Evaluating the Economic Impact of CMS coverage Delays for New Alzheimer's Drugs

by

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Abstract[1]

Historically, Medicare has reimbursed drugs approved by the Food and Drug Administration (FDA) including drugs granted accelerated approval. In 2021, FDA granted accelerated approval to plaque-targeting treatments for Alzheimer's disease (AD), but the Centers for Medicare and Medicaid Services (CMS) imposed a coverage paradigm for this entire class that requires patients to be enrolled in studies in order to receive coverage. This white paper uses the existing evidence base to calibrate the economic impact of such CMS coverage delays on this class of FDA approved new drugs for AD. Using historical data on such CMS delays show that the vast majority are ongoing and last as long as 17 years. We find that these data indicate expected losses from the imposed delay of the AD class ranging between $13.1 billion to $545.6 billion. We find that part of these losses stems from increased private and public healthcare spending ranging from $6.8 billion to $284.5 billion. These findings have important implications for how the Congressional Budget Office (CBO) should assess the budget impacts of these CMS delays as they likely raise, as opposed to lower, spending.

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Section 1: Introduction

While the FDA has granted approval to new Alzheimer's disease (AD) drugs that are shown to slow disease progression, the Centers for Medicare and Medicaid Services (CMS) is requiring new procedures that delay broad coverage of these same AD drugs. This causes delays in coverage and increases disease progression before such coverage. This paper aims to evaluate the losses induced by such coverage delays and thus is informative for potential Congressional Budget Office (CBO) budget scoring of the CMS actions.

Specifically, CMS has required certain AD drugs to go through Coverage with Evidence Development (CED) procedures, in which only patients participating in clinical trials would be given coverage. Removal of this requirement has been formally requested by the Alzheimer's Association, the leading professional group for practicing neurologists, as well as more than 100 bipartisan members of the House and Senate (Alzheimer's Association, 2022b; American Academy of Neurology, 2023; LaHood, 2023). Moreover, a bipartisan group of attorneys general is also advocating for access to AD treatments for patients and demanding the reversal of CMS's decision (Alzheimer's Association, 2023b). Despite these calls for reconsideration and broad concerns about how this decision is predicted to harm innovation on AD treatments (Grogan, 2022), CMS denied the request to reopen reconsideration (CMS, 2023). Despite CMS's decision, the Veteran's Administration announced coverage for one the new AD treatment (Alzheimer's Association, 2023a).

In this policy brief, we estimate the impact induced by such delays of coverage in terms of patient health and increased health care spending due to further progression of AD. Relying on previous estimates of the value of innovation slowing down the progression of AD reported in Philipson and Ling (2022), we investigate the losses for CED delays using evidence on their past durations ranging up to 17 years. In the base case we assume that 50% more eligible patients are treated without a CED than with a CED and that this reduction in treatment prevents a one-year disease progression delay from mild to moderate AD. In this base case we find the losses to range from $13.1 billion to $545.6 billion dependent on the length of CED delays. Of these total losses we find that between $4.4 billion to $182.1 billion would be due to increased Medicare and Medicaid spending. Additionally, these are conservative estimates as CED recruitment and patient registries are slower than coverage ramp-ups in the market, further delaying patient access to the treatments with no coverage for the first few years.

This policy brief is structured as follows: Section 2 discusses the new CMS policies governing the CEDs of AD drugs; Section 3 calculates the losses induced by such CMS delays using historical evidence on the durations of CED; Section 4 estimates the cost increases the delays entails for Medicare and Medicaid; Section 5 discusses implications for CBO scoring; Section 6 provides the conclusion.

Section 2: The Nature of CMS CED Decision

In certain situations, CMS will decide to write a National Coverage Determination (NCD) for a particular item, service, or procedure instead of deferring coverage to Medicare Administrative Contractors and Medicare Advantage (MA) plans. The process of establishing an NCD usually takes 9-12 months and involves a public comment period. The Façade of Evidence report found that between 2012 and 2022, 336 NCDs were issued by CMS. Most of these NCDs apply to medical devices, but when CMS has issued NCDs for FDA-approved drugs, it almost always provides coverage in accordance with the drug's label (Alliance for Aging Research, 2023). In April 2022, CMS issued an NCD for the entire class of FDA-approved monoclonal antibodies targeting amyloid for Alzheimer's disease. The NCD CMS imposed on this class requires CED (CMS, 2022b; Alzheimer's Association, 2022b). Under this construct, only participants enrolled in certain trials can receive Medicare coverage for the treatments. Specifically, CMS's NCD for anti-amyloid Alzheimer's treatments establishes two pathways of CED requirements. For drugs granted accelerated approval, CMS requires beneficiaries to be enrolled in randomized controlled trials to receive coverage. Anti-amyloid therapies that receive traditional approval will only be covered for patients who are enrolled in a "CMS-approved prospective comparative study." Nonetheless, since CED patient registries can take a substantial amount of time, coverage is hardly provided to patients during the first few years. Several sources have stressed burdens of this requirement. According to research by the USC Schaeffer Center, such requirements would limit access to such treatments to patients in rural areas (Grogan, 2022). The Alzheimer's Association requested the removal of such requirements in the NCDs and pointed to the publication of new clinical trial evidence verifying the benefits of such treatments subsequent to CMS's decision (Alzheimer's Association, 2022b). It is the first time that CMS issued such requirements for the on-label use of an FDA-approved drug (UsAgainstAlzheimer's, 2022).

Currently, there are two approved products subject to the NCD: Biogen's Aducanumab and Eisai's Lecanemab. The NCD will also apply to any future approved products in this same class, including Donanemab, an anti-amyloid treatment for which Eli Lilly recently announced positive Phase III results (Lilly, 2023).

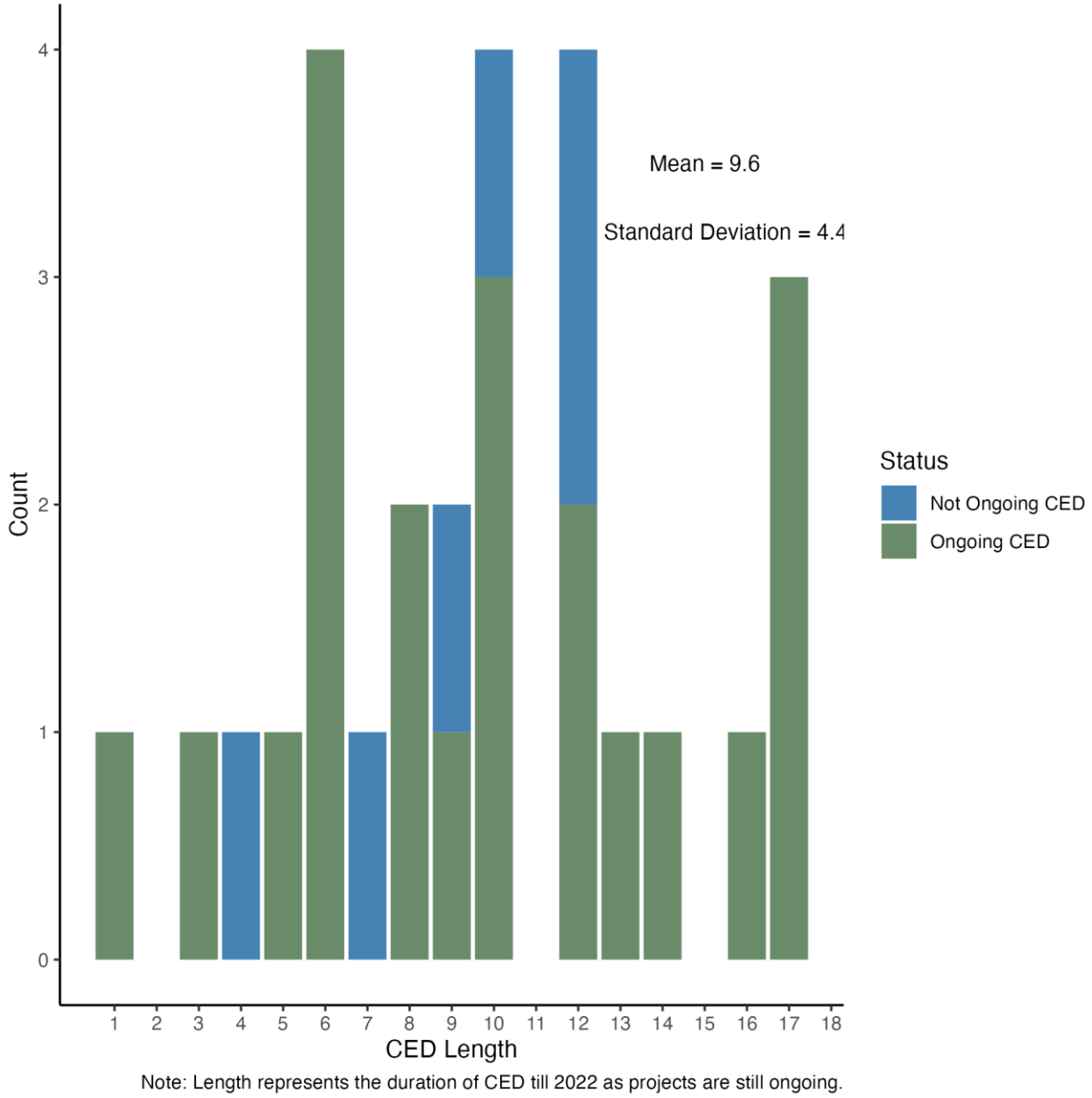
Section 3: The Impact on Patient Health from CMS CED Decision

In this section we estimate the aggregate value lost due to the delay to access of the drugs by CMS. Based on the value of delayed disease progression from Philipson and Ling (2022), we found the aggregate value lost to range from $6.5 billion to $545.6 billion across different additional coverage scenarios and the CED length up to 17 years at $150,000 Value of a Statistical Life Year (VSLY), a metric commonly used in scientific literature to describe how much a year in life is worth, assuming the drugs can delay disease progression for 1 year (Table 3). Among these, health outcomes from additional life years gained account for$2.3 billion to $195.6 billion (Table 4).

3.1 The Evidence on Length of CED Delays

As the AD drugs facing CED tend to delay the progression of the disease, the decision to postpone broad coverage of these treatments would essentially cause a “delay of the delay” in progression. While CED still provides limited coverage to only enrolled patients in trials or registries once traditional approval is obtained, much broader coverage and hence access to the treatments can be achieved if CED is not imposed. To estimate how the Alzheimer's NCD with CED may impact access, we looked at Zeitler et. al (2022) which reviews the past CED programs and reports a range of durations from 1 to 16 years. Using data reported in Zeitler et al. (2022), we plot the distribution of CED length in Figure 1. We present projects that are labeled “Converted to NCD without CED”, “coverage deferred to local contractors”, and “Limited NCD without CED” in blue (and ongoing CEDs in green) since they are technically not ongoing CMS CED programs, which can indicate historical lengths of ended CEDs. Since starting month of CED is not reported in Zeitler et al. (2022), our length estimates are obtained by deducting the CED year from 2022, resulting in slightly inconsistent results. The mean CED length is around 9.6 years, and the standard deviation is around 4.4. We use the 1 to 17 years range and 2023 as a baseline year in the following analysis. For 2023, denoted as baseline with 0 year of delay, we calculate the values lost to the cumulative eligible mild AD patients till 2022.

Figure 1 Distribution of Ongoing CED Length



Note: Length represents the duration of CED till 2022 for ongoing projects in green; Length represents the complete duration of CED for ended projects in blue

3.2 The Loss in Health Induced by Observed Delays in CEDs

To estimate how much observed delays due to CEDs postpone health gains we refer to Philipson and Ling (2022), which estimates the value of the delay in disease progression to mild AD patients (Table 1). For a one-year delay in disease progression from mild to moderate, cost-savings were $34,249 from market-based cost, and $7,882 from non-market cost in terms of informal care not transacted in the market. At varying levels of the VSLY indicated in the table, the health outcome improvement is valued from $15,700 to $76,930. At $150,000 VSLY, a standard threshold often used in policymaking, the value is $23,550, resulting in a total value of both cost savings and health of $65,681. As the disease progresses, treatment would become relatively less effective, increasing the cost of treatment due to disease progression, which is not captured by our assumption but is highly likely to happen by the delay in coverage; this renders our estimates conservative. The assumption of one-year disease progression delay implies the entire course of the disease will be delayed by one year for each patient, regardless of when the delay occurs (in what year after diagnosis).

Table 1 Estimated Value of 1-year Delayed Disease Progression for Mild AD patients

VSLY	Market-based Value	Non-market Value	QALY Improvement	Total Per Patient
		Mild AD		
$100,000	$34,249.0	$7,882.0	$15,700.0	$57,831.0
$150,000	$34,249.0	$7,882.0	$23,550.0	$65,681.0
$490,000	$34,249.0	$7,882.0	$76,930.0	$119,061.0

Source: Philipson and Ling (2022).

3.2.1 Survival Function within Mild AD

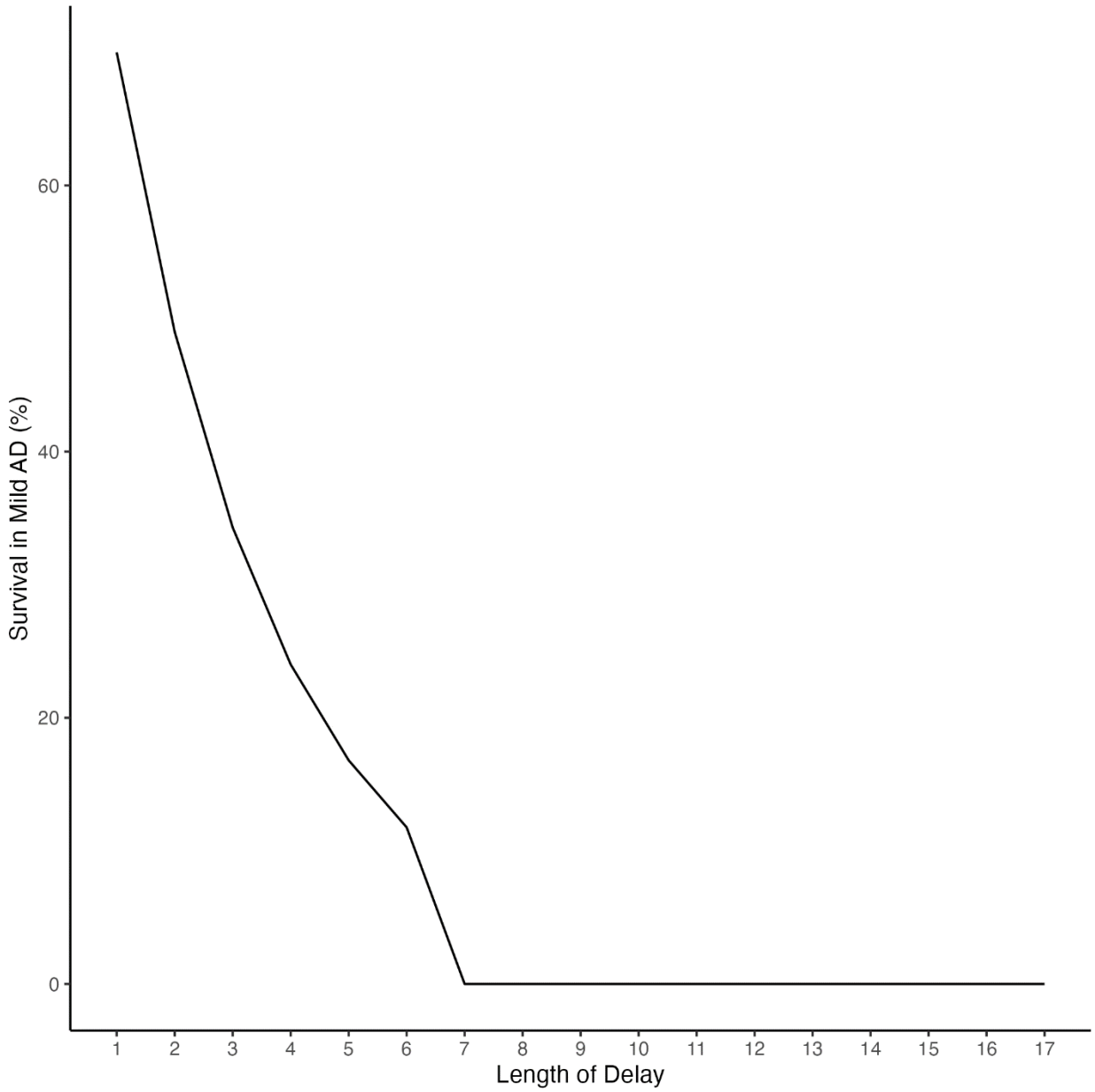
As each patient only experiences the transition from mild AD to moderate AD once, we consider survival functions within mild AD, defined as the percentage of remaining mild AD patients after certain periods of time. Vermunt et al. (2019) reports a duration range of 3.2 to 5.7 years in mild AD, where we round the upper bound and assume the course of mild AD can last as long as 6 years. After 6 years, we assume the patients either enter moderate AD or become deceased. Across several studies the literature reports constant annual transition probabilities over 30% (Potashman et al., 2021; ICER, 2021; Neumann et al., 2001). We assume the annual transition probability from mild to moderate AD to be 30% as a lower bound. Note both the maximum 6 years in mild AD and the 30% transition probability assumptions lead us to conservative estimates, as both assume a slower transition to moderate AD, and hence lower values lost from patients becoming ineligible for treatment.

The equation for the survival function is in equation 1, and a plot of such survival can be seen in Figure 2.

Equation 1 Survival Function in Mild AD

$$S(t) = (1 - annual\ transition\ probability)^t \mathbb{1}(t \leq maximum\ years\ in\ mild\ AD)$$

Figure 2 Survival Function across Length of CED Delay



Note: Assuming a constant annual transition probability of 30% from mild AD to moderate AD; assuming all mild AD patients leave the mild AD stage after 6 years

3.2.2 Values Lost across CED Lengths

A lengthy CED process precludes some individuals from taking advantage of new technology that delays the transition from the mild to moderate state. On an individual level, this occurs for people who transition before the CED is complete. For a given calendar year and set of individuals entering into mild AD that year, this occurs for those who transition before the calendar year of

the CED is completed. These losses from delayed coverage induce large aggregate losses due to the significant prevalence of AD.

Using the same method in estimating the mild AD population as in Philipson and Ling (2022), the estimated cumulative number of mild AD patients eligible for taking up the treatments from 2023 to 2040 (17 years from 2023; excluding 2023) can be seen in Table 2. For 2023 we estimate the value lost for the cumulative number of mild AD patients by 2022. Combining projected population by age groups, the prevalence of MCI across age groups, and transition rates between MCI and mild AD, we estimate there to be 25.5 million mild AD patients by 2040[2]. Details of the method for this estimation are provided in Philipson and Ling (2022). After obtaining the estimated population of mild AD patients, we multiply the population by the prevalence of amyloid abnormality in mild AD (85%; Jansen et al. (2022)) to arrive at the size of patients to whom the treatments can be applied, and further multiply such eligible population by 25% and 50% as the two scenarios in consideration. Within the 25.5 million mild AD patients, we estimate 21.6 million would exhibit amyloid abnormality. These two scenarios represent two hypothetical cases in which coverage without CED would increase by 25% and 50% on the margin, in addition to the coverage provided within CED, specifically evaluating the additional value of coverage that would have been gained if there is no CED procedure. We assume that patients will take up the treatments once provided coverage, hence we treat the scenarios equivalent to 25% and 50% additional take-up rates. Note we use the estimated mild AD patients as the baseline population – different baseline populations would simply yield proportional results.

Table 2 Estimated Cumulative Population of Mild AD Patients with Amyloid Abnormality by Year (Millions)

Years of Coverage Delay	Year	Cumulative Mild AD Population	25% Additional Coverage	50% Additional Coverage
0	2023	3.7	0.9	1.8
1	2024	4.6	1.1	2.3
2	2025	5.5	1.4	2.8
3	2026	6.5	1.6	3.2
4	2027	7.5	1.9	3.7
5	2028	8.5	2.1	4.2
6	2029	9.5	2.4	4.8
7	2030	10.6	2.6	5.3
8	2031	11.6	2.9	5.8
9	2032	12.7	3.2	6.3
10	2033	13.8	3.4	6.9
11	2034	14.9	3.7	7.4
12	2035	16.0	4.0	8.0
13	2036	17.1	4.3	8.6
14	2037	18.2	4.6	9.1
15	2038	19.4	4.8	9.7
16	2039	20.5	5.1	10.3
17	2040	21.6	5.4	10.8

Considering the impact of drugs enabling a 1-year delay on transitioning, the aggregate value lost by the delay in coverage is presented in Table 3. We estimate the aggregate value as the sum of two components: the delay for existent patients in 2022, and the delay for newly transitioned

[2] This number is not comparable to the more than 2000 cases from mild to moderate AD reported in Alzheimer's Association (2022b) since we look at transitions from Mild Cognitive Impairment (MCI) to mild AD; if we were to perform a similar analysis, our estimates are around 3000 transitions per day from MCI to mild AD.

patients each year after that, in which the lengths of delay are dependent on the specific year when they transition into the current disease stage (Equation 2).

With the newly transitioned patients, we define the cohorts by year, and apply the survival function mentioned above to calculate the value lost from the reduction in eligible patients for each length of CED delay, which can be interpreted as "what percentage of mild AD patients transitions due to the delay". For the cumulative mild AD patients till 2022, we apply the same logic with the assumption that this population is distributed uniformly across the mild AD durations of 0 to 6 years and consider each cohort separately.

Note in both calculating values from newly transitioned patients and cumulative patients, the survival functions give the reduction in eligible patients by comparing the survived patients after CED delay versus their current years in the mild AD stages. For example, for a CED that ends in 2025, we consider the loss in value of a 3-year delay of treatment for the 3.3 million mild AD cohort already with amyloid abnormality up to 2022, a 2-year delay for newly diagnosed mild cases in 2023, and a 1-year delay for those diagnosed in 2024.

Using this method, we find that for mild AD patients, at 50% additional coverage, the value ranges from $13.1 billion to $545.6 billion for delays from 0 year to 17 years. At 25% additional coverage and hence take-up, the value ranges from $6.5 billion to $272.8 billion. Other lengths of disease progression delay would lead to proportional results.

Equation 2 Value Lost Calculation

$$Value = \sum_{y=2023}^{delay\ end\ year} incidence_y \times takeup \times value\ per\ patient \times (1 - S(delay\ end\ year - y))$$
$$+ \sum_{current\ year\ of\ disease=0}^{6} \frac{existent\ patients_{2022}}{7} \times takeup \times value\ per\ patient$$
$$\times (S(current\ year\ of\ disease) - S(delay\ end\ year - 2022 + current\ year\ of\ disease))$$

Table 3 Aggregate Value Lost Due to Delay in Coverage by Length of Delay ($ billion)

Years of Coverage Delay	Year	25% Additional Coverage	50% Additional Coverage
0	2023	$6.5	$13.1
1	2024	$15.5	$31.0
2	2025	$26.2	$52.5
3	2026	$38.4	$76.8
4	2027	$51.7	$103.3
5	2028	$65.8	$131.6
6	2029	$80.6	$161.2
7	2030	$96.7	$193.5
8	2031	$113.2	$226.4
9	2032	$130.0	$260.1
10	2033	$147.2	$294.3
11	2034	$164.5	$329.1

12	2035	$182.1	$364.2
13	2036	$199.9	$399.8
14	2037	$217.9	$435.8
15	2038	$236.1	$472.1
16	2039	$254.4	$508.7
17	2040	$272.8	$545.6

Note: 1-year delay in disease progression; $150,000 VSLY

Specifically, we estimate the value lost from health outcomes in the same method as above (Table 4). For mild AD patients with amyloid abnormality at 50% additional coverage, the lost health outcome improvement is valued from $4.7 billion to $195.6 billion at $150,000 VSLY. With 25% additional coverage, the range becomes $2.4 billion to $97.8 billion.

Table 4 Aggregate Value Lost from Health Outcome Improvement Due to Delay in Coverage by Length of Delay ($ billion)

Years of Coverage Delay	Year	25% Additional Coverage	50% Additional Coverage
0	2023	$2.3	$4.7
1	2024	$5.5	$11.1
2	2025	$9.4	$18.8
3	2026	$13.8	$27.5
4	2027	$18.5	$37.0
5	2028	$23.6	$47.2
6	2029	$28.9	$57.8
7	2030	$34.7	$69.4
8	2031	$40.6	$81.2
9	2032	$46.6	$93.3
10	2033	$52.8	$105.5
11	2034	$59.0	$118.0
12	2035	$65.3	$130.6
13	2036	$71.7	$143.4
14	2037	$78.1	$156.3
15	2038	$84.6	$169.3
16	2039	$91.2	$182.4
17	2040	$97.8	$195.6

Note: 1-year delay in disease progression; $150,000 VSLY; Health outcome improvement only

To present the compositions of the values lost, assuming an additional 50% of mild AD patients with amyloid abnormality have coverage of the AD drugs, and the drugs are able to delay disease progression by 1 year, at $150,000 VSLY, we estimate the aggregate value lost to range from $13.1 billion to $545.6 billion for CED ranging from 0 to 17 years (Table 5; Figure 3). Specifically, $6.8 billion to $284.5 billion would be lost from market-based cost, $1.6 billion to $65.5 billion from non-market costs, and $4.7 billion to $195.6 billion from health outcome improvement.

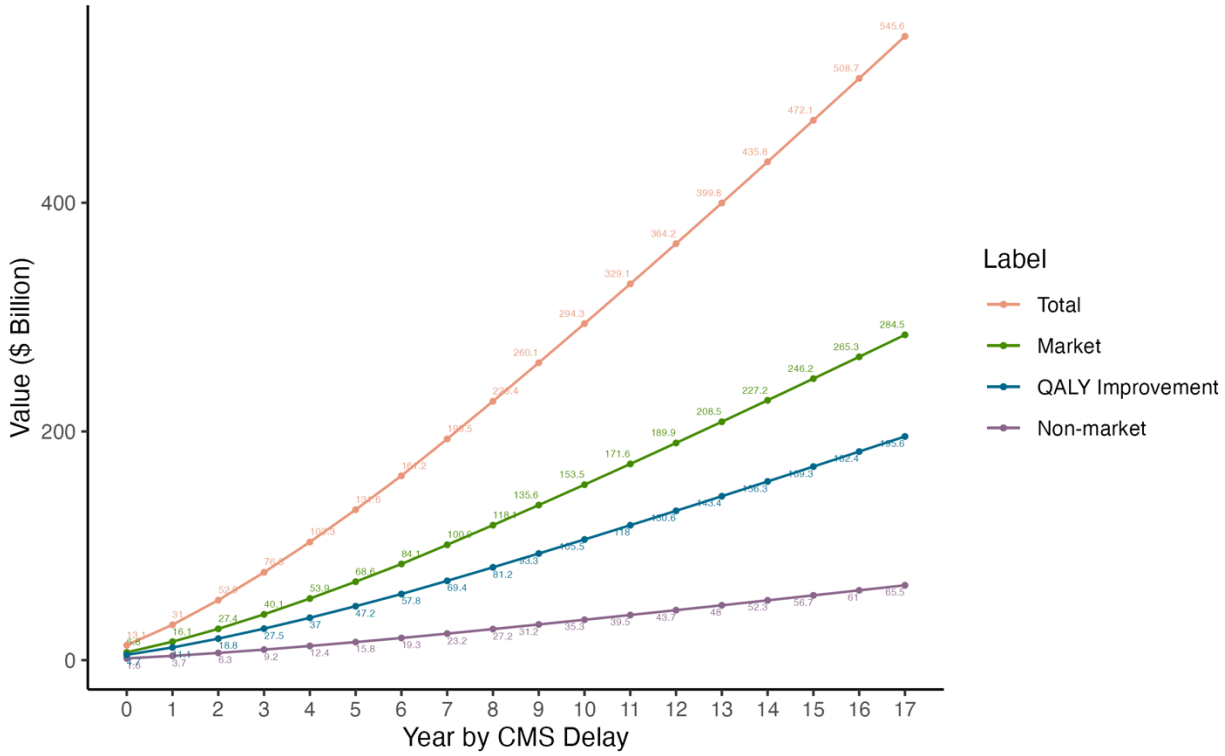
Table 5 Aggregate Value Lost Due to Delay in Coverage by Length of Delay ($ billion)

Years of Coverage Delay	Year	Market-based Value	Non-market Value	QALY Improvement	Aggregate Value
0	2023	$6.8	$1.6	$4.7	$13.1
1	2024	$16.1	$3.7	$11.1	$31.0
2	2025	$27.4	$6.3	$18.8	$52.5
3	2026	$40.1	$9.2	$27.5	$76.8
4	2027	$53.9	$12.4	$37.0	$103.3
5	2028	$68.6	$15.8	$47.2	$131.6
6	2029	$84.1	$19.3	$57.8	$161.2
7	2030	$100.9	$23.2	$69.4	$193.5

8	2031	$118.1	$27.2	$81.2	$226.4
9	2032	$135.6	$31.2	$93.3	$260.1
10	2033	$153.5	$35.3	$105.5	$294.3
11	2034	$171.6	$39.5	$118.0	$329.1
12	2035	$189.9	$43.7	$130.6	$364.2
13	2036	$208.5	$48.0	$143.4	$399.8
14	2037	$227.2	$52.3	$156.3	$435.8
15	2038	$246.2	$56.7	$169.3	$472.1
16	2039	$265.3	$61.0	$182.4	$508.7
17	2040	$284.5	$65.5	$195.6	$545.6

Note: 1-year delay in disease progression; $150,000 VSLY; 50% additional coverage

Figure 3 Aggregate Value Lost Due to Delay in Coverage by Length of Delay ($ billion)



Note: 1-year delay in disease progression; $150,000 VSLY; 50% additional coverage; Market: market-based care, non-market: non-market-based care

The non-linearity within Figure 3 can be brought by a few factors: non-linear estimation of future mild AD patient population for each cohort, the survival function involving exponentials, and the calculation methods assigning different waiting years to treatment for each cohort.

Section 4: The impact of the delayed CMS coverage on Medicare and Medicaid spending

The previous cost assessments concerned total healthcare costs. This section considers the impact on publicly financed Medicare and Medicaid spending. According to Alzheimer's Association (2022a), Medicare accounts for 45% of the market cost of dementia care, while Medicaid takes on 19%. We estimate the impact on Medicare and Medicaid in the same method as above but focusing only on federal and state budget costs excluding informal care. Considering the scenario with 50% additional coverage of AD drugs delaying disease progression by 1 year, the value lost impacting

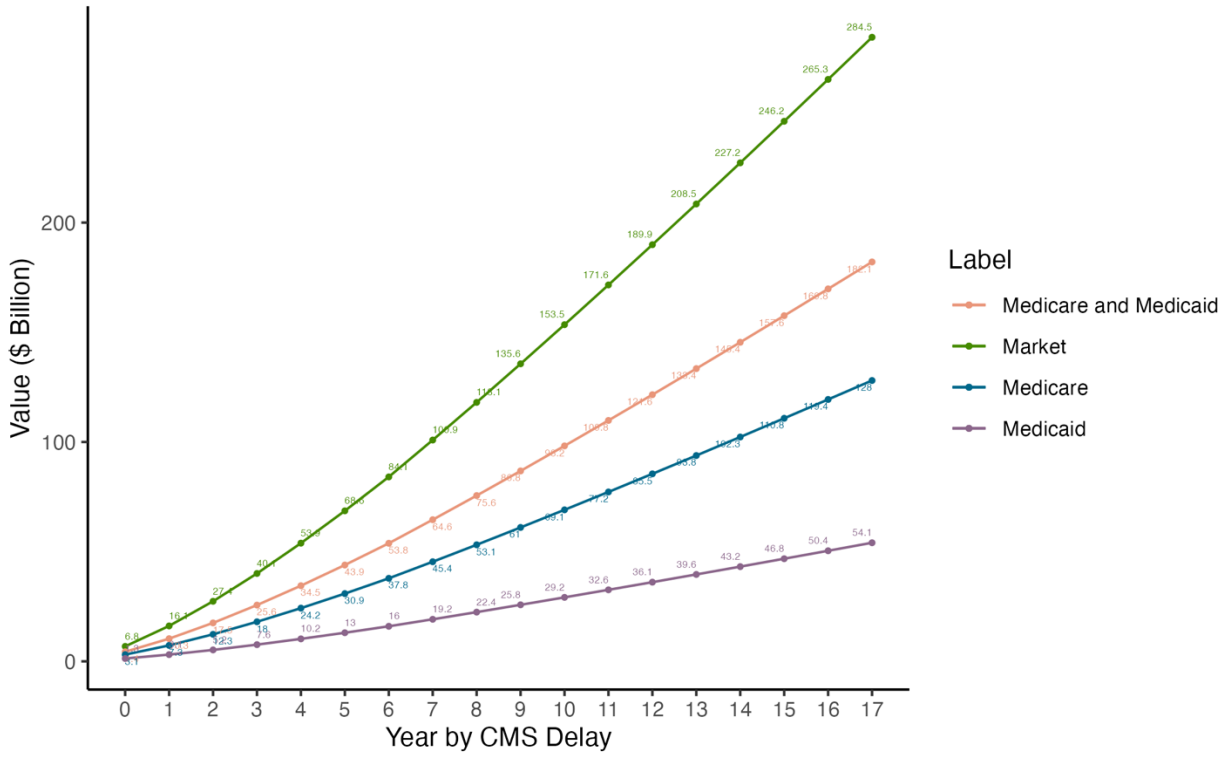
Medicare and Medicaid can be seen in Table 7. Across CED lengths of delay, the trends can be seen in Figure 3. For Medicare, the value lost ranges from $3.1 billion to $128 billion for CMS delay of 0 to 17 years, and for Medicaid the range is $1.3 billion to $54.1 billion. Combining Medicare and Medicaid, the value lost to public insurance would range from $4.4 billion to $182.1 billion.

Table 7 Aggregate Value Lost to Medicare and Medicaid ($ Billion)

Years of Coverage Delay	Year	Market-based Value	Medicare	Medicaid	Medicare and Medicaid
0	2023	$6.8	$3.1	$1.3	$4.4
1	2024	$16.1	$7.3	$3.1	$10.3
2	2025	$27.4	$12.3	$5.2	$17.5
3	2026	$40.1	$18.0	$7.6	$25.6
4	2027	$53.9	$24.2	$10.2	$34.5
5	2028	$68.6	$30.9	$13.0	$43.9
6	2029	$84.1	$37.8	$16.0	$53.8
7	2030	$100.9	$45.4	$19.2	$64.6
8	2031	$118.1	$53.1	$22.4	$75.6
9	2032	$135.6	$61.0	$25.8	$86.8
10	2033	$153.5	$69.1	$29.2	$98.2
11	2034	$171.6	$77.2	$32.6	$109.8
12	2035	$189.9	$85.5	$36.1	$121.6
13	2036	$208.5	$93.8	$39.6	$133.4
14	2037	$227.2	$102.3	$43.2	$145.4
15	2038	$246.2	$110.8	$46.8	$157.6
16	2039	$265.3	$119.4	$50.4	$169.8
17	2040	$284.5	$128.0	$54.1	$182.1

Note: 1-year delay in disease progression; $150,000 VSLY; 50% additional coverage

Figure 3 Aggregate Value Lost Due to Delay in Coverage by Length of Delay for Medicare and Medicaid ($ billion)



Note: 1-year delay in disease progression; $150,000 VSLY; 50% additional coverage; Market: market-based care

Section 5: Implications for Accurate CBO Scoring of CMS Actions

Though budget concerns should not directly enter CMS's decision, the budgetary effect of CMS coverage for such AD drugs could be taken into overall consideration of policymakers. However, such concerns, highly likely stemming from the CBO scoring of coverage, come from the mandated responsibility of CBO to only consider budgetary effect rather than the full value and benefits of policies. In addition, the Office of Actuary at CMS also projects spending on potential AD drugs as it impacts Medicare premiums. As discussed in the earlier sections, though delaying coverage of AD drugs may reduce spending on these specific drugs alone, it raises total health care spending and is also forfeiting substantial health gains that could have been realized from improved health and treatment savings with slower disease progression. Thus, taking the aggregate value into consideration, delaying AD drug coverage may eventually lead to net cost rather than gain, indicating the need for a more holistic valuation approach when it comes to scoring for CMS actions.

Section 6: Conclusion

CMS is requiring new procedures that delay coverage of FDA-approved drugs aimed at slowing the progression of Alzheimer's disease. Historically, Medicare has covered the cost of FDA-approved drugs for its beneficiaries, including drugs granted accelerated approval. However,

CMS-imposed requirements on CED procedures for the entire class of such AD drugs, only providing coverage for patients enrolled in CED trials. As such CEDs usually have lengthy durations, causing delays in broader coverage and leaving many patients with faster disease progression before such coverage.

This white paper assessed the values forgone by CMS's action to delay coverage for such AD drugs generating values regarding both patient health and cost of care. Using historical data on such CMS delays, we found that the healthcare system would induce losses of between $13.1 billion to $545.6 billion for the range of historically observed coverage delays at $150,000 VSLY, with 50% additional coverage and 1-year disease progression delay by the drugs. Under the same assumptions, private and public health care spending would rise by $6.8 billion to $284.5 billion –$4.4 billion to $182.1 billion in losses would be accounted for by Medicare and Medicaid. This raises important implications for how CBO should assess the budget impacts of these CMS measures as they raise, as opposed to lower, spending.

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