

Antidepressant use in Poland in the years 2010-2018

Katarzyna Bliźniewska-Kowalska, Julita Katarzyna Chęcińska,
Piotr Gałecki

Summary

Antidepressants are used in the treatment of both depressive and anxiety disorders. According to the latest data, the quantity of antidepressants and mood stabilizers used has almost doubled over the last eight years. These numbers are still growing, but the highest increase in the number of patients using this group of drugs was recorded in 2013 (12%) and 2014 (13.1%). The most commonly used group of antidepressants are selective serotonin reuptake inhibitors (SSRIs) (63% of prescribed antidepressants). SSRIs are considered first-choice drugs in the treatment of depressive disorders and chronic anxiety. The number of SSRIs used by patients has more than doubled over the last 8 years. Among selective serotonin reuptake inhibitors, sertraline (38.5% of all prescriptions) was the most commonly used active substance in Poland in 2018. The most frequently prescribed substance belonging to the group of antidepressants with a different mechanism of action was opipramol (23.8% of all prescriptions), followed by trazodone (19.1% of all prescriptions) and mianserin (15.4% of all prescriptions). Out of the two drugs from the group of serotonin and noradrenaline reuptake inhibitors (SNRI) available in Poland, many more patients use venlafaxine (84.2%) than duloxetine (15.8%).

A similar trend related to a constantly growing number of antidepressants used is also observed in other European countries and in the United States of America.

statistics, pharmaceutical treatment of mental illness, antidepressant, depression

INTRODUCTION

Antidepressants are a heterogeneous group of psychotropic drugs. They are used to treat not only depressive disorders, but also the entire spectrum of anxiety disorders.

In the 1950s, numerous scientific studies on new anti-tuberculosis drugs were carried out. In 1953, Fox and Gibas synthesized ipronazide – an isoniazide derivative used to treat tuberculosis [1]. It was observed that patients treated with ipronazide for tuberculosis presented sig-

nificant “side effects” of this drug in the form of euphoria, increased psychomotor drive, improved sleep and appetite [2, 3]. In 1957, Loomer and colleagues conducted a study on the efficacy of ipronazide in depressed patients. They showed significant improvement in as many as 70% patients [4]. Thus, ipronazide, a monoamine oxidase inhibitor (MAO), became the first antidepressant. Iparoniazide was withdrawn from the market after some time due to its non-selective mechanism of action. A combination of foods containing large amounts of tyramine, such as cheese and dairy products, with MAO inhibitors that increase the concentration of tyramine and noradrenaline in the sympathetic nervous system resulted in dangerous arte-

Katarzyna Bliźniewska-Kowalska, Julita Katarzyna Chęcińska,
Piotr Gałecki: Department of Adult Psychiatry, Medical University
of Lodz, Poland

Correspondence address: kblizniewska@gmail.com

rial pressure spikes, tachycardia and increased sweating. Currently, safer, reversible and selective MAO_A inhibitors (e.g. moclobemide) are used in clinical practice.

Also in the late 1950s, Swiss psychiatrist Roland Kuhn discovered the antidepressant effect of imipramine, which as the first tricyclic antidepressant was registered by the FDA (Food and Drug Administration) in 1959 [5, 6].

Fluoxetine was the first selective serotonin reuptake inhibitor approved and sold in the United States [7, 8]. In the early 1980s, zimelidine, which also belonged to the SSRI group, was introduced to the European market. It was derived from phenylamine and was soon withdrawn due to serious side effects such as Guillain-Barre syndrome [9]. Since then, many new selective serotonin reuptake inhibitors have been developed and have become the first-choice drugs in the treatment of patients with depressive disorders [10].

The aim of our study was to evaluate the popularity and dynamics of antidepressant prescription in Poland over the last ten years. The analysis of antidepressant prescription has been undertaken, because the significant increase of in the incidence of Major Depressive Disorders (MDD) during the last years is noticeable in Poland. The question arises whether the increase in morbidity is accompanied by the increase of the number of prescribed antidepressants and which groups of drugs are most often chosen by doctors.

The use of antidepressants and mood stabilisers

Data obtained from the IQVIA (formerly IMS Health and Quintiles) shows that the number of antidepressants and mood stabilizers used by patients has almost doubled over the last eight years (Figure 1).

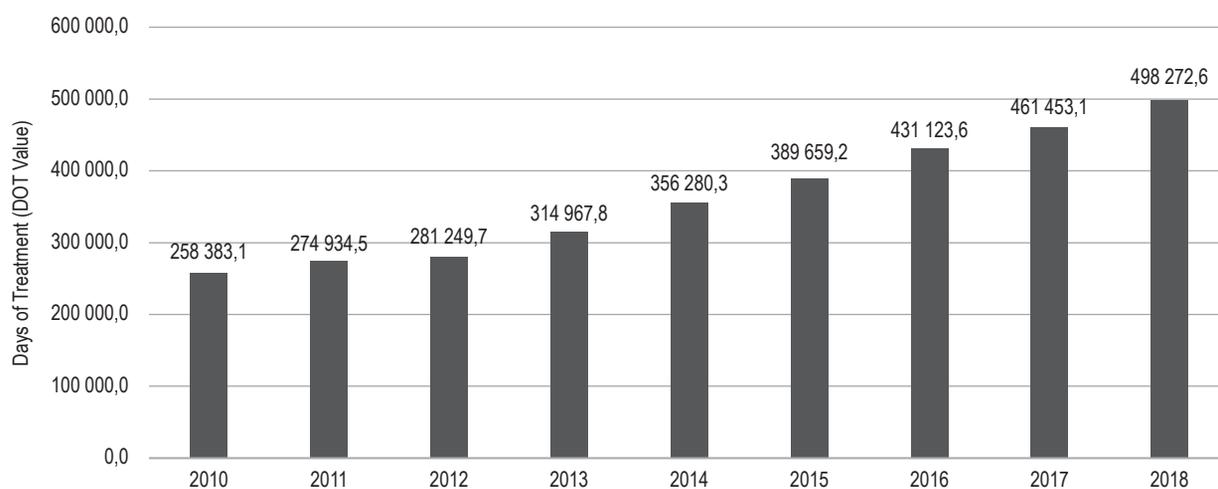


Figure 1. Days of treatment (DOT Value) of patients using antidepressants and mood stabilizers in Poland in the years 2010-2018. Data provided by IQVIA (formerly IMS Polska)

For the sake of uniformity, quantitative data is presented as a "DOT Value" (Days of Treatment), i.e. a measure defining the number of therapy days (according to Defined Daily Dosages) ensured by the number of packages of a given preparation sold in a given period of time. It is assumed that Defined Daily Dosages (DDD) correspond to the WHO guidelines defining the recommended daily dosage for each therapeutic substance [11].

The increase in the number of drugs from this therapeutic group is significant. The highest increase in the number of patients using antidepressants and mood stabilizers was observed in 2013 (12%) and 2014 (13.1%) (Figure 2).

The groups of drugs described above include: selective serotonin reuptake inhibitors (SSRIs), serotonin-norepinephrine reuptake inhibitors (SNRIs), antidepressants with a different mechanism of action, mood stabilizers and over-the-

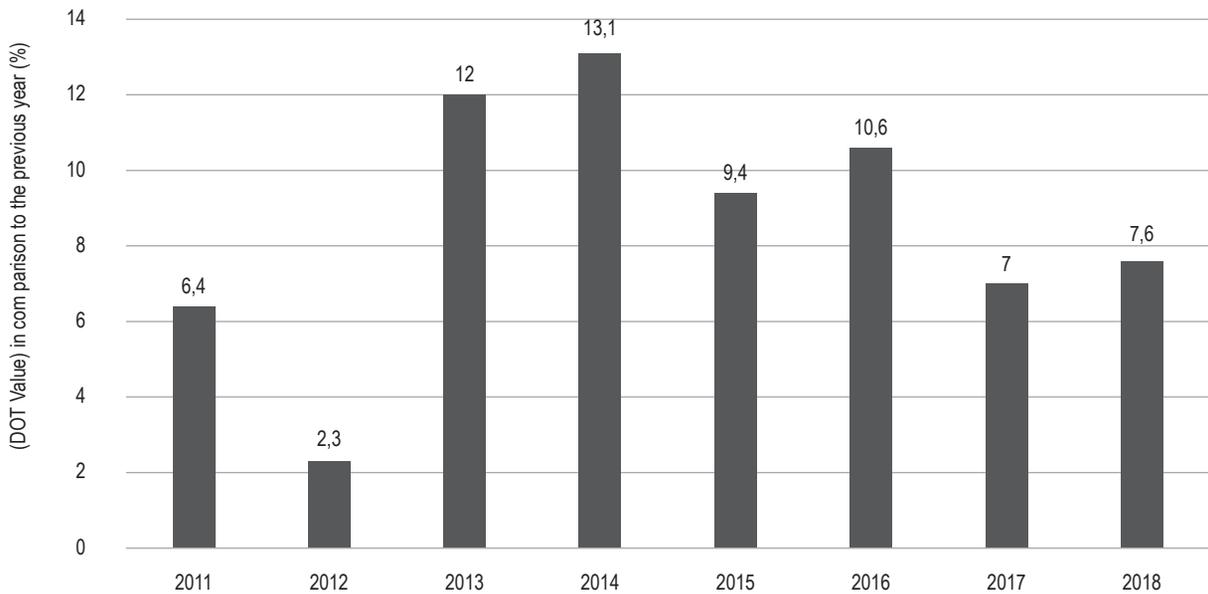


Figure 2. Increase in the number of Days of Treatment (DOT Value) in comparison to the previous year [%] in Poland. Data provided by IQVIA (formerly IMS Polska)

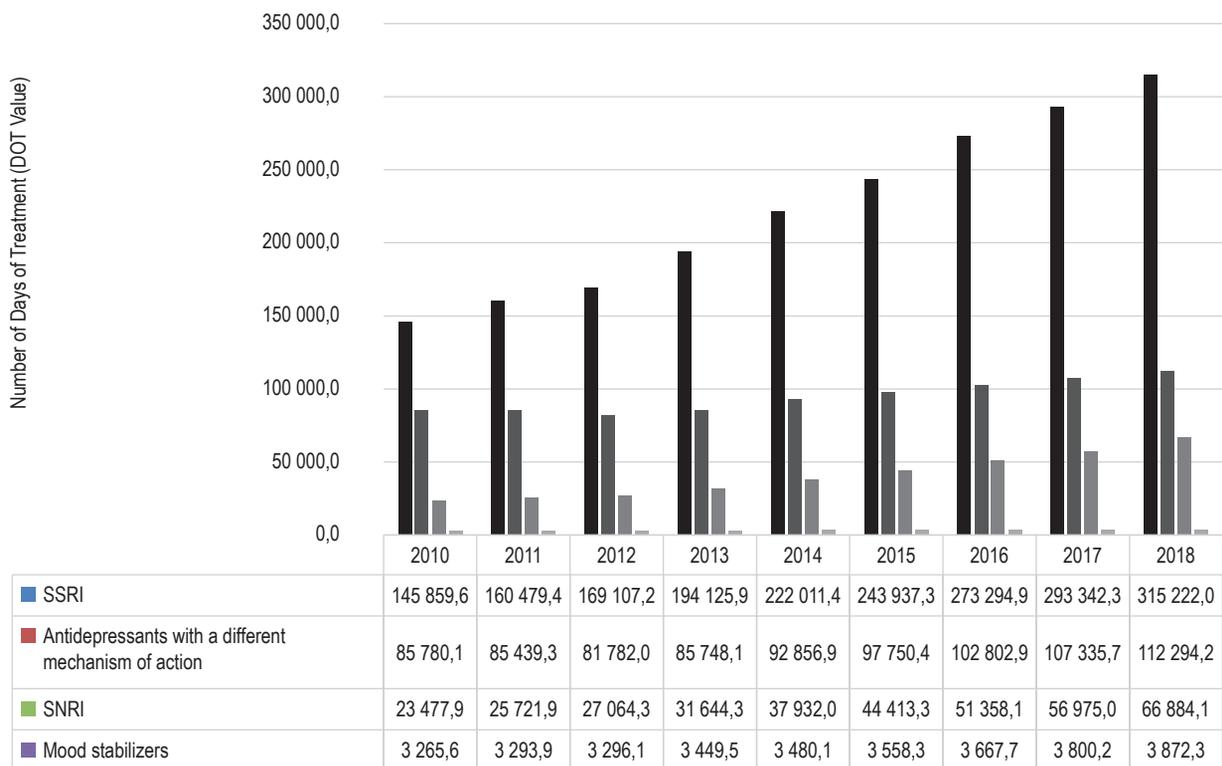


Figure 3. Number of Days of Treatment (DOT Value) of patients using antidepressants and mood stabilizers in Poland in the years 2010-2018 (with a breakdown by the group of drugs). Data provided by IQVIA (formerly IMS Polska)

counter herbal medicines. There is no detailed and reliable data on the sales of the abovementioned plant-based dietary supplements.

The most commonly used antidepressants are selective serotonin reuptake inhibitors (SS-

RI), followed by antidepressants with a different mechanism of action and serotonin-noradrenaline reuptake inhibitors (SNRIs). Moreover, it is clear that the number of SSRIs used by patients has more than doubled over the last 8

years, from a DOT Value of 145 859.6 in 2010 to 315 222.0 in 2018 (Figure 3).

In this group of drugs, SSRIs accounted for more than 63% of the drugs used in 2018 (Figure 4).

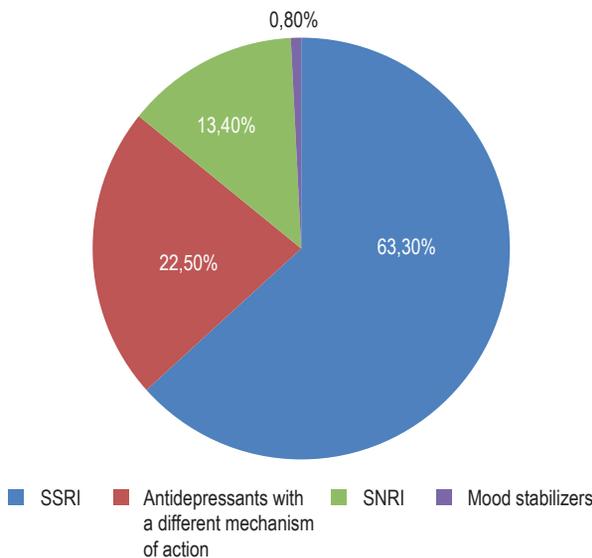


Figure 4. Percentage share of specific groups of antidepressants in Poland in 2018. Data provided by IQVIA company (formerly IMS Polska)

In the SSRI group, the active substance most commonly used in 2018 in Poland was sertraline (38.5% of all prescriptions). The second most commonly used active substance was escitalopram (21.8% of all prescriptions) (Figure 5). SSRIs are considered first-choice drugs in the treatment of depressive disorders and chronic anxiety.

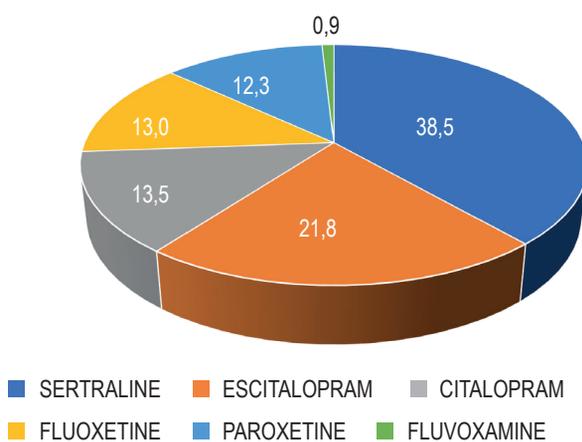


Figure 5. Percentage share of active substances from the SSRI group (by DOT Value) in Poland in 2018 [%]. Data provided by IQVIA (formerly IMS Polska)

The most commonly prescribed substance from the group of antidepressants with a different mechanism of action is opipramol (23.8% of all prescriptions), followed by trazodone (19.1% of all prescriptions) and mianserin (15.4% of all prescriptions) (Figure 6). Opipramol belongs to tricyclic antidepressants, which have been available in Poland for a very long time. Trazodone and mianserin are often used in patients with insomnia, which is very often associated with depressive disorders. These medications are well known among primary care physicians.

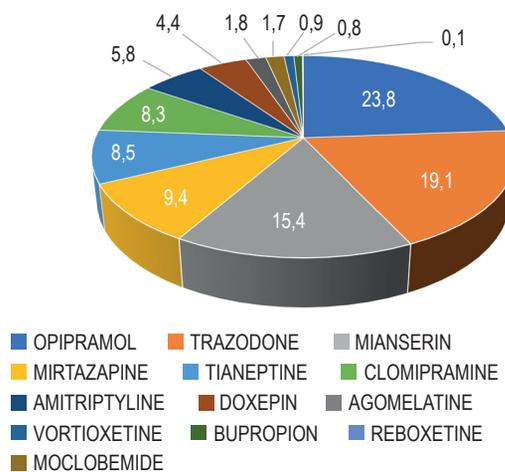


Figure 6. Percentage share of active substances from the group of antidepressants with a different mechanism of action (by DOT Value) in Poland in 2018 [%]. Data provided by IQVIA (formerly IMS Polska)

The group of serotonin and noradrenaline reuptake inhibitors (SNRI) registered in Poland includes venlafaxine and duloxetine. The former is prescribed by doctors much more frequently than the latter (84.2% versus 15.8%) (Figure 7). This may be due to the fact that duloxetine is

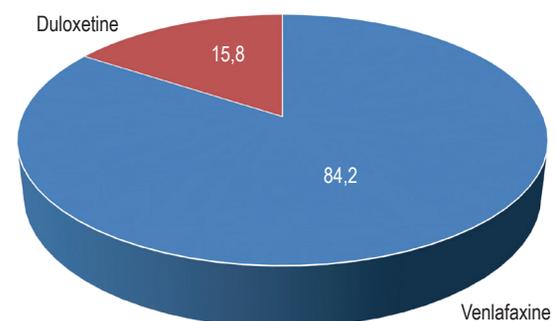


Figure 7. Percentage share of active substances from the SNRI group (by DOT Value) in Poland in 2018 [%]. Data provided by IQVIA (formerly IMS Polska)

not refundable in Poland, which makes it more expensive for patients. It is also available on the Polish market for a shorter period of time and this may reflect its less popularity.

Prescription of antidepressants by doctors

According to data on drug prescription at the national level (RECEPTometr 2.0) provided by PEX PharmaSequence, the main group of doctors prescribing antidepressants are psychiatrists, followed by primary care physicians (PCPs) [12].

DISCUSSION

Data presented by Gusmão et al. shows a continuous increase in the prevalence of antidepressants in European countries, with an average annual increase of 19.83% expressed in DDD (Defined Daily Dose) per 1000 inhabitants per day. The Netherlands and Switzerland recorded the lowest annual growth rates of only 3%, followed by Bulgaria, France and Luxembourg (all 5%), with the highest growth rates of 59% in Finland, followed by the Czech Republic (41%), Slovakia (40%) and Sweden (34%). The described growth rate for Poland in the period 2004-2009 was 10% DDD/1000 inhabitants/day per year [13].

The number of prescribed antidepressants varies considerably between European countries. In 2015, Iceland prescribed over 10 times more antidepressants per capita than Lithuania (129.6 DDD/1000/day versus 12.3 DDD/1000/day) [14]. It is difficult to find a single cause for these differences. Nevertheless, the differences in access to specialist medical services resulting from different healthcare systems and social awareness of mental disorders do not seem to be insignificant.

The frequency of long-term use of antidepressants in the Netherlands is significant and continues to increase; from 1995 to 2005, it amounted to 30.3% of all cases, while in the next decade (2005-2015) it increased to 43.7% [15].

A British study [16] based on Eurobarometer 2010, covering data from 27 EU Member States, found that 7.2% of Europeans had taken antidepressants in the previous year. As in other stud-

ies, significant differences in the prevalence of antidepressants were found between European countries. The Portuguese (15.7%) and Lithuanians (>10%) were the most frequent users of antidepressants, and Greeks (2.7%) the least frequent. Poles according to this study were below the European average for the frequency of antidepressants use.

According to American data [17], between 2011 and 2014, 12.7% people over 12 years of age (8.6% of men, 16.5% of women) in the USA admitted taking antidepressants in the past month. In each age group, women used antidepressants almost twice as often as men. Non-Hispanic white persons used antidepressants five times more often than Asian persons (16.5% versus 3.3%) and three times more often than Hispanic (5%) or black persons (5.6%). Long-term pharmacotherapy is quite common. Between 2011 and 2014, 68% of US residents over 12 years of age who admit using antidepressants took these drugs for over 2 years, and a quarter of these people have been using antidepressants for over 10 years. Research shows that the number of antidepressants used in the United States of America, both among men and women, is steadily increasing from 7.7% in 1999-2002 to 12.7% in 2011-2014 [17].

Differences between individual countries may result from different reimbursement strategies, time of availability of a given medication on the market in a particular country, and public awareness of affective disorders.

REFERENCES

1. Fox HH, Gibas JT. Synthetic tuberculostats. VII monoalkyl derivatives of isonicotinylhydrazine. *Journal of Organic Chemistry*. 1953;18:994-1002.
2. López-Muñoz F, Alamo C, Juckel G, Assion HJ. Half a century of antidepressant drugs: on the clinical introduction of monoamine oxidase inhibitors, tricyclics, and tetracyclics. Part I: monoamine oxidase inhibitors. *J Clin Psychopharmacol*. 2007; 27(6):555-559.
3. Delay J, Laine B, Buisson JF. The action of isonicotinylhydrazide used in the treatment of depressive states *Ann Med Psychol (Paris)*. 1952;110(2 5):689-692.
4. Loomer HP, Saunders JC, Kline NS. A clinical and pharmacodynamic evaluation of iproniazid as a psychic energizer. *Psychiatr Res Rep Am Psychiatr Assoc*. 1957;8:129-141.
5. Hillhouse TM, Porter JH. A brief history of the development of antidepressant drugs: From monoamines to glutamate. *Exp Clin Psychopharmacol*. 2015; 23(1): 1-21

6. Chaitra T, Ramachandrai H, Narayana Subramanyam,1 Kral Jurgen Bar,2 Glen Baker,3 and Vikram K. Yeragani. Antidepressants: From MAOIs to SSRIs and more. *Indian J Psychiatry*. 2011; 53(2): 180–182.
7. Fangmann P, Assion HJ, Juckel G, Gonzalez CA, Lopez-Munoz F. Half a century of antidepressants: On clinical introduction of monoamine oxidase inhibitors, tricyclics and tetracyclics. Part 2: Tricyclics and tetracyclics. *J Clin Pharmacol*. 2008; 28:1–4.
8. Pletscher A. The Discovery of antidepressants: A winding path. *Experientia*. 1991;47:4–8. [PubMed] [Google Scholar]
9. Fagius J, Osterman PO, Sidén A, Wiholm BE. Guillain-Barre syndrome following zimeldine treatment. *J Neurol Neurosurg Psychiatry*. 1985; 48(1):65-69.
10. Gałecki P. Zalecenia konsultanta krajowego w dziedzinie psychiatrii dotyczące leczenia epizodu depresji i zaburzeń depresyjnych nawracających. *Farmakoterapia w psychiatrii i neurologii*. 2018; 34 (3): 157-199.
11. WHO Collaborating Center for Drug Statistics Methodology, Last updated: 2018-12-13, cited 2019-06, Available from: https://www.whocc.no/atc_ddd_index/
12. Pex Pharma Sequence. RECEPTOmetr 2.0
13. Gusmão R, Quintão S, McDaid D, Arensman E, Van Audenhove C, Coffey C, Värnik A, Värnik P, Coyne J, Heggerl U. Antidepressant Utilization and Suicide in Europe: An Ecological Multi-National Study. *PLoS One*. 2013 Jun 19;8(6):e66455. doi: 10.1371/journal.pone.0066455. Print 2013.
14. Health at a Glance 2017: OECD Indicators – Chapter 10, Pharmaceutical Figure 10.9 Antidepressant drugs consumption, 2000 and 2005 (or nearest year).
15. Huijbregts KM, Hoogendoorn A, Slottje P, van Balkom AJLM, Batelaan NM. Long-Term and Short-Term Antidepressant Use in General Practice: Data from a Large Cohort in the Netherlands. *Psychother Psychosom*. 2017;86(6):362-369. doi: 10.1159/000480456. Epub 2017 Nov 3.
16. Lewer D, O'Reilly C, Mojtabai R, Evans-Lacko S. Antidepressant use in 27 European countries: associations with sociodemographic, cultural and economic factors. *Br J Psychiatry*. 2015 Sep;207(3):221-6. doi: 10.1192/bjp.bp.114.156786. Epub 2015 Jul 9.
17. Pratt LA, Brody DJ, Gu Q. Antidepressant Use among persons aged 12 and over: United States, 2011–2014. *NCHS Data Brief No. 283*, 2017.