Trends in the registration of anxiety in Belgian primary care from 2000 to 2021: A registry-based study

Beerten, Simon; Coteur, Kristien; Mamouris, Pavlos; van Nuland, Marc; Van Pottelbergh, Gijs; Casas, Lidia; Vaes, Bert

DOI: https://doi.org/10.3399/BJGP.2022.0196

To access the most recent version of this article, please click the DOI URL in the line above.

Received 14 April 2022
Revised 23 September 2022
Accepted 24 October 2022

© 2022 The Author(s). This is an Open Access article distributed under the terms of the Creative Commons Attribution 4.0 License (http://creativecommons.org/licenses/by/4.0/). Published by British Journal of General Practice. For editorial process and policies, see: https://bjgp.org/authors/bjgp-editorial-process-and-policies

When citing this article please include the DOI provided above.
Trends in the registration of anxiety in Belgian primary care from 2000 to 2021

A registry-based study

Simon Gabriël Beerten¹, MD, MSc
Research fellow
https://orcid.org/0000-0003-3695-2452

Kristien Coteur¹, MSc
Research fellow
https://orcid.org/0000-0002-3170-0195

Pavlos Mamouris¹, MSc
Research fellow
http://orcid.org/0000-0001-7902-5355

Marc Van Nuland¹, MD, PhD
Visiting professor
http://orcid.org/0000-0002-2976-6611

Gijs Van Pottelbergh¹, MD, PhD
Assistant professor
https://orcid.org/0000-0002-0844-8673

Lidia Casas²³, MD, PhD
Assistant professor
https://orcid.org/0000-0003-1820-8742

Bert Vaes¹, MD, PhD
Assistant professor
https://orcid.org/0000-0001-5244-1930

¹ Department of Public Health and Primary Care, KU Leuven, Belgium

² Social Epidemiology and Health Policy (SEHPO), Department of Family Medicine and Population Health (FAMPOP), University of Antwerp, Belgium
3 Institute for Environment and Sustainable Development (IMDO), University of Antwerp, Belgium.
**ABSTRACT**

*Background:* Anxiety is frequently encountered in general practice, but figures regarding prevalence and incidence in this healthcare setting remain scarce.

*Aim:* To provide insight in the trends of prevalence and incidence of anxiety in Belgian general practice, as well as the comorbidities and treatment of anxiety in this context.

*Design and setting:* A retrospective cohort study using the INTEGO morbidity registration network, collecting clinical data of over 600,000 patients in Flanders, Belgium.

*Methods:* Trends in age-standardized prevalence and incidence of anxiety from 2000 to 2021, as well as prescriptions in prevalent anxiety cases, were analysed with joinpoint regression. Comorbidity profiles were analysed using the Cochran-Armitage test and the Jonckheere-Terpstra test.

*Results:* During the 22-year study period, we identified 8,451 unique patients with anxiety. The prevalence of anxiety diagnoses rose significantly during this period, from 1.1% in 2000 to 4.8% in 2021. The incidence rate rose from 1.1/1000 patient-years (PY) in 2000 to 9.9/1000 PY in 2021. The average chronic disease count per patient increased significantly during the study period, from 1.5 to 2.3 chronic conditions. The most frequent comorbidities in patients with anxiety were malignancy (20.1%), hypertension (18.2%) and irritable bowel syndrome (13.5%). The proportion of patients treated with psychoactive medication rose from 25.7% to almost 40% over the study period.

*Conclusion:* We found a significantly increasing prevalence and incidence of physician-registered anxiety in our study. Patients with anxiety tend to become more complex, with more comorbidities. Treatment for anxiety in Belgian primary care is very dependent on medication.
**Keywords**: epidemiology, anxiety, general practice, Belgium

**HOW THIS FITS IN**

Figures on anxiety in general practice are scarce. This study shows increasing incidence and prevalence of physician-registered anxiety. Patients with anxiety had an increasing number of comorbidities over time. Treatment of anxiety in this setting seems very dependent on medication, particularly SSRIs and anxiolytics.

**INTRODUCTION**

Anxiety disorders are common, with a global prevalence of 4.1% in 2019, higher in women. In Belgium, the estimated prevalence in 2019 was 5.6% (6.5% for women and 4.7% for men). These results were derived from surveys (face-to-face interviews using the WMH-CIDI questionnaire) in the general population.

In primary care, the most commonly diagnosed anxiety disorder is generalized anxiety disorder (GAD). The 2018 Belgian Health Interview Survey put the prevalence of GAD at 11.2%. In this population-level self-report survey, the 7-item Generalized Anxiety Disorders Scale was used.

An important problem with data for mental health disorders is the discrepancy between diagnostic data in electronic medical records and self-reported data.

Regarding the trends in the epidemiology of anxiety, there are many sources with contradictory findings. For instance, in a population-level analysis by Booth et al. anxiety tended to increase more over time in specific populations (e.g. students). For most of these studies, surveys such as the State-Trait Anxiety Inventory (STAI) were used instead of clinical data.
Furthermore, there are generally high rates of comorbidity between depression and anxiety.\textsuperscript{11,12} This has raised doubts as to whether these disorders constitute separate clinical entities.\textsuperscript{13} Some studies found common overlap for anxiety and mood disorders in primary care.\textsuperscript{14,15}

Because of the paucity of data surrounding trends in anxiety in primary care, we sought to study the registration of anxiety, its comorbidities, as well as medication prescription over a 22-year period in primary care in Flanders, the northern region of Belgium.

**METHODS**

**Study design and data collection**

This study used the INTEGO database, a morbidity registration network in Flemish primary care.\textsuperscript{16} It started in 1994 and contains medical information of over 600,000 patients. Primary care practices apply for inclusion in this registry, which is a continuous process. Registration performance of these practices is compared with that of other applicants. Only those practices with optimal performance are included in this study. All diagnoses and new drug prescriptions are registered using codes.

In Belgium, patients are able to visit any GP they prefer. In INTEGO, their data is coded with a unique patient ID, to avoid double-counting when they visit multiple GPs in the network.

Currently, there are 104 practices in INTEGO. The patients of those practices are representative for the Flemish population in terms of age and gender.\textsuperscript{16} Our study period ran from January 1, 2000 to December 31, 2021. Only practices with at least 80% coded diagnoses were included in the study (86 practices), to minimize intra-practice variation.
The denominator used in this study is the Yearly Contact Group (YCG),\textsuperscript{16,17} which contains all the patients who visited a practice at least once in a given year. Given that Belgian GPs do not have fixed patient lists, using the YCG as a denominator is therefore the most realistic approach.\textsuperscript{17} We included patients at least 15 years of age.

**Anxiety, comorbidities and treatment**

Diagnoses in INTEGO are coded using the International Classification of Primary Care 2 (ICPC-2). To identify patients with anxiety, we used the ICPC code P74 “Anxiety disorder/Anxiety state”. In a sensitivity analysis, we have added the symptom code P01 “Feeling anxious/nervous/tense”, for comparison (see Supplementary Data).

In line with the view that anxiety disorders are considered chronic,\textsuperscript{18} we considered a case prevalent when the diagnosis of P74 was made at any point before the year of analysis during the study period. At the start of the study period (2000), a case was considered prevalent if the diagnosis had been made in 1999 or before. Similarly, a case was considered incident in a certain year if in that year the diagnosis was made for the first time ever. Incident cases were thus eligible to become prevalent cases in the next year. It was not possible to tell the severity of the disorder since this was not coded in the EHR.

For the comorbidities at the moment of diagnosis in incident cases (i.e. present the same day as the first anxiety diagnosis), we used a precompiled list of chronic diseases, as in our previous study.\textsuperscript{19} We assessed chronic kidney disease by the closest creatinine measurements in the 2 years preceding or following a P74 diagnosis.

To define treatment, we used the Anatomic Therapeutic Classification codes that are available in the INTEGO databases. Psychoactive medication was defined as: N05A (antipsychotics), N05B (anxiolytics), N05C (hypnotics/sedatives) and N06A
(antidepressants). The full list can be found in Supplementary Data. We assessed medication prescription in patients with anxiety (though not necessarily for anxiety) who received prescriptions at only one, or three or more, separate occasions per year, the latter serving as an approximation for chronic use. Intervventional trials aimed at deprescribing benzodiazepines defined 3 months or longer as long-term use.20

Data analysis

We calculated age-standardized prevalence proportions (/100 patients) and incidence rates (/1000 patient-years).

For age-standardization, we used the Flemish population in Belgium in 2000 as the reference population. The following age groups were used: 15-29, 30-44, 45-59, 60-74 and 75 plus. To analyse the trend in those age-standardized rates, we used joinpoint regression.21 From this model, the annual percentage change (APC) and the average annual percentage change (AAPC) are derived. The APC is calculated for each significant trend from a piecewise log-linear model on the logarithm of the age-standardized rate versus the year. The AAPC represents the average of APC estimates per significant trend weighted by the corresponding number of years in the trend.21

Based on the consensus in the paper of Nielen et al.,22 we also performed a sensitivity analysis using a contact-free interval of 1 year for the prevalence calculation (see Supplementary Data). The contact-free interval is defined as the period in which repeated visits with the same registered problem are considered to be part of the same episode of care.22

Trends in comorbidities in incident anxiety cases were analysed using the Cochran-Armitage and the Jonckheere-Terpstra tests, while medication prescription in prevalent anxiety cases was analysed using joinpoint regression. Medication prescription in
incident cases and per age group in prevalent cases, can be found in Supplementary Data.

Most statistical analysis was done using R, version 4.0.3. Joinpoint regression was done using the Joinpoint Regression Program, Version 4.9.0.1 of the US National Cancer Institute.

RESULTS
Trends in the prevalence and incidence of anxiety
During the study period, we identified 8451 unique patients with anxiety, using a chronic disease assumption. The prevalence of anxiety rose significantly over this period, from 1.1% in 2000 to 4.8% in 2021 (average annual percent change (AAPC): 6.8%, CI 5.3-8.4). The annual percent change (APC) from 2000 to 2015 was 3.4% (CI 1.8-5.1), with a steeper rise of 15.8% (CI 11.6-20.2) from 2015 to 2021. (Table 1, Figure 1) The same trend can be seen for the incidence of anxiety. The incidence rate in 2000 was 1.1/1000 patient-years (PY) and rose to 9.9/1000 PY in 2021 (AAPC 10.3%, CI 8.6-12.0). The largest increase in incidence was observed from 2014 to 2021, with an APC of 29.4% (CI 25.6-33.3). (Table 1, Figure 1)

The trends in prevalence and incidence for each gender were similar, with the prevalence in women being almost twice that of men. (Table 1)

We saw concurrent increases in prevalence proportions in all age groups, with the highest prevalence figures in the middle age groups (30-59 years old). The highest increase was in the youngest age group. Incidence rates also increased substantially in all age groups, with the youngest age group contributing the most. (Table 1)
When taking P74 and P01 together, we saw both the incidence and prevalence increase (due to the now increased number of cases available), but the trends were largely conserved (see Supplementary Data).

**Trends in anxiety comorbidities**

The relationship between anxiety and various groups of comorbidities are outlined in Table 2. The mean age at diagnosis showed a significantly positive trend, going from 44.1 to 45.4 years old.

Psychological diagnoses associated significantly with anxiety disorder, were depression and personality disorder. Various other somatic conditions were also associated with anxiety, for instance cardiovascular, metabolic and pulmonary disease.

The average chronic disease count per patient increased significantly during the study period, from 1.5 to 2.3.

**Trends in medication prescriptions in patients with anxiety**

Among prevalent cases with anxiety, the proportion of patients treated with psychoactive medication rose from 25.7% to almost 40% (Figure 2). The increase was statistically significant for the period 2014 to 2021, resulting in an APC of 4.0% (CI 3.0-5.1). Among incident cases with anxiety, the proportion of patients treated with medication rose from 18.6% to 31.2 %. This increase was also statistically significant with an AAPC of 2.0% (CI 0.6-3.5).

When looking at patients receiving prescriptions on once per year, the proportion was 3.8% in 2000, decreasing to 1.7% in 2021, with a significant AAPC of -4.4% (CI -6.8; -2.0). However, the proportion of patients receiving prescriptions 3 or more times per year went from 18.6% to 30.7% [AAPC of 2.3% (CI 1.2-3.3)].
This increase is predominantly caused by a larger proportion of the study population treated with selective serotonin reuptake inhibitors (SSRIs; APC 5.3% from 2014 to 2021, CI 3.8-6.7), while the use of anxiolytics tends to fall significantly, but not greatly (AAPC -0.5%, SI -0.8;-0.2). Other psychoactive drugs are prescribed much less, and their use stagnates or declines slightly, with the notable exception of neuromodulators (most commonly used as anti-epileptic drugs): their use more than doubled over the study period (from 4.5% to 10.5%, AAPC 4.0%, CI 1.2-6.9). While fluctuating in the beginning of the study period (significant APCs of 20% for 2000-2003 (CI 6.2-35.5) and -5.5% (CI -9.3;-1.6) for 2003-2009), their prescription rate steeply increased from 2018 to 2021 (APC 11.3%, CI 7.4-15.3).

Proportionally, women with anxiety are prescribed more psychoactive medication than men (two-tailed t-test: $P < 0.0001$; Figure 3). In both genders, medication use increased over the study period.

When looking at specific age groups, younger age groups were prescribed more medication in incident cases, whereas older groups were prescribed more in prevalent cases (see Supplementary Data).

DISCUSSION

Summary

In this study, we found that, from 2000 to 2021, the prevalence and incidence of anxiety in Flemish primary care increased steeply, but mostly in the last 5 years. The younger age groups seem to be responsible for most of this increase.

The number of comorbidities in patients with anxiety rose significantly during the study period. Medication prescription among patients with anxiety also increased, most notably for SSRIs.
Strengths and limitations

The major strength of this study is the inclusion of longitudinal data, reflecting the registration trends of anxiety as they developed during the 22-year study period. We had access to prescription and comorbidity data, allowing for a more balanced and multi-faceted view on anxiety as it presents to GPs in Flanders. Given the paucity of real-world data on anxiety in primary care, we believe this study to be a valuable addition to the evidence.

Our study comes with some limitations. The denominator of our study population can vary, due to the fact that patients in Belgium are not registered with a particular GP. Although only 40% of the population only go to one GP, the Usual Provider Continuity Index still remains acceptable (more than 75% consultations with a specific GP for over 65% of the Belgian population). Data of patients going to a GP outside of the INTEGO network, however, are not included.

The YCG also does not capture the whole practice population, but only the patients who visit at least once a year. It is however, as stated before, the most realistic approach in Belgium.

We did not know whether GPs over- or underdiagnosed anxiety in their patients, and what clinical tools they used to arrive at their diagnosis. Also, there might exist regional variations in coding practice (e.g. some practices are more likely to code anxiety as a symptom and not a diagnosis), something which this study did not specifically investigate. Diagnoses as free text were not included in this study.

Many patients with anxiety problems might not go to their GP, leading to an underestimation of the real disease burden. The effect of the COVID pandemic on anxiety...
was not specifically evaluated. Medication could have been prescribed for other indications than anxiety, as stated earlier (e.g. SSRI for depression).

The uptake of psychotherapy among patients could not be studied, because it was not registered in our database.

**Comparison with existing literature**

*Trends in the prevalence and incidence of anxiety*

The recent increase in the registration of anxiety corresponds to the international literature. Although methodologically different, recent increases were seen in young people across multiple studies in different countries.\textsuperscript{25-27} This may be due to actual disease burden or an increased acceptance and awareness of mental disorders in general, leading to earlier recognition. Some studies point in that direction.\textsuperscript{28,29} Other authors blame the emergence and importance of social media in the lives of young adults.\textsuperscript{30}

In our data, it is unclear whether the increase in the registration of anxiety is actual or perceived. Of note is that we used the ICPC-2 code P74, which is a clinical diagnosis. GPs might be hesitant to diagnose a disorder based solely on subclinical symptoms, which is why in some studies there seemed to be a recent tendency to code anxiety *symptoms* rather than *diagnoses*.\textsuperscript{26,31} This might also explain why the registered prevalence and incidence of anxiety in our study are decidedly lower than in other, similar studies.\textsuperscript{14,26,32} Furthermore, in a previous paper by our team, we have stated that this increase might also partly be brought about by a *registration effect*.\textsuperscript{19} This is a form of bias: anxiety could be more likely to be registered now than earlier in the study period, due to various reasons (for example more diligent and more frequent coding and registration).
The last two years of the study period were marked by the ongoing COVID-19 pandemic, during which mental health disorders, particularly anxiety, seemed on the increase.\textsuperscript{33,34} Our results show an increasing incidence and prevalence for anxiety in those years, but we did not perform a COVID-specific analysis. The Belgian public health institute Sciensano found that self-reported mental health in Belgium fluctuated during the pandemic, depending on the specific phase (restrictions versus relaxation of measures).\textsuperscript{35} It is conceivable that many patients did not seek help for anxiety during the first waves of the pandemic, making our figures likely underestimates.

For our calculations, we assumed anxiety disorder to be chronic, a stance shared by other authors as well.\textsuperscript{36} We also conducted a sensitivity analysis using a 1-year contact-free interval, and the conclusions remain robust. Using this much shorter period we arrived at a lower prevalence, which is mathematically evident (Supplementary Table 1). The trends were largely conserved (see Supplementary Figure 1).

**Trends in comorbidities**

The most salient finding here was the fact that the average number of chronic diseases for each patient increased significantly. This is in line with our previous findings concerning depression.\textsuperscript{19} Patients presenting with mental health disorders in primary care tend to become more complex over time. However, it is also possible that the awareness for anxiety might be increased specifically with multimorbid patients.

In any case, a multidisciplinary approach to these patients is warranted. The GP is perfectly placed to coordinate care between first- or second-line health professionals. In an analysis by Martín-Merino \textit{et al.}, patients with anxiety were more likely to abuse alcohol, have COPD or cancer, or be hospitalized or referred for another health problem.\textsuperscript{32} In our sample, there was no concurrent trend for alcohol abuse, although
anxiety was significantly associated with a number of somatic conditions, such as
asthma and COPD, cardiovascular problems and cancer.

The strong association with depression is not new, and controversy exists as to whether
the presence of anxiety might predict the onset of depression or vice versa, or even
whether they constitute different syndromes altogether.\textsuperscript{13,14}

\textit{Trends in medication}

In prevalent anxiety cases, the relative amount of psychoactive medication prescriptions
increased, albeit only significantly so for the last 6 years. This is consistent with a study
by Noordam \textit{et al.}, who also found an increase in prescriptions for mental health
disorders.\textsuperscript{37} Women with anxiety in our study received proportionally more
prescriptions than men, which was the case in the Noordam study as well.\textsuperscript{37} Chronic use,
which we defined as 3 or more prescriptions per year, increased significantly, while
occasional use (1 prescription per year) declined. For benzodiazepines specifically, the
definition of chronic use in international literature tends to vary and is rarely uniform
across studies.\textsuperscript{38}

The most frequently prescribed medications in our study were SSRIs, anxiolytics and
hypnotics. Initially, anxiolytics were prescribed more than SSRIs, whereas the two
switched positions around 2017. SSRIs are also a first-line treatment for depression, and
the important comorbidity between anxiety and depression might also have been a
driving force. According to the NICE guidelines, the recommended treatment for anxiety
disorder, besides psychotherapy, is SSRIs, followed by SNRIs.\textsuperscript{39} The use of
benzodiazepines is explicitly discouraged, except for short-term crisis management. This
might also have contributed to the prescription trends seen in our data.
Another interesting trend is the recent steep increase of the neuromodulator group, consisting mostly of anti-epileptic medication such as pregabalin, a drug that is also proposed as a second- or third-choice treatment for anxiety disorder.  

**Implications for research and practice**

In this registry-based study, we found a significantly increasing prevalence and incidence of physician-registered anxiety, particularly during the last 5 years and in the youngest age groups. Patients with anxiety tend to become more complex or multimorbid patients are at least more easily diagnosed with anxiety. A holistic, multi-disciplinary primary care approach for these patients, with the GP taking on a coordinating role, is important.

Without knowing referrals for psychotherapy, treatment for anxiety in Belgian primary care seemed to be heavily dependent on medication. In any case, there is more adherence to official guidelines recently; the use of SSRIs increases, while the use of anxiolytics declines.
### Tables and Figures

**Table 1. Trends in the age-standardized prevalence and incidence of anxiety in Flanders, Belgium (2000-2021).**

<table>
<thead>
<tr>
<th>Summary</th>
<th>Trend 1</th>
<th>Trend 2</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Year 2000</td>
<td>Year 2021</td>
</tr>
<tr>
<td><strong>Prevalence (/100)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1.07</td>
<td>4.82</td>
</tr>
<tr>
<td>Women</td>
<td>1.38</td>
<td>5.80</td>
</tr>
<tr>
<td>Men</td>
<td>0.73</td>
<td>3.57</td>
</tr>
<tr>
<td>15-29</td>
<td>0.56</td>
<td>3.92</td>
</tr>
<tr>
<td>30-44</td>
<td>1.17</td>
<td>5.55</td>
</tr>
<tr>
<td>45-59</td>
<td>1.44</td>
<td>5.15</td>
</tr>
<tr>
<td>60-74</td>
<td>1.25</td>
<td>4.58</td>
</tr>
<tr>
<td>75+</td>
<td>0.73</td>
<td>4.39</td>
</tr>
<tr>
<td><strong>Incidence rate (/1000 patient years)</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Total</td>
<td>1.14</td>
<td>9.94</td>
</tr>
<tr>
<td>Women</td>
<td>1.47</td>
<td>12.43</td>
</tr>
<tr>
<td>Men</td>
<td>1.40</td>
<td>6.76</td>
</tr>
<tr>
<td>15-29</td>
<td>0.96</td>
<td>13.58</td>
</tr>
<tr>
<td>30-44</td>
<td>1.48</td>
<td>12.00</td>
</tr>
<tr>
<td>45-59</td>
<td>1.11</td>
<td>7.95</td>
</tr>
<tr>
<td>60-74</td>
<td>0.87</td>
<td>6.30</td>
</tr>
<tr>
<td>75+</td>
<td>1.17</td>
<td>6.60</td>
</tr>
</tbody>
</table>

Abbreviations: AAPC = average annual percent change, APC = annual percent change.
Table 2: Trends in comorbidities in patients with anxiety in Flanders, Belgium (2000-2021)

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>STUDY POPULATION</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Patients with anxiety (n)</td>
<td>473</td>
<td>659</td>
<td>694</td>
<td>968</td>
<td>5657</td>
<td></td>
</tr>
<tr>
<td>Mean age (standard deviation)</td>
<td>44.1(17.4)</td>
<td>44.8(17.4)</td>
<td>42.7(18.2)</td>
<td>41.7(18)</td>
<td>45.4(19.6)</td>
<td>0.0006</td>
</tr>
<tr>
<td>Number of women (%)</td>
<td>300(63.4%)</td>
<td>446(67.7%)</td>
<td>474(68.3%)</td>
<td>602(62.2%)</td>
<td>3783(66.9%)</td>
<td>0.4447</td>
</tr>
<tr>
<td><strong>PREVALENCE OF COMORBIDITIES, n (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mean chronic disease count per patient (SD)</td>
<td>1.5(1.8)</td>
<td>1.7(1.9)</td>
<td>1.7(2)</td>
<td>2.1(2.4)</td>
<td>2.3(2.6)</td>
<td>0.0002</td>
</tr>
<tr>
<td><strong>ICPC code</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Depressive disorder</td>
<td>P76</td>
<td>40(8.5%)</td>
<td>37(5.6%)</td>
<td>33(4.8%)</td>
<td>71(7.3%)</td>
<td>556(9.8%) &lt;0.0001</td>
</tr>
<tr>
<td>Alcohol abuse</td>
<td>P15-16</td>
<td>9(1.9%)</td>
<td>25(3.8%)</td>
<td>16(2.3%)</td>
<td>49(5.1%)</td>
<td>184(3.3%) 0.4162</td>
</tr>
<tr>
<td>Dementia</td>
<td>P70</td>
<td>3(0.6%)</td>
<td>5(0.8%)</td>
<td>2(0.3%)</td>
<td>11(1.1%)</td>
<td>60(1.1%)  0.1071</td>
</tr>
<tr>
<td>Schizophrenia</td>
<td>P72</td>
<td>4(0.8%)</td>
<td>4(0.6%)</td>
<td>5(0.7%)</td>
<td>6(0.6%)</td>
<td>53(0.9%)  0.3822</td>
</tr>
<tr>
<td>Suicide/suicide attempt</td>
<td>P77</td>
<td>1(0.2%)</td>
<td>1(0.2%)</td>
<td>0(0%)</td>
<td>5(0.5%)</td>
<td>18(0.3%)  0.2938</td>
</tr>
<tr>
<td>Phobia/compulsive disorder</td>
<td>P79</td>
<td>14(3%)</td>
<td>19(2.9%)</td>
<td>23(3.3%)</td>
<td>43(4.4%)</td>
<td>166(2.9%) 0.7287</td>
</tr>
<tr>
<td>Personality disorder</td>
<td>P80</td>
<td>3(0.6%)</td>
<td>7(1.1%)</td>
<td>9(1.3%)</td>
<td>32(3.3%)</td>
<td>244(4.3%) &lt;0.0001</td>
</tr>
<tr>
<td>Anorexia nervosa/bulimia</td>
<td>P86</td>
<td>3(0.6%)</td>
<td>1(0.2%)</td>
<td>3(0.4%)</td>
<td>1(0.1%)</td>
<td>8(0.1%)   0</td>
</tr>
<tr>
<td>Substance abuse</td>
<td>P18-19</td>
<td>2(0.4%)</td>
<td>4(0.6%)</td>
<td>10(1.4%)</td>
<td>15(1.5%)</td>
<td>64(1.1%)  0.2067</td>
</tr>
<tr>
<td>Atrial fibrillation/flutter</td>
<td>K78</td>
<td>8(1.7%)</td>
<td>11(1.7%)</td>
<td>12(1.7%)</td>
<td>17(1.8%)</td>
<td>190(3.4%) 0.0002</td>
</tr>
<tr>
<td>Hypertension</td>
<td>K86-87</td>
<td>57(12.1%)</td>
<td>100(15.2%)</td>
<td>99(14.3%)</td>
<td>135(13.9%)</td>
<td>1032(18.2%) &lt;0.0001</td>
</tr>
<tr>
<td>Heart failure</td>
<td>K77</td>
<td>2(0.4%)</td>
<td>3(0.5%)</td>
<td>5(0.7%)</td>
<td>9(0.9%)</td>
<td>95(1.7%)  0.0002</td>
</tr>
<tr>
<td>Atherosclerosis</td>
<td>K92</td>
<td>9(1.9%)</td>
<td>11(1.7%)</td>
<td>9(1.3%)</td>
<td>25(2.6%)</td>
<td>102(1.8%) 0.8476</td>
</tr>
<tr>
<td>Ischemic heart disease</td>
<td>K74-75-76</td>
<td>14(3%)</td>
<td>27(4.1%)</td>
<td>29(4.2%)</td>
<td>34(3.5%)</td>
<td>183(3.2%) 0.3879</td>
</tr>
<tr>
<td>Diabetes Mellitus</td>
<td>T89-90</td>
<td>16(3.4%)</td>
<td>29(4.4%)</td>
<td>51(7.3%)</td>
<td>77(8%)</td>
<td>380(6.7%) 0.0054</td>
</tr>
<tr>
<td>Hypothyroidism</td>
<td>T86</td>
<td>8(1.7%)</td>
<td>12(1.8%)</td>
<td>5(0.7%)</td>
<td>22(2.3%)</td>
<td>216(3.8%) &lt;0.0001</td>
</tr>
<tr>
<td>Hyperthyroidism</td>
<td>T85</td>
<td>4(0.8%)</td>
<td>4(0.6%)</td>
<td>0(0%)</td>
<td>1(0.1%)</td>
<td>20(0.4%)  0.2456</td>
</tr>
<tr>
<td>Irritable bowel syndrome</td>
<td>D01-D93</td>
<td>66(14%)</td>
<td>96(14.6%)</td>
<td>101(14.6%)</td>
<td>150(15.5%)</td>
<td>761(13.5%) 0.3133</td>
</tr>
<tr>
<td>Condition</td>
<td>Code</td>
<td>2001</td>
<td>2002</td>
<td>2003</td>
<td>2004</td>
<td>2005</td>
</tr>
<tr>
<td>-------------------------------</td>
<td>------------</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>------</td>
<td>------</td>
</tr>
<tr>
<td><strong>Asthma</strong></td>
<td>R96</td>
<td>40(8.5%)</td>
<td>64(9.7%)</td>
<td>81(11.7%)</td>
<td>138(14.3%)</td>
<td>746(13.2%)</td>
</tr>
<tr>
<td><strong>COPD</strong></td>
<td>R95</td>
<td>10(2.1%)</td>
<td>22(3.3%)</td>
<td>23(3.3%)</td>
<td>32(3.3%)</td>
<td>227(4%)</td>
</tr>
<tr>
<td><strong>Osteoarthritis</strong></td>
<td>L89-90-91</td>
<td>57(12.1%)</td>
<td>87(13.2%)</td>
<td>69(9.9%)</td>
<td>114(11.8%)</td>
<td>613(10.8%)</td>
</tr>
<tr>
<td><strong>Cerebrovascular disease</strong></td>
<td>K90-91</td>
<td>7(1.5%)</td>
<td>9(1.4%)</td>
<td>12(1.7%)</td>
<td>20(2.1%)</td>
<td>143(2.5%)</td>
</tr>
<tr>
<td><strong>Malignancy</strong></td>
<td>A79-Y78-N74-Y77-U76-T71-D76-D74-U77-U75-D75-R84-B74-S77-R85-D77-X76-W72-X75-X77</td>
<td>18(3.8%)</td>
<td>36(5.5%)</td>
<td>52(7.5%)</td>
<td>94(9.7%)</td>
<td>1137(20.1%)</td>
</tr>
<tr>
<td><strong>Chronic Kidney Disease</strong></td>
<td></td>
<td>4(0.8%)</td>
<td>6(0.9%)</td>
<td>3(0.4%)</td>
<td>8(0.8%)</td>
<td>72(1.3%)</td>
</tr>
</tbody>
</table>

Bold indicates P values for trend < 0.05.
Figure 1: Age-stratified prevalence (top) and incidence (bottom) of anxiety (2000-2021).
Figure 2: Psychoactive medication prescriptions in prevalent anxiety cases (2000-2021).

Figure 3: Total prescription volume in prevalent anxiety cases (2000-2021).
Funding
This work was supported by a research project from the Research Foundation Flanders (FWO).

Ethical approval
The INTEGO procedures are approved by the ethical review board of the KU Leuven Faculty of Medicine (no. ML 1723) and by the Belgian Privacy Commission (no. SCSZG/13/079).

Competing interests
The authors declare that they have no competing interests.
REFERENCES


