

# Dementia clinical trials over the past decade: are women fairly represented?

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**To cite:** Pinho-Gomes A-C, Gong J, Harris K, *et al*. Dementia clinical trials over the past decade: are women fairly represented? *BMJ Neurology Open* 2022;4:e000261. doi:10.1136/bmjno-2021-000261

► Additional supplemental material is published online only. To view, please visit the journal online (<http://dx.doi.org/10.1136/bmjno-2021-000261>).

Received 17 December 2021  
Accepted 07 August 2022



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## ABSTRACT

**Background** Lack of progress in finding disease-modifying treatments for dementia may be due to heterogeneity in treatment effects among subgroups, such as by sex. Therefore, we investigated the characteristics of dementia trials completed in the last decade, with a focus on women's representation and sex-disaggregated outcomes.

**Methods** Clinical trials on dementia completed since 2010 were identified from ClinicalTrials.gov. Randomised, phase III/IV trials with ≥100 participants were selected to quantify women's representation among participants, by computing the participation to prevalence ratio (PPR) and investigate whether sex-disaggregated analyses had been performed.

**Results** A total of 1351 trials were identified between January 2010 and August 2021 (429 520 participants), of which 118 were eligible for analysis of women's representation and sex-stratified analysis. Only 113 reported the sex of participants and were included in the analysis of women's representation. Of the 110 469 participants in these 113 trials, 58% were women, lower than their estimated representation in the global dementia population of 64%. The mean PPR was 0.90 (95% CI 0.86 to 0.94). Women's participation tended to be higher when the first or last authors of the trial report were women. Eight out of the 118 trials reported sex-disaggregated outcomes, and three of those found significant sex differences in efficacy outcomes. None of the trials reported screening failures or adverse events stratified by sex.

**Conclusions** Overall, women and men were equally represented in dementia trials carried out over the past decade, but women's representation was lower than in the underlying dementia population. Sex-disaggregated efficacy and safety outcomes were rarely reported.

## INTRODUCTION

Notwithstanding the remarkable advances in our understanding of dementia, including Alzheimer's disease, over the past decades, similar developments in our therapeutic armamentarium have not been witnessed.<sup>1 2</sup> There have been no major improvements in treatment or prevention of dementia since the successful trial of memantine in 2003.<sup>3</sup> One possible explanation for the failure in developing disease-modifying treatments for dementia is the heterogeneity in the

## WHAT IS ALREADY KNOWN ON THIS TOPIC

- ⇒ Women are under-represented in clinical trials across multiple specialties and sex-disaggregated analysis are often lacking.
- ⇒ The incidence of dementia is higher among women than men.

## WHAT THIS STUDY ADDS

- ⇒ In a subsample of dementia clinical trials registered on ClinicalTrials.gov and published between 2010 and 2021, women comprised 58% of the 110 469 participants, which was lower than their estimated representation in the global dementia population (64%).
- ⇒ None of the trials reported screening failures or adverse events stratified by sex, and sex-disaggregated outcomes were only reported by 8 of the 118 dementia trials studied.

## HOW THIS STUDY MIGHT AFFECT RESEARCH, PRACTICE OR POLICY

- ⇒ Although there is broadly sex parity among participants in dementia trials, women's representation has remained lower than their representation in the underlying dementia population and sex-disaggregated analyses are seldom performed.
- ⇒ Addressing these issues is paramount to enable investigating heterogeneity in treatment effects based on sex differences and improve management of dementia across the globe.

population of patients enrolled into clinical trials. This heterogeneity may be explained by differences in underlying diseases or lifestyle risk factors, stages of disease, genetic susceptibility or sex differences.<sup>4</sup> In fact, incidence rates for dementia in general, and Alzheimer's disease in particular, are higher in women than in men, with rates diverging from about the age of 80.<sup>5</sup> Although this is at least partially explained by women's survival into older ages in comparison to men, evidence has been accruing on the substantial differences in risk factors, presentation and progression of dementia between women and men.<sup>6 7</sup> For instance, sex-specific associations between certain genetic polymorphisms and increased risk of Alzheimer's disease

have been identified.<sup>8-10</sup> There is also evidence that the association between blood pressure and dementia is log-linear in women, but U-shaped in men.<sup>11</sup>

It is, thus, plausible that some of the ‘failed’ drugs or interventions could be efficacious in a subgroup of patients, such as women. However, sex-disaggregated analyses are seldom performed, even if regulatory guidelines advise carrying out, and prespecifying, subgroup analyses by sex.<sup>12</sup> In addition, inadequate enrolment of women in clinical trials has been a long-standing issue across multiple medical fields, which may compromise the ability to identify clinically meaningful sex differences.<sup>13-17</sup>

Therefore, the aims of this study were to (1) investigate the characteristics of dementia trials completed since 2010, (2) estimate the representation of women among participants in those trials, (3) determine whether sex-disaggregated analyses were performed and, if so, whether sex differences in safety and/or efficacy were reported and (4) explore whether the proportion of women participants differed according to type of dementia, severity of disease, type of intervention, continent where the trial was conducted, funding agency, age of participants or gender of first and last authors.

## METHODS

### Data source and search strategy

We searched for clinical trials registered on ClinicalTrials.gov, a web-based registry of human clinical studies conducted around the world provided by the US National Library of Medicine and managed by the National Institutes of Health (NIH). The search terms were ‘dementia’ as disease condition, ‘interventional studies (clinical trials)’ as study type and ‘completed’ or ‘terminated’ as recruitment status. Searches were limited to trials with adults aged  $\geq 18$  years and with a primary completion between the 1 January 2010 and the 31 August 2021. Trials completed prior to 2010 were excluded as we were only interested in contemporary trials.

For the analysis of women’s representation, a subsample of the trials was selected using the following criteria: (1) trials that included both genders; (2) trials with at least 100 participants; (3) phase III or IV trials; and (4) trials whose interventions were on patients (rather than healthcare professionals or carers). Once the trials were identified on the ClinicalTrials.gov web page, full manuscripts were searched on PubMed using the national clinical trial identifier assigned to the trial, trial registered name and acronym and primary investigator’s name. If no matching publication was found, Google Scholar, Embase and Scopus databases were searched using the national clinical trial identifier, trial registered name and acronym and primary investigator’s name. When published reports could not be identified, the principal investigator was contacted whenever an email address was available, but no answers were received. All searches were performed in duplicate (A-CP-G and JG).

### Data extraction

Data were extracted by one author (A-CP-G) for the eligible trials. The variables extracted were National Clinical Trial number, completion date, trial location(s) (ie, country, continent or worldwide if across several continents), intervention type (ie, pharmacological, behavioural, radiation, dietary supplement, procedure, device or other), type of dementia (vascular dementia, Alzheimer’s disease, either and other), funding agency (ie, industry, vs other). For published articles, data were also extracted for mean age of participants, total sample size, proportion of women, reporting of screening failures by sex, reporting of sex-disaggregated outcomes, observed differences in efficacy and/or safety, the name of the journal, year of publication and gender of first and last authors were also extracted.

### Data analyses

To investigate the extent of women’s representation among participants in trials, we calculated the participation to prevalence ratio (PPR), the percentage of women among trial participants divided by the percentage of women in the underlying disease population.<sup>18</sup> A PPR close to 1 indicates that the sex composition of the trial is that of the disease population.<sup>19</sup> The percentage of women with dementia in the population was obtained from prevalence estimates from the Global Burden of Disease (GBD).<sup>20</sup> Where trials were conducted in a single country location, country-specific prevalence estimates were used. Where trials were conducted across multiple countries, regional or international (if more than one region) prevalence estimates were assigned to the respective trials.

For the published trials, the gender of the first and last author was determined according to their first name and pronouns used to describe them in their institutional biography. Gender was assigned using the binary terms: woman or man; there were no authors identified as non-binary in their biography.

Subgroup analyses were conducted according to type of dementia (Alzheimer’s disease vs other dementias), severity (mild cognitive impairment vs dementia), sponsor type (industry vs other), intervention (pharmacological, behavioural and other), continent, age (under vs over 80 years) and gender of first and last author (women vs men). To assess whether PPR varied by study sample size, we calculated a sample size weighted mean (SSWM) of the PPR across all trials. SSWM was calculated by multiplying the trial PPR by the trial sample size and dividing by the sum of participants in all trials included in this study. The sum of this quantity is the SSWM. Bootstrap methods were used to obtain 95% CIs for the mean PPR and SSWM of the PPR, using the percentile method with 100 000 iterations. Trends over time were displayed for number of trials for the overall analysis, and for mean PPR for the subset of trials included in the analysis of women’s representation. All data analyses were performed in R V.4.0.2 (R Core Team, 2020).

## Role of funding source

There was no specific funding for this study.

## RESULTS

### Overall dementia trials

A total of 1351 eligible trials related to dementia were identified between January 2010 and August 2021, with a total of 429 520 participants (online supplemental figure S1). The total number of participants ranged from 1 to 197 692, and 1043 (77%) trials had fewer than 100 participants. All trials included a mix of women and men. Just over half of the trials (720; 53%) were conducted in the Americas, with the remainder mainly carried out in Europe (307; 23%) or worldwide (175; 13%) (table 1; online supplemental table S1 and figure S2).

### Women's representation in dementia trials

A total of 172 trials were eligible for inclusion in the analysis of women's representation after applying the criteria mentioned in the methods (figure 1). For 24 (14%) of those trials, results were available on ClinicalTrials.gov, and for 78 (45%) trials, published reports could not be identified. Of the resulting 118 trials (69% of eligible trials), 5 did not report number of participants stratified by sex and, thus, were excluded from the analysis. Therefore, the final analysis of women's representation comprised 113 trials (table 2). These trials included a total of 110 469 participants, of whom 63 772 (57.7%) were women. The percentage of women in individual trials varied widely from 2.2% to 90.7%, with a mean of 57.3% (SD 13.9) and a median of 58.1% (interquartile interval (52.6–65.2)).

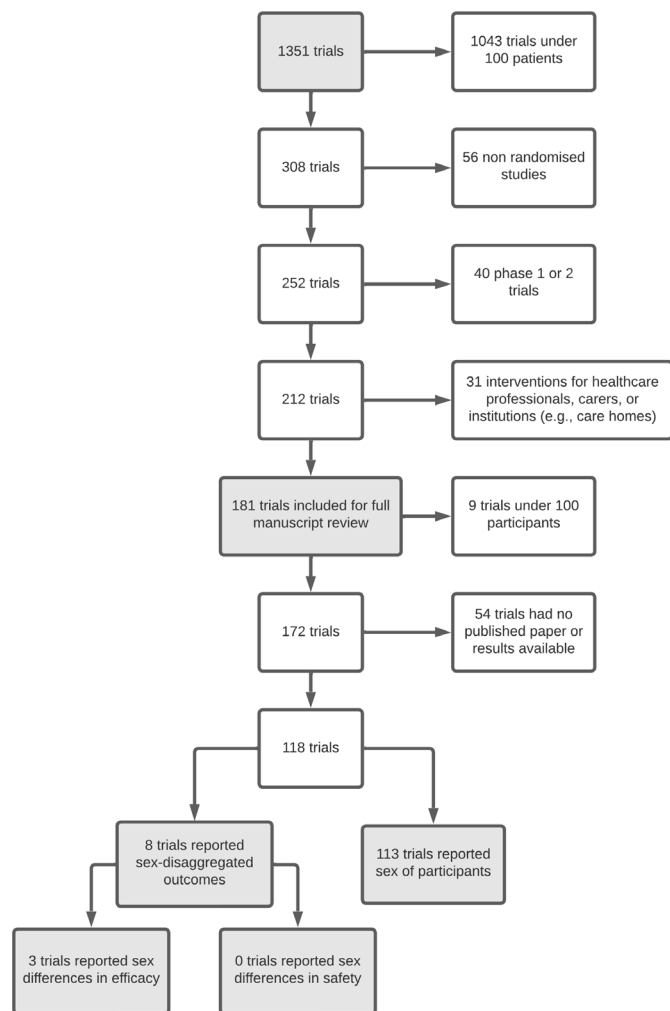
Overall, women were represented in clinical trials at a lower proportion relative to their proportion in the underlying dementia population, in which women account for 64.1% of the cases (mean PPR 0.90, 95% CI (0.86 to 0.94)). There was a large variation in the PPR across trials, ranging from 0.04 to 1.41. The SSWM, which gives more weight to larger trials, was similar to the PPR without weighing according to trial size (SSWM 0.91 (95% CI (0.52 to 1.58)) although with a wider CI.

Subgroup analyses (figure 2, online supplemental figure S3 and table S2) showed that the PPR was significantly higher for trials with a mean of 80 years and above (PPR 1.01, 95% CI (0.98 to 1.05)) than those with a mean age of under 80 years (PPR 0.85, 95% CI (0.80 to 0.89)). No other significant differences were observed in subgroup analyses. Women's representation was comparable in trials related to mild cognitive impairment (PPR 0.96, 95% CI (0.91 to 1.00)) and dementia (PPR 0.88, 95% CI (0.84 to 0.92)). Women's representation was broadly similar, irrespective of the type of dementia (Alzheimer's disease vs other dementias), type of intervention (pharmacological, behavioural or other interventions) and funding agency (industry vs other). There was also no significant heterogeneity in PPR across world regions (Europe PPR 0.96, 95% CI (0.89 to 1.01), Asia

**Table 1** Summary of 1351 dementia trials completed between 2010 and 2021

Characteristic	N trials	%
Results available on ClinicalTrials.gov (yes)	388	28.7
Type of dementia		
Alzheimer disease	832	61.6
Delirium	18	1.3
Dementia	321	23.8
Dementia with Lewy bodies	28	2.1
HIV dementia	14	1.0
Huntington disease	78	5.8
Mild cognitive impairment	47	3.5
Vascular dementia	13	1.0
Mild cognitive impairment (of any cause)	201	14.9
Type intervention		
Behavioural	266	19.7
Biological	38	2.8
Device	90	6.7
Diagnostic test	4	0.3
Dietary supplement	21	1.6
Drug	722	53.4
Genetic	1	0.1
Procedure	20	1.5
Radiation	16	1.2
Other	173	12.8
Trial phase		
Not applicable	534	39.5
Phase 1/2	582	43.1
Phase 3/4	235	17.4
Funding agency		
Industry	484	35.8
Industry and NIH	13	1.0
Industry and other	96	7.1
NIH	3	0.2
NIH and other	111	8.2
Other	644	47.7
Randomisation (yes)	914	67.7
Location (continent)		
Africa	5	0.4
Americas	720	53.3
Asia	133	9.8
Europe	307	22.7
Oceania	11	0.8
Worldwide	175	13.0

NIH, National Institutes of Health .



**Figure 1** Flowchart summarising the selection of trials for the overall analysis and analysis of women's representation.

PPR 0.97, 95% CI (0.91 to 1.03), Americas PPR 0.85, 95% CI (0.78 to 0.92) and worldwide PPR 0.88, 95% CI (0.83 to 0.92)). There was no evidence that women's representation increased between 2010 and 2019 (figure 3).

Among the 118 trials, 43 (36%) first authors and 28 (24%) last authors were women. Women's representation in trials appeared to be higher when the first author was a woman (PPR 0.95, 95% CI (0.70 to 1.20)) than a man (PPR 0.87, 95% CI (0.46 to 1.12)). Women also tended to account for a higher proportion of participants when the last author was a woman (PPR 0.98, 95% CI (0.79 to 1.14)) in comparison to a man (PPR 0.88, 95% CI (0.46 to 1.15)).

None of the trials reported screening failures or adverse events stratified by sex. Only 8 out of the 118 trials included in the analysis of women's representation reported sex-disaggregated outcomes. Of those eight trials, three reported significant differences between women and men. One of these trials showed that nilvadipine slowed cognitive decline to a greater extent among men than women (NCT02017340). The other two trials investigated the effects of behavioural interventions related to

physical activity, and both showed that women responded better than men (NCT02262104 and NCT02290912).

## DISCUSSION

In a subsample of 118 dementia trials registered on ClinicalTrials.gov and published between 2010 and 2021, which included both sexes, 5 failed to provide data on the percentage of women included. In the remaining 113 trials, 58% of the 110469 participants were women, which was lower than their estimated representation in the global dementia population (64%). Women's representation tended to be lower when the first or last authors of the published manuscripts were men than women. In addition, none of the trials reported screening failures or adverse events stratified by sex, and sex-disaggregated outcomes were only reported by 8 of the 118 dementia trials studied.

### Women's representation in clinical trials

Although dementia is now a leading cause of death among both women and men in many countries, it is most prevalent among women, particularly over the age of 80.<sup>21</sup> Despite this, women remain under-represented in dementia trials, in proportion to their representation in the dementia population overall. This is in keeping with a recent study showing that the proportion of women in clinical trials of Alzheimer's disease, although higher than the proportion of men, was significantly lower than that in the general population.<sup>22</sup> However, this earlier study did not estimate the PPR, which provides a better understanding of the discrepancy between representation in clinical trials and the general population. Furthermore, the lack of significant progress in women's representation over the past decade hints at a lack of commitment to addressing this situation. Importantly, our study suggests that women under-representation may be lower when the first or the last authors are women in comparison to men. Similar findings were seen in a previous study that showed a direct association between having women as authors and women's enrolment into clinical trials.<sup>23</sup> However, we found a striking gender gap with women accounting for about one in three first authors and one in four last authors of the dementia papers included in this study. This gender gap among authors of scientific papers has been compellingly demonstrated in myriad medical specialties and science in general.<sup>24 25</sup> Altogether, this evidence suggests that tackling the gender imbalance in authorship of papers and women's representation in clinical trials may go hand-in-hand. It is thus imperative that healthcare and academic institutions, funding agencies, journals and the scientific community more broadly commit to promoting gender equality in both policy and practice at all levels. In line with this, the American Society of Preventive Cardiology has recently published a practice statement to improve the enrolment of women and ethnically diverse populations in cardiovascular clinical trials,<sup>26</sup>

**Table 2** Baseline table of trial characteristics: number (and percentage)

Characteristic	Trials	Participants	Female participants
Total	113	110 469	63 772 (57.7)
Age			
<80 years	87 (77)	72 866 (66)	38 669 (61)
≥80 years	26 (23)	37 603 (34)	25 103 (39)
Intervention			
Drug	71 (63)	65 512 (59)	34 413 (54)
Behavioural	22 (19)	38 812 (35)	25 415 (40)
Other	20 (18)	6145 (6)	3944 (6)
Dementia type			
Alzheimer disease	74 (65)	89 223 (81)	53 522 (84)
Delirium	4 (4)	1320 (1)	837 (1)
Dementia	24 (21)	7747 (7)	4651 (7)
Dementia with Lewy bodies	2 (2)	403 (0)	137 (0)
Huntington disease	1 (1)	609 (1)	313 (0)
Mild cognitive impairment	6 (5)	10 341 (9)	4027 (6)
Vascular dementia	2 (2)	826 (1)	285 (0)
Continent			
Americas	49 (43)	66 729 (60)	38 240 (60)
Asia	15 (13)	4035 (4)	2336 (4)
Europe	21 (19)	7610 (7)	4992 (8)
Worldwide	28 (25)	32 095 (29)	18 204 (29)
Funding			
Industry	61 (54)	53 620 (48)	29 849 (47)
Other	52 (46)	56 849 (52)	33 923 (43)
First author			
Woman	34 (31)	48 085 (44)	30 889 (49)
Man	77 (69)	60 282 (56)	31 697 (51)
Last author			
Woman	20 (18)	7158 (7)	4535 (7)
Man	91 (82)	101 209 (93)	58 051 (93)

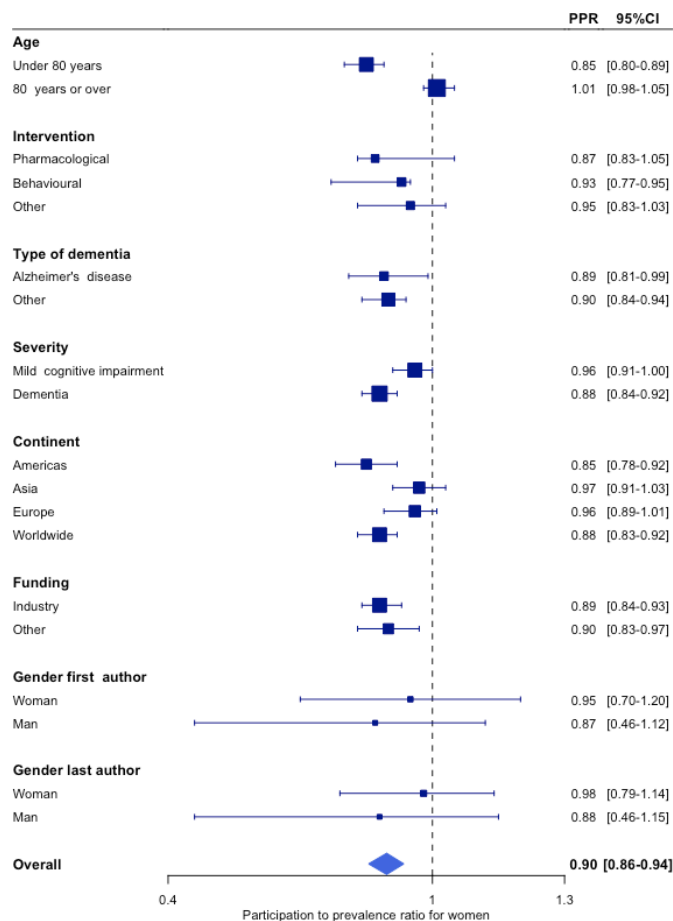
which should pave the way for other medical societies to promote equality and diversity in their fields.

### Sex-disaggregated outcomes

It is concerning that reporting of sex-disaggregated efficacy outcomes remains extremely uncommon (reported in only 8 out of 118 trials in our study). The importance of subgroup analysis by sex is emphasised by the fact that three out of these eight found clinically relevant sex differences. This supports the hypothesis that heterogeneity in treatment effects based on sex might underpin the lack of benefit of interventions for dementia.<sup>27</sup> This is in keeping with evidence demonstrating sex differences in the association between specific risk factors and dementia, such as high blood pressure, raised cholesterol or sex hormones.<sup>28 29</sup> This has two implications. First, even if treatment effects are broadly comparable among women

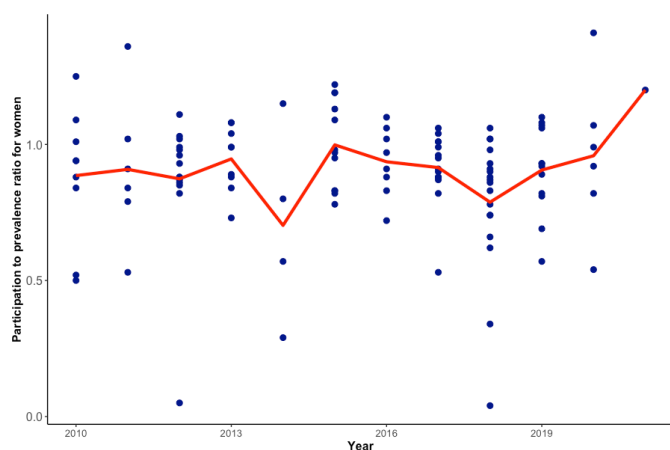
and men, the absolute risk reduction may be larger in one sex than another, depending on the strength of the association. Second, it is possible that different mechanisms underpin the development of dementia in women and men, at least partially mediated by sex chromosomes and hormones, which could lead to sex differences in treatment effects depending on the target pathways.<sup>30 31</sup> Therefore, sex-disaggregated analyses should be planned in trial protocols to avoid missing potential sex-specific benefits and comply with good research practice.<sup>32</sup>

Furthermore, safety outcomes should be reported stratified by sex as it is biologically plausible that women and men experience different adverse events or with different severity. A comprehensive review of the US Food and Drug Administration Adverse Event Reporting System, which identified sex differences in adverse events for



**Figure 2** Subgroup analysis of participation to prevalence ratio for women. Size of box is proportional to number of studies in each category. PPR, participation to prevalence ratio.

307 out of 668 drugs of the 20 most common treatment regimens in the USA.<sup>33</sup> This is in keeping with further evidence suggesting that sex differences in pharmacokinetics and pharmacodynamics underpin, at least partially,



**Figure 3** Women's representation in dementia trials, relative to prevalence, between 2010 and 2021. Dots represent participation to prevalence ratio for each trial plotted by year. Line represents the mean participation to prevalence ratio per year.

the increased risk of adverse events observed in women compared with men.<sup>34 35</sup> Considering that adverse events are, in general, more common among older adults, who are typically the population of dementia trials, it is critical that not only efficacy but also safety outcomes are reported disaggregated by sex.<sup>36</sup>

### Future perspectives

Our study suggested that trials led by women may have higher representation of women in comparison to trials led by men. This is in keeping with evidence showing cardiovascular trials with a woman as principal investigator were associated with a 7% mean higher enrolment of women as participants, in comparison to trials led by a man.<sup>37</sup> Furthermore, a recent study showed that women accounted for only 10% of clinical trials leadership committees, which may, at least partially, underpin women's under-representation among trial participants.<sup>38</sup> Gender diversity in the clinical trial workforce may improve understanding of diverse participant populations and, hence enable tailoring research products to participants, thus fostering participation of a more diverse population in trials.<sup>39</sup> In general, women authors appear to be more likely to publish sex-disaggregated outcomes than men,<sup>40</sup> but as only three dementia trials in our study reported sex-disaggregated outcomes, we were unable to investigate this issue in our study. Altogether, these findings suggest that closing the gender gap in clinical trial leadership may play a key role both in addressing under-representation of women among clinical trial participants and incorporating sex-disaggregated analysis in clinical trials.

Besides improving women's representation as principal investigators in trials, other strategies are important to increase women's participation in trials and promote systematic reporting of sex-disaggregated analyses. First, all scientific journals could require trials to include both sexes in adequate numbers and address sex and gender differences in order to be considered for publication.<sup>32</sup> Second, frameworks to integrate health equity considerations into the design of clinical trials should be implemented in research to promote recruitment of women.<sup>41 42</sup> This may involve avoiding women-specific exclusion criteria (ie, women of childbearing age) as well as more nuanced criteria that may preferentially select men due to sex differences in how diseases manifest and progress.<sup>43</sup> Third, addressing barriers that may disproportionately affect women is paramount, such as logistical or communication barriers. For instance, evidence suggests that women and men may make decisions differently and, thus, the same enrolment process may yield different enrolment rates by sex.<sup>44 45</sup> In addition, our finding that women's under-representation is larger among younger women suggests younger women may be particularly vulnerable to barriers, such as caring responsibilities.<sup>46</sup> Therefore, greater flexibility in study structures and processes to cater for the different preferences and needs of women and men, especially in younger age, may

promote gender equality among participants in clinical trials.<sup>47</sup>

### Limitations

This study has some limitations worth acknowledging. First, our only source of data was ClinicalTrials.gov. However, most journals require that trials are registered in an open platform to be published, and this is the most commonly used platform. Therefore, we expect our findings to represent the overall landscape of dementia trials. Second, we could not obtain full manuscripts for all the trials eligible for inclusion in the analysis of women's representation, even though we searched the largest databases of index publications (PubMed, Embase, Google Scholar and Scopus). This may be because trials were discontinued or achieved negative results, which are less likely to be of interest to journals. This may result in publication bias, which skews the evidence available, and raises concerns about research integrity and transparency, which may undermine public trust in research. Moreover, lack of published reports can lead to unnecessary repetition of trials, which is a waste of precious resources that would better be spent elsewhere. However, we do not expect those trials would have had a material impact on our findings, as there is no reason for those trials to have better representation of women than other trials. Third, the background population prevalence used to derive the PPR may not have been representative of the actual prevalence in the study population, particularly for trials that enrolled participants worldwide and older trials as we used the most recent data on prevalence provided by the GBD. However, any errors in prevalence estimates by population or time are unlikely to vary by sex, and it is the women to men relative prevalence that informs the PPR. Fourth, we used overall prevalence of Alzheimer's disease and other dementias, and there may be differences between different types of dementia within countries and regions. Fifth, we were unable to identify the funder of each trial, other than for industry and NIH, due to the limited information in the registry. Sixth, although we searched for any published articles currently for each trial, it is possible that some may eventually publish secondary analyses with sex-stratified outcomes. Seventh, we were unable to ascertain whether sex disaggregation of results was prespecified, precluding analysis of whether reporting of sex differences in primary publications tended to occur only when a sex variation was observed. Eighth, data extraction was performed by a single author, which may have introduced error.

### CONCLUSION

The lack of progress in disease-modifying strategies for dementia may be, at least partially, underpinned by pitfalls in clinical trials conducted over the past decade, which have mainly been small, underpowered studies, with a lack of geographical representation. Although there is broadly sex parity among participants in dementia

trials, women's representation has remained lower than their representation in the underlying dementia population. This, together with the lack of sex-disaggregated outcomes, limits our ability to explore heterogeneity in treatment effects based on sex differences, and hence may impair improvements to the care of the rapidly increasing number of women with dementia across the globe.

**Contributors** ACPG, CC and MW designed this study. ACPG extracted the data. ACPG and JG searched for manuscripts. ACPG and KH analysed the data. ACPG drafted the manuscript. All authors reviewed the manuscript. ACPG and CC are the guarantors for this study. They accept full responsibility for the conduct of the study, had access to the data, and controlled the decision to publish.

**Funding** The authors have not declared a specific grant for this research from any funding agency in the public, commercial or not-for-profit sectors.

**Map disclaimer** The inclusion of any map (including the depiction of any boundaries therein), or of any geographical or locational reference, does not imply the expression of any opinion whatsoever on the part of BMJ concerning the legal status of any country, territory, jurisdiction or area or of its authorities. Any such expression remains solely that of the relevant source and is not endorsed by BMJ. Maps are provided without any warranty of any kind, either express or implied.

**Competing interests** MW is a consultant for Amgen, Kyowa Kirin and Freeline.

**Patient consent for publication** Not applicable.

**Ethics approval** Not applicable.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request. Access to all data is possible upon reasonable request through the corresponding author.

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**Supplementary tables****Table S1: Number of trials by country**

<b>Country</b>	<b>Number of trials</b>
Argentina	1
Australia	10
Austria	6
Belgium	4
Brazil	11
Canada	64
China	24
Denmark	5
Egypt	3
Finland	4
France	88
Germany	39
Greece	3
Hong Kong	11
India	1
Iran	1
Ireland	1
Israel	8
Italy	17
Japan	18
Korea (South)	28
Mexico	2
Netherlands	12
New Zealand	1
Nigeria	1
Norway	23
Pakistan	1
Poland	1
Portugal	5
Russian Federation	2
Singapore	5
Slovakia	1
Spain	30
Sweden	6
Switzerland	10
Taiwan	28
Tanzania	1
Thailand	1

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<b>Turkey</b>	6
<b>United Kingdom</b>	50
<b>USA</b>	642
<b>Vietnam</b>	1
<b>International</b>	175

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**Table S2: Subgroup analysis for participation to prevalence ratio for women (N=113)**

<b>Variable</b>	<b>Factors</b>	<b>PPR with 95% CI</b>
<b>Age</b>	<80 years	0.85 [0.80 to 0.89]
	≥80 years	1.01 [0.98 to 1.05]
<b>Intervention</b>	Drug	0.87 [0.83 to 1.05]
	Behavioural	0.93 [0.77 to 0.95]
	Other	0.95 [0.83 to 1.03]
<b>Dementia type</b>	Alzheimer's disease	0.89 [0.81 to 0.99]
	Other	0.90 [0.84 to 0.94]
<b>Severity</b>	Mild cognitive impairment	0.96 [0.91 to 1.00]
	Dementia	0.88 [0.84 to 0.92]
<b>Continent</b>	Americas	0.85 [0.78 to 0.92]
	Asia	0.97 [0.91 to 1.03]
	Europe	0.96 [0.89 to 1.01]
	Worldwide	0.88 [0.83 to 0.92]
<b>Funding</b>	Industry	0.89 [0.84 to 0.93]
	Other	0.90 [0.83 to 0.97]
<b>Gender first author</b>	Woman	0.95 [0.70 to 1.20]
	Man	0.87 [0.46 to 1.12]
<b>Gender last author</b>	Woman	0.98 [0.79 to 1.14]
	Man	0.88 [0.46 to 1.15]

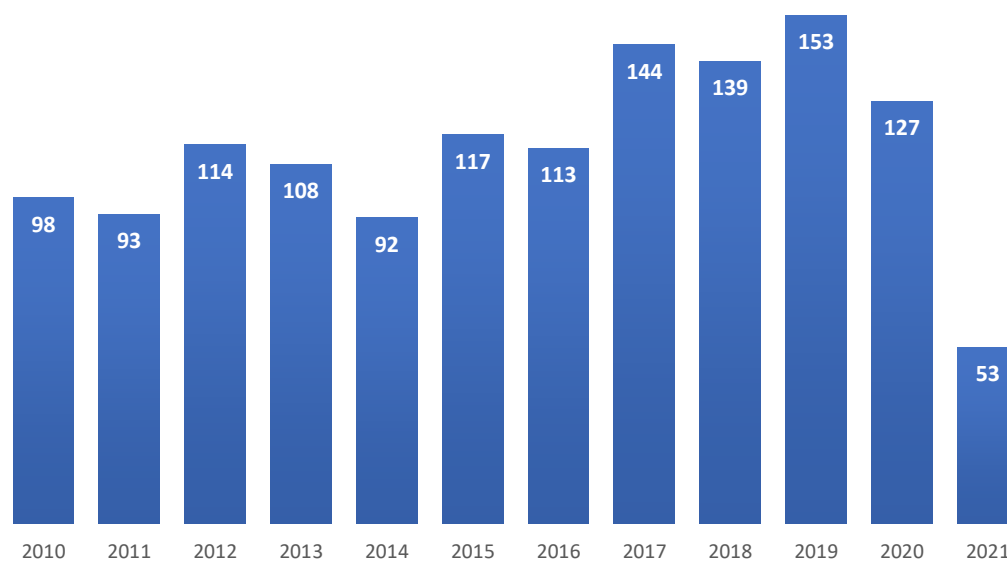
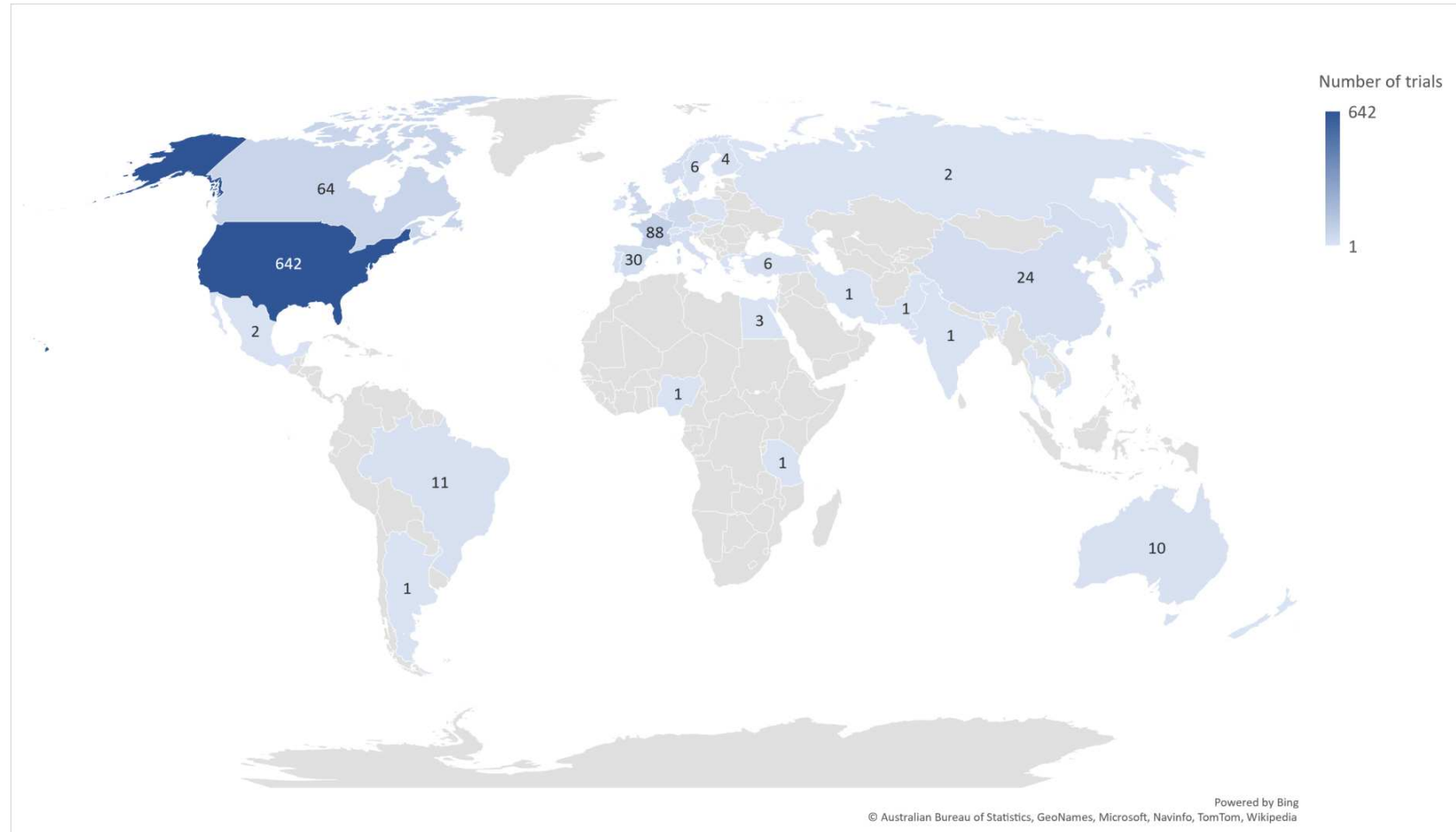
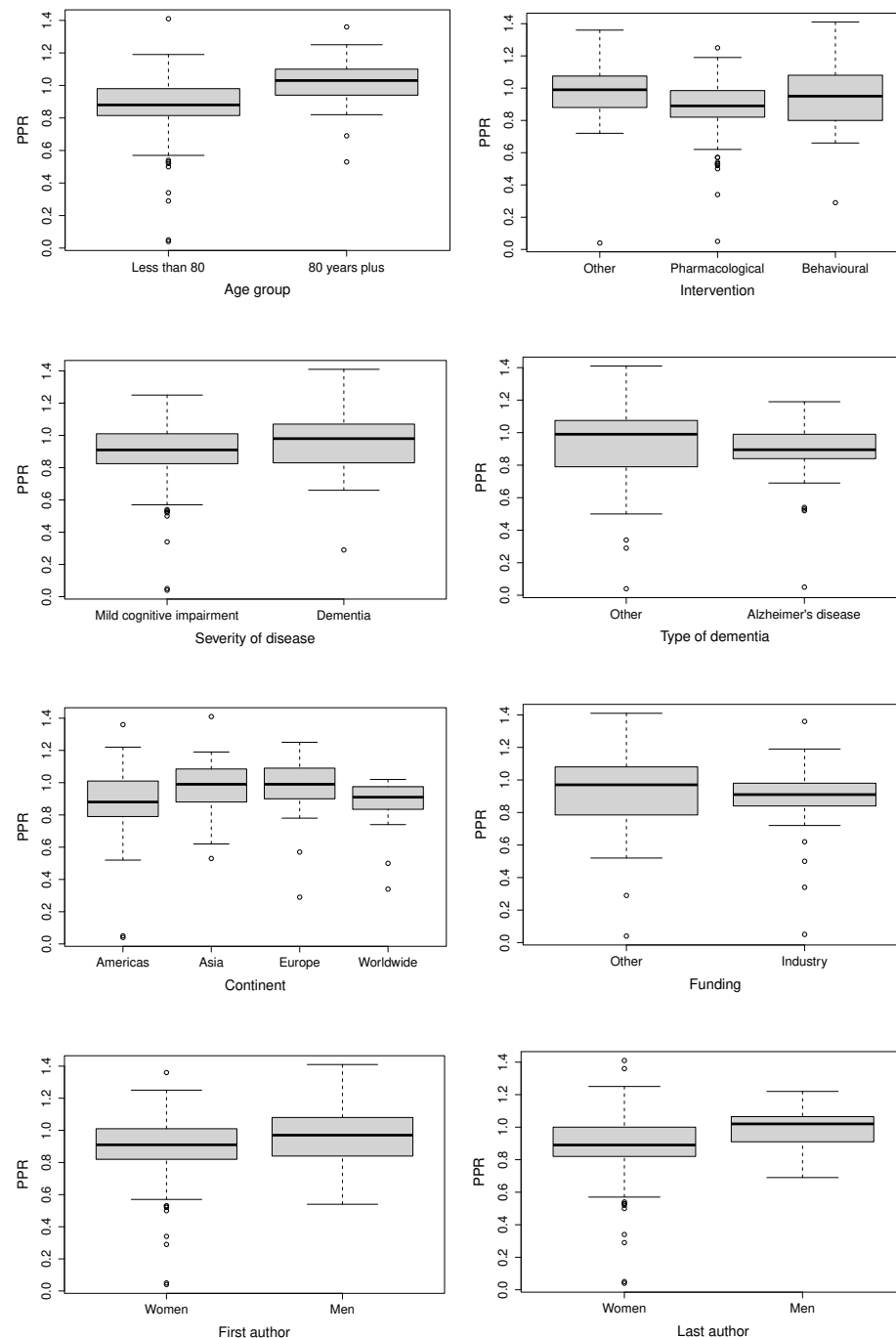
**Figure S1: Number of dementia trials 2010-2021**

Figure S2: World map displaying the number of trials conducted in each country



**Figure S3: Subgroup analysis of the distribution of participation to prevalence ratios (PPR)**

Box and whisker plots represent the distribution of PPR within each category. The thick black horizontal bar represents the median PPR within the category, with the grey box representing the interquartile interval between the first quarter and upper quarter of the dataset. The thin black lines represent “whiskers” that extends to one and a half times the interquartile interval, values beyond are extreme values represented as white dots with black outline.