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# Sex differences in incidence of respiratory symptoms and management by general practitioners

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## Abstract

**Background:** Differences between women and men play an important role in lung physiology and epidemiology of respiratory diseases, but also in the health care processes.

**Objective:** To analyse sex differences in patients encountering their general practitioner (GP) with respiratory symptoms with regard to incidence, GP's management and final diagnoses.

**Methods:** Retrospective cohort study, using data of the Dutch Practice Based Research Network. All patients who encountered their GP from 01-07-2013 until 30-06-2018 with a new episode of care starting with a reason for encounter in the respiratory category (R) of the ICPC-2 classification were included ($n$ = 16 773). Multi-level logistic regression was used to analyse influence of patients' sex on management of GPs with adjustment for possible confounders.

**Results:** We found a significant higher incidence of respiratory symptoms in women than in men: 230/1000 patient years [95% confidence interval (CI) 227–232] and 186/1000 patient years (95% CI 183–189), respectively. When presenting with cough, GPs are more likely to perform physical examination [odds ratio (OR) 1.22; 95% CI 1.11–1.35] and diagnostic radiology (OR 1.25; 95% CI 1.08–1.44), but less likely to prescribe medication (OR 0.88; 95% CI 0.82–0.95) in men. When visiting the GP with dyspnoea, men more often undergo diagnostic imaging (OR 1.32; 95% CI 1.05–1.66) and are more often referred to a specialist (OR 1.35; 95% CI 1.13–1.62).

**Conclusions:** Women encounter their GP more frequently with respiratory symptoms than men and GPs perform more diagnostic investigations in men. We suggest more research in general practice focussing on sex differences and possible confounders.

**Key words:** Family practice, general practice, respiration disorders, respiratory symptoms, sex bias, sex factors

## Background

Men and women differ in their health and diseases. This variation is caused by biological characteristics such as anatomy or hormonal factors (sex) (1), together with 'gender', meaning the different expected social roles, behaviours and cultural aspects related to being male or female (2,3). The past years, growing scientific interest in the role of gender and sex on health care and specific diseases has developed (4). Previous studies show several discrepancies in epidemiology and symptoms of conditions in males and females. However, these differences between sexes are not fully addressed by health care providers yet (5,6).

Although health research about sex and gender has mainly focussed on cardiovascular conditions, recent evidence has shown that

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**Key Messages**

- Women have a higher incidence of respiratory symptoms in primary care than men.
- Male sex possibly relates to more interventions performed in primary care.
- More research focussing on sex differences in primary care is needed.

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sex and gender influence lung physiology and respiratory diseases as well. This influence is seen throughout the whole lifespan. Starting in intra-uterine life, female foetuses show an earlier production of surfactant than males and have fewer number bronchi but these mature faster (7,8). During childhood, boys have a higher prevalence of asthma than girls. This difference is probably due to relatively smaller airway diameters in males compared with females (8). Asthma prevalence rises in females in puberty and decreases in men in puberty, reaching an equal prevalence for both sexes around the age of the menopause (1). Also in chronic obstructive pulmonary disease (COPD), previously seen as a '*smoking men's disease*', epidemiologic changes are noted. Incidence of COPD in females is rising, and evidence suggests that females are more susceptible to tobacco smoke than men (7).

Sex and gender do not only influence epidemiology and pathogenesis of diseases, they also impact the actions of health care providers. Evidence shows that despite presenting with similar complaints in several conditions, women are less likely to undergo additional diagnostic investigations and are more often classified in a category of non-specific diagnoses than men (9–11). Possible explanations for this phenomenon are that women tend to seek health care more often than men and have a less straightforward way of presenting their symptoms (3,11).

Little to no research has yet been conducted into sex differences of specifically respiratory symptoms and subsequent management hereof by the general practitioner (GP). This is problematic, as sex is an inevitable determinant in research and in clinical practice. Additionally a lack of knowledge may lead to bias and suboptimal treatment when differences between males and females are not taken into account. In this study, we aim to analyse the difference in incidence of respiratory symptoms presenting to the GP between men and women, as these symptoms are very common in primary care practice. Furthermore, we will analyse differences in the management and final diagnosis by the GP between men and women presenting with respiratory symptoms.

## Methods

### Design and data collection

This retrospective cohort study used electronic data from the Practice Based Research Network (PBRN) Family Medicine Network (FaMe-Net), a Dutch primary care research network from the Radboud University Medical Centre in Nijmegen (12). Since 1971, all encounters between patients and GPs are registered in this network, which consists of seven family practices (24 GPs and approximately 32 000 registered patients). GPs routinely code episodes of care according to the International Classification of Primary Care (ICPC-2) (13,14). An episode of care is defined here as an individual health problem, that starts at the first encounter and is completed at the final encounter linked to that health problem. Furthermore, GPs register the patient's initial reason for encounter (RFE) for each episode, all performed interventions during the episode and the final GP's diagnosis (15,16). Being the literal expression of the reason why patients encounter the GP, the RFE represents the demand of care for that person (17). RFEs can be complaints and symptoms, but also a particular diagnosis or a request for an intervention, such as prescription of medication.

### Population

We included patients of all ages who encountered their GP in the period 01-07-2013 until 30-06-2018 with a new episode of care starting with a RFE in the respiratory category (R) of the ICPC-2 (R-RFE). We excluded episodes of care that started solely with a request for intervention (R30–R69).

### Measurements

We collected the following patient characteristics: sex, age at start of episode of care, GP practice and comorbidity. Relevant comorbidities were selected by their ICPC code: cardiovascular disease (K22, K72, K47–80, K82–84, K86–92, K99), COPD/chronic bronchitis (R79 and R95), asthma (R96) and presence of malignancies (A79, B72–74, D74–77, F74, H75, L71, N74, N76, R84, R85, T71–73, U75–77, U79, X75–77, X81, Y77–79). From encounters we collected the following information: the RFE, status of the visit (first encounter or subsequent encounter within the episode), the type of encounter (consultation at the practice or at home, telephone or email consultation, both in daily practice as in evening or night shifts) and the final diagnosis of the episode of care.

#### Incidence of respiratory symptoms

We analysed the incidence (in patient years) of each RFE at exclusively the first visit of an episode, per sex and age category as used in previous research (18,19). Patient years were extracted from the Electronic Medical Health Record TransHis, the information system of GPs participating in the PBRN FaMe-Net. When GPs coded more than one initial R-RFE at the start of an episode of care, we included every initial R-RFE in our analysis.

#### Management and final diagnosis of GPs

We focussed on the four R-RFEs with the highest incidence number, namely cough, dyspnoea, acute upper respiratory infection and throat symptoms, and analysed all interventions that were performed by the GP in the entire corresponding episodes of care. Interventions were grouped by their ICPC code: physical examination (–30 and –31), laboratory diagnostics (–33 and –34), diagnostic radiology/imaging (–41), medication prescription (–50), referral to other primary care provider (–66) or referral to specialized care/hospital (–67). Furthermore, we analysed for both sexes the final diagnosis of each episode of care started with the particular RFE. These diagnoses were coded by the ICPC-2 classification. The validity of registration of diagnoses is high, as participating GPs meet regularly to discuss registration and diagnostic criteria. Moreover, the electronic medical record system that was used, warns the GP in case of error or inconsistency in registration.

### Data analysis

For data analysis we used tools provided in SPSS 25. We calculated incidence numbers and confidence intervals (CIs) using descriptive statistics. To investigate how patients' sex affects interventions delivered by GPs, we performed a multi-level analysis to determine the influence of variables on the presence or absence of an intervention. We corrected our findings for patients' sex, age, numbers

of encounters in the episode and presence of comorbidities at start of the episode.

## Results

We found 38 704 episodes of care starting with an R-RFE in 20 063 patients. We excluded 9063 episodes of care, because they started with a request for intervention as RFE (of which 66% was a request for influenza vaccination or a request for medication prescription). Finally, we analysed 29 641 episodes of care in 16 773 patients. Baseline characteristics of the included patients are shown in Table 1. Women encountered the GP more frequently with an R-RFE than men and women had more relevant comorbidities at the moment of encounter. We found no difference in the total number of encounters within an episode of care between male and female patients.

The total incidence of R-RFEs is 208/1000 patient years (95% CI 206–210), with a significant difference in the incidence between men and women: 186/1000 patient years (95% CI 183–189) and 230/1000 patient years (95% CI 227–232), respectively. Figure 1 shows the distribution of incidences for all R-RFEs per age category and sex. In the age category 0–4 years the incidence of R-RFEs is significantly higher in boys with an incidence of 537/1000 patient years (95% CI 525–550); for girls this incidence is 476/1000 patient years (95% CI 463–489). As age increases, the distribution of included R-RFEs per sex changes. The 10 most frequently coded R-RFEs for men and women are shown in Table 2, with their corresponding incidences per 1000 patient years.

The four RFEs with highest incidences were cough (R05), dyspnoea (R02), throat symptoms (R21) and acute upper respiratory tract infection (R74). Table 3 shows the interventions of GPs in episodes of care started with cough and dyspnoea. With a RFE cough, GPs more frequently perform a physical examination [odds ratio (OR) 1.22; 95% CI 1.11–1.35], and diagnostic imaging (OR 1.25; 95% CI 1.08–1.44) in men and prescribe medication less often (OR 0.88; 95% CI 0.82–0.95) compared with women. When visiting the GP with RFE dyspnoea, the odds to receive diagnostic imaging in the episode of care is 1.32 times (95% CI 1.05–1.66) higher for male patients than for females. In addition, men presenting with dyspnoea are more often referred to a specialist in the episode of care (OR 1.35; 95% CI 1.13–1.62). In throat symptoms and acute upper respiratory infection no significant differences were found between male and female patients for all types of interventions (data

**Table 1.** Baseline characteristics of all patients encountering general practice with respiratory symptoms (01-07-2013–30-06-2018)

| Characteristic | Men, no. (%) | Women, no. (%) | P value | Total |
|---|---|---|---|---|
| *Patients* | 7594 (45%) | 9179 (55%) | | 16 773 |
| New episodes of care | 13 009 (44%) | 16 632 (56%) | | 29 641 |
| Age at start of episode of care, mean (SD) | 34 (27) | 37 (25) | | |
| Number of R-RFEs at start of episode of care, mean (SD) | 1.15 (0.39) | 1.17 (0.40) | **<0.001** | |
| Number of encounters per episode, mean (SD) | 1.61 (1.66) | 1.60 (1.61) | | |
| Comorbidity at start of episode of care | 4269 (33%) | 5712 (34%) | **0.006** | 9981 |
|     Cardiovascular disease | 2999 (23%) | 4002 (24%) | **0.043** | 7001 |
|     Asthma, COPD or chronic bronchitis | 1751 (14%) | 2202 (13%) | 0.58 | 3953 |
|     Malignancy | 623 (5%) | 991 (6%) | **<0.001** | 1614 |

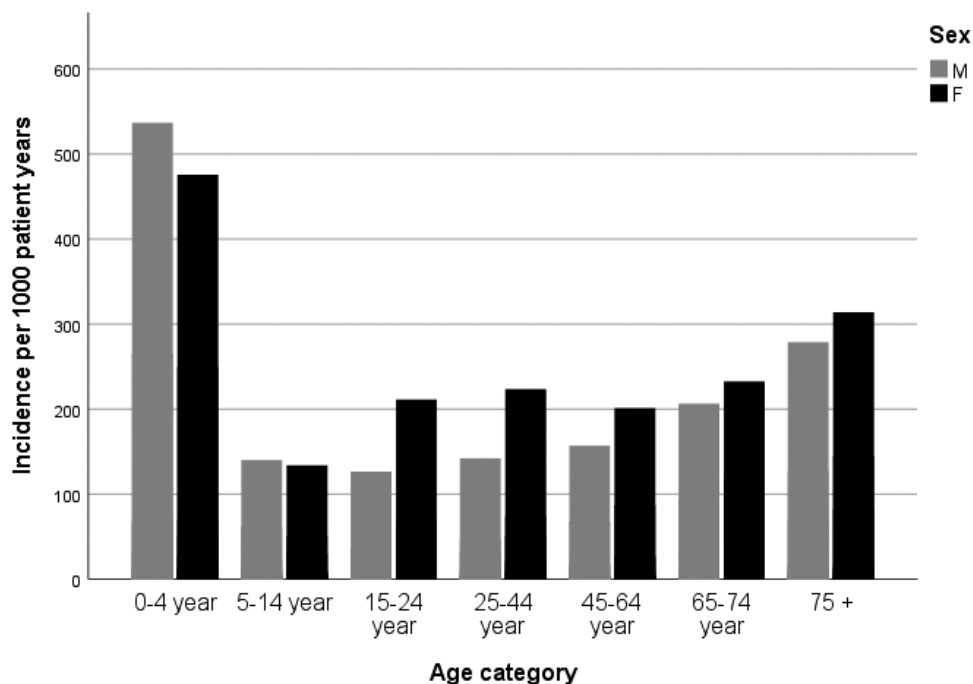Significant differences between men and women are marked in bold.



**Figure 1.** Total incidence number of all included respiratory reasons for encounter of general practice in the FaMe-Net database, divided per age category and sex (01-07-2013–30-06-2018).

**Table 2.** Incidence numbers of the ten most common respiratory reasons for encounter in general practice for both men and women (01-07-2013–30-06-2018)

Incidence per 1000 patient years (95% CI)

| Men | | Women | |
|---|---|---|---|
| *Total* | 186 (183–189) | *Total* | 230 (227–232) |
| Cough (R05) | 77.9 (76.0–79.8) | Cough (R05) | 93.2 (91.1–95.2) |
| Throat symptoms (R21) | 24.5 (23.4–25.6) | Throat symptoms (R21) | 38.1 (36.8–39.4) |
| Dyspnoea (R02) | 21.2 (20.2–22.3) | Dyspnoea (R02) | 28.1 (26.9–29.2) |
| Acute upper respiratory tract infection (R74) | 14.5 (13.6–15.3) | Acute upper respiratory tract infection (R74) | 18.3 (17.4–19.3) |
| Sneezing (R07) | 5.9 (5.3–6.4) | Sneezing (R07) | 5.9 (5.4–6.5) |
| Epistaxis (R06) | 5.0 (4.5–5.5) | Sinus symptoms (R09) | 5.7 (5.2–6.2) |
| Nose symptoms (R08) | 4.3 (3.8–4.7) | Nose symptoms(R08) | 4.2 (3.8–4.7) |
| Breathing problem (R04) | 2.3 (3.8–4.7) | Epistaxis (R06) | 4.2 (3.7–4.6) |
| Wheezing (R03) | 3.5 (3.1–3.9) | Sinusitis acute/chronic (R75) | 4.1 (3.6–4.5) |
| Allergic rhinitis (R97) | 3.4 (2.9–3.8) | Influenza (R80) | 3.7 (3.2–4.1) |

**Table 3.** Interventions performed by GPs in episodes of care starting with reasons for encounter 'cough' and 'dyspnoea' (01-07-2013–30-06-2018)

| Intervention | Male patients (% of total) | Female patients (% of total) | Total episodes | OR, *crude*[a] (95% CI) | OR, *adjusted*[b] (95% CI) | *P* value, *adjusted* |
|---|---|---|---|---|---|---|
| *Total episodes RFE cough* | 5903 | 7357 | 13 260 | | | |
| Physical examination | 5129 (86.9%) | 6192 (84.2%) | 11 321 | 1.25 (1.13–1.38) | 1.22 (1.11–1.35) | **<0.001** |
| Laboratory diagnostics | 992 (16.8%) | 1335 (18.1%) | 2327 | 0.92 (0.83 -1.01) | 0.96 (0.87–1.07) | 0.47 |
| Diagnostic radiology/imaging | 354 (6.0%) | 349 (4.7%) | 703 | 1.18 (1.02–1.35) | 1.25 (1.08–1.44) | **0.002** |
| Medication prescription | 2829 (47.9%) | 3870 (52.6%) | 6699 | 0.83 (0.77–0.90) | 0.88 (0.82–0.95) | **0.001** |
| Referral in first line | 10 (0.2%) | 23 (0.3%) | 33 | 0.98 (0.80–1.20) | 0.98 (0.80–1.20) | 0.83 |
| Referral to specialist/hospital | 189 (3.2%) | 204 (2.8%) | 393 | 1.07 (0.90–1.26) | 1.05 (0.89–1.24) | 0.54 |
| *Total episodes RFE dyspnoea* | 1610 | 2217 | 3827 | | | |
| Physical examination | 1483 (92.1%) | 2011 (90.7%) | 3494 | 1.16 (0.93–1.46) | 1.15 (0.92–1.44) | 0.23 |
| Laboratory diagnostics | 396 (24.6%) | 619 (27.9%) | 1015 | 0.85 (0.73–0.98) | 0.90 (0.77–1.05) | 0.18 |
| Diagnostic radiology/imaging | 155 (9.6%) | 175 (7.9%) | 330 | 1.20 (0.96–1.50) | 1.32 (1.05–1.66) | **0.016** |
| Medication prescription | 789 (49.0%) | 1016 (45.8%) | 1805 | 1.14 (0.99-1,30) | 1.12 (0.98–1.29) | 0.10 |
| Referral in first line | 56 (3.5%) | 76 (3.4%) | 132 | 1.01 (0.75–1.36) | 1.04 (0.77–1.41) | 0.79 |
| Referral to specialist/hospital | 289 (18.0%) | 317 (14.3%) | 606 | 1.31 (1.10–1.57) | 1.35 (1.13–1.62) | **0.001** |

Significant differences between male and female are marked in bold.

[a]Tested by multi-level logistic regression.

[b]Adjusted for possible confounders: age, number of encounters in episode of care, cardiovascular comorbidity, asthma, COPD, chronic bronchitis or known malignancy at moment of encounter.

not shown). The most frequent final diagnoses of the episodes of care starting with a cough and dyspnoea are presented in Table 4. For both symptoms cough and dyspnoea, men are more often diagnosed with pneumonia. Women are more often diagnosed with 'sinusitis' when presenting with a cough, and with a final (symptom)diagnosis 'dyspnoea' when presenting with dyspnoea. For men presenting with cough, the diagnoses 'acute otitis media/myringitis', 'wheezing' and 'asthma' are more often assigned.

## Discussion

### Summary

Female patients were found to have a significantly higher incidence of respiratory symptoms as RFE (230/1000 patient years) compared with male patients (186/1000 patient years). GPs perform different interventions in male and female patients presenting with the same RFE, especially in cough and dyspnoea. When presenting a cough, males are more likely to undergo physical examination and diagnostic radiology than females. Women, however, are more often prescribed medication for their cough than men. With regard to

dyspnoea, males are more likely to undergo diagnostic radiology when encountering the GP and are more often referred to a medical specialist during this episode of care than females. In the current research, these differences in GPs' actions are not explained by patient characteristics such as age, comorbidity or the number of encounters in the episode of care. Symptom-diagnoses such as 'dyspnoea' are more often assigned to women than to men, whose diagnoses are more clearly defined.

### Strengths and limitations

A major strength of this study is the high validity and reliability of the FaMe-Net database, based on regular discussions between participating GPs to ensure conformity regarding registration. Additionally, we included many patients and encounters, allowing for greater statistical power. However, the retrospective study design has its limitations. First, differences in symptom-presentation between men and women may have had a substantial impact on GPs' decisions. In addition, the severity of the symptoms at the moment of presentation may vary between women and men. Health care seeking behaviour may also influence decision making of GPs:

**Table 4**. Final diagnoses of episodes of care starting with reasons for encounter 'cough' and 'dyspnoea' (01-07-2013–30-06-2018)

| Final diagnosis (by ICPC-2) | Men | Women | *P* value |
| --- | --- | --- | --- |
| | N (% of episodes) | N (% of episodes) | |
| Episodes of care starting with cough (R05) | | | |
| R74 Acute upper respiratory infection | 2340 (39.6%) | 3001 (40.8%) | 0.18 |
| R05 Cough | 1691 (28.7%) | 2212 (30.1%) | 0.075 |
| R81 Pneumonia | 526 (8.9%) | 550 (7.5%) | **0.003** |
| R78 Acute bronchitis/bronchiolitis | 411 (7.0%) | 471 (6.4%) | 0.20 |
| R77 Acute laryngitis/tracheitis | 186 (3.15%) | 272 (3.7%) | 0.087 |
| R80 Influenza | 166 (2.8%) | 196 (2.7%) | 0.60 |
| H71 Acute otitis media/myringitis | 92 (1.6%) | 76 (1.0%) | **0.007** |
| R75 Sinusitis acute/chronic | 46 (0.78%) | 87 (1.2%) | **0.021** |
| R96 Asthma | 64 (1.1%) | 52 (0.71%) | **0.020** |
| R03 Wheezing | 43 (0.73%) | 26 (0.35%) | **0.003** |
| Episodes of care starting with dyspnoea (R02) | | | |
| R02 Dyspnoea | 358 (22.2%) | 613 (27.7%) | **<0.001** |
| R74 Acute upper respiratory infection | 291 (18.1%) | 416 (18.8%) | 0.59 |
| R81 Pneumonia | 172 (10.7%) | 181 (8.2%) | **0.008** |
| R78 Acute bronchitis/bronchiolitis | 143 (8.9%) | 164 (7.4%) | 0.095 |
| R96 Asthma | 70 (4.4%) | 94 (4.2%) | 0.87 |
| R77 Acute laryngitis/tracheitis | 54 (3.4%) | 71 (3.2%) | 0.80 |
| R98 Hyperventilation syndrome | 47 (2.9%) | 77 (3.5%) | 0.34 |
| R05 Cough | 39 (2.4%) | 49 (2.2%) | 0.67 |
| K77 Heart failure | 40 (2.5%) | 48 (2.2%) | 0.52 |
| R80 Influenza | 30 (1.9%) | 45 (2.0%) | 0.71 |

Significant differences between men and women are marked in bold.

women seek more care and at an earlier stage than men (20). Other possible confounding factors are the personal conceptions and experiences of a GP, such as former patients with similar complaints and experienced benefits or harms of certain interventions. We could not take these possible confounding factors into account, due to the retrospective nature of the study. Furthermore, we could not correct our analyses for additional possible confounders including smoking status, socio-economic status (SES) and family history of respiratory disease. Especially the absence of information on patient's smoking status in the context of respiratory diseases is of importance, as this may have substantial effects on actions performed by the GP. Lastly, despite the high validity of ICPC-2 coding of RFEs and diagnoses in our study, potential misclassification of final disease or diagnoses may have occurred.

## Comparison with previous literature

We found a total incidence of respiratory symptoms of 208/1000 patient years. This is in line with a Dutch study conducted in 2004 (19), which reports a total incidence of symptoms in the respiratory ICPC-category of 214/1000 patient years. Consistent with previous literature, we found that women seek more health care than men (11,21). Both the absolute frequency of GP encounters, as the incidence of respiratory RFEs is higher in women than men. Possible explanations for this are differences in socialization patterns and cultural norms between men and women, allowing women to more easily seek health care (22,23). In the ages 0–4 years, incidence of respiratory symptoms is higher in males, but after puberty incidence is higher in females. These findings are in line with previous research (19), which states that during childhood, male patients are more susceptible for respiratory disease due to anatomical development of the lungs, shifting to a higher prevalence of lung diseases in females from the age of puberty, possibly due to hormonal and physiological changes (1,7).

Our results of differences in GP interventions match results of previous studies, in which women are less likely to receive more advanced diagnostic interventions in a large variety of diseases. Especially in cardiovascular disease, research shows that women are less likely than men to be diagnosed, treated and referred when experiencing chest pain (3,10,24–26). These differences are seen prospectively in randomized trials and cohort studies, both in primary care and specialized care. Although in lesser amount, sex differences have been studied regarding respiratory symptoms or diseases (9,27,28). However, no studies were performed in the Netherlands and the only study we found in primary care focussing on respiratory complaints has been performed in Spain with significantly fewer patients than this cohort study (9).

A variety of factors may explain the differences in the nature and number of GP interventions. First, patients' biological factors might cause variations in type and severity of symptoms, which makes the GP decide upon different interventions. Also, additional patient characteristics including age, smoking status and family history are thought to be important factors for GPs to consider when deciding upon management of respiratory symptoms. However, after adjustment for age and the presence of relevant comorbidities, the influence of sex on GP's interventions remained present in our study. Second, differences in GPs' interventions might be explained by a differing likelihood for final diagnoses between men and women presenting with the same RFE. For example, men may receive the final diagnosis pneumonia more frequently than women. On the one hand, this could be due to a higher detection rate of pneumonia in men, as they receive more radiology than women. This situation may be self-sustaining: increased use of radiology in men leads to a higher detection rate of pneumonia in men compared with women. Consequently, the incidence of pneumonia in men increases, followed by an increased likelihood of GPs applying more radiology, as GPs base their actions on guidelines and personal experience. On the other hand, a truly higher incidence of pneumonia, irrespective

of diagnostic procedures, might be present in men compared with women. The current research, however, cannot clarify which situation is more likely. Lastly, wishes and communication patterns of patients may contribute to differences in GP's interventions. The presentation of complaints of women is often considered to be more extensive and vague; men communicate more demanding and straightforward, possibly resulting in the demand for more thorough examinations or referral (3).

## Implications for further research and clinical practice

The findings of this study show differences in the incidence in respiratory symptoms and the interventions by GPs that follow these symptoms, between men and women. However, as we could not include some possible confounding variables, further research is necessary to assess to which extent a sex bias contributes to these differences. We suggest future research that assesses possible factors that influence GPs' interventions. Such research could include patient's gender, smoking habits, SES and family history of respiratory disease, but also communication aspects and the sex of the GP. Furthermore, qualitative research in patients with respiratory symptoms who are considering seeking help from a GP and in patients who actually did seek help, may provide information on patients' expectations of and experiences with their GP and whether these expectations and experiences differ between women and men. Additionally, in clinical practice, more awareness of the influence of patients' sex could be raised when GPs are taught to reflect on their actions focussing on possible sex- and communication-related aspects. Results of studies focussing on sex differences could be incorporated in training programmes for GPs and in the curriculum of medical students and GP trainees. In conclusion, our study suggests the need for more awareness of sex differences in primary care itself, as well as in primary care research.

## Declaration

## Research checklist

This article was written according to the STROBE checklist for observational studies in epidemiology (29).

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