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RESEARCH ARTICLE

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Occurrence of mosaic Down syndrome and prevalence of co-occurring conditions in Medicaid enrolled adults, 2016–2019

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Abstract

Background: Mosaic Down syndrome is a triplication of chromosome 21 in some but not all cells. Little is known about the epidemiology of mosaic Down syndrome. We described prevalence of mosaic Down syndrome and the co-occurrence of common chronic conditions in 94,533 Medicaid enrolled adults with any Down syndrome enrolled from 2016 to 2019.

Methods: We identified mosaic Down syndrome using the International Classification of Diseases and Related Health Problems, tenth edition code for mosaic Down syndrome and compared to those with nonmosaic Down syndrome codes. We identified chronic conditions using established algorithms and compared prevalence by mosaicism.

Results: In total, 1966 (2.08%) had claims for mosaic Down syndrome. Mosaicism did not differ by sex or race/ethnicity with similar age distributions. Individuals with mosaicism were more likely to present with autism (13.9% vs. 9.6%) and attention deficit hyperactivity disorder (17.7% vs. 14.0%) compared to individuals without mosaicism. In total, 22.3% of those with mosaic Down syndrome and 21.5% of those without mosaicism had claims for Alzheimer's dementia (Prevalence difference: 0.8; 95% Confidence interval: −1.0, 2.8). The mosaic group had 1.19 times the hazard of Alzheimer's dementia compared to the nonmosaic group (95% CI: 1.0, 1.3).

Discussion: Mosaicism may be associated with a higher susceptibility to certain neurodevelopmental and neurodegenerative conditions, including Alzheimer's dementia. Our findings challenge previous assumptions about its protective effects in Down syndrome. Further research is necessary to explore these associations in greater depth.

KEYWORDS
Alzheimer's disease, Down syndrome, epidemiology, Medicaid, mosaicism

1 | INTRODUCTION

Down syndrome is a condition defined by the triplication of chromosome 21. In the majority of cases this triplication occurs within all cell lines and is evidenced in all tissue types; however, some people with Down syndrome exhibit mosiaicism (Papavassiliou et al., 2015). Mosaicism is the occurrence of two or more genetically distinct cell lines coming from the same zygote (Martínez-Glez et al., 2020). While having mosaic Down syndrome is a binary outcome, the percent of cells that are mosaic is continuous with variation within individuals (Papavassiliou et al., 2009). Conventional chromosomal testing, microarray tests, genotyping, and florescence in situ hybridization testing are commonly used to identify mosaicism from blood, skin, and buccal swab samples; however sensitivity of detection varies by method. Standard karyotyping for Down syndrome uses a level of 450 bands and can reliably detect mosaicism when >26% of cells are mosaic (Hook, 1977). Nevertheless, by evaluating more cells for lack of triplication, mosaicism can be identified with 1% of cells being mosaic.

Mosaic Down syndrome can present like nonmosaic Down syndrome (e.g. intellectual disability, morphological features) or with no evidence of Down syndrome traits. Mosaicism can only be uncovered through genetic testing (Papavassiliou et al., 2015). For health conditions associated with Down syndrome, there is some evidence of the increased risk of leukemia among individuals with mosaicism compared to individuals without mosaicism (Simon et al., 1987). Alzheimer's dementia presents earlier and more often in adults with Down syndrome compared to neurotypical peers (Rubenstein et al., 2020) due to the amyloid precursor protein being located on chromosome 21 (Fortea et al., 2021). Individuals with mosaicism still illustrate high risk of Alzheimer's dementia, but it has been hypothesized they may have less risk compared to individuals without mosaicism because of the decreased amount of the triplicated chromosome (Potter, 2016).

Given the important health questions surrounding mosaic Down syndrome, epidemiolocal research is warranted. However, population research has been challenging because of the rarity of mosaic Down syndrome (prevalence of Down syndrome is 1/800 live births (de Graaf et al., 2017) and less than 5% of those will be mosaic). A sample of mosaic Down syndrome with adequate power requires a very large population data set.

The International Classification of Diseases and Related Health Problems, tenth edition (ICD-10) (World Health Organization, 2004), was implemented into the US healthcare system in 2015. The ICD-10 is a comprehensive categorization of disease and health conditions used to track health and facilitate billing. ICD-10 codes have been extensively used across medical conditions for health- and health services research (Khera et al., 2018). The codes reflect conditions identified by providers and are affected by trends in coding practice, misclassification, and misidentification. When verified with electronic health records, developmental disabilities are reliably and accurately identified via ICD-9 and ICD-10 codes (McDermott et al., 2018; Straub et al., 2021). However, mosaic Down syndrome has not been evaluated. ICD-10 included a code for mosaic Down syndrome, enabling passive assessment of the occurrence of mosaicism in large health systems.

Medicaid is a public health insurance provider for low income and disabled adults in the United States, serving >120,000 adults with Down syndrome (Rubenstein et al., 2023). The large population of adults with Down syndrome in conjunction with the implementation of ICD-10 enabled us to examine mosaic Down syndrome at the population level. Our objective was to use a full Medicaid data set to identify documented mosaicism in adults with Down syndrome and compare chronic conditions (including Alzheimer's dementia) between those with and without mosaicism.

2 | METHODS

2.1 | Data source

We used data from the Down Syndrome Toward Optimal Trajectories and Health Equity using Medicaid Analytic eXtract (DS-TO-THE-MAX) project. DS-TO-THE-MAX is a cohort of approximately 5,000,000 Medicaid enrollees which includes all adults >18 with claims for Down syndrome from 2011 to 2019. Data include beneficiary demographics, all inpatient hospitalization, and other services claims and encounters, prescription drug claims, and long-term service care use.

2.2 | Inclusion criteria

We utilized data from 2011 to 2019 to identify chronic conditions, but limited our analyses to individuals diagnosed with Down syndrome using ICD-10 codes that had also claims between 2016 and 2019, in order to accurately identify cases of mosaicism. We did not assess 2015 since ICD-10 was not fully implemented.

2.3 | Down syndrome type

We classified Down syndrome type by ICD-10 code. Mosaicism was identified in claims with code Q90.1 (Down syndrome, mosaicism). Triplication included Q90.0 (Down syndrome, nonmosaic); Q90 (Down syndrome without specification) without claims for Q90.1, or Q90.9 (Down syndrome, unspecified) without claims for Q90.1. If one had claims for Q90.1 and Q90.0 we would classify that individual as mosaic. For this study we include those with translocation (Q90.2, one of the three copies of chromosome 21 attached to another) in the nonmosaic group because of the consistency with full triplication of chromosome 21 and phenotype (Zhu et al., 2013).

2.4 | Chronic conditions

Chronic conditions were identified from the Chronic Condition Warehouse algorithms for Medicare data. Algorithms are for specific conditions and have been widely used and validated (Center for Medicare

and Medicaid Services, 2021). We selected conditions that are prevalent in Down syndrome and/or related to key phenotypic features of Down syndrome. We assessed: anemia, autism spectrum disorder, attention deficit hyperactivity disorder, anxiety, bipolar disorder, chronic obstructive pulmonary disease, depressive disorders, epilepsy, heart failure, hyperlipidemia, hypothyroidism, hypertension, chronic kidney disease, leukemia and lymphomas, obesity, and deafness. We used all years of data (2011–2019) and evaluated diagnoses in inpatient, outpatient, and long-term care claims. We evaluated these chronic conditions as binary outcomes.

2.5 | Alzheimer's dementia

We examined Alzheimer's dementia using the Chronic Condition Warehouse algorithms (Center for Medicare and Medicaid Services, 2021). Because of the consistency of enrollment in Medicaid and high service use, we used a 1-year washout period rather than the three in the algorithm. The washout period for incident dementia was 1 year without dementia claims to ensure that the first claim in our data is incident.

2.6 | Other covariates

Demographic characteristics were from the Medicaid demographic enrollment file. These variables included sex, age, region, dual enrollment (enrolled in Medicare and Medicaid concurrently), source of Medicaid eligibility (disability and/or income) and death. For race and ethnicity variables, ca. 16% of data were missing. We used multiple imputation to account for the missing data. Our imputation approach is described elsewhere (Rubenstein et al., 2023).

2.7 | Analysis

We described demographic characteristics and compared distribution of person time and person years by mosaic status using a Kolmogorov–Smirnoff test. We calculated percentage with each chronic condition for mosaic and nonmosaic Down syndrome, the percentage point difference between the groups, and corresponding confidence interval around the point difference. We assumed that chronic conditions were static, that person time enrolled did not impact occurrence, and that age differences between the groups were minimal. We attempted to examine these assumptions by doing a sensitivity analyses estimating prevalence differences using an identity-Poisson model adjusted for age and person time. Those models did not converge so we calculated adjusted prevalence ratios using a log-Poisson model.

We plotted Kaplan–Meier survival curves by mosaic status for time to Alzheimer's dementia and compared the curves using a log-rank test. We used age as our time scale. We ran an unadjusted Cox proportional hazard model and an adjusted model that accounted for differences in enrollment length and age comparing incidence of Alzheimer's dementia for mosaic and nonmosaic Down syndrome.

3 | RESULTS

There were 94,533 adults with Down syndrome enrolled in Medicaid at some point between 2016 and 2019. Of those, 1966 (2.08%) had claims for mosaic Down syndrome. Of those with claims for mosaic Down syndrome, 143 also had claims for translocation (7.3%). All had at least one claim for triplication nonmosaic Down syndrome (Q90.0; 29.1%) or Down syndrome unspecified (Q90.9; 91.8%). Among individuals with mosaicism, 51.2% were male and 74.7% where white (Table 1). For individuals without mosaicism, 52.6% were male and 74.5% were white. By region, 31.5% of Individuals with mosaicism lived in the Midwest compared to 22.7% of individuals without mosaicism. More than three quarters of each group were eligible for Medicaid via disability and 56.9% of individuals with mosaicism and 61.3% of individuals without mosaicism were dual eligible with Medicare. Person time (2011–2019) and person time during ICD-10 (2016–2019) had different distributions between groups. There was a mean total person time difference of 3.4 more months of enrollment for individuals with mosaicism compared to individuals without mosaicism. Individuals without mosaicism had 1.1 months less of ICD-10 person time compared to individuals with mosaicism.

Individuals with mosaicism and individuals without mosaicism had significantly different distributions for age at study entry based on the Kolmogorov–Smirnoff test (Figure 1). Mean age at study entry for individuals with mosaicism was 35.2 years compared to 33.6 in individuals without mosaicism. By age category in years 2016–2019 (Table 2) a greater percentage of individuals with mosaicism were 18–25 in each year. In 2016–2018 a higher proportion of individuals with mosaicism were 55–59 compared to individuals without mosaicism. In 2019, a higher proportion of individuals with mosaicism were 60–64 compared to individuals without mosaicism.

The most common chronic conditions in both groups were hypothyroidism, hyperlipidemia, obesity, and anxiety. Conditions that were more common in the mosaic group compared to the nonmosaic group were anxiety, autism spectrum disorder, attention deficit hyperactivity disorder, and epilepsy (Table 3); although the biggest difference was only 3.7% points. There were no conditions that were significantly higher in the nonmosaic than in the mosaic group. In sensitivity analyses adjusting for age and person time using a Poisson model, there were no differences between adjusted and unadjusted ratios (Table S1).

In total, 22.3% of those with mosaic Down syndrome and 21.5% of those without mosaicism had claims for Alzheimer's dementia (Prevalence difference: 0.8; 95% Confidence interval: −1.0, 2.8). Time to dementia curves by age at study entry are presented in Figures 2a–d. There were no differences in the curves for mosaic and nonmosaic groups in the 25–34 and 55–64 age at study entry ranges. Failure

TABLE 1 Demographics of adults with mosaic and nonmosaic down syndrome enrolled in Medicaid between 2016 and 2019.

	Mosaic		Nonmosaic	
	N = 1966	%	*N* = 92,567	%
Sex				
Male	1007	51.2	48,646	52.6
Female	959	48.8	43,821	47.3
Race				
White NH	1428	74.7	66,778	74.5
Black	273	14.3	12,178	13.6
PI	26	1.4	946	1.1
Asian	61	3.2	3152	3.5
Mixed	110	5.8	5802	6.5
Missing	54		2967	
Ethnicity				
Hispanic	300	15.7	15,834	17.7
Non-Hispanic	1612	84.3	73,766	82.3
Missing	54		2967	
Region				
Midwest	619	31.5	21,050	22.7
Northeast	348	17.7	20,846	22.5
South	687	34.9	29,058	31.4
U.S. Territories	12	0.6	602	0.7
West	300	15.3	21,009	22.7
Death				
No	1780	90.5	82,335	89.9
Yes	186	9.5	10,232	11.1
Eligibility[a]				
Disability	1463	74.4	73,456	79.4
Income	1151	58.5	49,849	53.9
Dual	1118	56.9	56,729	61.3
Person months				
Mean, SD	80.7	31.1	84.8	28.7
Median, IQR	96.0	48	100.0	42
ICD-10 Person days				
Mean, SD	44.4	8.9	43.3	10.6
Median, IQR	48.0	0	48.0	1.3
Year[b]				
2016	1697	1.73	84,113	90.9
2017	1759	1.79	84,155	90.9
2018	1811	1.84	84,344	91.1
2019	1805	1.84	83,083	89.8

Abbreviations: ICD-10, International Classification of Diseases and Related Health Problems, tenth edition; IQR, inter quartile range; NH, non-Hispanic; PI, pacific Islander; SD, standard deviation.
[a]Not exclusive.
[b]Percentages are row percentages.

probability was significantly greater in the mosaic group compared to the nonmosaic group for the 35–44 and 45–54 age groups. Results from the unadjusted Cox proportional hazard model showed the mosaic group having 1.15 the hazard of dementia compared to nonmosaic (95% CI: 1.0, 1.3) and an adjusted hazard ratio of 1.19 (95% CI: 1.04, 1.31).

4 | DISCUSSION

Mosaic Down syndrome is an important area of research because of the potential implications of the partial trisomy of chromosome 21. With the implementation of ICD-10 in 2015, we are now able to assess mosaicism in a near full population adult sample of Down syndrome. Our findings illustrate the utility of claims data to assess epidemiology of mosaicism and co-occurring health conditions, although methodological refinement is still needed.

We found that over the four years, 2.08% of individuals with in our sample had claims mosaicism in Medicaid which is at the lower range of prevalence estimates in the literature (Papavassiliou et al., 2015). Our estimate is conditional on Medicaid enrollment and clinician identification, which may exclude those that do not present with clinical features of Down syndrome or do not have genetic testing (Papavassiliou et al., 2015). Devlin et al. in 2004 used a complete registry in Northern Ireland and found only 37.5% of mosaicism was identified clinically, with most being identified via karyotyping (Devlin & Morrison, 2004). While genetic testing is more common now for identifying genetic abnormalities (Carbone et al., 2020), Medicaid enrollment is still conditional on low income and/or disability. Intellectual disability is a phenotypic part of nonmosaic Down syndrome, but some with mosaic Down syndrome may not have intellectual disability (de A Moreira et al., 2000; Nuebling et al., 2021) and not qualify for Medicaid which would therefore not be captured in our dataset. Further, the coding of ICD-10 mosaicism may take longer than four years to be fully utilized (Khera et al., 2018), so optimal identification of mosaic Down syndrome may not be in practice. Therefore, our results likely reflect an underestimation of mosaic prevalence.

There is evidence that mosaicism increases with age, where people with Down syndrome, both classified as mosaic and nonmosaic, have a higher percentage of mosaic cells in older adulthood compared to younger ages (Jenkins et al., 1997). However, in our data we saw qualitatively similar age distributions, although there was a small uptick in older adults with mosaicism compared to nonmosaicism in 2019. Genetic karyotype and mosaicism are often measured at one point in time-prenatally or shortly after birth (Papavassiliou et al., 2015), with clinical rekaryotyping being uncommon. Therefore, our data may largely reflect survival rather than incident mosaicism. Zhu et al. found decreased mortality rate in individuals with mosaicism compared to individuals without mosaicism in a Danish national cohort (Zhu et al., 2013). We saw regional differences in mosaicism, which was unexpected. There may be different patterns in uptake of the ICD-10 code. Further investigation is needed to understand potential misclassification.

Chronic conditions were qualitatively similar for mosaic and nonmosaic Down syndrome even without adjustment for age or time enrolled in the study. Differences were in psychological and

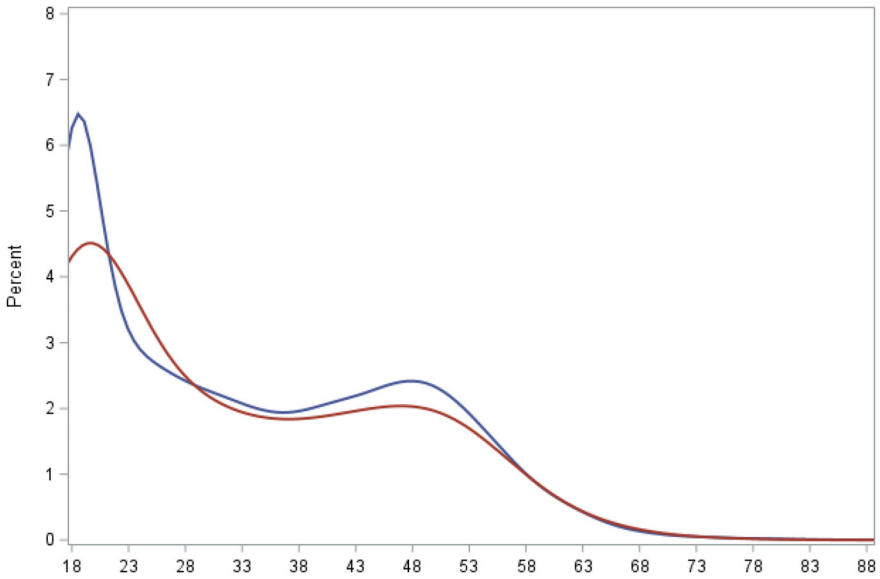

FIGURE 1 Age distribution of adults with mosaic and nonmosaic Down syndrome at study entry enrolled in Medicaid. Age at study entry is first year of claims in the data between 2011 and 2019.

TABLE 2 Age categories and summary statistics for years 2016–2019 by Mosaic status.

	2016		2017		2018		2019	
Age (years)	%mosaic	%nonmosaic	%mosaic	%nonmosaic	%mosaic	%nonmosaic	%mosaic	%nonmosaic
18–24	24.9	20.8	25.0	20.7	26.6	20.5	24.0	18.1
25–30	13.1	13.5	13.9	14.1	13.8	14.7	14.9	15.4
30–34	8.3	8.7	8.6	9.0	8.8	9.2	9.6	9.9
35–39	8.7	9.3	8.6	9.7	8.4	9.9	8.8	10.5
40–44	7.5	8.4	7.3	8.3	6.8	8.4	7.6	8.9
45–49	9.3	9.4	9.5	9.0	8.7	8.7	7.8	8.6
50–54	10.1	11.2	8.6	10.4	7.5	9.8	7.9	9.5
55–59	10.3	10.0	10.4	9.9	10.3	9.7	9.3	9.7
60–64	5.1	5.4	5.3	5.6	5.8	5.7	6.7	5.9
65+	2.8	3.2	2.8	3.3	3.2	3.4	3.5	3.6
Mean age	38.1	39.1	38.0	38.9	37.5	38.8	37.3	38.8
SD	14.5	14.4	14.7	14.4	14.8	14.4	14.8	14.3
Median age	36.0	37.0	35.0	37.0	34.0	37.0	36.0	34.0
IQR	26.0	25.0	26.0	21.0	26.0	25.0	21.0	19.0

Abbreviations: IQR, inter-quartile range; SD, standard deviation.

neurological conditions (attention deficit hyperactivity disorder, anxiety, autism, epilepsy). Anxiety, attention deficit hyperactivity disorder, and autism identification are affected by sociological factors and healthcare quality and access (Bilaver et al., 2021; Locke et al., 2017; Rubenstein et al., 2023; Santoro et al., 2016). It is possible that genetic screening, including the identification of mosaicism is also associated with sociological factors and healthcare quality and access (Swami et al., 2022). Therefore, the increased risk for these chronic conditions could be confounded and the association reflects just the sociological and healthcare factors that lead to diagnosis. These results could also reflect the fact that symptomatic persons with mosaic Down syndrome are more likely to seek medical attention. Those with mosaic Down syndrome, with less phenotypic manifestations, are likely under-represented in the data. As such, it is possible that these co-occurring conditions in people with mosaic down syndrome could be similar or even less than those with nonmosaic Down syndrome if the true incidence of mosaicism was known. Nevertheless, the point difference is small and may not be clinically relevant.

In our data, Alzheimer's dementia was either more common in individuals with mosaicism compared to individuals without mosaicism, or there was no difference, depending on age group. It is well established that mosaic trisomy 21 is a risk factor for Alzheimer's dementia in people without the hallmark phenotype of Down syndrome (Potter, 2016; Potter et al., 2016), but our findings contradicts

TABLE 3 Chronic conditions comparing Medicaid enrollees with mosaic and nonmosaic Down syndrome, 2011–2019.

	Mosaic		Non mosaic			
	N = 1966		*N* = 92,567			
Conditions	***N***	**%**	***N***	**%**	**% point difference**	**95% CI**
Anemia	486	24.7	22,939	24.8	−0.1	−2.0, 1.9
Anxiety	304	15.5	12,374	13.4	**2.1**	**0.5, 3.8**
Autism spectrum disorder	174	8.9	5350	5.8	**3.1**	**1.9, 4.4**
ADHD	193	9.8	7414	8.0	**1.8**	**0.5, 3.2**
Alzheimer's dementia	438	22.3	19,901	21.5	1.2	−1.0, 2.8
Bipolar disorder	133	6.8	5139	5.6	**1.2**	0.1, 2.4
COPD	404	20.5	17,955	19.4	1.1	−0.6, 2.9
Deafness	219	11.1	12,362	13.4	**−2.3**	−3.6, −0.7
Depressive disorders	410	20.9	18,536	20.0	0.5	−1.2, 2.3
Diabetes	208	10.6	10,797	11.7	−1.1	−2.4, 3.5
Epilepsy	261	13.3	10,248	11.1	**2.2**	**0.7, 3.8**
Heart failure	221	11.2	10,797	11.7	−0.5	−1.9, 1.0
Hyperlipidemia	668	34.0	34,303	37.1	3.1	−4.2, 0.1
Hypothyroidism	919	46.7	45,012	48.6	−1.9	−4.1, 0.4
Chronic kidney disease	165	8.4	8770	9.5	−1.1	−2.2, 0.2
Leukemia + lymphomas	23	2.5	882	1.0	1.5	−0.2, 0.7
Obesity	326	16.4	15,168	16.6	−0.2	−1.4, 1.9

Abbreviations: ADHD, attention deficit hyperactivity disorder; COPD, chronic obstructive pulmonary disease.

Note: Bold values indicate statistically significant prevalence differences.

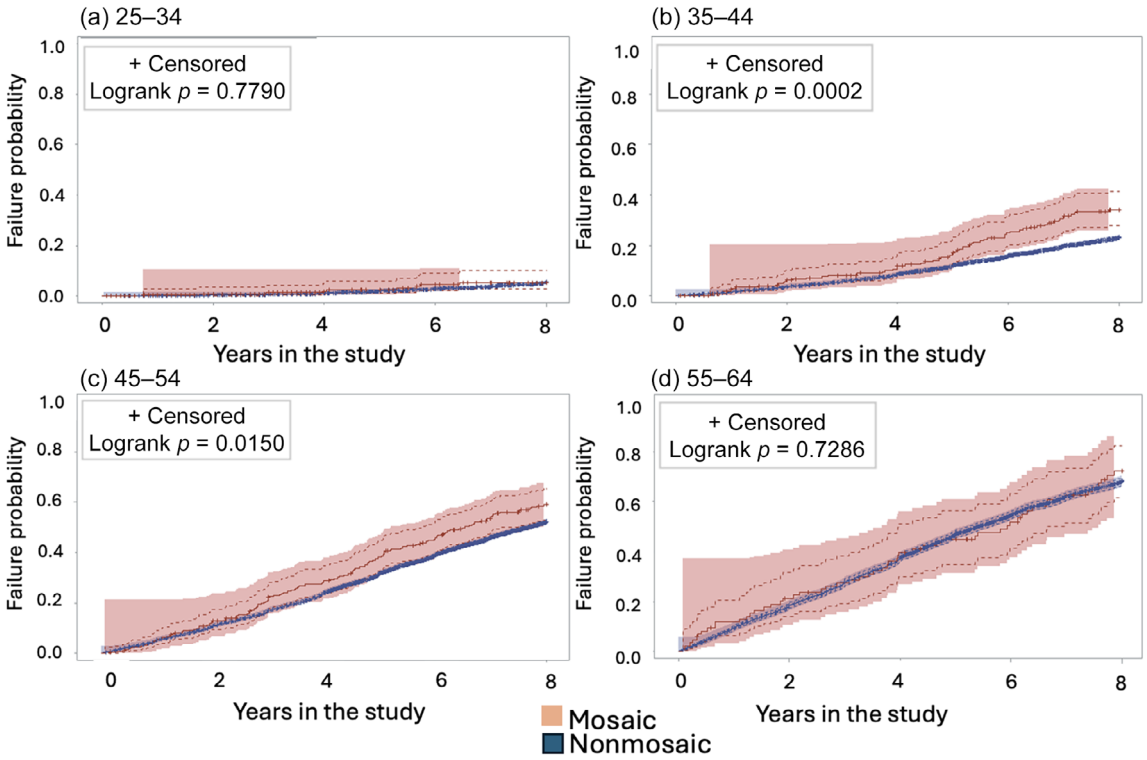

FIGURE 2 Age to Alzheimer's dementia by age at study entry comparing mosaic Down syndrome to nonmosaic Down syndrome in Medicaid, 2011–2019.

the hypothesis that the lower percentage of triplicated chromosome 21 would decrease risk for Alzheimer's dementia, as the dose of the amyloid precursor protein would be lower. Individuals with mosaicism may have more than enough amyloid to trigger the amyloid cascade and it is possible that the immune response with euploid cells is worse for Alzheimer's dementia; a hypothesis in this sense has been explained for the lesser occurrence of hemorrhages in Down syndrome compared to those with amyloid precursor protein duplication (Buss et al., 2016). It is also possible, again, that only the most clinically affected persons with mosaic Down syndrome sought medical attention, making cooccurring conditions disproportionately higher than persons with nonmosaic Down syndrome. With only ICD-10 codes, we could not ascertain what proportion of cells were mosaic, so it is possible that those in our sample had a low proportion of mosaic cells. Further, it could be that our Alzheimer's dementia results are confounded by sociological and healthcare factors that influence the same psychological and neurological conditions we found above. To overcome these issues, full karyotyping in a very large cohort may be needed to assess the dose–response relationship between mosaicism and Alzheimer's dementia.

Our study was limited by a lack of phenotypic and genotypic data that cannot be captured by claims data. ICD-10 codes for mosaic Down syndrome are relatively new and should continue to be assessed for validity and trends in use over time. We analyzed chronic conditions as static and did not evaluate timing of onset. However, we saw little difference when comparing individuals with and without mosaicism after adjusting for age and person time enrolled. Individuals in our sample had to be enrolled in 2016 to be observed for ICD-10 codes, but we used their data from 2011 to 2015 as well. This could impart an immortal person time bias (Agarwal et al., 2018) since everyone in our cohort had to survive until 2016. We believe there is minimal bias because we did not see major differences in age distributions, person-time, or age at death (data not shown).

We were able to utilize a full Medicaid sample of adults with Down syndrome and the updated ICD-10 with codes for mosaicism to describe occurrence of mosaic Down syndrome and related chronic conditions. The similar and higher rates of Alzheimer's dementia suggest that, at least in Medicaid, individuals with mosaicism might not have a decreased rate of Alzheimer's dementia compared to individuals without mosaicism. The use of the ICD-10 mosaic Down syndrome code should be evaluated over time and comparison with nonmosaic Down syndrome should be continued to be made.

AUTHOR CONTRIBUTIONS

ER—had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis, conceptualization, data curation, formal analysis, funding acquisition, investigation, methodology, project administration, resources, software, supervision, validation, visualization, writing—original draft, and writing—review & editing. ST—visualization, formal analysis, writing—review and editing. BS—Funding acquisition, writing-review. AM—data curation, formal analysis, methodology, validation. JF—conceptualization, writing—review.

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CONFLICT OF INTEREST STATEMENT

JF reported receiving personal fees for service on the advisory boards, adjudication committees or speaker honoraria from AC Immune, Lilly, Lundbeck, Roche, Esteve, Laboratorios Carnot, Adamed, LMI, Perha, Alzheon, Zambon, and Biogen outside the submitted work. JF report holding a patent for markers of synaptopathy in neurodegenerative disease (licensed to Adx, EPI8382175.0). Dr. Skotko occasionally consults on the topic of Down syndrome through Gerson Lehrman Group. He receives remuneration from Down syndrome nonprofit organizations for speaking engagements and associated travel expenses. In the past 2 years, Dr. Skotko received annual royalties from Woodbine House, Inc., for the publication of his book, *Fasten Your Seatbelt: A Crash Course on Down Syndrome for Brothers and Sisters*. Within the past 2 years, he has received research funding from AC Immune and LuMind IDSC Down Syndrome Foundation to conduct clinical trials for people with Down syndrome. Dr. Skotko is occasionally asked to serve as an expert witness for legal cases where Down syndrome is discussed. Dr. Skotko serves in a nonpaid capacity on the Honorary Board of Directors for the Massachusetts Down Syndrome Congress and the Professional Advisory Committee for the National Center for Prenatal and Postnatal Down Syndrome Resources. Dr. Skotko has a sister with Down syndrome. Funders did not have a say in the analysis or choice to publish data.

DATA AVAILABILITY STATEMENT

Data are not available due to restrictions in the Data Use Agreement between Boston University and the Centers for Medicare and Medicaid Services.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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