Incidence and care pathways of patients with chest pain at the out-of-hours general practitioner office

Master Thesis proposed to achieve the degree of Master of Family Medicine by

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II. ABSTRACT

Background

Chest pain as presenting complaint poses diagnostic challenges in general practice, especially in settings with limited resources. A low threshold for referral to the emergency department (ED) is warranted when urgent differential diagnoses, such as cardiac causes, are suspected. To date, the epidemiology of chest pain in out-of-hours primary care in Flanders, Belgium, has not been described.

Methods

This retrospective analysis examined the incidence and care trajectories of patients presenting with chest pain in the Flanders region using data from a single out-of-hours GP office (KHOBRA, May 2019 to April 2023) and a multicentre database covering several out-of-hours GP offices (iCAREdata, January 2014 to June 2024). Chi-squared tests (with Bonferroni correction) were applied to compare ED referral rates across datasets and among grouped out-of-hours GP offices categorized by population density. Incidence rates were also compared to data from an in-hours primary care registry (INTEGO, January 2003 to December 2022).

Results

We included 852 (KHOBRA) and 21,133 (iCAREdata) patient contacts with a median age of 47 and 53 years, respectively. Chest pain accounted for 7.3 (iCAREdata) to 10.1 (KHOBRA) cases per 1,000 patient contacts. Overall, 28.5% (iCAREdata) to 33.6% (KHOBRA) of contacts were classified as urgent or higher, with higher urgency observed during home visits (iCAREdata 45.1% versus KHOBRA 51.4%) and in older age groups. Potential cardiac ischemic causes were assigned in 12.0% (iCAREdata) to 16.1% (KHOBRA) of chest pain working diagnoses. ED referral rate ranged from 24.4% (KHOBRA) to 25.7% (iCAREdata). Rural areas showed a higher incidence of chest pain, an older patient population, and a significantly higher referral rate to the emergency department (29.0%) compared to their urban counterpart (19.5%). In comparison, the in-hours GP dataset (INTEGO) revealed a higher incidence of ischemic heart disease diagnoses albeit this encompassed both acute and chronic care.

Conclusion

The incidence and urgency of chest pain in out-of-hours primary care are associated with contact type and demographical factors such as age and rurality. Understanding regional healthcare patterns is crucial to optimize care pathways between primary care and emergency services.

III. SAMENVATTING

Achtergrond

Thoracale pijn als aanmeldingsklacht brengt diagnostische uitdagingen mee in de huisartsensetting, voornamelijk in omstandigheden met beperkte middelen. Een laagdrempelige verwijzing naar de spoedgevallendienst is aangewezen wanneer urgente differentiaaldiagnosen, zoals cardiale oorzaken, vermoed worden. Op heden werd de epidemiologie van thoracale pijn op huisartsenwachtposten (HWP) in Vlaanderen, België, nog niet beschreven.

Methodologie

Deze retrospectieve studie onderzocht de incidentie en zorgstromen van patiënten die zich presenteerden met thoracale pijn in Vlaanderen, gebruikmakend van gegevens van één HWP (KHOBRA, mei 2019 tot april 2023) en een multicentrische database met verschillende aangesloten HWP's (iCAREdata, januari 2014 tot juni 2024). Chi-kwadraat testen (met Bonferroni correctie) werden toegepast ter vergelijking van verwijzingsgraad naar de spoedgevallendienst tussen beide datasets en tussen HWP's gegroepeerd volgens bevolkingsdichtheid. De incidenties werden vergeleken met gegevens van een huisartsenregistratienetwerk in reguliere zorgsetting (INTEGO, januari 2003 tot december 2022).

Resultaten

We includeerden 852 (KHOBRA) en 21 133 (iCAREdata) patiëntcontacten met een mediane leeftijd van 47 en 53 jaar respectievelijk. Thoracale pijn betrof 7,3 (iCAREdata) tot 10,1 (KHOBRA) per 1000 patiëntcontacten. Globaal werden 28,5% (iCAREdata) tot 33,6% (KHOBRA) van de contacten gescoord als urgent of hoger, toenemend bij huisbezoeken (iCAREdata 45,1% versus KHOBRA 51,4%) en oudere leeftijdscategorieën. Potentieel cardiaal ischemische oorzaken vormden 12,0% (iCAREdata) tot 16,1% (KHOBRA) van thoracale pijn werkdiagnosen. De spoedverwijzingsgraad varieerde van 24,4% (KHOBRA) tot 25,7% (iCAREdata). Landelijke gebieden toonden een hogere incidentie van thoracale pijn, een oudere patiëntpopulatie en een significant hogere spoedverwijzingsgraad (29,0%) in vergelijking met stedelijke werkregio's (19,5%). In vergelijking toonde de reguliere zorgdatabase (INTEGO) een hogere incidentie van ischemische hartziektediagnosen hoewel dit zowel acute als chronische zorg omvatte.

Conclusie

De incidentie en urgentie van thoracale pijn in de huisartsenwachtpost zijn geassocieerd met het type patiëntcontact en demografische factoren zoals leeftijd en landelijke regio's. Begrip van regionale zorgpatronen is cruciaal om de stromen tussen eerstelijnszorg en spoedgevallendiensten te optimaliseren.

IV. LIST OF ABBREVIATIONS

Abbreviations	
ACS	Acute coronary syndrome
ECG	Electrocardiogram
ED	Emergency department
GP	General practitioner
hs-cTn	High-sensitivity (analysis of) cardiac troponin
iCAREdata	Improving Care and Research Electronic Data Trust Antwerp
ICPC-2	International Classification of Primary Care - Second Edition
KHOBRA	Kring Huisartsen Oost-Brabant
NOS	Not otherwise specified
NSTEMI	Non-ST-elevation myocardial infarction
POCT	Point-of-care test
STEMI	ST-elevation myocardial infarction

Recurring ICPC-2 codes	
ICPC-2 A11	Chest pain not otherwise specified
ICPC-2 K01	Heart pain
ICPC-2 K02	Pressure/tightness of heart
ICPC-2 K03	Cardiovascular pain not otherwise specified
ICPC-2 K74	Ischemic heart disease with angina
ICPC-2 K75	Acute myocardial infarction
ICPC-2 K76	Ischemic heart disease without angina

V. INTRODUCTION

A patient presenting with symptoms suggestive of cardiac ischemia, such as acute onset chest pain, must always be carefully evaluated. The presence or absence of anamnestic arguments contributes to diagnostic probability and the decision to perform technical investigations to confirm or exclude this serious condition. These include a 12-lead electrocardiogram (ECG) and sequential measurements of cardiac biomarkers to differentiate between a high or low likelihood of acute coronary syndrome (ACS) (1). The term ACS applies to patients with suspected or confirmed acute myocardial injury or infarction, with differentiation between unstable angina, ST-elevation myocardial infarction (STEMI), and non-ST-elevation myocardial infarction (NSTEMI) (2). Unstable angina is characterized by ACS symptoms without an elevation in cardiac biomarkers, with or without ischemic ECG changes, while a STEMI or NSTEMI is always accompanied by an increase in cardiac biomarkers. With a sensitivity of > 90% and a specificity of 68-80%, the most reliable diagnostic tool for NSTEMIs is the high-sensitivity analysis of cardiac troponins (hs-cTn) in serum, a biomarker for myocardial injury (3,4). Its use in two serial measurements has a high negative predictive value of > 99% and thus plays a central role in the current guidelines of the European Society of Cardiology (4–7).

A general practitioner-based registry in the Flemish region of Belgium reports that the incidence of 'heart pain' as registered complaint in the general population between 2000 and 2023 ranged from 0.10 to 0.56 per 1,000 patient years (8,9). For 'pressure/tightness of heart' the incidence ranged from 0.08 to 0.46 per 1,000 patient years, whilst 'chest pain not otherwise specified (NOS)' varied between 0.83 to 5.75 per 1,000 patient years (8,9). Observational studies report chest pain in 0.7-3.0% of general practitioner (GP) encounters (10–12). In a primary care setting, the diagnostic arsenal of the GP is currently limited to clinical evaluation, including vital parameters, and, if available, an ECG device. A rapid laboratory analysis of cardiac troponins, as is common in an emergency department (ED), is typically not available. Consequently, GP's often lack the resources to reliably exclude cardiac ischemia in suspected ACS if the ECG shows no abnormalities. A low-threshold referral to the ED is therefore recommended for sequential hs-cTn determination, in addition to ECG and hemodynamic monitoring in case of clinical deterioration (1,13,14). Validated clinical decision-making algorithms with (such as HEART score, T-MACS Decision Aid, ADAPT Protocol for Cardiac Event Risk) and without troponin (such as HEAR score, HEAR-GP score, INTERCHEST score, Marburg Heart score, HE-MACS score, EDACS score, Bruins Slot rule, and Gencer rule) can help assess the risk of ACS (7,15–23). However, a clinician should keep in mind that without hs-cTn analysis the sensitivity of these risk scores might be insufficient for a reliable ACS rule-out in primary care setting (1,13). Apart from broad cardiovascular causes (such as aortic dissection, heart failure, pericarditis, and pulmonary embolism), the differential diagnoses of chest pain include other organ systems such as respiratory (such as pneumothorax and pneumonia), gastrointestinal (such as gastroesophageal reflux disease) and musculoskeletal (such as chest wall pain and costochondritis) causes as well (10,14,24–26). Albeit that in a GP setting the pre-test probability of urgent chest pain diagnoses is lower than non-urgent causes, vigilance is indicated (10,14,24–29).

The rise of hs-cTn analysis by point-of-care test (POCT) could have a large impact on risk stratification of possible cardiac chest pain in primary care (4,30,31). Several analytical and clinical studies validating these hs-cTn POCT's report favorable results or are ongoing, both in laboratory, prehospital, ED, and rural GP settings (32–42). Further research is needed to support its evidence before implementation in primary care guidelines (26,31). In preparation for clinical validation studies in Belgian primary care, as foreseen in the future, regional epidemiological data is needed.

Currently, comprehensive descriptive literature on the incidence and care pathways in patients presenting with (suspected cardiac) chest pain in Flemish Belgian primary care, particularly out-of-hours GP care, is missing. This study aims to address these gaps by analysing three primary care datasets at different geographical levels.

VI. MATERIALS AND METHODS

Study design and objectives

This retrospective analysis of three anonymized datasets aimed to explore the incidence and care pathways of (non-)cardiac chest pain in patients presenting at the out-of-hours versus in-hours GP care on different geographical levels in the Flanders region of Belgium. Additionally, for future research purposes in the context of a foreseen hs-cTn POCT clinical validation study, the incidence of chest pain specifically at the KHOBRA out-of-hours GP office is determined.

Study population

Inclusion criteria were as follows: patients ≥ 18 years old presenting at the out-of-hours or in-hours GP office within the study period of the corresponding dataset with at least one of relevant ICPC-2 (International Classification of Primary Care - Second Edition) codes registered as either chief complaint and/or diagnosis. Included ICPC-2 codes of interest were A11 (chest pain NOS), K01 (heart pain), K02 (pressure/tightness of heart), K03 (cardiovascular pain NOS), K74 (ischemic heart disease with angina), K75 (acute myocardial infarction), K76 (ischemic heart disease without angina).

The first dataset, supplied by local GP association KHOBRA (Kring Huisartsen Oost-Brabant), included patients presenting at the out-of-hours GP office in Leuven, Belgium, from May 24, 2019 to April 1, 2023 (43). The onset of the study period corresponds with the start of its latest data collection method. A data sharing agreement was concluded. The second dataset, iCAREdata (Improving Care and Research Electronic Data Trust Antwerp, University of Antwerp), collects data of multiple affiliated out-of-hours GP offices spread over the Flanders region of Belgium (44,45). After application, the independent Scientific Advisory Council decided favourably to provide anonymized data of relevant patient contacts within the period of January 1, 2014 to June 30, 2024 (44,45). Incidentally, data from the KHOBRA out-of-hours GP office is also collected by iCAREdata. After demographical analysis, out-of-hours GP offices had to be reported in a pseudonymized manner. As a third dataset, INTEGO (Integrated Computer Network, University of Leuven) collects and analyses registered data of in-hours primary care electronic health records of about 500 GPs at the time of writing (8,9). A query based on our inclusion criteria was performed within their yearly contact group (patients with at least one contact per year) between January 1, 2003, and December 31, 2022. Repeated registrations of the same ICPC-2 code within ≤ 28 days of first registration were excluded to avoid multiple registrations per episode. All patient data were anonymized prior to analysis and ethical approval of this project has been granted by the Educational-Support Committee of the Research Ethics Committee UZ/KU Leuven.

Data collection

Regarding the out-of-hours GP datasets, KHOBRA and iCAREdata, following data was collected: age (years), sex (male/female), type of patient contact (home visit/consultation/telephone consult), date of patient contact, name of out-of-hours GP office, ICPC-2 coded chief complaint and diagnosis, graded level of urgency (see Table 1), and plan of action (coded or free text) (46). Annual number of contacts with patients aged ≥ 18 years old per out-of-hours GP office was provided as denominator to calculate incidence. Five out-of-hours GP offices (B3, B8, B9, C1, and C12) contain missing data from 2022 onwards and two (X1, X2) have been out of order since 2018. Available data was used for analysis yet insufficient to calculate incidence for X1 and X2. For in-hours primary care, INTEGO provided the absolute number and incidence proportions of ICPC-2 coded registrations per age category (years), sex (male/female) and year of patient contact.

Table 1: Interpretation of graded levels of urgency (46)	
Level of urgency	**Interpretation**
Not evaluated	No level of urgency was registered
Plannable care	Inappropriate use: evaluation could have waited until in-hours GP care
Unplanned care	Appropriate use: evaluation was needed during out-of-hours GP care
Urgent	Needed evaluation within two hours
Highly urgent	Needed evaluation within one hour
Life-threatening	Immediate intervention was required

Statistical methods

Descriptive statistics were performed. Per out-of-hours GP dataset, patient contacts during their respective study period were categorized per age group to compare the number and percentage of ICPC-2 coded chief complaints and diagnoses, graded level of urgency, and plan of action if registered. Population density of each out-of-hours GP office work area was calculated based on demographical characteristics of the resident population in 2011 to assign each office in one of three arithmetic population density clusters (> 1,000, 500-1,000, or < 500 inhabitants per km²) (47,48). Afterwards, out-of-hours GP offices were pseudonymized and randomized in order within their respective cluster prior to demographical comparison between clusters. As proxy, incidence was calculated using the number of registrations divided by the total number of contacts with patients ≥ 18 years old during the study period and expressed as per 1,000 patient contacts. The ED referral rate was computed through the number of registered ED referrals divided by the total number of included patient contacts. The Chi-squared test was used to explore differences in ED referral rates between datasets and population density clusters. A p-value < 0.05 was considered statistically significant when comparing two groups. Bonferroni correction was applied when comparing four groups with an adjusted p-value < 0.008 considered significant. Incidence proportions of the in-hours primary care results were calculated by INTEGO based on their yearly contact group and expressed as per 1,000 patient years.

Statistical and descriptive analysis was performed using MedCalc® Statistical Software, version 20.015 (MedCalc Software Ltd, Ostend, Belgium), and IBM® SPSS® Statistics for Windows, version 30.0.0.0 (IBM Corp., New York, United States). Graphical illustrations were provided through Microsoft® Excel® for Microsoft 365 MSO, version 2411 (Microsoft Corp., Washington, United States), and open-source SankeyMATIC, version 1.2.0.

VII. RESULTS

1. Study population characteristics

The KHOBRA out-of-hours GP office had 70,318 contacts with patients aged 18 years or older (47,380 consultations, 12,203 home visits, and 10,735 telephone consults). Applying the inclusion criteria, 852 patient contacts were further selected. Likewise, in the iCAREdata study population, 21,133 out of 2,757,533 patient contacts at affiliated out-of-hours GP offices were included. The in-hours INTEGO query included 46,653 registrations within their yearly contact group, which ranged between 158,638 and 400,919 patients, corresponding to 5,172,772 patient years. Study population characteristics and yearly number of patient contacts are presented in Table 2 and Supplementary Table 1-2. Comparatively, mostly younger age categories with slightly more women are represented in out-of-hours datasets, in contrast to an older, male-skewed population in the in-hours registry. Age distributions per population density cluster in iCAREdata study population are described in Supplementary Table 3. Remarkably, the proportion of younger age categories was higher in the cluster of out-of-hours GP offices with higher population density. The types of patient contacts (home visit, consultation, telephone consult) per age category are described in Supplementary Table 4, where a decrease in absolute number of patient contacts yet proportional increase in home visits was observed in elder age categories.

Table 2: Study population characteristics of general practice datasets

	Out-of-hours primary care		In-hours primary care
	KHOBRA (n = 852)	**iCAREdata (n = 21,133)**	**INTEGO (n = 46,653)**
Age			
Median age in years (Q1-Q3)	47 (30-69)	53 (35-71)	
Number of patient contacts per age category (% of total)			
18-35 years old	295 (34.6%)	5,480 (25.9%)	4,199 (9.0%)
36-45 years old	113 (13.3%)	2,967 (14.0%)	4,380 (9.4%)
45-55 years old	85 (10.0%)	2,993 (14.2%)	7,350 (15.8%)
56-65 years old	116 (13.6%)	2,927 (13.9%)	10,374 (22.2%)
66-75 years old	71 (8.3%)	2,517 (11.9%)	10,136 (21.7%)
76-85 years old	78 (9.2%)	2,468 (11.7%)	7,463 (16.0%)
≥ 86 years old	94 (11.0%)	1,781 (8.4%)	2,751 (5.9%)
Number of patient contacts per sex (% of total)			
Female	452 (53.0%)	11,047 (52.3%)	19,177 (41.1%)
Number of patient contacts per contact type (% of total)			
Consultation	555 (65.1%)	13,157 (62.2%)	
Home visit	210 (24.7%)	3,671 (17.4%)	
Telephone consult	87 (10.2%)	4,305 (20.4%)	
Number of patient contacts per level of urgency (% of total)			
Not evaluated	1 (0.1%)	365 (1.7%)	
Plannable care	30 (3.5%)	1,589 (7.5%)	
Unplanned care	535 (62.8%)	13,163 (62.3%)	
Urgent	209 (24.5%)	4,060 (19.2%)	
Highly urgent	70 (8.2%)	1,683 (8.0%)	
Life-threatening	7 (0.8%)	273 (1.3%)	

Age: lower and upper quartiles are specified between brackets. KHOBRA: Kring Huisartsen Oost-Brabant, a single out-of-hours GP office; iCAREdata: a database of multiple affiliated out-of-hours GP offices in Flanders, Belgium; INTEGO: an in-hours primary care registry in Flanders, Belgium. Multiple presentations of patients during the study period were not excluded except for INTEGO, where repeated registrations of the same ICPC-2 code within ≤ 28 days of first registration were excluded.

2. Out-of-hours general practice datasets (KHOBRA, iCAREdata)

2a. Level of urgency

The number of patient contacts by level of urgency per contact type and age category in the KHOBRA and iCAREdata study population are graphically represented in Figure 1. Over all ages, 33.6% (n = 286/852) of patient contacts were graded as either urgent, highly urgent, or life-threatening in the KHOBRA dataset, as compared to 28.5% (n = 6,016/21,133) in the iCAREdata study population. With age, an increasing trend in proportionally more urgent clinical presentations is observed, as described in Supplementary Table 4.

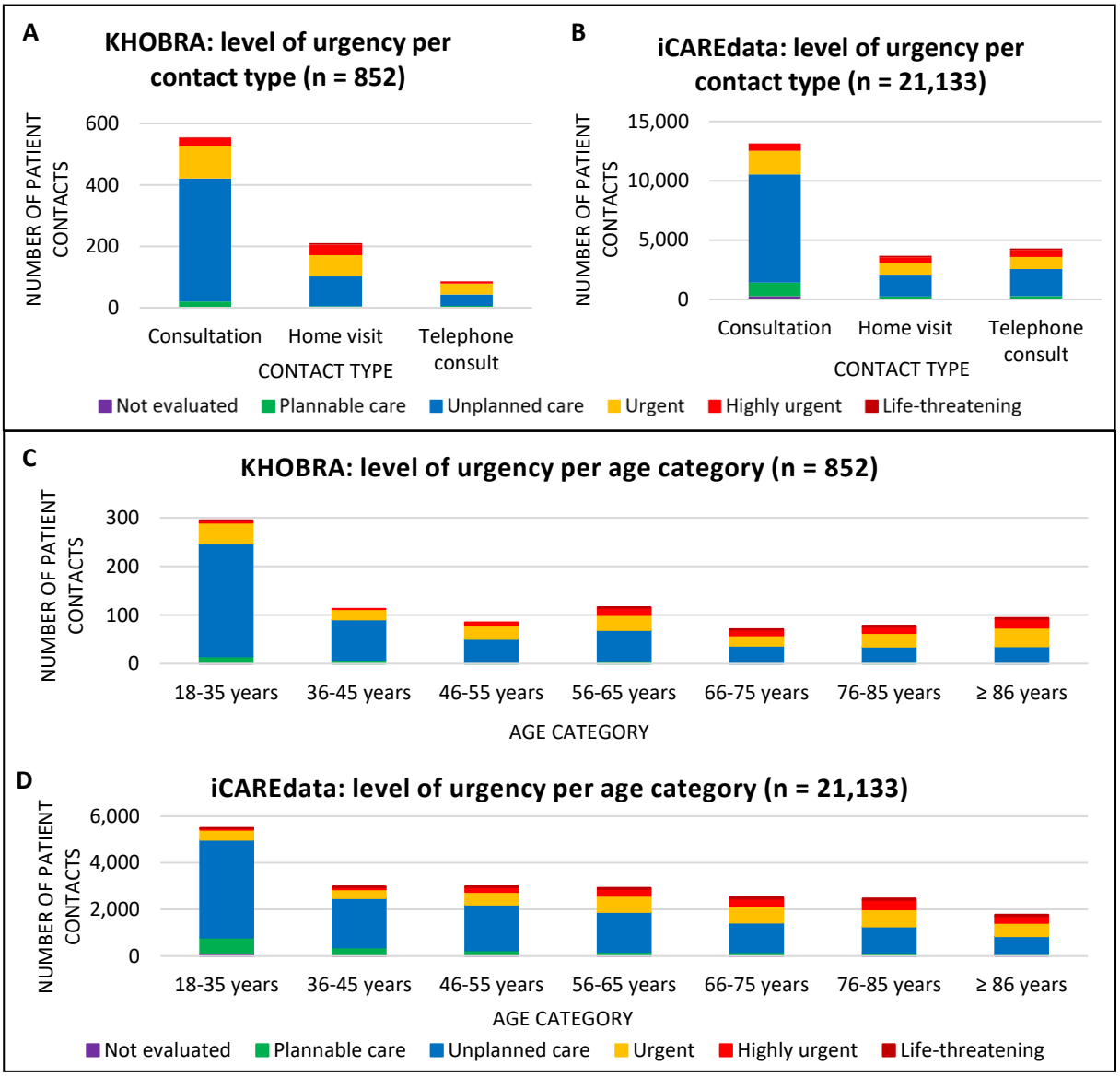

Figure 1: *Number of patient contacts per level of urgency and contact type over all age categories in KHOBRA (A) and iCAREdata study population (B). Number of patient contacts per level of urgency and age category over all contact types in KHOBRA (C) and iCAREdata study population (D).*

2b. Chief complaints and diagnoses

Predominantly ICPC-2 code A11 (chest pain NOS) is represented as chief complaint with 71.3% (n = 608/852) in the KHOBRA dataset versus 82.2% % (n = 17,363/21,133) in the iCAREdata study population. Aggregated per ICPC category in Figure 2, a shift is observed from the general category as chief complaint towards more musculoskeletal, respiratory, cardiovascular, digestive, and psychiatric categories. Supplementary Table 5 supplies a detailed overview of ICPC-2 coded chief complaints and diagnoses.

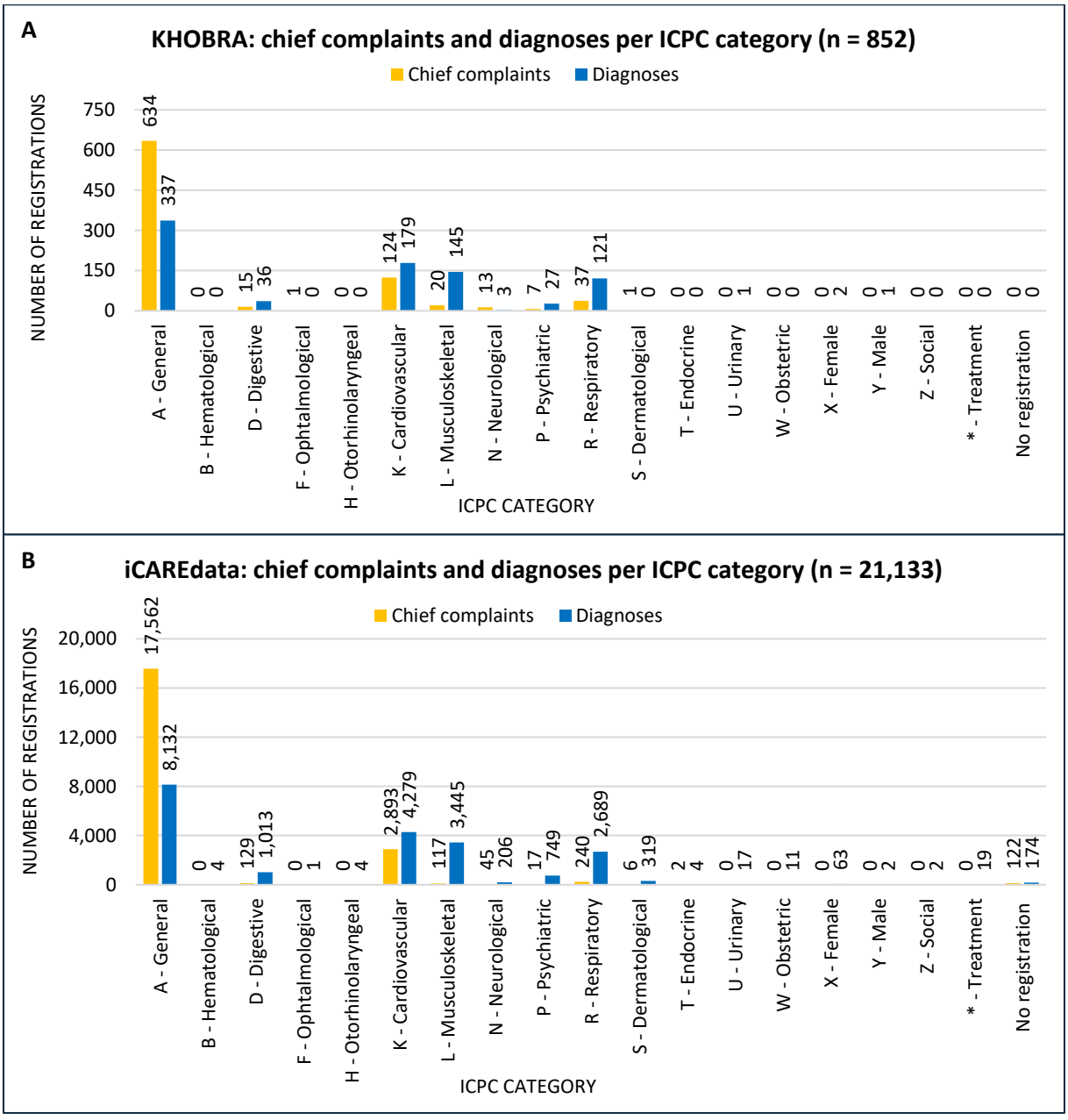

Figure 2: *Number of registered chief complaints versus diagnoses per ICPC category in KHOBRA (A) and iCAREdata (B) study populations. A detailed overview is provided in Supplementary Table 5.*

Registered diagnoses of interest per age category are illustrated in Figure 3. The cardiovascular codes of interest (K01, K02, K03, K74, K75, and K76) constituted 12.0% (n = 102/852) in KHOBRA versus 16.1% (n = 3,404/21,133) in the iCAREdata study population. As a diagnosis, A11 (chest pain NOS) was registered in 35.0% (KHOBRA, n = 298/852) and 33.7% (iCAREdata, n = 7,127/21,133) of cases. The graded level of urgency in this subgroup is provided in Supplementary Table 6 to further distinguish in severity. Remarkably, over all ages in the KHOBRA dataset, 36.9% (n = 110/298) of patient contacts with A11 as diagnosis were still graded as urgent or higher as compared to > 50% in the three eldest age categories. Likewise, in the iCAREdata study population, the proportional severity of graded level of urgency in this subgroup increases with age.

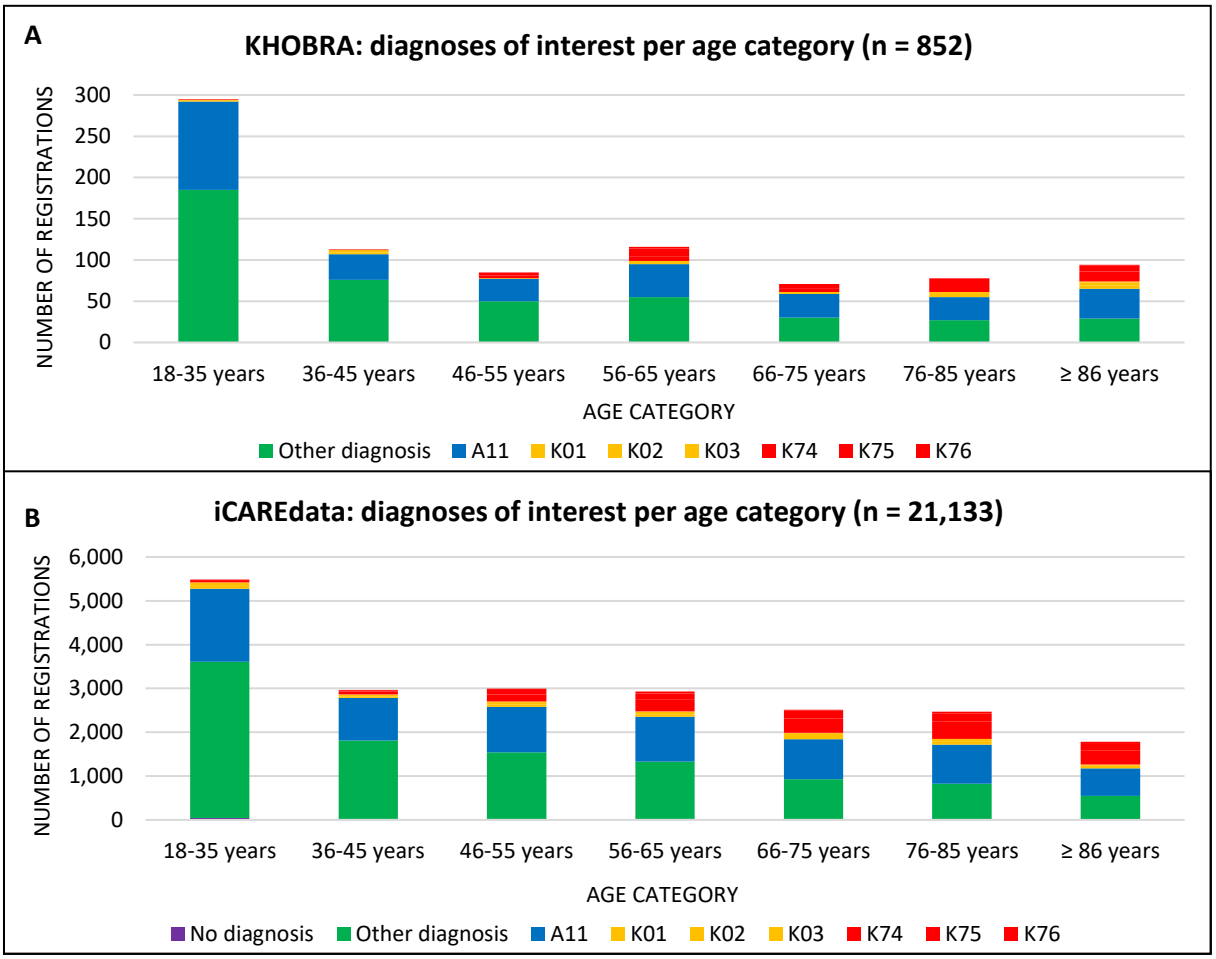

Figure 3: *Number of registered diagnoses of interest per age category in KHOBRA (A) and iCAREdata (B) study populations. Supplementary Table 6 provides a detailed overview. ICPC-2 codes: A11 (chest pain not otherwise specified), K01 (heart pain), K02 (pressure/tightness of heart), K03 (cardiovascular pain not otherwise specified), K74 (ischemic heart disease with angina), K75 (acute myocardial infarction), K76 (ischemic heart disease without angina).*

2c. Incidence of chest pain

Table 3 compares the incidence between the two out-of-hours GP datasets regarding the summed-up registrations of ICPC-2 code A11 (chest pain NOS) and cardiac diagnoses of interest (K01, K02, K03, K74, K75, and K76) as chief complaint, versus as diagnosis, versus cardiac diagnoses of interest alone. The KHOBRA dataset has a higher incidence on all three respects compared to the iCAREdata study population. Comparing out-of-hours GP offices clustered within the same population density category in the latter dataset, an association between higher incidence and lower population density is observed.

Table 3: Incidence of chest pain in out-of-hours general practice datasets

KHOBRA study population (n = 852)			
Population density (inhabitants/km²)	Incidence (per 1,000 patient contacts)		
	Chest pain [A11 + cardiac diagnoses of interest] as chief complaint	Chest pain [A11 + cardiac diagnoses of interest] as diagnosis	Cardiac chest pain [cardiac diagnoses of interest] as diagnosis
555.4 inh/km²	10.1 per 1,000 contacts	5.7 per 1,000 contacts	1.5 per 1,000 contacts

iCAREdata study population (n = 21,133)			
Population density (inhabitants/km²)	Incidence (per 1,000 patient contacts)		
	Chest pain [A11 + cardiac diagnoses of interest] as chief complaint	Chest pain [A11 + cardiac diagnoses of interest] as diagnosis	Cardiac chest pain [cardiac diagnoses of interest] as diagnosis
Cluster A: > 1,000 inh/km²	6.7 per 1,000 contacts	3.3 per 1,000 contacts	1.0 per 1,000 contacts
Cluster B: 500-1,000 inh/km²	7.1 per 1,000 contacts	3.5 per 1,000 contacts	1.1 per 1,000 contacts
Cluster C: < 500 inh/km²	7.6 per 1,000 contacts	4.2 per 1,000 contacts	1.4 per 1,000 contacts
Cluster X: Out of order	Incidence unavailable	Incidence unavailable	Incidence unavailable
Total	7.3 per 1,000 contacts	3.8 per 1,000 contacts	1.2 per 1,000 contacts

Incidence of out-of-hours GP datasets was calculated by dividing the number of registrations by the total number of contacts with patients ≥ 18 years old during study period and expressed as per 1,000 patient contacts. Registrations include ICPC-2 codes A11 (chest pain not otherwise specified), and cardiac diagnoses of interest constitute K01 (heart pain), K02 (pressure/tightness of heart), K03 (cardiovascular pain not otherwise specified), K74 (ischemic heart disease with angina), K75 (acute myocardial infarction), and K76 (ischemic heart disease without angina). Incidence could not be calculated for cluster X because of missing data.

2d. Emergency department referral rate

Comparing the KHOBRA and iCAREdata study populations, plans of action were specified in 48.8% (n = 416/852) and 43.9% (n = 9,275/21,133) of patient contacts respectively. In this subgroup, 50.0% (KHOBRA, n = 208/416) and 58.7% (iCAREdata, n = 5,441/9,275) of contacts were referred to the ED. Table 4 explores differences in the proportion of ED referrals, if registered, between KHOBRA and iCAREdata. In the latter dataset, the proportion of ED referral registrations out of total patient contacts was significantly different between the three population density clusters (Chi-squared, $p < 0.001$ overall and clusters compared individually). A higher ED referral rate was observed in clusters with lower population densities. The ED referral rate in the KHOBRA dataset (555.4 inhabitants/km²) was not significantly different from Cluster B (500-1,000 inhabitants/km²) ($p = 0.846$) nor the total iCAREdata study population ($p = 0.342$), yet a statistically significant difference was observed when compared with Cluster A ($p = 0.002$) and C ($p = 0.003$). Supplementary Table 7 provides the ED referral rate per individual GP office. The proportion of ED referrals varies per age category, as summarized in Supplementary Table 8. In contacts without specified plan of action, over all ages, 21.1% (KHOBRA, n = 92/436) and 18.4% (iCAREdata, n = 2,184/11,858) were still graded as urgent or higher. Supplementary Figures 1-2 provide a graphical illustration of care pathways in both KHOBRA and iCAREdata respectively.

Table 4: Emergency department referral rate in out-of-hours general practice datasets

KHOBRA study population (n = 852)

Population density (inhabitants/km²)	Total number of patient contacts	Number of contacts with registered ED referral (% of total)	Number of contacts with other plan of action (% of total)	Number of contacts without specified plan of action (% of total)
555.4 inh/km²	852	208 (24.4%)	208 (24.4%)	436 (51.2%)

iCAREdata study population (n = 21,133)

Population density (inhabitants/km²)	Total number of patient contacts	Number of contacts with registered ED referral (% of total)	Number of contacts with other plan of action (% of total)	Number of contacts without specified plan of action (% of total)
Cluster A: > 1,000 inh/km²	4,007	781 (19.5%)	700 (17.5%)	2,526 (63.0%)
Cluster B: 500-1,000 inh/km²	7,000	1,722 (24.6%)	1,479 (21.1%)	3,799 (54.3%)
Cluster C: < 500 inh/km²	10,115	2,935 (29.0%)	1,654 (16.4%)	5,526 (54.6%)
Cluster X: Out of order	11	3 (27.3%)	1 (9.1%)	7 (63.6%)
Total	21,133	5,441 (25.7%)	3,834 (18.1%)	11,858 (56.1%)

Cluster X is separated because of missing data.

3. In-hours general practice dataset (INTEGO)

Regarding the in-hours primary care registry INTEGO, Table 5 and 6 describe the incidence of relevant diagnoses per ICPC code and age category respectively. The increasing incidence of K74-K75-K76 with age was higher in males and more pronounced than A11-K01-K02-K03.

Table 5: Overall incidence of chest pain within the in-hours general practice dataset (INTEGO)

ICPC-2 diagnoses of interest	Absolute number of registrations	Incidence (per 1,000 patient years)
A11 - Chest pain not otherwise specified	14,950	2.9 per 1,000 PY
K01 - Heart pain	1,512	0.3 per 1,000 PY
K02 - Pressure/tightness of heart	1,016	0.2 per 1,000 PY
K03 - Cardiovascular pain not otherwise specified	71	0.01 per 1,000 PY
K74 - Ischemic heart disease with angina	9,665	1.9 per 1,000 YPY
K75 - Acute myocardial infarction	8,154	1.6 per 1,000 PY
K76 - Ischemic heart disease without angina	11,285	2.2 per 1,000 PY
Sum of [A11 + cardiac diagnoses of interest]	46,653	9.0 per 1,000 PY
Sum of [cardiac diagnoses of interest]	31,703	6.1 per 1,000 PY

Incidence proportion (number of registrations per 1,000 patient years) calculated in yearly contact group (number of patients with at least one contact in GP office per year, n = 5,172,772 patient years). Cardiac diagnoses of interest constitute K01, K02, K03, K74, K75, and K76.

Table 6: Incidence of diagnoses of interest per demography within the in-hours general practice dataset (INTEGO)

Age category per sex		Sum of diagnoses A11-K01-K02-K03		Sum of diagnoses K74-K75-K76	
		Absolute number of registrations	Incidence (per 1,000 patient years)	Absolute number of registrations	Incidence (per 1,000 patient years)
Male	18-35 years old	1,935	3.2 per 1,000 PY	265	0.4 per 1,000 PY
	36-45 years old	1,541	3.8 per 1,000 PY	834	2.1 per 1,000 PY
	46-55 years old	1,768	4.1 per 1,000 PY	2,912	6.7 per 1,000 PY
	56-65 years old	1,596	4.0 per 1,000 PY	5,242	13.0 per 1,000 PY
	66-75 years old	1,101	3.8 per 1,000 PY	5,132	17.5 per 1,000 PY
	76-85 years old	616	4.0 per 1,000 PY	3,371	21.7 per 1,000 PY
	≥ 86 years old	198	5.0 per 1,000 PY	965	24.5 per 1,000 PY
Female	18-35 years old	1,768	2.3 per 1,000 PY	231	0.3 per 1,000 PY
	36-45 years old	1,572	3.3 per 1,000 PY	433	0.9 per 1,000 PY
	46-55 years old	1,588	3.2 per 1,000 PY	1,082	2.2 per 1,000 PY
	56-65 years old	1,464	3.3 per 1,000 PY	2,072	4.7 per 1,000 PY
	66-75 years old	1,215	3.6 per 1,000 PY	2,688	7.9 per 1,000 PY
	76-85 years old	856	3.9 per 1,000 PY	2,620	11.9 per 1,000 PY
	≥ 86 years old	331	4.0 per 1,000 PY	1,257	15.3 per 1,000 PY

Incidence proportion (number of registrations per 1,000 patient years) calculated in yearly contact group (number of patients with at least one contact in GP office per year, n = 5,172,772 patient years). ICPC-2 codes: A11 (chest pain not otherwise specified), K01 (heart pain), K02 (pressure/tightness of heart), K03 (cardiovascular pain not otherwise specified), K74 (ischemic heart disease with angina), K75 (acute myocardial infarction), K76 (ischemic heart disease without angina).

VIII. DISCUSSION

Summary of findings

This retrospective analysis describes the incidence and care pathways of patients presenting with (possible cardiac) chest pain at the levels of a single out-of-hours GP office (KHOBRA) and a regional database with multiple affiliated out-of-hours GP offices (iCAREdata), compared with an in-hours primary care registry (INTEGO). Out-of-hours GP offices were clustered in three categories of population density to allow for demographical comparison.

First, mainly younger patients presented at the out-of-hours GP office, as opposed to the in-hours primary care dataset. The ages from 18 to 55 years old represented over half of patient contacts (KHOBRA 57.9%, iCAREdata 54.1%, INTEGO 34.1%), with the age category of 18-35 years old being the largest group (KHOBRA 34.6%, iCAREdata 25.9%, INTEGO 9.0%). In out-of-hours setting, the proportion of younger patient contacts was larger in clusters with higher population density. The male-female distribution is similar in KHOBRA (47% vs. 53%) and iCAREdata (46.7% vs. 52.3%) but notably different from INTEGO (58.9% vs. 41.1%).

With most chief complaints being registered as general (74.4-83.1%), predominantly A11 (chest pain NOS), the ICPC-coded categories of diagnoses were distributed as general (33.7-35.0%), cardiovascular (20.2-21.0%), musculoskeletal (16.3-17.0%), respiratory (12.7-14.2%), gastro-intestinal (4.2-4.8%), and psychiatric (3.2-3.5%). The codes of interest correlating with cardiac chest pain (K01, K02, K03) and myocardial infarction (K74, K75, K76) constituted 12.0% (KHOBRA) and 16.1% (iCAREdata) of total diagnoses. To further distinguish in severity, over a third of A11 diagnoses were considered urgent or higher. The share of patient contacts graded urgent or higher over all ages and contact types was 33.6% (KHOBRA) versus 28.5% (iCAREdata), increasing proportionally with age.

Remarkably, the KHOBRA study population had a higher incidence than iCAREdata on all three respects of chest pain as chief complaint (10.1 versus 7.3 per 1,000 patient contacts), chest pain as diagnosis (5.7 versus 3.8 per 1,000 patient contacts), and cardiac chest pain as diagnosis (1.5 versus 1.2 per 1,000 patient contacts). Demographical analysis within iCAREdata clusters revealed a higher incidence associated with a lower population density. The incidence of ischemic heart disease registrations was lower than the in-hours INTEGO dataset (6.13 per 1,000 patient years), but incidence was computed differently, and the latter includes registrations in both acute and chronic care. This in-hours GP registry revealed the incidence of myocardial infarction increasing with age, especially in males.

The ED referral rate did not differ significantly when comparing KHOBRA (24.4%) with the overall iCAREdata (25.7%) study population. Within iCAREdata, a significant difference in ED referral rate was observed when individually comparing population density clusters, ranging from 19.5% in the urban (> 1,000 inhabitants/km²) to 29.0% in the rural cluster (< 500 inh/km²). Interestingly, the ED referral rate in the KHOBRA study population (555.4 inh/km²) was not significantly different from the iCAREdata cluster with intermediate population density (500-1,000 inh/km²), yet notably different from the abovementioned urban and rural iCAREdata clusters.

Comparison with literature

Mainly younger age categories are represented in the out-of-hours KHOBRA and iCAREdata study populations, whereas older in the in-hours INTEGO dataset. Observational studies (Hoorweg et al., Frese et al.) and the FaMe-Net in-hours primary care registry reported most patients presenting with chest pain as older than 45-50 years (8–11,49–51). Our share of mostly benign diagnoses is in line with the meta-analysis by Haasenritter et al. and the more recent observational study by Hoorweg et al. (10,24). Different from our results, the first made a distinction between cardiovascular diseases (13.8-16.1%), stable coronary heart disease (6.6-11.2%), and ACS (1.5-3.6%) (24). The latter reported a higher incidence of acute chest pain of 12.6 per 1,000 patient contacts (n = 281) during their two-week study period but a lower ED referral rate of 14.2% (10). They noted that life-threatening causes were

considered in 17.1% of patients yet withheld in 8.4% of final diagnoses (10). After review of final diagnoses, the calculated incidence rate of life-threatening causes of chest pain was 0.76 per 1,000 contacts (10). Similarly, a German cross-sectional study reported ACS as the cause of chest pain in primary care in 3.6% of cases (12). In contrast, a Norwegian prospective study reported a remarkably higher proportion of suspected ischemic heart disease (50%, of which n = 43/50 admitted to the hospital) in patients presenting with chest pain at out-of-hours primary care (52). In their study population about half of patient contacts graded potentially life-threatening were suspected cardiac ischemia (52). Comparatively, a Belgian cross-sectional study confirmed a significantly higher percentage of serious cardiovascular diseases (myocardial infarction, pericarditis, heart failure and pulmonary embolism) as root of chest pain in an ED (28.1%) compared to in-hours GP setting (4.8%), as well as serious respiratory diseases (8.8% versus 3.5% respectively) (29).

The observed lower ED referral rate in urban areas might be related to the larger representation of younger age categories, hence a lower pre-test probability of urgent chest pain causes (12). More relevant than rural areas, selection bias should be considered in urban regions with hospitals more easily accessible, as patients might refer themselves or be referred directly to the ED after contacting emergency services (53). Its availability might lower the threshold for patients with urgent conditions to refer themselves to the ED, as opposed to rural areas where an out-of-hours GP office might be the easiest accessible healthcare provider (54). Interestingly, two Flemish studies investigated differences in use of ED and out-of-hours primary care: one found that lower socio-economic status rather than distance was associated with more ED use, and another noted a relation with having a non-native background (55,56). A Dutch study reported that a higher population density and lower socioeconomic status are significant predictors for higher demand of out-of-hours primary care services (57). These studies, however, concern general use instead of chest pain specifically.

Compared to our INTEGO results, the Dutch FaMe-Net primary care registry reported a higher overall incidence of 3.8 chest pain NOS (A11) registrations per 1,000 patient years between 2014 and 2021 (49–51). For cardiac diagnoses, the incidence of heart pain (K01, K02) was higher, ranging from 1.5-2.2 per 1,000 patient years, whilst myocardial infarction (K74, K75, K76) was lower with only 0.8-0.9 per 1,000 patient years (49–51). Similarly, they remarked a difference in incidence between males (1.3 per 1,000 patient years) and females (0.5 per 1,000 patient years), and an increasing incidence of myocardial infarction with age (49,50). The authors emphasized that these statistics refer predominantly to chronic care associated with ischemic heart disease (50).

Strengths and limitations

An extensive dataset over multiple years on different demographical levels and settings was gathered for this retrospective study, which represents a major strength for our study. Electronic health care systems widely used in Flemish out-of-hours GP setting oblige (ICPC-2 coded) registration of chief complaint, diagnosis, and level of urgency for every patient contact (46). This system, however, does not allow registration of multiple diagnoses within the same contact. Coded registration of plan of action is optional and might introduce registration bias.

Other biases should be considered as well. First, the development of electronic health care records, regional GP associations, and out-of-hours GP offices in Belgium have been a notable trend in the past decades, with increasing awareness and use by the population (58,59). Registration bias and missing data are presumably more prominent further in the past. The influence of the COVID-19 pandemic on healthcare-seeking behavior should be considered, since out-of-hours GP offices played a non-negligible role in SARS-CoV-2 testing in Flanders (60). Second, the lower representation of elder age categories might be related to their higher incidence of emergency department visits (61). The availability of a nearby hospital, such as in an urban region, might lower this threshold. Third, the datasets were fully anonymized, thus no consideration of patients with multiple presentations during the study period was possible. The number of unique patients in the three datasets was not provided. Since no reference standard was registered, the working diagnoses could not be verified, nor the

outcome after ED referral. Data collection of additional interventions such as ECG, radiology, and prescribed medication were lacking or of insufficient quality for analysis. In registered diagnoses no clear differentiation was possible between stable ischemic heart disease and ACS, impacting comparability with literature. For INTEGO, no differentiation was possible between ischemic heart disease registration in chronic or acute care setting. No distinction in patient contacts was made between the resident population and non-resident higher education students living in the working area of out-of-hours GP offices such as KHOBRA (43,47,62). Further, clinical decision-making skills and ICPC-2 coded registrations per contact are subject to interobserver variability. Registered diagnoses should be considered working hypotheses. Another example is the subjective grading of level of urgency: some diagnoses corresponding with cardiac chest pain were graded as unplanned care as opposed to urgent or higher, and one patient contact with diagnosis A96 (death) was graded as life-threatening. Lastly, the full range of cardiac symptoms such as syncope and arrythmia were not retained specifically in inclusion criteria to focus on chest pain as chief complaint or diagnosis. Seasonal analysis and further exploration of other urgent causes within the dataset, such as respiratory, might be an interesting addition for the future.

Future perspectives

This retrospective study is the first to describe chest pain epidemiology in out-of-hours primary care on different demographical levels in Belgium. For future research purposes in the context of a foreseen hs-cTn POCT clinical validation study, the incidence of chest pain specifically at the KHOBRA out-of-hours GP office was determined. Given that hs-cTn analysis is crucial for risk stratification in suspected ACS, its recent emergence could have an impact on the ambulatory workup of patients with acute chest pain, especially in combination with a clinical decision rule (4,26,30,31,63,64). Should it become sufficiently scientifically validated in the future, this could bring about significant changes to current primary care practice guidelines, with the possibility to exclude ACS with a high negative predictive value as a GP and avoid an ED referral if reassured (31). Implementation could be useful especially in rural areas, where our study revealed a higher incidence of chest pain in proportionally older patients and a higher ED referral rate.

In turn, insight into the incidence and care pathways in out-of-hours GP offices provides opportunity for identification and optimization of gaps. With increasing complex care needs in an aging population, non-gatekeeping health care systems face a challenge to have the right patient in the right place and time with the appropriate healthcare provider (65,66). Epidemiological data are required to assess and address healthcare needs within the local population and on a larger scale (57). This approach could help shape a future striving for closer cooperation and improvement of flow between GP offices and emergency departments, for example with a common triage point using validated clinical decision rules (15,21,26,65–69). Current data collection and analysis could be extended to identify which clinical-anamnestic signs led to an ED referral and provide more in-depth demographical analyses. With our results considered exploratory, future repetition of this study on a more comprehensive scale is strongly suggested to validate and extend these findings.

Conclusion

Mainly younger patients presented with chest pain at out-of-hours GP care. However mostly benign, 24.4-25.7% patients of chest pain were referred to the ED, and a higher level of urgency was associated with home visits and elder age. Potential cardiac ischemic disease represented 12.0-16.1% of chest pain working diagnoses. Demographical differences were of relevance: rural out-of-hours GP offices had a higher incidence of chest pain, in older patients and a significantly higher referral rate to the ED. Assessing regional healthcare needs should be kept in mind to optimize care pathways between primary care and ED.

IX. KEY POINTS

What is already known about the topic:

- Acute chest pain accounts for 0.7 to 3.0% of consultations in general practice.
- Although chest pain is often benign, potentially life-threatening causes must be considered during the diagnostic process.
- General practitioners typically lack access to reliable tools such as high-sensitivity cardiac troponin analysis that can rapidly exclude cardiac ischemia with high negative predictive value.
- Epidemiological data from out-of-hours GP services might provide insights on incidence and care pathways for patients presenting with chest pain.

What this study might add:

- In out-of-hours primary care, chest pain as the main complaint occurred in 7.3 to 10.1 per 1,000 patient contacts with most patients aged between 18 and 55 years.
- Approximately one-third of patients were classified as urgent or higher, with urgency increasing among older patients and home visits. The overall ED referral rate was 24.4-25.7%.
- Suspected cardiac ischemia was noted in 12.0-16.1% of chest pain working diagnoses. Additionally, some patients were referred to the ED with a nonspecific yet still urgent diagnosis.
- Compared to urban regions, rural out-of-hours GP offices reported a higher incidence of chest pain, a proportionally older patient population, and a significantly higher referral rate to the emergency department.

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XI. ADDENDUM

Supplementary Table 1: Number of patient contacts per year in KHOBRA dataset during the study period from May 24, 2019 to April 1, 2023 (n = 852).

Supplementary Table 1: Number of patient contacts per year in KHOBRA out-of-hours general practitioner office			
Year	Number of patient contacts	Number of contacts with patients ≥ 18 years old	Number of included patient contacts according to selection criteria
2019	10,628	7,820	111
2020	33,145	26,709	231
2021	24,975	17,948	241
2022	19,578	13,734	191
2023	5,884	4,107	78
Total	94,210	70,318	852

Supplementary Table 2: Annual number of included patient contacts in iCAREdata dataset during the study period from January 1, 2014 to June 30, 2024 (n = 21,133). Out-of-hours GP offices were clustered based on population density and randomly assigned in order. Five out-of-hours GP offices (B3, B8, B9, C1, and C12) contain missing data from 2022 onwards and two (X1, X2) have been out of order since 2018. Empty cells indicate zero (included) patient contacts.

Supplementary Table 2: Annual number of included patient contacts per out-of-hours general practitioner office, clustered by population density, in iCAREdata study population													
GP office		**2014**	**2015**	**2016**	**2017**	**2018**	**2019**	**2020**	**2021**	**2022**	**2023**	**2024**	**Total**
A: Population density > 1,000 inhabitants/km²	A1						1	150	255	354	355	185	1,300
	A2	1	62	73	91	89	61	243	148	115	174	95	1,152
	A3						5	132	61	55	62	28	343
	A4		21	24	24	35	26	225	126	74	107	68	730
	A5			20	14	17	15	158	82	65	61	50	482
B: Population density 500-1,000 inhabitants/km²	B1						51	158	63	82	74	30	458
	B2						153	317	263	232	259	169	1,393
	B3		83	72	58	54	67	126	7				467
	B4						41	205	168	129	130	62	735
	B5				3	1	19	97	146	106	270	156	798
	B6							169	97	76	102	46	490
	B7							116	126	132	276	158	808
	B8							52	3				55
	B9							43	4				47
	B10											27	27
	B11					9	73	212	91	77	84	59	605
	B12						87	319	222	184	199	106	1,117
C: Population density < 500 inhabitants/km²	C1							147	9				156
	C2											3	3
	C3						66	228	200	120	181	90	885
	C4							57	47	42	65	31	242
	C5		114	119	106		96	206	171	133	269	117	1,331
	C6		236	240	266	232	129	488	344	285	297	138	2,655
	C7						79	249	245	197	248	108	1,126
	C8		40	26	31	22	13	94	68	61	61	43	459
	C9					59	158	179	115	94	126	67	798
	C10						160	311	178	164	210	98	1,121
	C11						1	259	271	256	310	157	1,254
	C12							77	8				85

X: Out of order	X1				10								10
	X2				1								1
Total		1	556	574	604	518	1,301	5,017	3,518	3,033	3,920	2,091	21,133

Supplementary Table 3: Age distribution of patient contacts per population density cluster in iCAREdata study population (n = 21,133). Percentage of total patient contacts within each cluster is provided between brackets.

Supplementary Table 3: Age distribution of patient contacts per population density cluster in iCAREdata study population								
Population density (inhabitants/km²)	**18-35 years**	**36-45 years**	**46-55 years**	**56-65 years**	**66-75 years**	**76-85 years**	**≥ 86 years**	**Total of cluster**
Cluster A: > 1,000 inh/km²	1,319 (32.9%)	640 (16.0%)	486 (12.1%)	446 (11.1%)	380 (9.5%)	418 (10.4%)	318 (7.9%)	4,007 (100%)
Cluster B: 500-1,000 inh/km²	1,848 (26.4%)	1,014 (14.5%)	1,018 (14.5%)	974 (13.9%)	773 (11.0%)	781 (11.2%)	592 (8.5%)	7,000 (100%)
Cluster C: < 500 inh/km²	2,310 (22.8%)	1,312 (13.0%)	1,488 (14.7%)	1,506 (14.9%)	1,361 (13.5%)	1,267 (12.5%)	871 (8.6%)	10,115 (100%)
Cluster X: Out of order	3 (27.3%)	1 (9.1%)	1 (9.1%)	1 (9.1%)	3 (27.3%)	2 (18.2%)	(0.0%)	11 (100%)
Total within age category (% of total of cluster)	**5,480** (25.9%)	**2,967** (14.0%)	**2,993** (14.2%)	**2,927** (13.9%)	**2,517** (11.9%)	**2,468** (11.7%)	**1,781** (8.4%)	**21,133** (100%)

Supplementary Table 4: Number of patient contacts per age category and contact type in out-of-hours GP datasets. Percentage of total patient contacts per contact type within age category is provided between brackets. Levels urgent, highly urgent, and life-threatening are grouped as 'urgent or higher'.

Supplementary Table 4: Level of urgency per contact type and age category in out-of-hours general practice datasets KHOBRA study population								
Contact type	**18-35 years**	**36-45 years**	**46-55 years**	**56-65 years**	**66-75 years**	**76-85 years**	**≥ 86 years**	**Total**
Consultation (% of total within age category)	231 (78.3%)	80 (70.8%)	69 (81.2%)	88 (75.9%)	49 (69.0%)	25 (32.1%)	13 (13.8%)	555 (65.1%)
Urgency not evaluated (% of consultations within age category)	1 (0.4%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.2%)
Plannable care (% of consultations within age category)	9 (3.9%)	5 (6.3%)	1 (1.4%)	3 (3.4%)	0 (0.0%)	1 (4.0%)	0 (0.0%)	19 (3.4%)
Unplanned care (% of consultations within age category)	195 (84.4%)	63 (78.8%)	42 (60.9%)	54 (61.4%)	25 (51.0%)	15 (60.0%)	7 (53.8%)	401 (72.3%)
Urgent or higher (% of consultations within age category)	26 (11.3%)	12 (15.0%)	26 (37.7%)	31 (35.2%)	24 (49.0%)	9 (36.0%)	6 (46.2%)	134 (24.1%)
Home visit (% of total within age category)	24 (8.1%)	17 (15.0%)	5 (5.9%)	17 (14.7%)	20 (28.2%)	52 (66.7%)	75 (79.8%)	210 (24.6%)
Urgency not evaluated (% of home visits within age category)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Plannable care (% of home visits within age category)	1 (4.2%)	1 (5.9%)	0 (0.0%)	1 (5.9%)	0 (0.0%)	2 (3.8%)	0 (0.0%)	5 (2.4%)
Unplanned care (% of home visits within age category)	17 (70.8%)	11 (64.7%)	3 (60.0%)	8 (47.1%)	12 (60.0%)	17 (32.7%)	29 (38.7%)	97 (46.2%)
Urgent or higher (% of home visits within age category)	6 (25.0%)	5 (29.4%)	2 (40.0%)	8 (47.1%)	8 (40.0%)	33 (63.5%)	46 (61.3%)	108 (51.4%)
Telephone consult (% of total within age category)	40 (13.6%)	16 (14.2%)	11 (12.9%)	11 (9.5%)	2 (2.8%)	1 (1.3%)	6 (6.4%)	87 (10.2%)
Urgency not evaluated (% of telephone consults within age category)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Plannable care (% of telephone consults within age category)	4 (10.0%)	1 (6.3%)	0 (0.0%)	1 (9.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (6.9%)

Unplanned care (% of telephone consults within age category)	20 (50.0%)	10 (62.5%)	5 (45.5%)	2 (18.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	37 (42.5%)
Urgent or higher (% of telephone consults within age category)	16 (40.0%)	5 (31.3%)	6 (54.5%)	8 (72.7%)	2 (100%)	1 (100%)	6 (100%)	44 (50.6%)
Total within age category	**295**	**113**	**85**	**116**	**71**	**78**	**94**	**852**
Urgency not evaluated (% of total within age category)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Plannable care (% of total within age category)	14 (4.7%)	7 (6.2%)	1 (1.2%)	5 (5.3%)	0 (0.0%)	3 (3.8%)	0 (0.0%)	30 (3.5%)
Unplanned care (% of total within age category)	232 (78.6%)	84 (74.3%)	50 (58.8%)	64 (55.2%)	37 (52.1%)	32 (41.0%)	36 (38.3%)	535 (62.8%)
Urgent or higher (% of total within age category)	48 (16.3%)	22 (19.5%)	34 (40.0%)	47 (40.5%)	34 (47.9%)	43 (55.1%)	58 (61.7%)	286 (33.6%)

iCAREdata study population

Contact type	**18-35 years**	**36-45 years**	**46-55 years**	**56-65 years**	**66-75 years**	**76-85 years**	**≥ 86 years**	**Total**
Consultation (% of total within age category)	4,219 (77.0%)	2,290 (77.2%)	2,217 (74.1%)	2,010 (68.7%)	1,403 (55.7%)	819 (33.2%)	199 (11.2%)	13,157 (62.3%)
Urgency not evaluated (% of consultations within age category)	98 (2.3%)	42 (1.8%)	37 (1.7%)	36 (1.8%)	38 (2.7%)	19 (2.3%)	3 (1.5%)	273 (2.1%)
Plannable care (% of consultations within age category)	534 (12.7%)	268 (11.7%)	141 (6.4%)	92 (4.6%)	69 (4.9%)	35 (4.3%)	7 (3.5%)	1,146 (8.7%)
Unplanned care (% of consultations within age category)	3,277 (77.7%)	1,667 (72.8%)	1,538 (69.4%)	1,287 (64.0%)	798 (56.9%)	457 (55.8%)	103 (51.8%)	9,127 (69.4%)
Urgent or higher (% of consultations within age category)	310 (7.3%)	313 (13.7%)	501 (22.6%)	595 (29.6%)	498 (35.5%)	308 (37.6%)	86 (43.2%)	2,611 (19.8%)
Home visit (% of total within age category)	150 (2.7%)	109 (3.7%)	202 (6.7%)	375 (12.8%)	571 (22.7%)	1,089 (44.1%)	1,175 (66.0%)	3,671 (17.4%)
Urgency not evaluated (% of home visits within age category)	5 (3.3%)	1 (0.9%)	2 (1.0%)	11 (2.9%)	12 (2.1%)	21 (1.9%)	27 (2.3%)	79 (2.2%)
Plannable care (% of home visits within age category)	17 (11.3%)	8 (7.3%)	22 (10.9%)	20 (5.3%)	28 (4.9%)	42 (3.9%)	34 (2.9%)	171 (4.7%)
Unplanned care (% of home visits within age category)	104 (69.3%)	73 (67.0%)	99 (49.0%)	176 (46.9%)	271 (47.5%)	504 (46.3%)	539 (45.9%)	1,766 (48.1%)
Urgent or higher (% of home visits within age category)	24 (16.0%)	27 (24.8%)	79 (39.1%)	168 (44.8%)	260 (45.5%)	522 (47.9%)	575 (48.9%	1,655 (45.1%)
Telephone consult (% of total within age category)	1,111 (20.3%)	568 (19.1%)	574 (19.2%)	542 (18.5%)	543 (21.6%)	560 (22.7%)	407 (22.9%)	4,305 (20.4%)
Urgency not evaluated (% of telephone consults within age category)	2 (0.2%)	3 (0.5%)	2 (0.3%)	5 (0.9%)	0 (0.0%)	0 (0.0%)	1 (0.2%)	13 (0.3%)
Plannable care (% of telephone consults within age category)	137 (12.3%)	48 (8.5%)	37 (6.4%)	18 (3.3%)	16 (2.9%)	10 (1.8%)	6 (1.5%)	272 (6.3%)
Unplanned care (% of telephone consults within age category)	817 (73.5%)	372 (65.5%)	324 (56.4%)	249 (45.9%)	206 (37.9%)	177 (31.6%)	125 (30.7%)	2,270 (52.7%)
Urgent or higher (% of telephone consults within age category)	155 (14.0%)	145 (25.5%)	211 (36.8%)	270 (49.8%)	321 (59.1%)	373 (66.6%)	275 (67.6%)	1,750 (40.7%)
Total within age category	**5,480**	**2,967**	**2,993**	**2,927**	**2,517**	**2,468**	**1,781**	**21,133**
Urgency not evaluated (% of total within age category)	105 (1.9%)	46 (1.6%)	41 (1.4%)	52 (1.8%)	50 (2.0%)	40 (1.6%)	31 (1.7%)	365 (1.7%)
Plannable care (% of total within age category)	688 (12.6%)	324 (10.9%)	200 (6.7%)	130 (4.4%)	113 (4.5%)	87 (3.5%)	47 (2.6%)	1,589 (7.5%)
Unplanned care (% of total within age category)	4,198 (76.6%)	2,112 (71.2%)	1,961 (65.5%)	1,712 (58.5%)	1,275 (50.7%)	1,138 (46.1%)	767 (43.1%)	13,163 (62.3%)
Urgent or higher (% of total within age category)	489 (8.9%)	485 (16.3%)	791 (26.4%)	1,033 (35.3%)	1,079 (42.9%)	1,203 (48.7%)	936 (52.6%)	6,016 (28.5%)

Supplementary Table 5: Number of registered ICPC-2 codes as chief complaints and diagnoses in out-of-hours GP datasets. Empty cells indicate zero registrations. Abbreviations: NOS (not otherwise specified).

Supplementary Table 5: Registrations of chief complaints and diagnoses in out-of-hours general practice datasets				
ICPC-2 code	**KHOBRA study population (n = 852)**		**iCAREdata study population (n = 21,133)**	
	Number of registrations as chief complaint (% of total)	Number of registrations as diagnosis (% of total)	Number of registrations as chief complaint (% of total)	Number of registrations as diagnosis (% of total)
ICPC A - General	634 (74.4%)	337 (39.6%)	17,562 (83.1%)	8,132 (38.5%)
A01 - Pain general/multiple sites	8	4	75	154
A02 - Chills			7	16
A03 - Fever	1			
A04 - Weakness/tiredness general	3		19	14
A05 - Feeling ill	6		51	20
A06 - Fainting/syncope	5		26	8
A07 - Coma			1	
A08 - Swelling			1	
A09 - Sweating problem			1	
A11 - Chest pain NOS	608	298	17,363	7,127
A13 - Concern/fear medical treatment			1	1
A29 - General symptom/complaint other			1	4
A38 - Other lab test		3		
A72 - Chickenpox				2
A73 - Malaria			1	
A76 - Viral exanthem other				3
A77 - Viral disease other/NOS	1	20	5	230
A78 - Infectious disease other/NOS				16
A79 - Malignancy NOS				1
A80 - Trauma/injury NOS			1	12
A81 - Multiple trauma/injuries				2
A82 - Secondary effect of trauma				1
A85 - Adverse effect medical agent		1		7
A86 - Toxic effect non-medicinal substance				3
A87 - Complication of medical treatment		3	2	23
A88 - Adverse effect physical factor				4
A89 - Effect prosthetic device		1		7
A91 - Abnormal result investigation NOS		2		6
A92 - Allergy/allergic reaction NOS	1		1	9
A96 - Death			2	1
A97 - No disease				5
A98 - Health maintenance/preventive medicine			3	6
A99 - Disease/condition unspecified nature/site		6	1	450
ICPC B - Hematological	0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.1%)
B02 - Lymph gland(s) enlarged/painful				1
B26 - Fear cancer blood/lymph				1
B82 - Anemia other/unspecified				2
ICPC D - Digestive	15 (1.8%)	36 (4.2%)	129 (0.6%)	1,013 (4.8%)
D01 - Abdominal pain/cramps general		3	12	51
D02 - Abdominal pain epigastric	7	4	52	145
D03 - Heartburn		2	2	61
D05 - Perianal itching				1
D06 - Abdominal pain localized other			1	2

	D07 - Dyspepsia/indigestion			1	9
	D08 - Flatulence/gas/belching			1	4
	D09 - Nausea	4		42	6
	D10 - Vomiting	4		18	4
	D11 - Diarrhea				1
	D12 - Constipation		1		13
	D13 - Jaundice				1
	D21 - Swallowing problem		1		4
	D29 - Digestive symptom/complaint other				3
	D70 - Gastrointestinal infection		1		21
	D73 - Gastroenteritis presumed infection				8
	D78 - Neoplasm digestive benign/unspecified				1
	D80 - Injury digestive system other				4
	D81 - Congenital anomaly digestive system				1
	D84 - Esophagus disease		14		374
	D86 - Peptic ulcer other				8
	D87 - Stomach function disorder		9		260
	D90 - Hiatus hernia				2
	D91 - Abdominal hernia other				2
	D93 - Irritable bowel syndrome				2
	D98 - Cholecystitis/cholelithiasis		1		15
	D99 - Disease digestive system other				10
ICPC F - Ophtalmological		1 (0.1%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
	F05 - Visual disturbance other				1
	F79 - Injury eye other	1			
ICPC H - Otorhinolaryngeal		0 (0.0%)	0 (0.0%)	0 (0.0%)	4 (0.1%)
	H71 - Acute otitis media/myringitis				1
	H72 - Serous otitis media				1
	H82 - Vertiginous syndrome				2
ICPC K - Cardiovascular		124 (14.6%)	179 (21.0%)	2,893 (13.7%)	4,279 (20.2%)
	K01 - Heart pain	39	18	1,041	435
	K02 - Pressure/tightness of heart	41	9	1,130	350
	K03 - Cardiovascular pain NOS	15	2	134	57
	K04 - Palpitations/awareness of heart		38		137
	K05 - Irregular heartbeat other		12		29
	K07 - Swollen ankles/oedema	1		2	6
	K22 - Risk factor cardiovascular disease			4	
	K24 - Fear of heart disease	3	4	51	20
	K25 - Fear of hypertension			1	1
	K27 - Fear cardiovascular disease other	2		40	9
	K28 - Limited function/disability				2
	K29 - Cardiovascular symptom/complaint other				3
	K70 - Infection of circulatory system				12
	K73 - Congenital anomaly cardiovascular				1
	K74 - Ischemic heart disease with angina	9	37	374	1,600
	K75 - Acute myocardial infarction		32	41	802
	K76 - Ischemic heart disease without angina		4	7	160
	K77 - Heart failure		1	8	61
	K78 - Atrial fibrillation/flutter		2		84
	K79 - Paroxysmal tachycardia		2		13
	K80 - Cardiac arrhythmia NOS	6	1	9	76
	K81 - Heart/arterial murmur NOS				3
	K82 - Pulmonary heart disease		1		1

	K84 - Heart disease other		4	4	142
	K85 - Elevated blood pressure		1	1	5
	K86 - Hypertension uncomplicated	7	7	34	157
	K87 - Hypertension complicated				2
	K88 - Postural hypotension	1	1	8	16
	K89 - Transient cerebral ischemia				4
	K90 - Stroke/cerebrovascular accident				5
	K92 - Atherosclerosis/peripheral vascular disease		2		32
	K93 - Pulmonary embolism				13
	K94 - Phlebitis/thrombophlebitis				12
	K95 - Varicose veins of leg				1
	K96 - Hemorrhoids				10
	K99 - Cardiovascular disease other		1	4	18
ICPC L - Musculoskeletal		20 (2.4%)	145 (17.0%)	117 (0.6%)	3,445 (16.3%)
	L01 - Neck symptom/complaint	1		4	29
	L02 - Back symptom/complaint	1	14	9	176
	L03 - Low back symptom/complaint				5
	L04 - Chest symptom/complaint	17	45	67	1,106
	L08 - Shoulder symptom/complaint				2
	L09 - Arm symptom/complaint			18	8
	L14 - Leg/thigh symptom/complaint			1	1
	L17 - Foot/toe symptom/complaint				1
	L18 - Muscle pain		32	2	702
	L19 - Muscle symptom/complaint NOS		1		13
	L20 - Joint symptom/complaint NOS			1	8
	L76 - Fracture: other			1	64
	L79 - Sprain/strain of joint NOS		3	1	124
	L80 - Dislocation/subluxation		1		5
	L81 - Injury musculoskeletal NOS		4	1	44
	L83 - Neck syndrome				17
	L84 - Back syndrome without radiating pain				17
	L86 - Back syndrome with radiating pain				7
	L87 - Bursitis/tendinitis/synovitis NOS				16
	L88 - Rheumatoid/seropositive arthritis				4
	L91 - Osteoarthrosis other				12
	L92 - Shoulder syndrome	1		11	23
	L94 - Osteochondrosis		1		7
	L95 - Osteoporosis				2
	L98 - Acquired deformity of limb				1
	L99 - Musculoskeletal disease other		43	1	1,051
ICPC N - Neurological		13 (1.5%)	3 (0.4%)	45 (0.2%)	206 (1.0%)
	N01 - Headache	2			
	N03 - Pain face			7	2
	N05 - Tingling fingers/feet/toes	1		2	2
	N08 - Abnormal involuntary movements			1	2
	N17 - Vertigo/dizziness	9		32	7
	N18 - Paralysis/weakness				1
	N29 - Neurological symptom/complaint other	1	2		24
	N81 - Injury nervous system other				2
	N88 - Epilepsy			1	
	N89 - Migraine			1	1
	N92 - Trigeminal neuralgia			1	
	N91 - Facial paralysis/bell's palsy				2
	N94 - Peripheral neuritis/neuropathy				45
	N95 - Tension headache				3
	N99 - Neurological disease other		1		115
ICPC P - Psychiatric		7 (0.8%)	27 (3.2%)	17 (0.1%)	749 (3.5%)
	P01 - Feeling anxious/nervous/tense			5	38

	P02 - Acute stress reaction		6		183
	P03 - Feeling depressed				4
	P04 - Feeling/behaving irritable/angry	3		2	14
	P06 - Sleep disturbance			1	1
	P15 - Chronic alcohol abuse				2
	P16 - Acute alcohol abuse		1		1
	P17 - Tobacco abuse				1
	P19 - Drug abuse			1	2
	P20 - Memory disturbance	1		1	1
	P29 - Psychological symptom/complaint other		4	1	150
	P70 - Dementia				3
	P71 - Organic psychosis other				2
	P72 - Schizophrenia				1
	P74 - Anxiety disorder/anxiety state	2	13	5	280
	P75 - Somatization disorder		1		14
	P76 - Depressive disorder				4
	P78 - Neurasthenia/surmenage	1			22
	P79 - Phobia/compulsive disorder				1
	P80 - Personality disorder				1
	P99 - Psychological disorders other		2	1	24
ICPC R - Respiratory		37 (4.3%)	121 (14.2%)	240 (1.1%)	2,689 (12.7%)
	R01 - Pain respiratory system	6	4	12	35
	R02 - Shortness of breath/dyspnoea	18	1	184	149
	R03 - Wheezing				3
	R04 - Breathing problem other	1		1	1
	R05 - Cough	2		12	53
	R08 - Nose symptom/complaint other				2
	R21 - Throat symptom/complaint	1		10	7
	R24 - Hemoptysis				1
	R27 - Fear of respiratory disease other		2		57
	R29 - Respiratory symptom/complaint other			2	7
	R72 - Strep throat				1
	R74 - Upper respiratory infection acute		4	4	175
	R75 - Sinusitis acute/chronic				11
	R76 - Tonsillitis acute				1
	R77 - Laryngitis/tracheitis acute		4		22
	R78 - Acute bronchitis/bronchiolitis		1		131
	R80 - Influenza	8	59	5	1,000
	R81 - Pneumonia		7		182
	R82 - Pleurisy/pleural effusion				86
	R83 - Respiratory infection other	1		2	3
	R87 - Foreign body nose/larynx/bronchus				1
	R92 - Neoplasm respiratory unspecified				2
	R95 - Chronic obstructive pulmonary disease		1	1	21
	R96 - Asthma		1		35
	R97 - Allergic rhinitis				5
	R98 - Hyperventilation syndrome		34	2	592
	R99 - Respiratory disease other		3	5	106
ICPC S - Dermatological		1 (0.1%)	0 (0.0%)	6 (0.1%)	319 (1.5%)
	S01 - Pain/tenderness of skin			1	
	S02 - Pruritus				1
	S04 - Lump/swelling localized				2
	S06 - Rash localized				2
	S08 - Skin color change	1		4	
	S10 - Boil/carbuncle				1
	S12 - Insect bite/sting				3
	S16 - Bruise/contusion				164

S17 - Abrasion/scratch/blister				1
S18 - Laceration/cut				1
S19 - Skin injury other			1	64
S70 - Herpes zoster				60
S71 - Herpes simplex				1
S72 - Scabies/other acariasis				1
S74 - Dermatophytosis				1
S76 - Skin infection other				7
S90 - Pityriasis rosea				1
S93 - Sebaceous cyst				1
S98 - Urticaria				2
S99 - Skin disease other				6
ICPC T - Endocrine	0 (0.0%)	0 (0.0%)	2 (0.1%)	4 (0.1%)
T03 - Loss of appetite			1	
T11 - Dehydration				2
T85 - Hyperthyroidism/thyrotoxicosis				1
T99 - Endocrine/metabolic/nutritional disease other			1	1
ICPC U - Urinary	0 (0.0%)	1 (0.1%)	0 (0.0%)	17 (0.1%)
U70 - Pyelonephritis/pyelitis				3
U71 - Cystitis/urinary infection other				11
U80 - Injury urinary tract				1
U95 - Urinary calculus		1		2
ICPC W - Obstetric	0 (0.0%)	0 (0.0%)	0 (0.0%)	11 (0.1%)
W19 - Lactation symptom/complaint				3
W81 - Toxemia of pregnancy				1
W94 - Puerperal mastitis				5
W95 - Breast disease in pregnancy/puerperium other				1
W99 - Disorder of pregnancy/delivery other				1
ICPC X - Female	0 (0.0%)	2 (0.2%)	0 (0.0%)	63 (0.3%)
X18 - Breast pain female				7
X19 - Breast lump/mass female				2
X21 - Breast symptom/complaint female other		2		2
X84 - Vaginitis/vulvitis NOS				1
X85 - Cervical disease NOS				2
X88 - Fibrocystic disease breast				3
X99 - Genital disease female other				46
ICPC Y - Male	0 (0.0%)	1 (0.1%)	0 (0.0%)	2 (0.1%)
Y73 - Prostatitis/seminal vesiculitis				1
Y99 - Genital disease male other		1		1
ICPC Z - Social problems	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.1%)
Z27 - Fear of a social problem				1
Z29 - Social problem NOS				1
ICPC * - Treatment	0 (0.0%)	0 (0.0%)	0 (0.0%)	19 (0.1%)
*38 - Other laboratory test NOS				19
Not evaluated	0 (0.0%)	0 (0.0%)	122 (0.6%)	174 (0.8%)
Total	852 (100%)	852 (100%)	21,133 (100%)	21,133 (100%)

Supplementary Table 6: Number of registered diagnoses per age category in out-of-hours GP datasets. To further distinguish in severity, the graded level of urgency is specified in patients with diagnosis ICPC-2 A11 (chest pain NOS). Abbreviations: NOS (not otherwise specified).

Supplementary Table 6: Number of registered diagnoses per age category in out-of-hours general practice datasets								
KHOBRA	**18-35 years**	**36-45 years**	**46-55 years**	**56-65 years**	**66-75 years**	**76-85 years**	**≥ 86 years**	**Total**
ICPC-2 diagnoses of interest (% of total in age category)	110 (37.3%)	37 (32.7%)	35 (41.2%)	61 (52.6%)	41 (57.7%)	51 (65.4%)	65 (69.1%)	400 (46.9%)
A11 - Chest pain NOS (% of total within age category)	107 (36.3%)	31 (27.4%)	27 (31.8%)	40 (34.5%)	29 (40.8%)	28 (35.9%)	36 (38.3%)	298 (35.0%)
Graded urgent or higher (% of A11 diagnoses within age category)	20 (18.7%)	9 (29.0%)	13 (48.1%)	17 (42.5%)	16 (55.1%)	15 (53.6%)	20 (55.6%)	110 (36.9%)
K01 - Heart pain (% of total within age category)	1 (0.3%)	2 (1.8%)	1 (1.2%)	4 (3.4%)	2 (2.8%)	4 (5.1%)	4 (4.3%)	18 (2.1%)
K02 - Pressure/tightness of heart (% of total within age category)	1 (0.3%)	3 (2.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	4 (4.3%)	9 (1.1%)
K03 - Cardiovascular pain NOS (% of total within age category)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.3%)	1 (1.1%)	2 (0.2%)
K74 - Ischemic heart disease with angina (% of total within age category)	1 (0.3%)	1 (0.9%)	3 (3.5%)	5 (4.3%)	5 (7.0%)	10 (12.8%)	12 (12.8%)	37 (4.3%)
K75 - Acute myocardial infarction (% of total within age category)	0 (0.0%)	0 (0.0%)	4 (4.7%)	10 (8.6%)	5 (7.0%)	6 (7.7%)	7 (7.4%)	32 (3.8%)
K76 - Ischemic heart disease without angina (% of total within age category)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (1.7%)	0 (0.0%)	1 (1.3%)	1 (1.1%)	4 (0.5%)
Other ICPC-2 diagnoses (% of total within age category)	185 (62.7%)	76 (67.3%)	50 (58.8%)	55 (47.4%)	30 (42.3%)	27 (34.6%)	29 (30.9%)	452 (53.1%)
No diagnosis registered (% of total within age category)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Total within age category	**295**	**113**	**85**	**116**	**71**	**78**	**94**	**852**
iCAREdata	**18-35 years**	**36-45 years**	**46-55 years**	**56-65 years**	**66-75 years**	**76-85 years**	**≥ 86 years**	**Total**
ICPC-2 diagnoses of interest (% of total within age category)	1,870 (34.1%)	1,154 (38.9%)	1,454 (48.6%)	1,595 (54.5%)	1,587 (63.1%)	1,641 (66.5%)	1,230 (69.1%)	10,531 (49.8%)
A11 - Chest pain NOS (% of total within age category)	1,667 (30.4%)	968 (32.6%)	1,041 (34.8%)	1,019 (34.8%)	913 (36.3%)	893 (36.2%)	626 (35.1%)	7,127 (33.7%)
Graded urgent or higher (% of A11 diagnoses within age category)	246 (14.8%)	256 (26.4%)	337 (32.4%)	432 (42.4%)	434 (47.5%)	481 (53.9%)	343 (54.8%)	2,529 (35.5%)
K01 - Heart pain (% of total within age category)	66 (1.2%)	38 (1.3%)	57 (1.9%)	64 (2.2%)	75 (3.0%)	79 (3.2%)	56 (3.1%)	435 (2.1%)
K02 - Pressure/tightness of heart (% of total within age category)	73 (1.3%)	39 (1.3%)	52 (1.7%)	52 (1.8%)	60 (2.4%)	49 (2.0%)	25 (1.4%)	350 (1.7%)
K03 - Cardiovascular pain NOS (% of total within age category)	7 (0.1%)	3 (0.1%)	11 (0.4%)	11 (0.4%)	12 (0.5%)	3 (0.1%)	10 (0.6%)	57 (0.3%)
K74 - Ischemic heart disease with angina (% of total within age category)	48 (0.9%)	70 (2.4%)	165 (5.5%)	279 (9.5%)	330 (13.1%)	399 (16.2%)	309 (17.3%)	1,600 (7.6%)
K75 - Acute myocardial infarction (% of total within age category)	6 (0.1%)	32 (1.1%)	104 (3.5%)	132 (4.5%)	170 (6.8%)	180 (7.3%)	178 (10.0%)	802 (3.8%)
K76 - Ischemic heart disease without angina (% of total within age category)	3 (0.1%)	4 (0.1%)	24 (0.8%)	38 (1.3%)	27 (1.1%)	38 (1.5%)	26 (1.5%)	160 (0.8%)
Other ICPC-2 diagnoses (% of total within age category)	3,565 (65.1%)	1,787 (60.2%)	1,517 (50.7%)	1,306 (44.6%)	911 (36.2%)	806 (32.7%)	536 (30.1%)	10,428 (49.3%)
No diagnosis registered (% of total within age category)	45 (0.8%)	26 (0.9%)	22 (0.7%)	26 (0.9%)	19 (0.8%)	21 (0.9%)	15 (0.8%)	174 (0.8%)
Total within age category	**5,480**	**2,967**	**2,993**	**2,927**	**2,517**	**2,468**	**1,781**	**21,133**

Supplementary Table 7: Plan of action registrations and its proportion of total patient contacts per out-of-hours GP office in iCAREdata study population. Out-of-hours GP offices were clustered based on population density and randomly assigned in order.

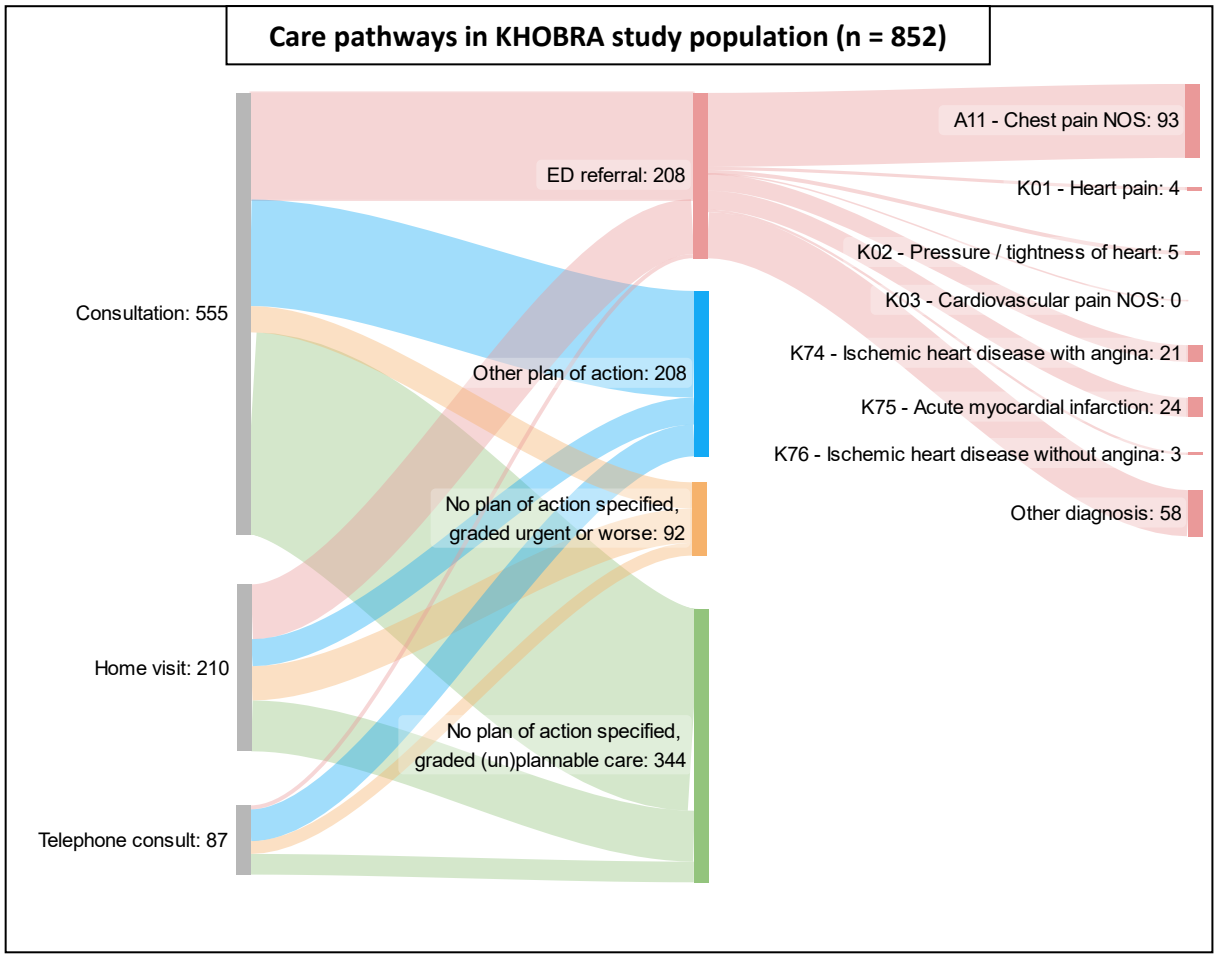
Supplementary Table 7: Plan of action registrations per out-of-hours general practitioner office in iCAREdata study population					
Out-of-hours GP office		Total number of patient contacts	Number of contacts with registered ED referral (% of total)	Number of contacts with other plan of action (% of total)	Number of contacts without specified plan of action (% of total)
A: Population density > 1,000 inhabitants/km²	A1	1,300	251 (19.3%)	232 (17.8%)	817 (62.8%)
	A2	1,152	265 (23.0%)	136 (11.8%)	751 (65.2%)
	A3	343	63 (18.4%)	51 (14.9%)	229 (66.8%)
	A4	730	124 (17.0%)	216 (29.6%)	390 (53.4%)
	A5	482	78 (16.2%)	65 (13.5%)	339 (70.3%)
B: Population density 500-1,000 inhabitants/km²	B1	458	132 (28.8%)	67 (14.6%)	259 (56.6%)
	B2	1,393	319 (22.9%)	221 (15.9%)	853 (61.2%)
	B3	467	110 (23.6%)	357 (76.4%)	0 (0.0%)
	B4	735	193 (26.3%)	83 (11.3%)	459 (62.4%)
	B5	798	211 (26.4%)	169 (21.2%)	418 (52.4%)
	B6	490	112 (22.9%)	100 (20.4%)	278 (56.7%)
	B7	808	244 (30.2%)	81 (10.0%)	483 (59.8%)
	B8	55	12 (21.8%)	43 (78.2%)	0 (0.0%)
	B9	47	8 (17.0%)	39 (83.0%)	0 (0.0%)
	B10	27	9 (33.3%)	1 (3.7%)	17 (63.0%)
	B11	605	153 (25.3%)	139 (23.0%)	313 (51.7%)
	B12	1,117	219 (19.6%)	179 (16.0%)	719 (64.4%)
C: Population density < 500 inhabitants/km²	C1	156	35 (22.4%)	121 (77.6%)	0 (0.0%)
	C2	3	0 (0.0%)	0 (0.0%)	3 (100.0%)
	C3	885	249 (28.1%)	102 (11.5%)	534 (60.3%)
	C4	242	77 (31.8%)	27 (11.2%)	138 (57.0%)
	C5	1,331	549 (41.2%)	300 (22.5%)	482 (36.2%)
	C6	2,655	710 (26.7%)	274 (10.3%)	1,671 (62.9%)
	C7	1,126	368 (32.7%)	158 (14.0%)	600 (53.3%)
	C8	459	104 (22.7%)	142 (30.9%)	213 (46.4%)
	C9	798	207 (25.9%)	113 (14.2%)	478 (59.9%)
	C10	1,121	279 (24.9%)	176 (15.7%)	666 (59.4%)
	C11	1,254	339 (27.0%)	174 (13.9%)	741 (59.1%)
	C12	85	18 (21.2%)	67 (78.8%)	0 (0.0%)
X: Out of order	X1	10	3 (30.0%)	1 (10.0%)	6 (60.0%)
	X2	1	0 (0.0%)	0 (0.0%)	1 (100.0%)
Total		**21,133**	**5,441 (25.7%)**	**3,834 (18.1%)**	**11,858 (56.1%)**

Supplementary Table 8: Number of patient contacts with and without specified plan of action per age category in out-of-hours GP datasets with percentages provided. Level of urgency is provided as substitute in patient contacts without specified plan of action.

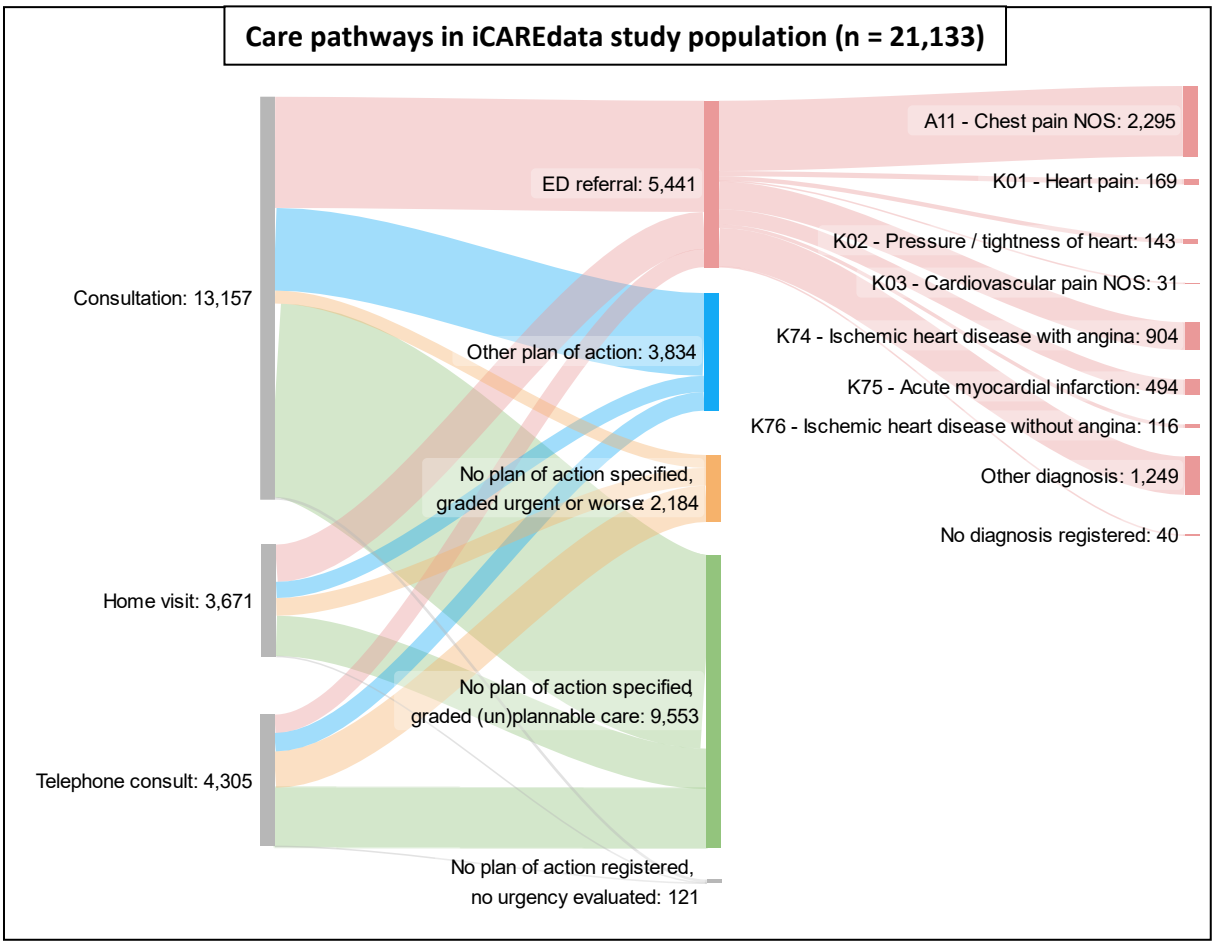
Supplementary Table 8: Plan of action per age category in out-of-hours general practice datasets								
KHOBRA study population								
Number of patient contacts	**18-35 years**	**36-45 years**	**46-55 years**	**56-65 years**	**66-75 years**	**76-85 years**	**≥ 86 years**	**Total**
With registered plan of action	130	49	44	67	40	38	48	416
Referral to emergency department (% of total contacts in age category)	45 (15.3%)	16 (14.2%)	22 (25.9%)	37 (31.9%)	25 (35.2%)	31 (39.7%)	32 (34.0%)	208 (24.4%)
Referral to specialist (% of total contacts in age category)	2 (0.7%)	2 (1.8%)	1 (1.2%)	2 (1.7%)	1 (1.4%)	0 (0.0%)	1 (1.1%)	9 (1.1%)
Referral to general practitioner (% of total contacts in age category)	13 (4.4%)	5 (4.4%)	1 (1.2%)	8 (6.9%)	5 (7.0%)	2 (2.6%)	5 (5.3%)	39 (4.6%)
Referral to physiotherapist (% of total contacts in age category)	2 (0.7%)	3 (2.7%)	1 (1.2%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	7 (0.8%)
Referral to other (% of total contacts in age category)	6 (2.0%)	1 (0.9%)	1 (1.2%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	2 (2.1%)	11 (1.3%)
Radiograph lungs (% of total contacts in age category)	1 (0.3%)	0 (0.0%)	1 (1.2%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.2%)
Radiograph musculoskeletal (% of total contacts in age category)	1 (0.3%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Radiograph other (% of total contacts in age category)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Blood test (% of total contacts in age category)	2 (0.7%)	1 (0.9%)	1 (1.2%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (0.7%)
Injection (% of total contacts in age category)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.1%)
Medication prescription or administration (% of total contacts in age category)	0 (0.0%)	1 (0.9%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.1%)	2 (0.2%)
Polymerase chain reaction test for SARS-CoV-2 (% of total contacts in age category)	46 (15.6%)	17 (15.0%)	10 (11.8%)	6 (5.2%)	7 (9.9%)	3 (5.3%)	5 (5.3%)	94 (11.0%)
Counseling (% of total contacts in age category)	3 (1.0%)	0 (0.0%)	1 (1.2%)	2 (1.7%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (0.7%)
Other treatment (% of total contacts in age category)	9 (3.1%)	3 (2.7%)	5 (5.9%)	6 (5.2%)	2 (2.8%)	2 (2.6%)	2 (2.1%)	29 (3.4%)
Without specified plan of action	165	64	41	49	31	40	46	436
Urgency not evaluated (% of total without specified plan of action in age category)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)
Graded plannable care (% of total without specified plan of action in age category)	8 (4.8%)	2 (3.1%)	1 (2.4%)	2 (4.1%)	0 (0.0%)	3 (7.5%)	0 (0.0%)	16 (3.7%)
Graded unplanned care (% of total without specified plan of action in age category)	141 (85.5%)	54 (84.4%)	33 (80.5%)	35 (71.4%)	23 (74.2%)	17 (42.5%)	25 (54.3%)	328 (75.2%)
Graded urgent or higher (% of total without specified plan of action in age category)	16 (9.7%)	8 (12.5%)	7 (17.1%)	12 (24.5%)	8 (25.8%)	20 (50.0%)	21 (45.7%)	92 (21.1%)
Total within age category	**295**	**113**	**85**	**116**	**71**	**78**	**94**	**852**
iCAREdata study population								
Number of patient contacts	**18-35 years**	**36-45 years**	**46-55 years**	**56-65 years**	**66-75 years**	**76-85 years**	**≥ 86 years**	**Total**
With registered plan of action	1,869	1,194	1,423	1,519	1,277	1,240	753	9,275
Referral to emergency department (% of total contacts in age group)	649 (11.8%)	524 (17.7%)	818 (27.3%)	1,039 (35.5%)	914 (36.3%)	955 (38.7%)	542 (30.4%)	5,441 (25.7%)

	Referral to specialist (% of total contacts in age group)	22 (0.4%)	18 (0.6%)	18 (0.6%)	15 (0.5%)	21 (0.8%)	15 (0.6%)	8 (0.4%)	117 (0.6%)
	Referral to general practitioner (% of total contacts in age group)	418 (7.6%)	261 (8.8%)	241 (8.1%)	194 (6.6%)	166 (6.6%)	120 (4.9%)	92 (5.2%)	1,492 (7.1%)
	Referral to physiotherapist (% of total contacts in age group)	73 (1.3%)	31 (1.0%)	11 (0.4%)	10 (0.3%)	11 (0.4%)	3 (0.1%)	0 (0.0%)	139 (0.7%)
	Referral to nurse (% of total contacts in age group)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.03%)	0 (0.0%)	0 (0.0%)	2 (0.1%)	3 (0.01%)
	Referral to psychologist (% of total contacts in age group)	1 (0.02%)	1 (0.03%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.01%)
	Referral to other (% of total contacts in age group)	44 (0.8%)	23 (0.8%)	18 (0.6%)	28 (1.0%)	10 (0.4%)	17 (0.7%)	7 (0.4%)	147 (0.7%)
	Radiograph lungs (% of total contacts in age group)	30 (0.5%)	18 (0.6%)	14 (0.5%)	12 (0.4%)	6 (0.2%)	2 (0.1%)	0 (0.0%)	82 (0.4%)
	Radiograph abdomen (% of total contacts in age group)	0 (0.0%)	1 (0.03%)	0 (0.0%)	1 (0.03%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	2 (0.01%)
	Radiograph musculoskeletal (% of total contacts in age group)	13 (0.2%)	3 (0.1%)	13 (0.04%)	2 (0.1%)	3 (0.1%)	4 (0.2%)	1 (0.1%)	39 (0.2%)
	Radiograph other (% of total contacts in age group)	1 (0.02%)	3 (0.1%)	0 (0.0%)	2 (0.1%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	6 (0.03%)
	Ultrasound abdomen (% of total contacts in age group)	1 (0.02%)	1 (0.03%)	1 (0.03%)	0 (0.0%)	0 (0.0%)	2 (0.1%)	0 (0.0%)	5 (0.02%)
	Ultrasound other (% of total contacts in age group)	6 (0.1%)	2 (0.1%)	2 (0.1%)	0 (0.0%)	0 (0.0%)	1 (0.04%)	1 (0.1%)	12 (0.1%)
	Blood test (% of total contacts in age group)	47 (0.9%)	21 (0.7%)	38 (1.3%)	30 (1.0%)	13 (0.5%)	9 (0.4%)	3 (0.2%)	161 (0.8%)
	Urinalysis (% of total contacts in age group)	0 (0.0%)	1 (0.03%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.01%)
	Injection (% of total contacts in age group)	8 (0.1%)	7 (0.2%)	5 (0.2%)	8 (0.3%)	11 (0.4%)	4 (0.2%)	8 (0.4%)	51 (0.2%)
	Medication prescription or administration (% of total contacts in age group)	19 (0.3%)	8 (0.3%)	12 (0.4%)	10 (0.3%)	13 (0.5%)	16 (0.6%)	17 (1.0%)	95 (0.4%)
	Polymerase chain reaction test for SARS-CoV-2 (% of total contacts in age group)	272 (5.0%)	132 (4.4%)	104 (3.5%)	73 (2.5%)	29 (1.2%)	18 (0.7%)	9 (0.5%)	637 (3.0%)
	Wound suturing (% of total contacts in age group)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (0.04%)	0 (0.0%)	1 (0.01%)
	Counseling (% of total contacts in age group)	37 (0.7%)	21 (0.7%)	14 (0.5%)	14 (0.5%)	6 (0.2%)	14 (0.6%)	4 (0.2%)	110 (0.5%)
	Other treatment (% of total contacts in age group)	160 (2.9%)	87 (2.9%)	78 (2.6%)	67 (2.3%)	56 (2.2%)	55 (2.2%)	52 (2.9%)	555 (2.6%)
	No follow-up necessary (% of total contacts in age group)	68 (1.2%)	31 (1.0%)	36 (1.2%)	13 (0.4%)	18 (0.7%)	4 (0.2%)	7 (0.4%)	177 (0.8%)
Without specified plan of action		3,611	1,773	1,570	1,408	1,240	1,228	1,028	11,858
	Urgency not evaluated (% of total without specified plan of action in age category)	30 (0.8%)	11 (0.6%)	13 (0.8%)	15 (1.1%)	22 (1.8%)	14 (1.1%)	16 (1.6%)	121 (1.0%)
	Graded plannable care (% of total without specified plan of action in age category)	536 (14.8%)	244 (13.8%)	138 (8.8%)	98 (7.0%)	80 (6.5%)	68 (5.5%)	41 (4.0%)	1,205 (10.2%)
	Graded unplanned care (% of total without specified plan of action in age category)	2,872 (79.5%)	1,346 (75.9%)	1,179 (75.1%)	997 (70.8%)	745 (60.1%)	693 (56.4%)	516 (50.2%)	8,348 (70.4%)
	Graded urgent or higher (% of total without specified plan of action in age category)	173 (4.8%)	172 (9.7%)	240 (15.3%)	298 (21.2%)	393 (31.7%)	453 (36.9%)	455 (44.3%)	2,184 (18.4%)
Total within age category		**5,480**	**2,967**	**2,993**	**2,927**	**2,517**	**2,468**	**1,781**	**21,133**

Supplementary Figure 1: Care pathways in KHOBRA (n = 852) study population. Nodes (left to right) include contact type, plan of action with or without graded level of urgency, and registered diagnosis in case of ED referral. Abbreviations: NOS (not otherwise specified).



Supplementary Figure 2: Care pathways in iCAREdata (n = 21,133) study population. Nodes (left to right) include contact type, plan of action with or without graded level of urgency, and registered diagnosis in case of ED referral. Abbreviations: NOS (not otherwise specified).



XII. CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

XIII. FINANCIAL DISCLOSURE

None.

XIV. FUNDING

None.

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