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RESEARCH ARTICLE

Trends in the incidence of dementia in people with hypertension in the UK 2000 to 2021

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Abstract

INTRODUCTION: We investigated trends in the incidence of dementia in UK adults with hypertension.

METHODS: Primary care electronic health records from IQVIA Medical Research Data UK, previously known as THIN, were used to identify 2,133,118 adults aged ≥40 years with hypertension over 2000 to 2021. The annual incidence rate and average annual percentage change in recorded dementia diagnoses were estimated and stratified by sex, 10-year age bands, Townsend deprivation quintiles and dementia subtype.

RESULTS: The crude incidence rate of dementia in people with hypertension increased from 1.98 (95% confidence internal [CI] 1.89–2.07) per 1000 person-years at risk (PYAR) in 2000 to 5.29 per 1000 PYAR (95% CI 5.07–5.53) in 2021, corresponding to an average annual increase of 4.1% (95% CI 3.3–5.0). Those aged ≥80 years, the most economically deprived (Townsend = 5), and Alzheimer's disease subtype reported the highest incidence rate within their respective categories.

DISCUSSION: The annual incidence rate of dementia in the hypertensive population has increased over the last 22 years.

KEYWORDS
dementia, electronic health records, epidemiology, hypertension, incidence

Highlights

- New dementia diagnosis in the hypertensive population has increased over 22 years.
- The Alzheimer's disease subtype reported the highest incidence rate in people with hypertension.
- Difference in dementia incidence between hypertensive females and males has reduced.
- Difference in dementia incidence among deprivation categories has reduced in recent years.

1 | BACKGROUND

Dementia is estimated to affect 57 million people globally and cases are predicted to increase to 157 million by 2050.[1] In the United Kingdom (UK), dementia is the leading cause of death among females and second highest cause of death among males.[2] There is no cure for dementia nor treatment that can slow neurodegeneration. Therefore, a focus on identifying risk factors that can be managed is an approach that can prevent or delay up to 40% of dementias.[3]

Hypertension has consistently been associated with an increased risk of dementia.[4,5] Studies have shown that hypertension starting in midlife (aged ≥ 40 years),[6] may exacerbate the mechanisms of cognitive decline and increase dementia risk through oxidative damage and systemic inflammation.[7] Moreover, hypertension has a direct effect on the risk of atherosclerotic and cerebrovascular disease, which are leasing causes of vascular dementia.[8] Hypertension is common with an estimated 1.28 billion adults worldwide living with the condition.[9] In 2019, the Health Survey of England estimated that 28% of all adults aged 16 and above were living with hypertension, including 12% with untreated hypertension.[10]

Previous studies describing the trends in dementia incidence rates have drawn from a sample of the general UK population,[11,12] but have not described trends in those specifically at risk from living with hypertension. Therefore, an epidemiology study describing the trends in dementia incidence among a representative sample of the hypertensive population in the UK is required. This study measured the changes in the annual rate of new dementia occurrence in the hypertensive population over the last 22 years. An investigation of the incidence of dementia in the hypertensive population may serve as the foundation for exploring interventions to slow the effects of hypertension on the rates of incident dementia.

1.1 | Aim

The aim of this study was to describe changes in the incidence of dementia in adults with hypertension aged ≥40 years between 2000 and 2021 in the UK.

RESEARCH IN CONTEXT

1. **Systematic review**: The authors reviewed the literature using MEDLINE and Embase. Hypertension has consistently been associated with an increased risk of incident dementia. However, the trends in new dementia cases within this high-risk group have not previously been described in the UK population.
2. **Interpretation**: The incidence of dementia diagnosis in a large representative sample of the UK hypertensive population has increased over the last 22 years. The gap in the rate of dementia diagnosis between the sexes has reduced over time and the impact of socioeconomic differences on dementia incidence in people with hypertension has decreased in recent years.
3. **Future directions**: Further studies are required to investigate if measures to manage hypertension may reduce the risk of incident dementia in this population. Additionally, studies have shown there are ethnic disparities in dementia risk factors such as hypertension. Future work should investigate if such disparities affect dementia incidence.

2 | METHODS

2.1 | Data source

We used IQVIA Medical Research Data (IMRD) incorporating data supplied by The Health Improvement Network (THIN), a proprietary database of Cegedim SA for this study. This database contains pseudonymized primary care data from > 16 million patients in the UK, representing ≈6% of the population.[13] The validity of the IMRD-UK database for research has been demonstrated in several studies,[14–16] including the generalizability and study-specific accuracy of dementia and hypertension diagnoses.[17,18]

2.2 | Ethics approval

This study was approved by the IMRD-UK Scientific Review Committee in March 2022 (Reference Number: 20SRC073).

2.3 | Study population

All patients in the IMRD-UK database with a diagnosis of hypertension and aged ≥ 40 years between January 1, 2000 and November 2, 2021 were included in this study. Hypertension was defined based on a validated method[18] that demonstrated comparable hypertension prevalence between IMRD-UK and the National Health Survey for England.[10] This method identified individuals with hypertension based on read codes (Table S1 in supporting information) linked to a clinical term describing hypertension or two blood pressure (BP) readings ≥140/90 mmHg within a 2-year period. For the year 2000, individuals were included if they had an initial BP reading in the previous 12 months and the second in the year 2000. We excluded read codes linked to pre-eclampsia or hypertension in pregnancy, as this type of hypertension is often resolved after pregnancy.[19] Any dementia case prior to the diagnosis of hypertension was also excluded. Individuals diagnosed with dementia within 6 months of registration with their general practitioner (GP) practice were excluded from the study, as this was unlikely to represent an incident case. Dementia cases, including subtypes, were identified using read codes linked to a clinical diagnosis of dementia (Table S2 in supporting information) or a prescription for

symptomatic treatment of dementia (Table S3 in supporting information). For the annual incidence calculation, the start of follow-up began from the latest of January 1 in each year or 40th birthdate. The end of follow-up was the earliest of incident dementia, death, transfer out of GP practice, last date of data collection in IMRD-UK, or end of study period (November 2, 2021).

2.4 | Statistical analysis

Descriptive statistics were used to describe the characteristics and common comorbidities associated with individuals with hypertension and dementia.[3] Continuous data were reported as mean ± standard deviation (SD) and categorical data reported as percentages. The annual incidence rate over a 22-year period was calculated by totaling the number of hypertensive patients with a new diagnosis of dementia in each year and dividing by the total number of person-years at risk (PYAR) of dementia in the same year, while accounting for deaths, last date of data collection, and those who transferred out of the GP practice. Crude incidence rates were expressed as per 1000 PYAR with confidence intervals (95% CI) estimated assuming the Poisson distribution. Annual incidence rates were also stratified by sex, 10-year age bands, Townsend deprivation quintiles,[20] and dementia subtype.

A linear regression model was used to estimate the average annual percentage change in incidence rates over the study period. We fitted our model with calendar year as the predictor variable and cumulative percentage change in incident rate as the dependent variable. Sex, 10-year age bands, and Townsend deprivation quintile-specific analyses were also conducted. A P-value < 0.05 was considered statistically significant.

All statistical analyses were conducted in Stata v17 (StataCorp LLC).

TABLE 1 Characteristics of individuals with hypertension and incident dementia.

	Incident dementia cases
Total (N)	85,245
Mean [SD] age,[a] years	80.0 [7.7]
Median [IQR] time to dementia diagnosis, years	9.6 [5.3–13.8]
Sex (%)	
Male	32,120 (37.7)
Female	53,125 (62.3)
Dementia subtypes (%)	
Alzheimer's disease	31,053 (36.4)
Unspecified dementia	30,905 (36.3)
Vascular dementia	19,581 (23.0)
Other dementias[b]	3706 (4.3)
Comorbidities (%)	
Renal disease	28,167 (33.0)
Ischemic heart disease	24,614 (28.9)
Depression	24,364 (28.6)
Cerebrovascular disease	23,099 (27.1)
Diabetes	17,127 (20.1)
Dyslipidemia	17,015 (20.0)
Arrhythmias	16,356 (19.2)
Heart failure	7,350 (8.6)
Peripheral vascular disease	5,674 (6.7)

Abbreviations: IQR, interquartile range; SD, standard deviation.
[a]Age at first dementia diagnosis.
[b]Other dementias = dementia with Lewy bodies, frontotemporal dementia, and dementias with other secondary cause.

3 | RESULTS

In a hypertensive population of 2,133,118 individuals aged ≥ 40 years, the mean age at hypertension diagnosis was 54.2 years (SD 13.6) and 53% (1,129,466) were female. Within this population we identified 85,245 (4%) incident cases of dementia between 2000 and 2021. Patient characteristics are described in Table 1. The median time from start of follow-up to dementia diagnosis was 9.6 years (interquartile range 5.3–13.8) and the mean age at diagnosis of dementia was 80 years (SD 7.7).

The annual trend in crude incidence rates of deme,ntia in individuals with hypertension between 2000 and 2021 is illustrated in Figure 1. Incidence rates increased from 1.98 (95% CI 1.89–2.07) per 1000 PYAR in 2000, to a peak of 5.29 (95% CI 5.07–5.53) per 1000 PYAR in 2021. There was a relatively large 1-year decline in the incidence rate from 2019; 5.19 (95% CI 5.01–5.37) per 1000 PYAR to 2020; 3.81 (95% CI 3.65–3.98) per 1000 PYAR, which recovered in 2021. Results from linear regression showed an average annual increase of 4.1% (95% CI 3.3–5.0; Table S4 in supporting information) in the incidence rate of dementia diagnosis.

Annual incidence rates stratified by sex (Figure 2) showed that the incidence rate of dementia in females with hypertension increased from 2.29 (95% CI 2.16–2.43) per 1000 PYAR in 2000 to 5.83 (95% CI 5.51–6.17) per 1000 PYAR in 2021, corresponding to an average annual increase of 3.7% (95% CI 2.8–4.6). In males with hypertension, the incidence rate also increased; from 1.58 (95% CI 1.46–1.71) per 1000 PYAR in 2000 to 4.69 (95% CI 4.38–5.01) per 1000 PYAR in 2021, an average annual increase of 5.1% (95% CI 4.3–6.0). The difference in dementia incidence between hypertensive females and males reduced from 44.9% in 2000 to 24.3% in 2021 (Table S5 in supporting information).

Figure 3 details annual incidence rates stratified by 10-year age bands. Incidence rates were greatest in the ≥ 80 years category, reaching a peak of 27.43 (95% CI 26.54–28.34) per 1000 PYAR in 2014. The average annual increase within this age category was 4.2% (95% CI 3.1–5.4). The 70 to 79 age category had a relatively small but gradual

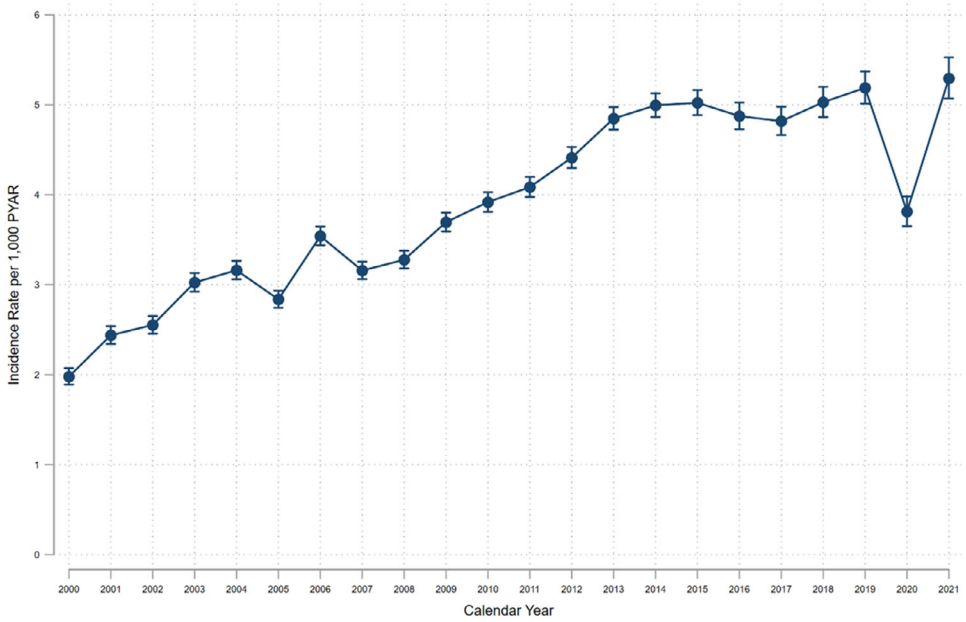

FIGURE 1 Annual incidence rate of dementia in the hypertensive population 2000–2021. PYAR, person-years at risk.

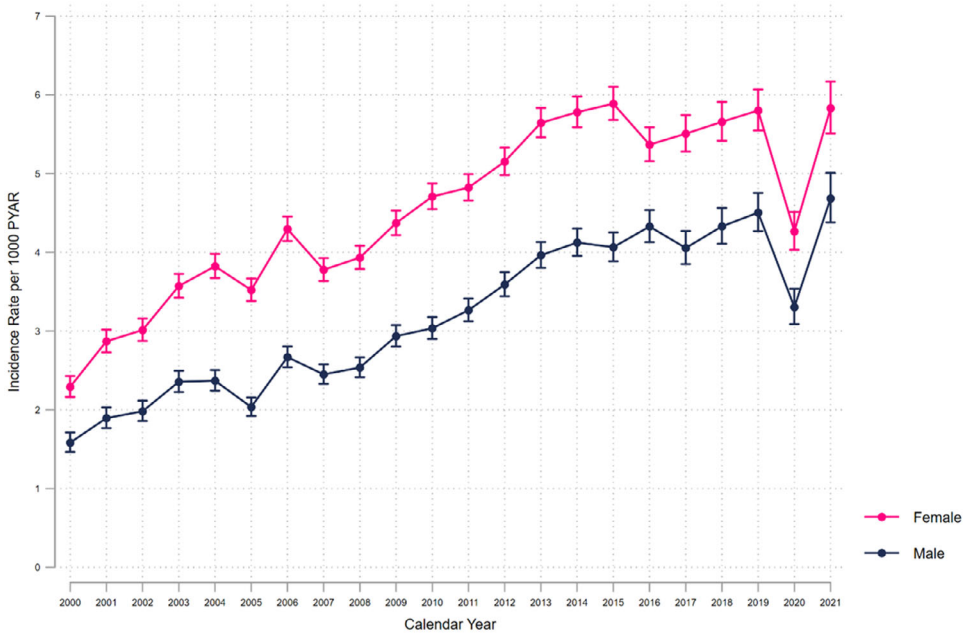

FIGURE 2 Sex-stratified annual incidence rate of dementia in the hypertensive population 2000–2021. PYAR, person-years at risk.

increase in incidence over the entire study period, except in 2020 when the rate decreased in a similar trend to results in the primary analysis (Figure 1). The average annual increase within the 70 to 79 age category was 2.7% (95% CI 1.8–3.7). The remaining age categories reported low incidence rates over the entire study period, with < 100 cases of dementia recorded in the 40 to 49 age category (Table S6 in supporting information).

Annual incidence rates stratified by Townsend quintile are shown in Figure 4. Townsend quintile 1 (least deprived) was shown to have the lowest dementia incidence rate of all Townsend quintile groups for every year, except in 2021. Townsend quintile 5 (most deprived) reported the greatest incident rate across all years compared to other Townsend quintile groups, with a peak of 5.80 (95% CI 5.16–6.51) per 1000 PYAR in 2021. However, the average annual change in incidence rate was highest in Townsend quintile 1; 5.5% (95% CI 4.8–6.2). The difference in dementia incidence rates between the most deprived and other Townsend quintiles reduced over the 22-year study period (Table S7 in supporting information).

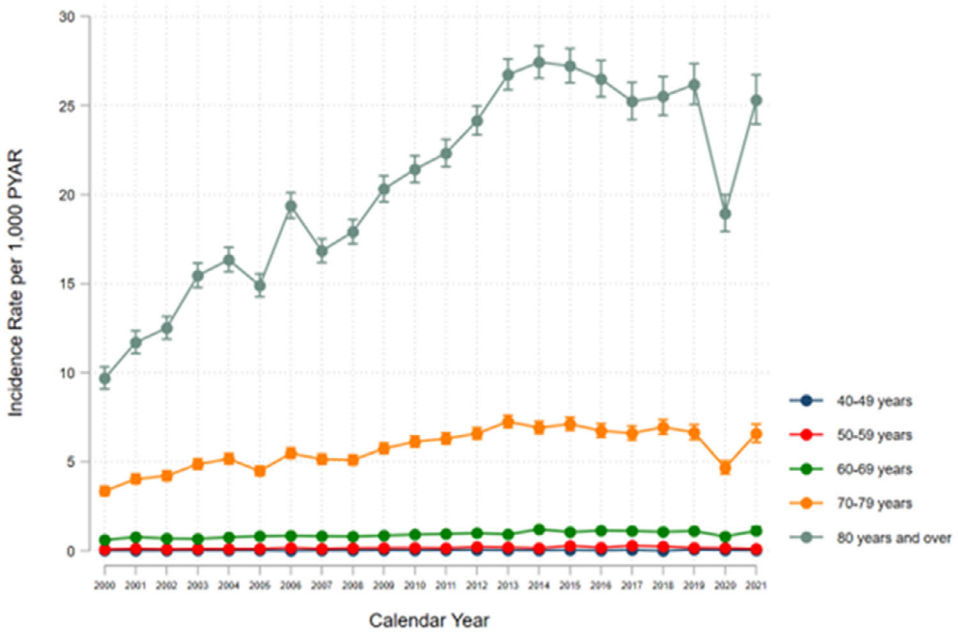

FIGURE 3 Age-stratified annual incidence rate of dementia in the hypertensive population 2000–2021. PYAR, person-years at risk.

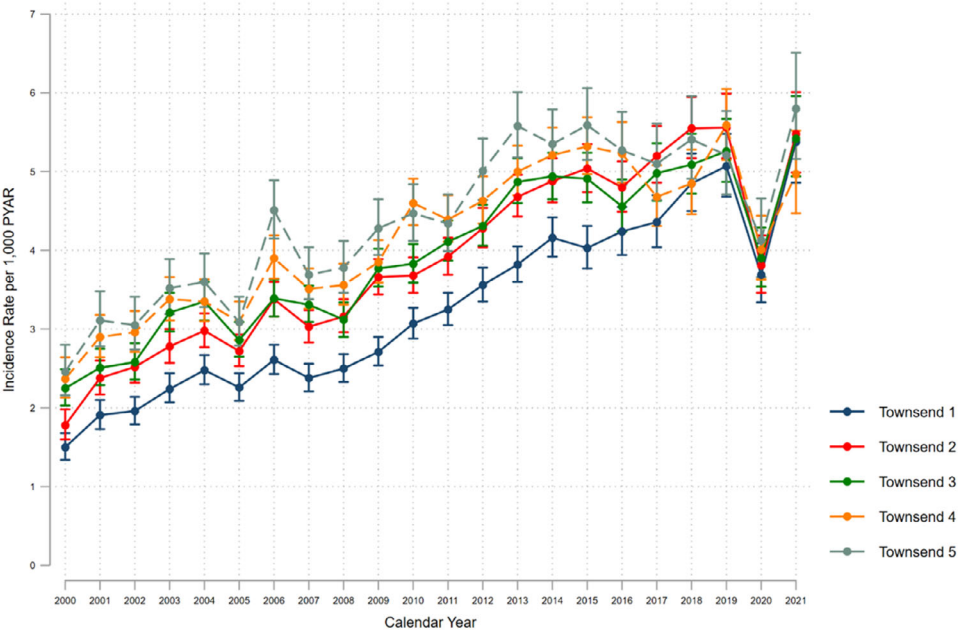

FIGURE 4 Townsend quintile stratified annual incidence rate of dementia in the hypertensive population 2000–2021. PYAR, person-years at risk.

Annual incidence rates stratified by dementia subtype (Figure 5) were initially highest among cases of "unspecified dementia" until 2012. From this point onward, rates of Alzheimer's disease (AD) continued to exceed diagnosis of all other subtypes. Within the AD subtype the average annual change in incidence rates was 7.3% (95% CI 6.5–8.1), which was higher than any other subtype. Vascular dementia (VaD) incidence rates followed a similar trend to AD from 2000 to 2010. Thereafter, the rate of AD increased sharply, while the incidence of VaD in the hypertensive population decreased from 2015 onward. The incidence rate of "other dementias" remained stable throughout the study period with a relatively small average annual increase of 0.3% (95% CI 0.1–0.4).

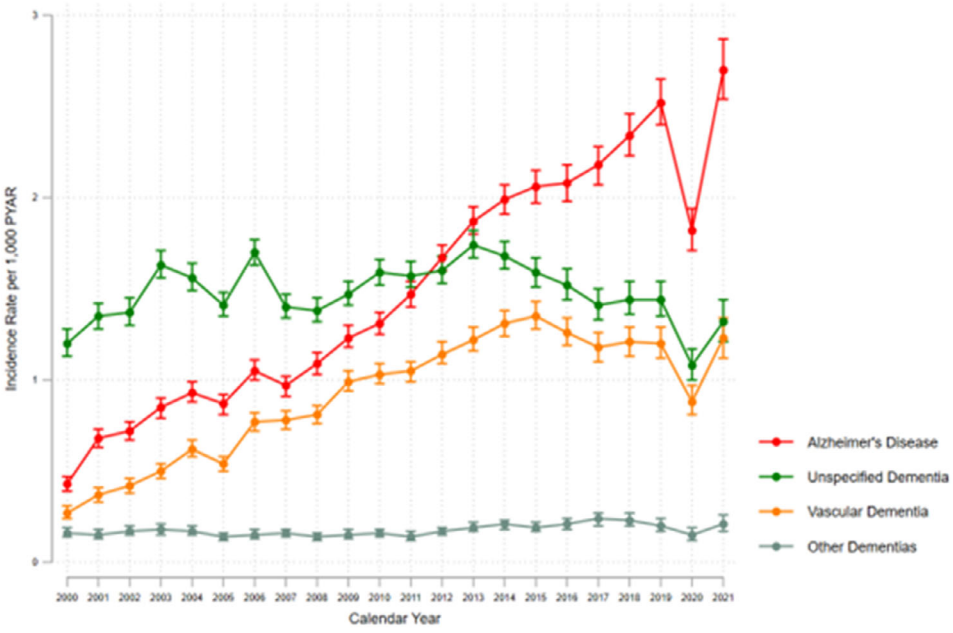

FIGURE 5 Dementia subtype stratified annual incidence rate of dementia in the hypertensive population 2000–2021. PYAR, person-years at risk.

4 | DISCUSSION

Our results show that the rate of incident dementia in adults aged ≥ 40 with hypertension increased from 2000 to 2019. The increasing trend temporarily decreased in 2020 but recovered in 2021. This reduction reflects the coronavirus (COVID-19) outbreak and associated lockdown and closure of dementia diagnosis services in the UK.[21] Similarly, the UK government reported a reduction in the diagnosis rate of dementia by up to 5.4% in 2020 compared to 2019.[22] This was the result of a reduction in primary care activities such as quality outcome framework (QOF) targets and secondary care referrals, therefore minimizing pressure on the National Health Service (NHS) and prioritizing COVID-19 vaccinations.[23]

Stratified analyses identified that in the hypertensive population, female sex had a greater incidence of dementia than male sex. However, this difference between sexes reduced over the study period. In the UK, the difference in life expectancy between male and female sex has also reduced over the last 40 years[24] and dementia is primarily a disease diagnosed in older age. Therefore, this finding may be the result of improved survival into later life among males who are predisposed to developing dementia due to age. Furthermore, those aged ≥ 80 living with hypertension accounted for the greatest number of dementia cases (Table S6 in supporting information). Increasing age is the strongest risk factor for dementia.[25] Our study supports this and has shown an increasing trend in the incidence of dementia with increasing age categories of individuals with hypertension.

The average annual change in dementia incidence was largest within the least deprived group (Townsend score = 1). However, this group had the lowest incidence rate of dementia. The difference in incidence rates between all Townsend quintile groups reduced throughout the study period, with a minimal difference between the least and most deprived in 2021. Social inequalities have been linked to incident dementia diagnosis and studies have reported an association between area deprivation, lower education attainment, occupational position (including financial resource), and an increased risk of incident dementia in the general population.[26,27] Our results show that in the hypertensive population, the risk from differences in socio-economic status has reduced over time and the effect of deprivation on dementia in the general population may be mediated by cardiovascular risk factors such as hypertension.

AD is the most common type of dementia accounting for up to 75% cases in the UK.[28] Our results show that AD had the highest incidence rate of all recorded dementia subtypes and accounted for the most cases of dementia. Hypertension and VaD have a strong associated risk,[29] developed through the effects of high BP on atherosclerotic and cerebrovascular disease.[8] Despite this link, the incidence of VaD in our hypertensive population decreased between 2015 and 2021. Recent trends in the incidence of stroke in England between 2005 and 2017 have also been reported to have decreased.[30,31] Stroke is a leading cause of VaD and this reduction may have impacted the observed decrease in VaD incidence in our study. Furthermore, this reduction may also be a reflection of improved lifestyle, BP control, and the uptake of other preventative cardiovascular risk management strategies that have also contributed to a reduction in coronary heart disease and cardiovascular disease mortality.[32] Categorization of "unspecified dementia" initially had the greatest incidence rate, but from 2013 onward continued to decrease. An improved understanding of dementia and subtypes over the last decade is likely to have contributed to the increased reporting of new dementia diagnosis and specific categorization of subtypes in primary care. This may have been the result

of national campaigns and initiatives such as the 2009 Living Well with Dementia national strategy,[33] the 2012 and 2015 UK Prime Minister's challenge on dementia,[34,35] and the introduction of dementia as a quality QOF target in 2014.[36] These national interventions set ambitions to improve the awareness, research, and diagnosis of dementia and have resulted in a significant acceleration in the rate of dementia diagnosis.[11] Our findings are a manifestation of the effectiveness these interventions have in enhancing the recognition and recording of incident dementia in primary care.

4.1 | Comparison to other studies

To the best of our knowledge this is the first study to estimate the incidence of dementia in a representative sample of the UK hypertensive population over the last 22 years. Our findings are consistent with other UK primary care database studies that have reported increasing trends, but in the general[11,12,37] and diabetes population.[38] This study also uniquely reports the incidence of dementia by different subtypes in people living with hypertension. Despite differences in the subpopulation and calendar years, stratified analyses in other studies[12,37,38] demonstrated similar increasing incidence rates in female sex, rising age categories, and those most deprived (Townsend score = 5). A study of aggregated data from prospective cohort studies between 1988 and 2015[39] showed a 13% decrease per calendar decade in incident dementia among individuals > 65 years. Although not a study conducted in a population with hypertension, their findings were attributed to improved lifestyle education and health interventions over the last 27 years. We also report a decline in dementia diagnoses, but only within the VaD and unspecified subtypes over the last 6 years.

4.2 | Strengths and limitations

The strength of this study is the inclusion of a large representative sample of the UK hypertension population. Unlike previous studies that have either included a relatively small sample size or short follow-up period, we have reported the annual trend over 22 years of new dementia diagnosis in > 2 million adults with hypertension. We were also able to report stratified results by sex, 10-year age bands, Townsend score (quintiles), and dementia subtype. Stratification by Townsend score has its limitations, as it is linked to deprivation by postcode, which does not always represent household deprivation. However, this is a relative measure of deprivation that has been used by UK health authorities to establish relationships between health and deprivation and has been used widely in research to demonstrate a high level of correlation with measures of health.[20] Other limitations include the quality of electronic primary care records in drawing meaningful conclusions. For example, our study does not include undiagnosed hypertensive patients. However, we used a validated method[17] to identify a representative study population of hypertensive individuals in the UK. Another limitation is that we did not have information from diagnostic brain imaging and autopsy to confirm the accuracy of dementia diagnosis based on clinical read codes. We attempted to mitigate this limitation by including prescriptions for symptomatic management of dementia as an additional definition for dementia diagnosis. In addition, the positive predictive value of dementia read codes in UK primary care databases is 83% with minimal false negatives in a sample without recorded dementia.[40] Therefore, we expect that our estimates are reflective of a representative sample of dementia cases.

5 | CONCLUSION

The annual incidence of dementia diagnosis in a large representative sample of the UK hypertensive population has increased over the last 22 years. The rate of new dementia is greatest in older-aged females and those living in deprived areas of the UK. The gap in the rate of dementia diagnosis between the sexes has reduced over time and the impact of socioeconomic differences on dementia incidence in people with hypertension has decreased in recent years. Further studies are required to investigate if measures to manage hypertension may reduce the risk of incident dementia in this population.

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The individual contributory roles of each author are outlined below using the Contributor Roles Taxonomy (CRediT). M. Adesuyan: conceptualization, methodology, software, formal analysis, investigation, data curation, writing- original draft, visualization and project administration. Y. H. Jani: writing—review & editing, supervision and funding acquisition. D. Alsugeir: writing—review & editing, validation and formal analysis. R. Howard: writing—review & editing and funding acquisition. L. Wei: Writing—review & editing and methodology. I. C. K. Wong: writing—review & editing and funding acquisition. R. Brauer: methodology, validation, writing—review & editing, funding acquisition, and supervision.

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CONFLICTS OF INTEREST STATEMENT

Mr. Matthew Adesuyan, Dr. Yogini H. Jani, Ms. Dana Alsugeir, Professor Robert Howard, Professor Li Wei, and Dr. Ruth Brauer all have no conflicts of interest to declare in relation to the subject matter and content discussed in this manuscript. Author disclosures are available in the supporting information.

CONSENT STATEMENT

Pseudo-anonymized data from electronic health records was used to carry out this study and can confirm that individual human participant consent was not necessary. This study was approved by the IQVIA Medical Research Data (IMRD) UK Scientific Review Committee in March 2022 (Reference Number: 20SRC073).

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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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