Sexual adverse drug reactions: patient impact and potential for pharmaceutical care

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Chapter 3

An estimation of patients at potential risk for drug-induced sexual dysfunction using pharmacy dispensing data

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Abstract

Background and objectives

Adverse drug reactions on sexual functioning (sADRs) may seriously decrease a person's quality of life. A multitude of diseases and drugs are known risk factors for sexual dysfunction. To inform patients better about these potential effects, more insight is needed on the estimated number of patients at high risk for sADRs and their characteristics.

Method

This cross-sectional study estimated the number of patients in the Netherlands who were dispensed drugs with a potential very high risk (>10%) or high risk (1–10%) for sADRs as registered in the Summary of Product Characteristics, the official drug information text in Europe.

Results

In April 2019, 2.06% of the inhabitants of the Netherlands received drugs with >10% risk for sADRs and 7.76% with 1–10% risk. The majority of these patients had at least one additional risk factor for decreased sexual function such as high age or depression. Almost half of the patients were identified with two or more morbidities influencing sexual functioning. Paroxetine, sertraline and spironolactone were the most dispensed drugs with a potential >10% risk for sADRs. One-third of their first dispenses were not followed by a second dispense, with a higher risk of discontinuation for a decreasing number of morbidities.

Conclusion

About 1 in 11 inhabitants of the Netherlands was dispensed a drug with a potentially high risk for sADRs, often with other risk factors for sexual complaints. Further research is needed whether these users actually experience sADRs, to understand its impact on multimorbid patients and to provide alternatives if needed.

Introduction

Sexual functioning is considered an important factor for quality of life, also for individuals with medical conditions and those who are older [1-4]. The burden of sexual dysfunction can be as high as the burden of a disease, as expressed by patients with schizophrenia [5]. In addition, patients with depression acknowledged low adherence to drug treatment because they associated it with sexual complaints [6]. Assuming that the drug efficacy is more important than potential sexual adverse drug reactions (sADRs) may not correspond with patients' considerations, as shown by a recent citizen petition that requested a serious warning for sADRs on the product labels of SSRIs and SNRIs [7]. Thus, the possible impact of sADRs should be taken seriously by healthcare providers in the choice for treatment.

Patients can experience sexual complaints from various drug groups. In Europe, 346 drugs were registered with sADRs according to the Summary of Product Characteristics (SmPC) [8]. SmPC-texts provide reliable drug information to healthcare professionals, mainly based on registration trials. More than 10% of the trial participants had reported sADRs for 16 drugs, and 1–10% of the participants for 82 drugs. These potential risks may be different in clinical practice. Firstly, the validity and completeness of the reporting numbers might be influenced by the methods used in registration trials to gather information on non-serious ADRs such as sADRs [9]. Bonierbale *et al*. exemplified this when they determined the prevalence of sexual dysfunction under 4557 depressed patients; 35% of the subjects reported sexual dysfunction spontaneously, whereas the prevalence doubled to 69% when a physician directly questioned the patient [10]. Secondly, both patients and healthcare providers might not recognize sexual complaints as sADRs or feel a barrier to discuss sexual dysfunction [11-15]. Lastly, the user of the drug may have medical conditions that hamper sexual functioning [16]. This impedes to identify a drug as the cause of sexual dysfunction. In registration trials, sexual problems may be easier relatable to the drug treatment than in other clinical studies with generally more diverse and multimorbid patients. This is a reason to focus on registered sADRs when identifying potential risks of drugs to decrease sexual functioning.

The complex relations between sexual functioning, medical condition and treatment have not yet been untangled. In comparison, the risks of isolated morbidities on sexual dysfunction are already widely described [16]. With the growing number of multimorbid persons, more insight is needed on the possible interactions between medical conditions, drug treatment and sexual function. As a first step to understand the influence of drug treatment, this study aimed to estimate the number of patients in the Netherlands that use drugs with a potential high risk for sADRs according to their SmPC leaflet.

Methods

Design

This cross-sectional study identified user numbers of drugs with a potential high risk for sADRs with pharmacy dispensing data from community-dwelling patients, a method that has been applied before [17, 18].

Source of drug dispensing data

In the Netherlands, the Foundation for Pharmaceutical Statistics collects drug dispensing data from ~95% of community pharmacies [19]. Within these pharmacies, dispensing data are aggregated on patient level. For each patient, information on the year of birth and sex are accessible. Drugs are specified by the Anatomic, Chemical, Therapeutic (ATC) classification system [20], drug formulation and number of units dispensed. Additional information is available on the dispensing date, the specialism of the prescriber (e.g. General Practitioner (GP)) and the prescribed daily dose, as registered in the computerized pharmacy system. No information is collected on diagnoses.

Inclusion of community pharmacies

To assess repeat dispensings of first prescriptions, community pharmacies were eligible that had supplied a complete data history of 14 months. Conventionally, first dispensings are defined as a dispensing without a previous dispensing within the prior 12 months and a notification for a first dispensing fee as registered in the community pharmacy [21]. In the Netherlands, first dispensings for drugs with separate entities for daily use generally cover a period of 14 days. This enables pharmacists to evaluate patients' experiences, reconsider treatment choices with prescribers and avoid medication waste. Thus, to establish whether a dispensing in the observation month was a first dispensing and whether it was followed by a second dispensing during the remaining days in the observation month or subsequent month, a history of 12 months before and one month after the observation month was needed. Correspondingly, pharmacies with complete data from March 2018 until May 2019 were included.

Patient selection

From eligible community pharmacies, those patients were selected who used at least one drug with a high risk for sADRs during the observation month. In previous research, 16 drugs with a potential >10% (very high) risk and 82 drugs with 1–10% (high) risk as

registered in the SmPC were collected and adopted for this study [8]. For spironolactone and cyproterone, the registered risk for sADRs was lower for females (1–10%) than males (>10%). Thus, user numbers for these drugs were counted as >10% risk for sADRs for males and 1–10% risk for females.

Data collection

Data aggregation on patient level

Data of community pharmacies was collected on patient level. Patients were followed for dispensings from different community pharmacies, which contributed to the validity of the results. A third trusted party aggregated different patient codes for one patient who visited multiple pharmacies, to one anonymous identification number for each patient.

Observation period

An observation period of 1 month was chosen because 1 month was considered as a reasonable time period to assume that dispensed drugs available within this period were used concomitantly. April 2019 was the most recent month at start of data collection. Additionally, the month April was likely to resemble usual patterns for chronic drug use and was not likely to be influenced by different dispensing behaviors due to holidays or end of year drug storage.

Periods of drug use

Drug use during the observation month could result from dispensings during the observation month and from earlier dispensings, if according to the amount of dispensed units and the prescribed daily dose, the amount of the earlier dispensing included use during the observation month [21]. If the prescribed daily dose was not registered in the pharmacy system (circa 6% of dispenses), the period of use was standardized to one day. For each patient, multiple high-risk drugs with a period of use during the observation month were calculated as in concomitant use.

Selection of morbidities

Morbidities that might decrease sexual function were identified for each patient. As the dispensing database did not include information on diagnosis, comorbidities were estimated by corresponding drug use. Morbidities that might decrease sexual function according to

literature [16] and could be identified by specific drug use were the following: depression (ATC code: N06A), diabetes (A10), lower urinary tract symptoms (G04BD), cardiovascular diseases (C02, C03, C07, C08, C09, C10), epilepsy (N03), hypothyroidy (H03AA) and COPD or asthma (R03). Patients were labelled for a morbidity if they received at least 3 dispensings of a relevant drug during the last 12 months of data available. Two of the possible morbidities are also the main indication of very high-risk (>10%) drugs: three drugs are antidepressants and one is used in treatment for cardiovascular diseases.

Drug discontinuation

Of the drugs with >10% risk for sADRs, only paroxetine, sertraline, clomipramine and spironolactone are generally used daily for a longer period of time and eligible to a first dispensing of 14 days. Therefore, only for these drugs discontinuation rates were calculated. First dispenses were considered discontinued if there was no follow-up dispensing until the end of the post-measurement month, May 2019.

Data analysis

Patient numbers were calculated for drug use with a potential >1% risk for sADRs in the observation month together with information on age, sex, first dispensing of >10% risk drugs, concomitant use of drugs with >1% risk for sADRs and morbidities as described above.

To estimate the proportion of drug users with a potential high risk for sADR, patient numbers were first extrapolated to the amount of all 1996 community pharmacies in the Netherlands (2019) and then divided by the population number for April, 2019 from the Statistics Netherlands' database [22].

Multivariate logistic regression was performed to identify risk factors for discontinuation of paroxetine, sertraline, clomipramine and spironolactone after first dispenses. The following variables were included as potential risk factors: age, sex, comorbidity and comedication with 1–10% or >10% risk for sADR. Analysis was performed with IBM Corp SPSS statistics, Chicago IL, USA, version 26.

Ethical approval of the study protocol

The board of the Dutch Foundation of Pharmaceutical Statistics approved the use of their data for this research. Data from pharmacies and patients were coded and anonymized before analyses. Use of observational data in descriptive retrospective studies in the Netherlands is not considered as an interventional trial according to Directive 2001/20/

EC and Dutch legislation [23]. Therefore, the study protocol did not need approval by a medical ethic committee.

Results

Data were available from 1782 (91%) community pharmacies in the Netherlands. During the month of April 2019, drugs with very high (>10%) risk for sADRs were dispensed to 318 821 patients and drugs with a high risk (1–10%) for sADRs to 1 198 754 patients (see Table 3.1). About 1.7% of users was <18 years old. When extrapolating to all 1996 community pharmacies in the Netherlands [19], there were 1 614 934 users of drugs with >1% risk for sADRs. Compared with a population number of 17 306 978, the user numbers of drugs with >10% and 1–10% risk correspond with 2.06% and 7.76% of the inhabitants of the Netherlands, respectively [22].

Table 3.1: Population in the Netherlands at risk to endure reduced sexual functioning from a sADR in April, 2019

	Users (% of NL)[a]	FD (%)	Age (μ)	Female (%)	Proportions with morbidity known to affect sexual functioning as identified by specific drug use(%)							
					DM	DP	CV	LUTS	EP	HT	AS/CO	≥2 mor
Drugs with >10% risk for sADR	318 821 (2.06%)	3.2	58.3 (SD=17)	52.2	12.4	66.6	48.0	2.1	5.9	6.1	11.3	43.9
Drugs with 1–10% risk for sADR	1 198 754 (7.76%)	NA	58.7 (SD=19)	55.8	12.6	41.4	50.6	2.5	10.2	6.0	11.4	38.3
Drugs with >1% risk for sADR	1 441 790 (9.33%)	NA	58.5 (SD=19)	55.6								

AS/CO=Asthma or COPD; FD=First dispense; CV=Cardiovascular diseases; DM=Diabetes Mellitus; DP=Depression; EP=Epilepsy; HT=Hypothyroidy; LUTS=Lower Urinary Tract Symptoms; NA=not available; NL=The Netherlands; ≥2 mor=proportion of users with two or more morbidities.

[a] These numbers were generated with data from 1782 community pharmacies in the Netherlands (91% of all community pharmacies in the Netherlands). Percentages of the population of the Netherlands were calculated by extrapolation to all community pharmacies in the Netherlands and divided by a population number of 17 306 978 (April 2019) from the Statistics Netherlands' database.

Patients that received a drug with >10% risk for sADRs had a mean age of 58.3 years and 52.2% were female. More than half of these patients were treated for depression (66.6%) or cardiovascular diseases (48.0%). Almost half were treated for more than one medical condition (43.9%). Without the users of spironolactone 37.8% of the patients were treated for cardiovascular diseases. Similarly 14.8% of the patients were treated for depression when adjusted for the antidepressants registered with >10% risk for sADRs. About a quarter of

drug users with a potential >10% risk for sADRs was dispensed another drug with at least a >1% potential risk for sADRs during the observation month: 23.8% for an additional drug with high risk and 2.23% for an additional drug with a very high risk for sADRs. The users of two or more drugs with >10% risk for sADRs most often combined olanzapine with sertraline (22.7% of the combinations) or paroxetine (18.9%), see Table 3.2.

Table 3.2: Users of two or more drugs with very high risk for sexual adverse drug reactions (>10%) in the Netherlands in April, 2019

Concomitant use of drugs with >10% risk for sADR	Number of users	Additionally using ≥1 drug with 1–10% risk for sADRs	Most prevalent drug combinations
Two drugs with >10% risk	7013	2387	Olanzapine + sertraline Olanzapine + paroxetine Olanzapine + clomipramine
Three drugs with >10% risk	102	43	Olanzapine + paroxetine + spironolactone Spironolactone + cyproterone + leuprorelin
Four drugs with >10% risk	2	1	Sertraline + silodosin + cyproterone + goserelin Olanzapine + sertraline + clomipramine + paroxetine

In Table 3.3, patient characteristics that may contribute to decreased sexual functioning are shown for each drug with >10% risk for sADRs. Of these, paroxetine, sertraline and spironolactone were dispensed most. The majority of paroxetine users was female (69.1%), with a mean age of 58.8 years, and almost half of the paroxetine users was also treated for cardiovascular disease (43.2%). Users of spironolactone were older (mean 71.2 years) and a quarter concomitantly used drugs with 1–10% risk for sADRs. Moreover, one in four patients who received spironolactone was labelled for diabetes comorbidity. Half of the users of paroxetine and spironolactone were identified with more than one medical condition associated with sexual complaints, of which 14.2% of the spironolactone users and 18.7% of the paroxetine users for two or more additional medical conditions besides cardiovascular diseases or depression.

During the observation month, 3.2% of drug users with very high risk for sADRs received a first dispensing. The proportion of first users was highest for lynestrenol (67.5%). First dispenses of the antidepressants, lynestrenol and terazosin were mainly prescribed by GPs. 36.2% of the patients with a first dispense for antidepressants and 29.9% of first-time spironolactone users did not receive a second dispense. Logistic regression showed an increased risk for discontinuation for a decreasing number of comorbidities (Table 3.4). The risk to discontinue an antidepressant was decreased by a higher number of concomitant drugs in use with high risk for sADRs.

Table 3.3: Characteristics of users of drugs with very high risk for sexual adverse drug reactions (>10%) in the Netherlands in April, 2019

	Age (μ)	Female (%)	1–10% drug (%)	FD [%] (% GP)	Dispenses of drugs that are characteristic for the following morbidities (%)[a]						
					DM	DP	CV	LUTS	EP	HT	AS/CO
N06 PSYCHOANALEPTICS[b] (n=205 113)	55.6	68.5	19.5	1.7 (63.5)	9.0	94.9[c]	38.7	1.7	5.4	7.0	10.4
Paroxetine (n=119 070)	58.8	69.0	15.5	1.0 (86.9)	9.5	95.2[c]	43.6	1.7	4.3	7.3	11.2
Sertraline (n=65 403)	48.7	67.4	23.9	3.3 (52.5)	6.9	93.8[c]	28.8	1.5	6.3	5.8	9.4
Clomipramine (n=20 948)	58.7	68.3	29.2	1.3 (50.4)	12.5	96.5[c]	47.4	1.9	8.4	8.3	9.5
C03 DIURETICS (n=51 641)	71.2	-	27.7	3.4 (25.6)	30.0	7.9	99.5[c]	2.5	5.0	4.2	18.3
Spironolactone[d] (n=51 641)	71.2	-	27.7	3.4 (25.6)	30.0	7.9	99.5[c]	2.5	5.0	4.2	18.3
N05 PSYCHOLEPTICS (n=35 153)	52.7	47.4	42.8	3.7 (27.8)	9.2	46.6	32.9	1.7	13.6	6.8	9.1
Olanzapine (n=34 834)	52.7	47.4	42.8	3.7 (27.8)	9.2	46.8	32.8	1.7	13.6	6.8	9.1
Bromperidol (n=333)	59.3	49.5	48.3	0.6 (0.0)	15.3	30.0	45.3	3.0	10.2	6.9	10.5
L02 ENDOCRINE THERAPY[b] (n=19 265)	61.9	34.8	25.2	7.1 (5.2)	8.9	6.0	39.2	4.4	2.9	2.7	7.3
Leuprorelin (n=7961)	62.7	38.6	25.0	5.5 (8.0)	9.3	7.5	39.9	4.5	3.3	2.8	8.1
Goserelin (n=7096)	72.3	11.9	32.1	4.3 (8.9)	11.7	5.9	52.7	5.9	3.4	2.5	8.6
Triptorelin (n=4202)	42.6	67.0	13.3	14.7 (1.5)	3.6	3.2	14.2	1.7	1.3	3.0	3.5
Nilutamide (n=86)	80.1	0.0	40.7	4.7 (0.0)	14.0	8.1	66.3	9.3	2.3	2.3	9.3
Flutamide (n=1)	18	100	100	0.0	0.0	100	0.0	0.0	0.0	0.0	0.0
G03 SEX HORMONES AND MODULATORS[b] (n=6742)	44.9	74.2	17.9	25.7 (81.9)	5.0	9.9	23.4	2.7	3.2	3.7	7.3
Lynestrenol (n=5044)	37.5	99.2	11.9	67.5 (86.8)	2.9	9.2	13.3	0.8	2.6	4.2	5.7
Cyproterone[d] (n=1698)	66.1	-	35.9	5.8 (10.0)	11.5	11.8	53.5	8.3	2.3	2.7	12.1
G04 UROLOGICALS[b] (n=7724)	73.5	1.8	34.1	5.5 (17.0)	17.0	9.7	68.9	10.3[e]	6.1	3.8	14.9
Silodosin (n=7074)	73.7	1.2	34.6	5.7 (14.3)	17.1	9.8	69.4	10.5[e]	6.3	3.7	15.1
Terazosin (n=653)	70.7	7.8	28.8	2.8 (77.8)	16.5	8.7	64.5	7.4	4.4	4.9	13.0
L01 ANTINEOPLASTIC AGENTS (n=0)	-	-	-	-	-	-	-	-	-	-	-
Thiotepa (n=0)	-	-	-	-	-	-	-	-	-	-	-

AS/CO=Asthma or COPD; CV=Cardiovascular diseases; DM=Diabetes Mellitus; DP=Depression; EP=Epilepsy; FD=first dispense; GP=amount of first dispenses prescribed by a general practitioner; HT=Hypothyroidy; LUTS=Lower Urinary Tract Symptoms.

[a] A morbidity is indicated with at least 3 dispensings of the corresponding drug class during 12 months.

[b] Total user number is lower than the sum of the users of the separate drugs due to combined use of these drugs.

[c] This drug is used as treatment for this morbidity and therefore approaches 100.

[d] Spironolactone and cyproterone are registered with >10% risk for sADRs for men and 1–10% risk for women. For this reason, female users of spironolactone and/or cyproterone were excluded for the analysis of the characteristics of spironolactone and cyproterone users.

[e] Though not indicated for LUTS, silodosin is indicated for benign prostatic hyperplasia, associated with LUTS.

Table 3.4: Influence of patient characteristics on discontinuation after first dispense of paroxetine, sertraline, clomipramine and spironolactone in the Netherlands (April, 2019)

	ANTIDEPRESSANTS (stop after FD=36.2%)	SPIRONOLACTONE (stop after FD=29.9%)
Age	1.01 (1.01–1.01)	0.98 (0.98 0.99)
Female sex	0.99 (0.86–1.14)	NA[a]
Number of comorbidities[b]	0.82 (0.73–0.92)	0.79 (0.68–0.92)
Number of drugs with 1–10% risk for sADR	0.81 (0.72–0.91)	0.99 (0.83–1.18)
Number of other drugs with >10% risk for sADR[c]	0.72 (0.48–1.07)	0.84 (0.44–1.62)

Results are shown as odds ratio (95% confidence interval), statistically significant results are printed in bold; Stop after FD=the proportion of users that discontinued drug treatment after receiving a first dispense of one of these drugs in April, 2019; NA=not available.
a As spironolactone is registered with >10% risk for sADRs for men and 1–10% risk for women, female users of spironolactone were excluded from this regression model.
[b] For analysing cessation with antidepressants, depression was not included and for cessation with spironolactone cardiovascular diseases was not included as a covariate into the multivariate logistic regression model.
[c] Paroxetine, sertraline, clomipramine and spironolactone were not included into the covariate for other drugs with a very high risk for sADR.

Discussion

In this cross-sectional study, almost 10% of the population in the Netherlands received drugs with a (very) high risk for sADRs. This equals on an average per pharmacy, 179 users of drugs with >10% risk for sADRs and 673 users with 1–10% risk for sADRs. Per pharmacy, five to six patients started with a drug with >10% risk for sADRs in one month. Additional risk factors for decreased sexual function were common. For example, one of every three antidepressant users was treated for cardiovascular disease. Since antidepressants users have rated sADRs as 'difficult to live with' [6], prescribers and pharmacists should be more alert for sADRs in almost 1 in 10 of their patients, often on top of other risk factors for decreased sexual functioning.

To our knowledge, this is the first study that estimated the number of persons at potential risk to experience sexual complaints as an adverse drug event. Morbidities affecting sexual functioning were present in 4 of 10 users of drugs with >1% risk for sADRs. Moreover, we found that one in three first dispenses of paroxetine, sertraline, clomipramine and spironolactone were not continued. Earlier, Holvast *et al.* showed, with pharmacy dispensing data in the Netherlands, that 10% of antidepressant users (ATC: N06A) discontinued therapy within a comparable period (the first four weeks) [24]. Also based on pharmacy dispensing data, Alfian *et al.* reported that 18% of diabetes patients in the North of the Netherlands stopped their cardiovascular drug treatment (ATC: C03, C07, C08, C09) within the first year [25]. Compared to both studies, our analysis was more specific, focusing on spirono-

lactone and antidepressants that are registered with >10% risk for sADRs. Compared with the longer observation period of Alfian *et al*., our discontinuation rates after first dispense were already considerable higher. Reasons for these high rates should be further explored.

Unexpectedly, in our study more morbidities decreased the risk for treatment cessation. For the antidepressants, additional drug use with 1–10% risk for sADRs also contributed to a lower risk for of stopping. Similarly, Holvast *et al*. reported that antidepressants users were less likely to stop treatment with increasing numbers of drugs [24]. Possibly, patients who already suffer from medical conditions were more willing or accustomed to taking chronic medication and thus less likely to stop. Also, if decreased sexual function was already present due to another disease or treatment, additional (s)ADRs might be considered less important.

In comparison, Appa *et al*. showed a linear relationship between the number of morbidities and low sexual desire (OR 1.10 (CI 1.03–1.18)) in 1997 women over 40 years old [26]. In their study population, 72% had two or more chronic morbidities. For each additional morbidity, the risk of reporting sexual problems such as difficulty with arousal, lubrication, orgasm or pain during intercourse increased with 10–16% [26]. Thus, future research should clarify to what extent the experience of sADRs depends on comorbidities and concomitant drug use and if the linear relationship found by Appa *et al*. also applies for the number of high-risk drugs or a combination of medical risk factors. With the assumption that more medical risk factors increase the risk for sexual dysfunction, physicians and pharmacists should give patients at high risk for sADRs additional attention and adapt drug treatment if necessary.

This study used dispensing data to calculate prevalence numbers of medication-related risks in a population. The database has also been utilised to improve drug prescribing and patient outcomes [27]. Nevertheless, performing an observational study with dispensing data comes with limitations. First, drug dispensing does not equal drug use. Therefore, (concomitant) drug use might be overestimated from our data. On the other hand, only considering a period of drug use for one day in case of missing information on daily drug use, our estimations may have been too conservative. Additionally, some drugs such as thiotepa were not dispensed by community pharmacies and thus not covered by our dispensing data. Thirdly, the validity of predicting morbidities by dispensing data depends on the specificity of the drugs for a certain disease. For example, antidepressants and anti-epileptics may also be used for other indications than depression or epilepsy. On the other hand, morbidities such as diabetes, hypertension and depression do not always require drug treatment, indicating an underestimation when identified solely by drug dispensing. Additionally, for the 82 drugs with 1–10% risk for sADRs, the morbidity prevalence numbers included the main indication for eight anti-diabetic drugs, two anti-epileptic

drugs and nine drugs targeting cardiovascular diseases, but the influence on the proportions detected was regarded as limited. Moreover, medical conditions such as arthritis or end-stage renal disease are likely to contribute to patients experiencing decreased sexual functioning, but cannot be identified from drug dispensings. This also applies for risk factors such as smoking, physical activity, or mental or cultural characteristics.

Importantly, we relied on SmPC-information for the quantification of drug users with a potential high risk for sADRs. In clinical practice, also drugs that are not registered with high risk for sADRs were reported to decrease sexual functioning, e.g. betablockers [28]. ADRs in the SmPC are reported during registration trials with generally more healthy and homogenous groups of patients. Nevertheless, by evaluating only drugs registered with a high risk, a drug's potential to cause sADRs in clinical practice may be underestimated by our results. Additionally, the SmPC-texts sometimes showed sex-specific differences in the risk for sADRs. This difference should be studied further in clinical practice.

Conclusion

This study showed that 1 in 11 inhabitants of the Netherlands used drugs with a (very) high risk for sADRs according to their registration files. The majority of these patients had additional risk factors for sexual dysfunction such as high age, depression and concomitant use of other drugs with high risk for sADRs. One-third of starters with antidepressants or spironolactone did not continue their treatment with a second dispense. More research is needed on patients' actual experience of sADRs and the consequences for their drug adherence and quality of life. In the meantime, physicians and pharmacists should be alert to patients experiencing sexual dysfunction, especially to those with a high risk for sADRs.

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