Atypical antipsychotics: Decades of use, unfathomable harms

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Background

Beginning in the late 1980's, multiple pharmaceutical companies developed and marketed drugs that would come to be known as atypical antipsychotics (or AAPs). These drugs – including Johnson and Johnson's Risperdal, Eli Lilly's Zyprexa, AstraZeneca's Seroquel, Bristol Myers Squibb's Abilify, and Pfizer's Geodon -- racked up massive US sales, including $100B between 2000 to 2019 alone (Table 1). Sales at this level are noteworthy, particularly given that at the beginning of this period it was strongly suspected, and a few years later firmly established, that these drugs, as a class, caused premature death when prescribed to elderly patients with dementia. Moreover, for most of these patients, the drugs provided no therapeutic benefit.

The first studies suggesting AAPs increased mortality appeared in the medical literature at the end of the 1990's. By 2002, Johnson and Johnson had warned Canadian (but not US) physicians that its AAP – Risperdal – had potentially deadly side effects. By 2003, warnings that AAPs were explicitly not for the treatment of dementia-related psychosis due to increased risk of cerebrovascular events began to appear on US drug labels. By 2005 – the year a comprehensive meta-analysis demonstrated an increased risk of death – a 'black box' warning was added to the entire class: if taken for a period of 10 weeks by an elderly patient with dementia, AAPs were associated with an absolute increase in the risk of death of 1.9% compared to placebo (detailed timeline of key events in Supplement Table 1).

This drumbeat of increasingly alarming studies and FDA regulatory actions did not impede AAP manufacturers from aggressively seeking to increase sales to the elderly. When numerous attempts to obtain labeled indications in this group faltered, the companies promoted use 'off label', ultimately resulting in collective fines and penalties of nearly $5 billion (Table 1). By 2007, according to an investigation by the Office of the Inspector General, an average of 14% of elderly nursing home residents at any one time were receiving AAPs, 88% of which was associated with the indication specified in the boxed warning.

We attempted to measure the toll wrought by AAPs on our elderly citizens over the course of the past two decades, applying a basic epidemiologic method referred to as 'attributable risk'. Based on indirect measures, we describe how AAP prescriptions written for elderly patients over the last two decades have led to somewhere between 300,000 and 1,200,000 needless deaths – a toll of the same order of magnitude as that exacted by the opiate epidemic over that same time period, which the CDC estimates to be 500,000.

Attributable risk calculation for measuring adverse harms of atypical antipsychotics

Attributable risk – a method familiar to any epidemiologist – enables estimation of population level impact of harmful exposures. The toll is determined by combining an estimate of how long people were exposed to the

drug (*exposure time*) with an estimate of the harm from the treatment per unit of exposure time. The latter is obtained either from a direct estimate of the *absolute risk* associated with the treatment, or by combining an estimate of the risk of the event absent the treatment (*baseline risk)* with an estimate of the relative increase in risk (*relative risk*) associated with the treatment. For AAPs, the *absolute risk* and the *exposure time* needed for that harm to occur are each listed on the drugs' labels: ten-week exposure causes 1.9% increase in the risk of death.

Exposure time across the population itself is optimally measured by counting filled prescriptions. Those data are not freely available, but Medicare possesses these data, and the FDA can demand this information from companies. Lacking prescription data, there are two indirect ways to gauge exposure -- sales data and survey data. We illustrate both approaches, relying on a standard assumption that risk is constant. The implication of this assumption is that it does not matter how exposure time is distributed across a population. For instance, the number of people harmed when 500 patients receive a harmful drug for 10 weeks equals the number of people harmed when half as many people (250 people) receive it for twice as long (20 weeks).

Sales-based estimate of exposure time: The dollar value of AAP sales divided by the yearly cost of an AAP provides one estimate of *exposure time*. There are limitations to this approach – companies may not report sales of products individually if they do not constitute a large enough share of their business, and this method does not capture free product given as samples or through corporate charities. If anything, these limitations underestimate the exposure time, and thus underestimate population-level harms. In the case of AAPs, however, the drugs generated massive sales and the manufacturers reported their revenues quarterly. Another challenge that often arises, especially for drugs with longstanding use in the market, is that the drug ends up being offered in multiple doses and formulations, each associated with a different price. Sales figures are typically reported for all versions of the drug combined. In this setting, it is safer to evaluate a range of estimates, from the most conservative (when every dispensing was the most expensive formulation) to least conservative (every dispensing was the least expensive formulation). Another challenge emerges if the focus is only on a subsegment of the population receiving the drug, as sales data are typically reported across the population.

When we applied the sales-based method, we started with reported US revenue from company financial filings for all branded versions of their AAPs (see Supplemental Methods). To account for the entry and uptake of generics during the analysis period, we estimated the market share of generics using CMS' Medicare Part D Spending Dashboard and Bloomberg. We utilized historic wholesale acquisition cost price data from 2000-2006 and net price data from 2007-2019. As our interest was in prescriptions for elderly patients with dementia, the use highlighted on the drug's boxed warning and associated with an increased risk of death, we estimated the share of AAP sales to elderly patients with dementia or other psychosis during that period using published reports.

Survey-based estimate of exposure time: Surveys of health care services among representative populations provide an alternative means of estimating *exposure time.* These surveys take two forms: cross-sectional surveys and audits. Cross-sectional population-based surveys produce estimates of the number of people who are receiving the medication on any day, month, or year. These surveys can safely be assumed to generalize to the period during which they were administered. A weakness of these data is that such surveys routinely exclude critical populations, such as patients residing in nursing homes or long-term care facilities. Audits represent another flavor of survey – they often target critical populations, but they are rare, meaning that changes over time are challenging to track. To estimate AAP use among the elderly, we combined insights from each type of survey. We relied primarily on estimates from the Office of the Inspector General (OIG) audit of the first half of 2007. This audit was specific to elderly nursing home residents, and according to its findings, we assumed the non-nursing home elderly population accounted for the remaining 80% of all AAP use. We analyzed a routinely conducted survey of representative samples of outpatient prescriptions to assess whether results from the OIG

audit could be generalized to our entire analysis period. We found that utilization in 2007 was 6% higher than average yearly utilization between 2000-2019. Therefore, we scaled down the OIG's reported AAP utilization by 6% and assumed prescribing did not change over time.

Quantifying how many premature deaths resulted from atypical antipsychotic use in the elderly:

Taking each of these approaches, and incorporating flexibility across our assumptions, our results find that the number of additional deaths due to AAP use between 2000 and 2019 falls in the range of 300,000 to 1,200,000 individuals (Table 2, Figure 1). The lower end of this range was estimated using the sales-based method, assuming the highest price per prescription. The upper end reflects the estimate from the survey-based method. All the possible values within this range support the same conclusion – AAP's have wrought an unfathomable toll on vulnerable elderly patients.

Table 1. Atypical antipsychotic drugs (AAPs) approved for use in the US, associated sales and fines paid for marketing violations

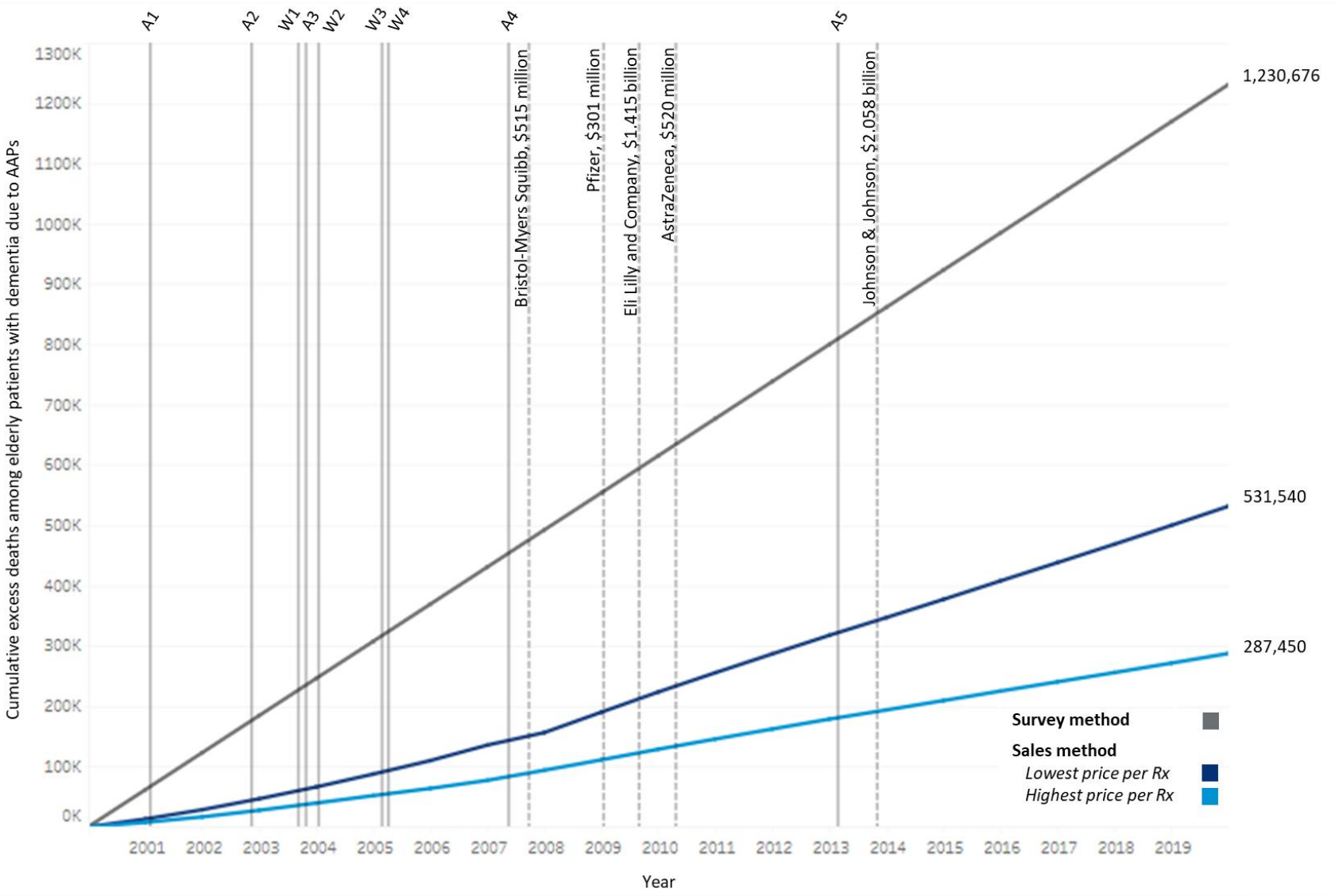
Manufacturer	Drug name	Approval year	Year of first generic entrant	Sales, $mn (2000-2019)	Fines and charges, $mn, related to marketing to elderly patients (year).
Bristol Myers Squibb/Otsuka	Abilify (aripiprazole)	2002	2015	$17,567	$515 (2007) Illegal marketing and pricing
	Abilify Maintena (aripiprazole)	2013	N/A	$405	
Pfizer	Geodon (ziprasidone hydrochloride)	2001	2012	$6,234	$301 (2009) Illegal marketing
Johnson and Johnson	Risperdal (risperidone)	1993	2008	$14,197	$2,058 (2013) Misbranding, off-label marketing, kickbacks to nursing home pharmacies[1]
	Risperdal Consta (risperidone)	2003	N/A	$5,920	
AstraZeneca	Seroquel IR (quetiapine fumarate)	1997	2012	$25,443	$520 (2010) Illegal marketing
	Seroquel XR (quetiapine fumarate)	2007	2016	$5,559	
Eli Lilly	Zyprexa (olanzapine)	1996	2011	$28,010	$1,415 (2009) Illegal marketing

[1]Not included in this estimate is the $6.8 billion Johnson and Johnson must pay in punitive damages for failing to adequately warn about the risk of gynecomastia in children and adolescents prescribed Risperdal.

Table 2. Attributable deaths among elderly patients with dementia, 2000-2019, based on sales and survey-based methods of estimation

	Excess deaths, 2000-2019
Survey method	1,230,676
Sales method	
Highest price per prescription	287,450
Lowest price per prescription	531,540

Figure 1. Cumulative attributable deaths among elderly patients with dementia, 2000-2019, based on sales and survey-based methods of estimation



AAPs: Atypical antipsychotics. We included the top five atypical antipsychotic (AAP) molecules according with the largest share of the Medicare market, according to beneficiary data from the Medicare Part D Spending Dashboard (Abilify, Geodon, Risperdal, Seroquel, Zyprexa).

Key events:

Initial FDA approvals for atypical antipsychotics:

A1: Geodon, February 2001
A2: Abilify, November 2002
A3: Risperdal Consta, October 2003
A4: Seroquel XR, May 2007
A5: Abilify Maintena, February 2013

FDA warning added to FDA label for cerebrovascular adverse events in elderly patients with dementia. Warning section includes the following language for the first time: “Risperdal is not approved for the treatment of patients with dementia-related psychosis.”

W1: Risperdal, September 2003
W2: Zyprexa, January 2004
W3: Abilify, March 2005

Boxed warning added to FDA label for increased mortality in elderly patients with dementia-related psychosis.

W4: Atypical antipsychotics, April 2005

Legal settlements related to marketing to elderly patients are notated by doted vertical lines.

Supplemental Methods

In this analysis, we included the top five atypical antipsychotic (AAP) molecules defined by those with the largest share of the Medicare market, according to beneficiary data from the Medicare Part D Spending Dashboard.

Sales-based estimate

The sales-based estimate required the following data points:

1. Annual US revenue for each branded drug
2. Annual cost of therapy for each branded drug
3. Annual person-years on generic drugs for each molecule of interest
4. Proportion of all patients treated with AAPs that are aged 65 and older
5. Proportion of patients 65 and older treated with AAPs that have the condition specified in the boxed warning
6. The absolute risk of death

Annual US revenues for the branded drugs of interest were primarily sourced through company financial filings. Risperdal sales data from 2000-2005 were pulled from a 2013 lawsuit against Johnson and Johnson. We excluded years with negative reported revenues. In limited cases, we estimated the product revenue when not available through financial disclosures. Generally, the product was at the beginning of its life cycle and revenues were relatively small. Any differences from actual sales are unlikely to be material to our conclusions. The products for which there are estimated revenues include:

- Risperdal: 2006
- Risperdal Consta: 2005-2006
- Seroquel IR: 2000-2001

Yearly cost of therapy for each drug was calculated by multiplying the drug price per tablet or vial by the recommended yearly dose. To account for the possible range of appropriate doses, we calculated the yearly cost assuming both the lowest and highest recommended dose for adults with schizophrenia, excluding initial doses (Supplement Table 2). Net price data were available from 2007-2019 from SSR Health. To estimate prices in earlier years, we pulled historic wholesale acquisition (WAC) prices from the RED BOOK Flat File. Although the cost per year of treatment was slightly higher using WAC than net prices, rebating had a much less significant influence on prices during the pre-2007 period than it does today.

The estimate of **person-years on each generic** in the first year or two after generic introduction is based on the market share of the branded and generic drug according to Bloomberg utilization data. The split between patients on branded versus generic drugs was cross-referenced with beneficiary counts from CMS' Medicare Part D Spending Dashboard. CMS beneficiary counts are skewed during partial years, e.g., when generics are first launched, because a beneficiary is counted as receiving a drug if they have at least one claim submitted for it. As such, the market share is overstated during these years. Companies also frequently stop reporting drug-specific revenues after the patent expiry and when sales become immaterial. This affects our ability to

estimate the generic market. Therefore, a growth rate based on CMS beneficiaries' utilization was applied from the second or third year after generic introduction through 2019.

We used estimates of the **proportion of elderly people prescribed AAPs** from existing literature. A 2007 report finds that 19% of people with at least one prescription for atypical antipsychotics were aged 65 or older. This proportion is likely an underestimate because the analysis used retail prescription data and therefore excludes data on patients in nursing homes or long-term care facilities.

The **proportion of elderly patients prescribed AAPs with dementia or other psychosis** differs depending setting. According to the Office of the Inspector General (OIG) audit of AAP use in nursing homes, claims for elderly nursing home residents accounted for one fifth of all Medicare claims analyzed during the first half of 2007. Therefore, we assumed 20% of elderly individuals exposed to AAPs in the sales-based estimate resided in nursing homes and the remaining 80% lived elsewhere in the community. Among elderly nursing home residents, 88% of claims were associated with the indication in the boxed warning. In contrast, 37% of patients prescribed atypical antipsychotics in the non-nursing home population were treated for dementia, Alzheimer's, or other psychosis.

The final estimates were derived by first dividing US revenue by the cost per year of therapy to estimate the number of person-years of branded therapy. We then scaled up the person count to account for the generic market where appropriate, using the brand to generic ratio from Bloomberg and the CMS Spending Dashboard, and scaled down to focus on the population aged 65 and older with dementia or other psychosis. For each year from 2000-2019, we multiplied the person-years estimate by the **absolute risk from the boxed warning** (1.9% for each 10-week period) to quantify excess deaths among elderly patients from AAPs (Risperdal example, Supplement Table 3).

Survey-based estimate

The survey-based estimate relied primarily on estimates from the OIG audit of AAP use in elderly nursing home patients. For the first 6-months of 2007, the report identified 1,678,874 Medicare Part B and Part D claims for AAPs among elderly nursing home residents. We assumed that each claim is associated with a one-month prescription.

To assess whether utilization data from the OIG audit could be generalized to our entire analysis period, we evaluated AAP utilization among the elderly as reported in the Medical Expenditure Panel Survey (MEPS). MEPS is a population-based survey of families and individuals, their medical providers, and employers across the United States. We did not use the MEPS Household Component for the main analysis because it excludes institutionalized populations (i.e. those in nursing homes, long terms care facilities, and hospitals) and does not capture exposure time, only the number of elderly patients with at least one AAP prescription. Though AAP utilization according to MEPS data increased substantially between 2000-2019, utilization in 2007 was only 6% higher than the mean during that period. Therefore, we scaled down the OIG's reported AAP utilization by 6% and assumed prescribing did not change over time.

Mirroring the sales-based estimate, we assumed 37% of elderly non-nursing home patients with an AAP prescription had a condition specified in the boxed warning. Within the nursing home

estimate, we assume that proportion was 88%. We multiplied the exposure estimates by the absolute risk from the boxed warning (1.9% for each 10-week period) to quantify excess deaths among elderly patients from AAPs among the nursing home and non-nursing populations, (Supplement Table 4).

Supplement Table 1. Timeline summarizing key atypical antipsychotic approval, safety, and legal settlement events

Date	Drug/Class	Event
December 29, 1993	Risperdal	**FDA approval** for Risperdal for the management of "manifestation of psychotic disorders" (later referred to as schizophrenia).
September 30, 1996	Zyprexa	**FDA approval** for Zyprexa for the management of "manifestation of psychotic disorders" (later referred to as schizophrenia).
September 26, 1997	Seroquel IR	**FDA approval** for Seroquel IR for the management of "manifestation of psychotic disorders" (later referred to as schizophrenia).
February 5, 2001	Geodon	**FDA approval** for Geodon for the treatment of schizophrenia.
October 17, 2002	Risperdal	**Safety warning** for Risperdal for increased risk of stroke and stroke-like events in elderly patients with dementia advised by Johnson & Johnson to Canadian government.
November 15, 2002	Abilify	**FDA approval** for Abilify for the treatment of schizophrenia.
September 10, 2003	Risperdal	**Safety warning** for Risperdal added to FDA label for cerebrovascular adverse events in elderly patients with dementia. Warning section includes the following language for the first time: "Risperdal is not approved for the treatment of patients with dementia-related psychosis."
October 29, 2003	Risperdal Consta	**FDA approval** for Risperdal Consta for the treatment of schizophrenia.
January 14, 2004	Zyprexa	**Safety warning** for Zyprexa added to FDA label for cerebrovascular adverse events in elderly patients with dementia. Warning section includes the following language for the first time: "Olanzapine is not approved for the treatment of patients with dementia-related psychosis."
March 1, 2005	Abilify	**Safety warning** for Abilify added to FDA label for cerebrovascular adverse events in elderly patients with dementia. Warning section includes the following language for the first time: "Aripiprazole is not approved for the treatment of patients with dementia-related psychosis."
April 11, 2005	Atypical antipsychotics	**Boxed warning** for all atypical antipsychotics added to FDA label for increased mortality in elderly patients with dementia-related psychosis "Analyses of seventeen placebo controlled trials (modal duration of 10 weeks) in these patients revealed a risk of death in the drug-treated patients of between 1.6 to 1.7 times that seen in placebo-treated patients. Over the course of a typical 10 week controlled trial, the rate of death in drug-treated patients was about 4.5%, compared to a rate of about 2.6% in the placebo group. Although the causes of death were varied, most of the deaths appeared to be either cardiovascular (e.g., heart failure, sudden death) or infectious (e.g., pneumonia) in nature. RISPERDAL (risperidone) is not approved for the treatment of patients with Dementia-Related Psychosis."
May 17, 2007	Seroquel XR	**FDA approval** for Seroquel XR for the treatment of schizophrenia.
September 28, 2007	Abilify	Bristol-Myers Squibb to pay $515 million in **settlement** for illegal marketing and pricing of Abilify.
June 16, 2008	Antipsychotics	**Boxed warning** extended to all antipsychotics for increased mortality in elderly patients with dementia-related psychosis.

January 15, 2009	Zyprexa	Eli Lilly and Company to pay $1.415 billion in **settlement** for promoting Zyprexa for uses not approved by the FDA.
February 10, 2009	Risperdal	FDA issues **complete response letter** for Risperdal Consta for the adjunctive maintenance treatment of bipolar disorder.
September 2, 2009	Geodon	Pfizer to pay $301 million in **settlement** for off-label marketing of Geodon.
April 27, 2010	Seroquel	AstraZeneca to pay $520 million in **settlement** for off-label marketing of Seroquel.
February 28, 2013	Abilify Maintena	**FDA approval** of Abilify Maintena for the treatment of schizophrenia.
November 4, 2013	Risperdal, Invega	Johnson & Johnson to pay more than $2.058 billion in **settlement** for misbranding, targeting vulnerable populations for off-label uses, and kickbacks to nursing home pharmacies with respect to antipsychotic drugs Risperdal and Invega.

Supplement Table 2. Annual price dosing assumptions

		Lowest price per prescription			Highest price per prescription		
Drug Name	**Dosing recommendation for the treatment of schizophrenia in adults**	**Strength**	**Doses/day of admin**	**Days of admin**	**Strength**	**Doses/day of admin**	**Days of admin**
Abilify	Initial dose: 10-15 mg daily; recommended dose: 10-15 mg daily; max dose: 30 mg daily	10MG	1	365	30MG	1	365
Abilify Maintena	Recommended starting and maintenance dose is 400 mg administered monthly as a single injection	400MG	1	12	400MG	1	12
Geodon	Initiate at 20 mg twice daily. Daily dosage may be adjusted up to 80 mg twice daily.	20MG	2	365	80MG	2	365
Risperdal	Initial dose: 2 mg daily; target dose: 4 to 8 mg daily; effective dose range: 4 to 16 mg daily	4MG	1	365	4MG	4	365
Risperdal Consta	25 mg intramuscular every 2 weeks. Patients not responding to 25 mg may benefit from a higher dose of 37.5 mg or 50 mg. The maximum dose should not exceed 50 mg every 2 weeks	25MG/2ML	1	26	50MG/2ML	1	26
Seroquel IR[a]	Initial dose: 25 mg twice daily; recommended dose: 150 - 750 mg daily; max dose: 750 mg daily	**2000-2005:** 100MG, 25MG **2006-2019:** 100MG, 50MG	**2000-2005:** 100MG x 1, 25MG x 2 **2006-2019:** 100MG x 1 50MG x 1	365	**2000-2005:** 300MG, 100MG, 25MG **2006-2019:** 400MG, 300MG, 50MG	**2000-2005:** 300MG x 2, 100MG x 1, 25MG x 2 **2006-2019:** 400MG x 1, 300MG x 1, 50MG x 1	365
Seroquel XR	Initial dose: 300 mg daily; recommended dose: 400-800 mg daily; max dose: 800 mg daily	400MG	1	365	400MG	2	365
Zyprexa	Initial dose: 5-10mg daily; target dose: 10mg daily	10MG	1	365	10MG	1	365

[a] Seroquel IR 50MG and 400MG tablet prices became available in 2006

Supplement Table 3. Example excess death calculation for Risperdal (not including Risperdal Consta) assuming the highest price per prescription and an elderly proportion of 19%

Year	Risperdal US Revenue, millions	Risperdal highest price per year[a]	Risperdal person-years of exposure, all ages	Generic market share[b]	Growth rate of risperidone market[c]	Generic risperidone person-years of exposure, all ages	Total risperidone person-years of exposure, all ages	Total risperidone person-years of exposure, elderly[d]	Total risperidone person-years of exposure, elderly, boxed warning conditions[e]	Excess deaths[f]
2000	$ 1,083	$ 8,375	129,313	---	---	---	129,313	24,570	11,597	1,146
2001	$ 1,240	$ 8,785	141,146	---	---	---	141,146	26,818	12,658	1,251
2002	$ 1,404	$ 9,579	146,566	---	---	---	146,566	27,848	13,144	1,299
2003	$ 1,448	$ 10,681	135,569	---	---	---	135,569	25,758	12,158	1,201
2004	$ 1,602	$ 11,107	144,239	---	---	---	144,239	27,405	12,935	1,278
2005	$ 1,726	$ 11,818	146,054	---	---	---	146,054	27,750	13,098	1,294
2006	$ 1,962	$ 13,249	148,089	---	---	---	148,089	28,137	13,281	1,312
2007	$ 2,198	$ 11,704	187,803	---	---	---	187,803	35,683	16,842	1,664
2008	$ 1,287	$ 10,090	127,551	25%	---	42,517	170,068	32,313	15,252	1,507
2009	$ 247	$ 14,269	17,311	88%	---	126,946	144,256	27,409	12,937	1,278
2010	---	---	---	---	9.0%	138,371	138,371	26,290	12,409	1,226
2011	---	---	---	---	4.6%	144,736	144,736	27,500	12,980	1,282
2012	---	---	---	---	3.6%	149,946	149,946	28,490	13,447	1,329
2013	---	---	---	---	1.5%	152,195	152,195	28,917	13,649	1,349
2014	---	---	---	---	-3.8%	146,412	146,412	27,818	13,130	1,297
2015	---	---	---	---	-3.7%	140,995	140,995	26,789	12,644	1,249
2016	---	---	---	---	-3.5%	136,060	136,060	25,851	12,202	1,206
2017	---	---	---	---	-3.5%	131,298	131,298	24,947	11,775	1,163
2018	---	---	---	---	-2.2%	128,409	128,409	24,398	11,516	1,138
2019	---	---	---	---	-2.2%	125,584	125,584	23,861	11,262	1,113

[a] Wholesale acquisition price used from 2000-2006. Net prices from SSR Health used from 2007 onward.

[b] Estimated using the brand to generic ratio from Bloomberg.

[c] Estimated using the growth rate of beneficiaries' utilization from CMS' Medicare Part D Spending Dashboard.

[d] Assumed 19% of people prescribed atypical antipsychotic are aged 65 or older.

[e] Among the nursing home population, assumed 88% of individuals prescribed atypical antipsychotics had the condition specified on the boxed warning. For the non-nursing home population, we assumed this proportion was 37%.
[f] Assumed 1.9% absolute rate of death in 10 weeks and 5.2 10-week periods in one year.

Supplement Table 4. Attributable deaths among elderly patients, 2000-2019, survey-based methods of estimation, detailed calculations

Cohort	2007 Rx for atypical antipsychotics[c]	Adjustment for average Rx across 2000-2019 period[d]	Rx for individuals with condition listed on the boxed warning[e]	Count of 10-week periods of exposure[f]	Excess deaths[g]
Elderly nursing home population					
Individual year[a]	3,357,748	3,156,283	2,777,529	1,207,621	22,945
Total, 2000-2019	67,154,960	63,125,662	55,550,583	24,152,427	458,896
Elderly non-nursing home population[b]					
Individual year[a]	13,430,992	12,625,132	4,671,299	2,031,000	38,589
Total, 2000-2019	268,619,840	252,502,650	93,425,980	40,619,991	771,780

[a] Assumed prescribing practices did not change over time.
[b] Assumed non-nursing home population was four times larger than the nursing home population, based on OIG audit of atypical antipsychotic use in elderly nursing home residents.
[c] Based on OIG audit of atypical antipsychotic use in elderly nursing home residents. As the review period was based on data from the first six months of 2007, we doubled the number of prescriptions for atypical antipsychotics identified in that period to estimate a full year of exposure.
[d] Based on our review of longitudinal data from the Medical Expenditure Panel Survey, we found that atypical antipsychotic utilization in 2007 was 6% higher than average yearly utilization between 2000-2019. Therefore, we scaled down the OIG audit's reported atypical antipsychotic utilization by 6%.
[e] Among the nursing home population, assumed 88% of individuals prescribed atypical antipsychotics had the condition specified on the boxed warning. For the non-nursing home population, this proportion was 37%.
[f] Assumed each prescription was for a 30-day fill and 2.3 prescriptions were administered in each 10-week period.
[g] Assumed 1.9% absolute rate of death in 10 weeks.