die verdacht worden van een ACS. Recente audio-opnames (<14 dagen oud) van telefoongesprekken van de triagisten werden gebruikt om hun reflectie te stimuleren. Het werd duidelijk dat triagisten een 'mentaal plaatje' van de patiënt creëren; "Hoe ziet de patiënt

er aan de andere kant van de telefoon uit?” Ze gebruikten bekende klinische redeneerstrategieën zoals kennis over ziektes gebruiken, hypotheses testen en patroonherkenning. Specifiek voor telefonische triage bleken de triagisten de paralinguïstische communicatie (non-verbale communicatie zoals de toon van de stem en ademhalingssnelheid) te interpreteren om dit mentale plaatje te creëren, om te compenseren voor het gebrek aan visuele informatie. Vervolgens vergeleken de triagisten hun eigen afwegingen over de meest passende urgentie met de NTS urgentie. Op basis van de ‘grounded theory benadering’ vonden we dat ‘congruentie’ essentieel is voor triagisten in het gebruik van de NTS, wat betekent dat de NTS hun beslissingsproces ondersteunt. Wanneer congruentie afwezig was pasten triagisten vier strategieën toe: (i) ze sleutelden aan de NTS-invoer zodat hun gewenste urgentie eruit kwam, (ii) ze pasten de NTS urgentie aan (‘overrulen’), (iii) ze schikten zich naar de NTS urgentie, of (iv) ze droegen de verantwoordelijkheid van de urgentiebepaling over aan de superviserende huisarts. Het werd duidelijk dat triagisten in hun werk met de NTS tegen diverse interactionele dilemma’s aanliepen. Begrijpen welke strategieën triagisten toepassen en welke factoren hierbij van de invloed zijn kan helpen om onderwijs te verbeteren. NTS ontwikkelaars kunnen er baat bij hebben triagisten te betrekken om de NTS zo aan te passen dat congruentie beter wordt.

Aanknopingspunten ontdekken voor verbetering

In **Hoofdstuk 5**, hebben we geanalyseerd of het tijdstip van bellen kan helpen om de urgentiebepaling van patiënten met acute borstkasklachten te verbeteren. Uit eerdere ziekenhuisstudies bleek namelijk dat een ACS vaker optreedt in de vroege ochtend, wat waarschijnlijk te relateren is aan het biologisch ritme waarbij ‘s ochtends vroeg de bloeddruk en de hartfrequentie stijgen.¹¹⁻¹³ We ontdekten dat het risico op een ACS onder 1655 patiënten met borstkasklachten bijna twee keer zo hoog was wanneer ze ‘s nachts belden (tussen 0.00 en 9.00) dan wanneer ze op andere tijden belden. Dit verhoogde risico was evident aanwezig bij mannen met een risico ratio van 2.33 (95% BI 1.68–3.22), maar minder uitgesproken bij vrouwen met een risico ratio van 1.29 (95% BI 0.83-1.99). De voor leeftijd- en geslacht gecorrigeerde risico ratio was 1.82 (95% BI 1.07–3.10). Op basis hiervan adviseren we bij patiënten die ‘s nachts bellen met borstkasklachten laagdrempelig een ambulance te sturen, met name bij mannen.

Zou triage voor mannen en vrouwen anders gedaan moeten worden?

In **Hoofdstuk 6**, hebben we patiënt- en gesprekskenmerken vergeleken van 85 vrouwen met ACS (8.6%) versus 908 vrouwen zonder ACS, alsmede voor 120 mannen met ACS (15.0%) versus 682 mannen zonder ACS. We ontdekten dat symptomen die een ACS voorspellen meer overeenkomstig dan verschillend waren voor mannen en vrouwen.

In beide geslachten was retrosternale pijn voorspellend voor ACS (vrouwen met ACS vs. zonder 62.3% vs. 40.3%, $p=0.002$, mannen met ACS vs. zonder 52.5% vs. 39.7%, $p=0.032$), net als drukkende zware pijn (vrouwen 78.6% vs. 61.5%, $p=0.011$, mannen 82.1% vs. 57.4%, $p<0.001$) en uitstraling naar de arm (vrouwen 75.6% vs. 45.9%, $p<0.001$, mannen 56.0% vs. 34.8%, $p<0.001$). Bij vrouwen waren daarnaast hevige pijn (65.4% vs. 38.1%, $p=0.006$), bleekheid (50.0% vs. 22.9%, $p=0.007$) en uitstraling naar de arm (50.0% vs. 29.8%, $p=0.017$) ook voorspellend voor ACS, en in mannen bleek zweten voorspellend voor ACS (52.4% vs. 38.1%, $p=0.015$), en stekende pijn juist te pleiten tegen ACS (8.4% vs. 26.5%, $p<0.001$). Naar vrouwen en mannen met een ACS werd even vaak een ambulance gestuurd (72.9% en 70.0%, respectievelijk).

In **Hoofdstuk 7**, hebben we de eerste geslachtsspecifieke klinische beslisregels ontwikkeld om de diagnose ACS te stellen op basis van symptomen. Onze beslisregel voor vrouwen bevat zeven klinische voorspellers (leeftijd, zweten, uitstraling, drukkende zware pijn, hevige pijn, tijdsduur van de pijn korter dan 12 uur en diabetes mellitus) met een intern gevalideerd discriminerend vermogen (c-statistiek) van 0.76 (95% BI 0.71-0.80). Onze predictieregel voor mannen bevat acht klinische voorspellers (leeftijd, zweten, uitstraling, drukkende zware pijn, diabetes mellitus, tijdstip van bellen in de nacht, herkennen van hartklachten en kortademigheid) met een intern gevalideerd discriminerend vermogen (c-statistiek) van 0.72 (95% BI 0.68-0.76). Na externe validatie kunnen deze beslisregels toegepast worden voor de telefonische triage van patiënten met borstkasklachten die de huisartsenpost bellen.

Aanbevelingen voor toekomstig onderzoek en de klinische praktijk

In **Hoofdstuk 8**, vatten we de onderzoeksresultaten van dit proefschrift samen en discussiëren over het belang de diagnose te betrekken in triage-onderzoek en triage in de praktijk. Tot slot reflecteren we op de klinische casus van de introductie van dit proefschrift.

Voor onderzoek naar triagesystemen raden we aan de urgentiebepaling altijd te valideren op de diagnoses van de patiënt, om zo te kunnen beoordelen hoe accuraat het systeem is, en dat de validatie gedaan moet worden in de setting (telefonische of fysieke triage, huisartsenpost of ziekenhuis) waar het systeem gebruikt gaat worden. Bij voorkeur vindt validatie daarbij plaats *voordat* een triagesysteem breed in gebruik wordt genomen. Verder kan het nuttig zijn de gebruikers (de triagisten) van een triagesysteem te betrekken in de ontwikkeling en implementatie, met als doel de congruentie te verbeteren en het risico op interactionele problemen te verkleinen. De input van triagisten kan ook waardevol zijn om onderwijs te verbeteren, o.a.

voor interpretatie van paralinguïstische communicatie. Verder benadrukken we de noodzaak dat managers van triagisten bij de kwaliteitsevaluatie van triagegesprekken ook de uiteindelijke diagnose van de patiënt betrekken.

Voor verbetering van de NTS raden we aan om leeftijd te includeren als triagecriterium bij de ingangsklacht 'pijn thorax' omdat het een sterke voorspeller is voor de diagnose ACS. Ook is het te overwegen wanneer patiënten 's nachts bellen laagdrempelig een ambulance te sturen, met name bij mannen.

Verder verwachten we dat onze geslachtsspecifieke klinische beslisregels ook toepasbaar kunnen zijn voor triage van patiënten met borstkasklachten die de ambulancemeldkamer ('112') bellen, omdat de voorafkans op ACS bij deze patiënten vergelijkbaar is met die van patiënten die de huisartsenpost bellen.¹⁴

Onze studies laten duidelijk zien dat er een grote overlap is in symptomen die een ACS voorspellen bij mannen en vrouwen. Deze bevinding staat in contrast met internationale richtlijnen en publieke campagnes, die daardoor een ongebalanceerde boodschap uitzenden. Dit kan onbewust ertoe leiden dat vrouwen gaan denken dat ze alleen bij 'atypische' klachten een risico hebben op een ACS en daardoor misschien typische klachten negeren. Het is tijd voor verandering.

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LIST OF PUBLICATIONS

This thesis

1. Erkelens DCA, **Wouters LTCM**, Zwart DLM, Damoiseaux RAMJ, de Groot Esther, Hoes AW, Rutten FH. Optimisation of telephone triage of callers with symptoms suggestive of acute cardiovascular disease in out-of-hours-primary care: observational design of the Safety First study. *BMJ Open* 2019 Jul 1;9(7):e027477.
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Other publications

5. Erkelens DCA, Rutten FH, **Wouters LTCM**, De Groot E, Damoiseaux RAMJ, Hoes AW, Zwart DLM. Limited reliability of experts' assessment of telephone triage in primary care patients with chest discomfort. *J Clin Epidemiol.* 2020 July 28;127:117-124.
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Loes Wouters was born on the 20th of May 1988 in Eindhoven, the Netherlands. After graduation from the gymnasium at secondary school S.G. Augustinianum in 2006, she studied medicine at the University of Maastricht and graduated in 2012. She worked as a resident from 2013 to 2015 at the surgery department of the st. Laurentius Ziekenhuis in Roermond, the dermatology department of the Catharina Ziekenhuis in Eindhoven, and at the psychiatry department of



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