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Diagnostic Challenges and Disparities in Young-Onset Dementia: Insights from a Southeast London Memory Clinic Study

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Presentation with dementia is not uncommon in people under the age of 65 years (young-onset dementia, YOD) with significant impact on patients and their families (Hendriks *et al.*, 2022). Subjective cognitive complaints are associated with a higher risk for dementia (Perna *et al.*, 2023), but are similar in their prevalence in working age and older populations (Begum *et al.*, 2014). Aim of this study was to determine the proportion of younger people attending memory clinics eventually diagnosed with dementia, and to characterise dementia subtypes, time to diagnosis, and risk factors in a diverse population.

We carried out a retrospective analysis of people aged under 65 years referred to diagnostic memory service in Southeast London, UK, between March 2011 to March 2022 using data from the Clinical Record Interactive Search (CRIS) system. CRIS provides researchers access to more than 500,000 anonymised mental health and dementia care records (Perera *et al.*, 2016) and has full approval for secondary analysis by the Oxford Research Ethics Committee (reference: 18/SC/0372).

Between 2011 and 2022, 2,738 patients aged under 65 years were referred to memory services in Southeast London. Mean age(SD) at referral was 57.1(+/- 6.8) years and 41.2% were male. Of those 408 (14.8%) were eventually diagnosed with dementia and mean age(SD) at dementia diagnosis was 61.6(+/- 4.7) years. Those diagnosed with dementia were older at the time of first referral and more frequently male (see Table 1). In the White British group 12.8% and in the Black group (combining Black Caribbean and Black African) 21.5% were eventually diagnosed with dementia ($p<0.001$; corrected $p<0.002$).

Dementia subtypes are presented in Table 1 with Alzheimer's disease (AD) being commonest followed by vascular dementia (VD). Average time from first referral to diagnosis was 1.4 years, whereby this was longest in those diagnosed with a Lewy body dementia (LBD; 2.9 years), followed by AD (1.6 years), unspecified dementia (1.4 years), vascular and frontotemporal dementia (0.8 years), and dementia in other diseases (0.6 years).

Compared to their White counterparts, patients of Black background had higher odds of being diagnosed with any dementia (Odds ratio (OR): 1.86; 95% confidence interval (CI): 1.42-2.43;

p<0.001), AD (OR: 1.53; 95%CI: 1.08-2.15; p=0.016; comparison with no dementia), and VD (OR: 3.75; 95%CI: 2.18-6.46; p<0.001; comparison with no dementia) in logistic regression models adjusted for age at first referral and gender. There was no significant difference in time to diagnosis between White (1.6 years) and Black (1.2 years) patients (p=0.123).

Diagnosing YOD can be challenging due to atypical presentations. Our findings of Alzheimer's being the most common followed by VD are in keeping with previous reports of YOD subtypes (Harvey *et al.*, 2003; Kvello-Alme *et al.*, 2019). For LBD it took almost 3 years, and twice as long than in all-cause dementia, from first referral to reach a dementia diagnosis. Whereby delays in LBD diagnosis are known from older populations, with 1.2 years in one UK study (Surendranathan *et al.*, 2020), this seems to be more pronounced in our working age sample. A recent retrospective Australian study also mentions other dementias including LBD as predictors for delayed diagnosis in people with YOD (Loi *et al.*, 2022). LBD frequently has a psychiatric onset with low mood or hallucinations being common early complaints (Moylett *et al.*, 2019). In younger patients, it is likely that affective or psychotic symptoms are attributed to functional mental illness.

Black patients presenting with cognitive concerns had almost two-times higher odds of being diagnosed with any dementia and four-times higher odds of being diagnosed with VD. Previous studies in this catchment showed that people from ethnic minority groups are diagnosed younger, with more advanced cognitive impairment and non-cognitive symptoms (Mukadam *et al.*, 2019; Tsamakis *et al.*, 2021). Our study extends those findings to a young-onset population. VD was more common in our sample, which was drawn from a catchment where Black and Ethnic minorities represent up to 40% of the population, than in other

populations (Harvey *et al.*, 2003; Kvello-Alme *et al.*, 2019) suggesting that a higher prevalence of vascular risk factors could contribute to more people with Black backgrounds receiving a diagnosis of dementia.

In conclusion, we found that about one in seven people under 65 years referred to memory services were eventually diagnosed with dementia, with AD and VD being the most common subtypes. Challenges known from older adult services, as delayed diagnosis of DLB and higher rates of VD in Black populations, appear to be more pronounced in this younger populations. Clinicians ought to be aware of the possibility of DLB in psychiatric presentations in middle-aged patients and public health measures should target vascular risk factors and encourage earlier memory clinic assessments in Black minority groups.

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Table 1: Patient characteristics in those with and without dementia diagnosis and dementia subtypes

	Diagnosed with dementia (n=408)	Not diagnosed with dementia (n=2,330)	P-values[1]	Corrected P-values[2]
Age at first referral (mean, SD)	60.2 (4.3)	56.5 (7.0)	<0.001	<0.002
Male (%)	47.6%	40.1%	0.005	0.012
Ethnicity (%)				
White – British	33.3%	39.9%	0.012	0.021
White – Irish & Other	9.3%	12.1%	0.111	0.130
Black – Caribbean & African	34.6%	22.1%	<0.001	<0.002
Asian	12.0%	10.7%	0.444	0.444
Other or missing	10.8%	15.2%	0.065	0.091
Dementia subtype (%)				
Alzheimer's disease	58.3%			
Vascular dementia	22.3%			
Frontotemporal dementia	3.9%			
Lewy body dementia	4.4%			
Dementia in other diseases	2.9%			
Unspecified dementia	8.1%			

1 – P-values are calculated using t-test for age and chi^2 test for gender and ethnicity
2 – P-values corrected for multiple testing using the Benjamini-Hochberg procedure (Benjamini and Hochberg, 1995)