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RESEARCH LETTER

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Estimated wasteful spending on aducanumab dispensing in the U.S. Medicare population: A cross-sectional analysis

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INTRODUCTION

Aducanumab, a weight-dosed Alzheimer's drug with uncertain benefits and high cost, could strain Medicare's budget if approved for widespread use.[1] In April 2022, Medicare issued a final determination restricting aducanumab's use in clinical trials. However, Medicare's coverage decision may still be overturned by legal challenges, potentially leading to much higher uptake.[2] Moreover, several other Alzheimer's infusion drugs similar to aducanumab are currently in the development pipeline.[3]

Because aducanumab is available in two fixed-dose vial sizes, its use may result in large amounts of discarded drugs and wasteful spending.[4,5] To quantify the amount of discarded drug and potential savings that could be generated from more efficient aducanumab vial sizes, we analyzed patient weight distributions from a nationally representative sample of Medicare beneficiaries with mild cognitive impairment (MCI) or mild dementia.

METHODS

We used nationally representative data from the 2016 Health and Retirement Study (HRS), focusing on participants aged ≥65 years with Medicare Part B insurance. Using validated cognitive measures to identify patients with MCI or mild dementia and self/proxy-reported patient weights, we estimated a lower and upper bound of potentially eligible patients to receive aducanumab (Figure S1, Tables S1 and S2, and Appendix S1).[6,7]

The manufacturer created two vial sizes: 170 mg/1.7 ml and 300 mg/3.0 ml. Assuming a 10 mg/kg monthly dose, we counted the number of vials needed for each patient weight category, and multiplied the per-vial costs by the survey-weighted population (e.g., 7.96% of the upper-bound survey-weighted population weighing 85–90 kg required three 300 mg/3 ml vials, or $2538 × 0.0796 per month, Table 1), and summarized across categories to derive a weighted average for drug spending. To estimate annualized per-patient discarded drug, we subtracted the milligrams of the patient weight-based dose

TABLE 1 Estimated per-person weight-based drug pricing

Self/proxy-reported patient weight (kg)	Percentage of lower bound sample	Percentage of upper bound sample	Number of 170 mg/1.7 ml vials	Number of 300 mg/3.0 ml vials	Calculated spending for full dose ($)	Lower bound population components of weighted average of monthly cost	Upper bound population components of weighted average of monthly cost	Estimated discarded drug for lower bound population (mg)	Estimated discarded drug for upper bound population (mg)
<47	2.48	2.61	1	1	1325.40	$32.93	$34.56	3,033,458	7,882,033
47–51	1.98	3.17	3	0	1438.20	$28.44	$45.59	1,043,217	4,400,109
51–60	10.87	12.72	0	2	1692.00	$184.00	$215.24	9,185,707	38,441,456
60–64	7.37	7.94	2	1	1804.80	$133.02	$143.34	3,169,158	11,182,838
64–68	6.89	6.05	4	0	1917.60	$132.20	$116.04	4,037,259	10,431,323
68–77	21.73	20.19	1	2	2171.40	$471.93	$438.38	33,839,476	87,899,037
77–81	8.25	9.27	3	1	2284.20	$188.44	$211.70	5,632,743	18,889,066
81–85	8.57	8.71	5	0	2397.00	$205.50	$208.70	5,639,236	16,748,895
85–90	7.31	7.96	0	3	2538.00	$185.54	$201.98	6,741,486	18,793,248
90–94	6.44	5.44	2	2	2650.80	$170.69	$144.20	4,905,492	11,170,689
94–98	3.52	3.70	4	1	2763.60	$97.22	$102.36	2,309,264	6,424,301
98–102	4.15	3.54	6	0	2876.40	$119.27	$101.97	2,555,988	5,978,532
102–107	3.70	3.09	1	3	3017.40	$111.77	$93.23	3,248,677	8,230,369
107–111	2.58	2.18	3	2	3130.20	$80.69	$68.24	1,434,515	3,549,658
111–115	1.07	1.11	5	1	3243.00	$34.70	$35.94	696,256	1,680,668
115–119	1.16	0.55	7	0	3355.80	$39.09	$18.43	544,384	814,880
119–120	0.07	0.02	0	4	3384.00	$2.43	$0.83	14,427	14,427
120–124	0.64	0.41	2	3	3496.80	$22.51	$14.50	477,235	790,158
124–128	0.97	0.68	4	2	3609.60	$34.96	$24.67	875,269	1,223,690
128–132	0.00	0.12	6	1	3722.40	$0.00	$4.29	0	187,876
132–136	0.07	0.04	8	0	3835.20	$2.57	$1.67	41,869	81,037
136–137	0.10	0.14	1	4	3863.40	$3.88	$5.35	26,425	105,942
137–141	0.00	0.00	3	3	3976.20	$0.00	$0.00	0	0
141–145	0.00	0.06	5	2	4089.00	$0.00	$2.53	0	136,173
145–149	0.00	0.22	7	1	4201.80	$0.00	$9.04	0	138,224
149–150	0.00	0.05	0	5	4230.00	$0.00	$2.24	0	13,835
>150	0.06	0.02	9	0	4314.60	$32.93	$34.56	33,520	33,520

TABLE 1 (Continued)

Self/proxy-reported patient weight (kg)	Percentage of lower bound sample	Percentage of upper bound sample	Number of 170 mg/1.7 ml vials	Number of 300 mg/3.0 ml vials	Calculated spending for full dose ($)	Lower bound population components of weighted average of monthly cost	Upper bound population components of weighted average of monthly cost	Estimated discarded drug for lower bound population (mg)	Estimated discarded drug for upper bound population (mg)
Total average per-person monthly cost (with 3% markup)						$2352.89	$2313.28	—	—
Total average per-person annualized cost (with 3% markup)						$28,234.68	$27,759.30	—	—
Total amount of monthly discarded drug (milligrams)						—	—	89,485,061	255,241,984

Note: To estimate the average per-person drug price for 1 year of aducanumab, we used the self-reported weight distribution of the lower and upper bound populations. For these calculations, we used data for all patients in the sample and did not incorporate expected drug uptake or exclusions based on plaque burden, which we later account for in calculating total discarded drug (see Figure 1). We defined 27 categories of self-reported weights in the population and used the most efficient dosing for each category to calculate the number of vials needed given the fixed-dose per vial. We multiplied the number of vials by the per-vial cost obtained from publicly available sources. We multiplied these category-specific costs by their percentage of the weighted population and summed these costs. For example, patients who weigh between 77 and 81 kg would require three 170 mg/1.7 ml vials, costing $479.40 × 3, plus one 300 mg/3 ml vial, costing $846 × 1, or $2284.20 in total. Given that 8.25% of the lower bound sample falls in this weight range, we then multiply $2284.20 × 0.0825 to obtain $188.44 per month for the lower bound group. For the upper bound group, we would multiply $2284.20 × 0.0927 to yield $211.70 per month. We repeated this process for each of the categories. We summed these values to obtain a per-person monthly cost for the lower and upper bounds, including a 3% markup. Because our cohort restricts to Medicare Part B beneficiaries, we include a 3% markup to reflect that Medicare initially pays 103% of wholesale acquisition cost (WAC) until an Average Sales Price (ASP) becomes available. We then multiplied these monthly values by 12 months to obtain an annualized drug price estimate for each group.

needed for each patient in the non-survey-weighted sample from the total dose provided in the most cost-efficient combination of vials. For example, an 85 kg patient requires 850 mg of drug provided by three 300 mg/3.0 ml vials (900 mg total), with 50 mg of discarded drug per month. We multiplied monthly discarded drug (mg) for each survey participant by the survey-weighted population (e.g., for the same 85 kg patient, multiply 50 mg of discarded drug per month by the survey-weighted population of 10,707 patients representing the 85 kg HRS survey participant), multiplied by 12 months to annualize estimates. We accounted for expected amyloid plaque rates[7,8] in the lower (37%) and upper-bound (68%) populations (Figure 1). We tabulated costs using the 300 mg/3.0 ml vial price. Hypothesizing that smaller vials could reduce the amount of discarded drug, we simulated three alternative size combinations (100 and 170 mg; 170 and 250 mg; and 80 mg, 170, and 300 mg), retaining at least one original vial size, and quantified potential savings.

We used SAS version 9.4, accounting for clustering, survey weights, and non-response to generate nationally representative estimates. The University of California, Los Angeles Institutional Review Board approved this study, which follows Strengthening the Reporting of Observational Studies in Epidemiology guidelines.

RESULTS

We identified lower and upper estimates of 737–2035 participants, representing approximately 2,882,893 (95% CI 2.6–3.2 million) to 8,405,858 (95% CI 7.7–9.1 million) Medicare Part B beneficiaries aged ≥65 years with MCI or mild dementia. Conservatively assuming a 10% drug uptake, the equivalent of between 132,398 (95% CI 115,220–149,655) and 694,258 (95% CI 628,458-760,059) 300 mg/3.0 ml vials of aducanumab would be discarded annually (Figure 1), costing between $115.4 (95% CI $100.4–$130.4) million and $604.9 (95% CI $547.6–$662.3) million each year. If the 300 mg/3.0 ml vial was reduced to 100 mg/1.0 ml, savings would range between $70.9 (95% CI $60.8–$81.1) and $369.0 (95% CI $331.1–$406.9) million per year.

DISCUSSION

In this nationally representative analysis, a 10% drug uptake would waste hundreds of thousands of aducanumab vials annually, burdening Medicare with $115–$605 million in wasteful spending each year. While Medicare set limits on aducanumab's use, Medicare's decision may still be overturned.[2] With several other

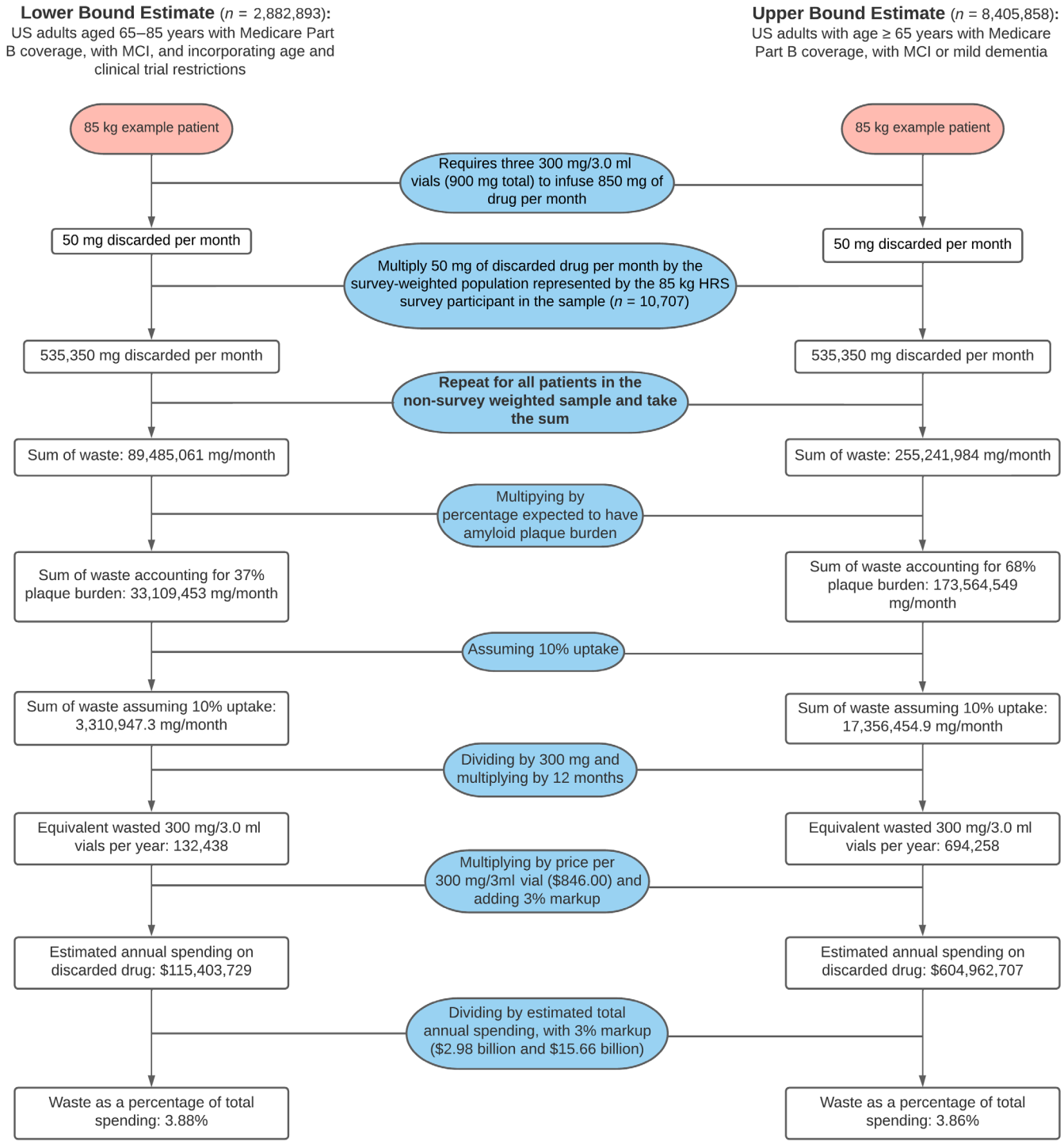

FIGURE 1 Estimated aducanumab wasted 300 mg/3.0 ml vials and spending on discarded drug. To estimate the sum of waste for those who would be eligible for aducanumab (i.e., those with amyloid plaque burden), we assumed that the patient weight distribution of participants with plaque (included) was the same as the weight distribution for those without plaque (excluded). The HRS does not collect data on amyloid plaque burden, so we used a range of population estimates of amyloid plaque burden seen on PET (37% for the lower bound, 68% for the upper bound). We conservatively assumed 10% uptake in our analysis and assumed that the patient weight distribution and plaque burden of those wiestimated to take aducanumab was the same as the 90% estimated to not take aducanumab.

Alzheimer's infusion drugs in the pipeline, aducanumab will not be the last Part B infusion drug to threaten Medicare's solvency. Given Medicare's 15% premium increase in 2022 due to anticipated aducanumab uptake, greater attention to efficient vial packaging could improve the value of future of Part B spending, constrain Part B premium growth, and limit beneficiaries' out-of-pocket spending.

This study has limitations. While self/proxy-reported cognitive measures and weights were previously validated,[6] surveys may misclassify some cases. We used plaque prevalence rates from population studies rather than PET scans on HRS participants.[7,8] We assumed patient weights would be randomly distributed by plaque presence and by aducanumab uptake, that vial and manufacturing costs would be negligible and that drug pricing would not change.

Reducing vial size could decrease wasteful spending from discarded vials by over 60%, with policy implications for all weight-based infusion drugs.

AUTHOR CONTRIBUTIONS

Carlos Irwin A. Oronce wrote the initial draft of the manuscript. Carlos Irwin A. Oronce, Julia Cave Arbanas, and John N. Mafi conceived the idea and design of the study. Cheryl L. Damberg, Bruce E. Landon, and Catherine Sarkisian provided input on the conceptualization of the study. Mei Leng performed the initial construction of the cohort. Carlos Irwin A. Oronce, Julia Cave Arbanas, and Mei Leng performed the analyses. Julia Cave Arbanas created the tables and figures. All authors provided critical feedback and revisions to the manuscript.

CONFLICT OF INTEREST

The authors have no conflicts of interest to declare.

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SUPPORTING INFORMATION

Additional supporting information may be found in the online version of the article at the publisher's website.

Appendix S1. Detailed description of methods, including cohort design, weight-based dosing assumptions, and weight-based calculations.

Figure S1. Flow Diagram of Cohort Design Using the 2016 Health and Retirement Study (HRS) CORE Sample.
Table S1. STROBE Checklist for Cross-Sectional Studies.
Table S2. Presence of Reported Informal Caregivers Stratified by Dementia Stage.
Table S3. Comparison of Measured Weight and Self-Reported Weight Distributions Among HRS Participants in 2016.

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