A comprehensive assessment of risk factors for falls in middle-aged adults: co-ordinated analyses of cohort studies in four countries

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Acknowledgements

Some of the research on which this article is based was conducted as part of the Australian Longitudinal Study on Women's Health by The University of Newcastle and The University of Queensland. We are grateful to the women who provided the survey data and to the Australian Government Department of Health for funding. The NSHD is funded by the UK Medical Research Council. We are grateful to NSHD study members for their continuing support. NSHD data used in this publication are available to bona fide researchers upon request to the NSHD Data Sharing Committee via a standard application procedure. Further details can be found at http://www.nshd.mrc.ac.uk/data doi: 10.5522/NSHD/Q101; doi: 10.5522/NSHD/Q102. The Longitudinal Aging Study Amsterdam is supported by a grant from the Netherlands Ministry of Health Welfare and Sports, Directorate of Long-Term Care. The data collection [in 2012-2013 and 2013-2014] was financially supported by the Netherlands Organization for Scientific Research (NWO) in the framework of the project "New Cohorts of young old in the 21st century" (file number 480-10-014). The Irish Longitudinal Study on Ageing (TILDA) is funded by the Irish Government, the Atlantic Philanthropies and Irish Life PLC. We are grateful to all of the TILDA respondents for participating in

the study. Researchers interested in using TILDA data may access the data for free from the following sites:

-Irish Social Science Data Archive at University College Dublin http://www.ucd.ie/issda/data/tilda/;

-Interuniversity Consortium for Political and Social Research (ICPSR) at the University of Michigan http://www.icpsr.umich.edu/icpsrweb/ICPSR/studies/34315.

GP was supported by a Global Brain Health Institute Fellowship. RC was supported by the UK Medical Research Council (programme code: MC_UU_12019/4). The funders had no role in the study design, data collection, data analysis, data interpretation, writing of the report or the decision to submit the article for publication.

Conflict of interest

Geeske Peeters, Rachel Cooper, Leigh Tooth, Natasja van Schoor and Rose Anne Kenny declare that they have no conflicts of interest.

Abstract

Purpose: Between ages 40-44 and 60-64 years, the annual prevalence of falls triples suggesting that middle-age may be a critical life stage for preventive interventions. We aimed to identify demographic, health and lifestyle factors associated with falls in adults aged 50-64 years.

Methods: Harmonised data were used from four population-based cohort studies based in Australia (Australian Longitudinal Study on Women's Health, n=10641, 51-58 years in 2004), Ireland (The Irish Longitudinal Study on Ageing, n=4663, 40-64 years in 2010), the Netherlands (Longitudinal Aging Study Amsterdam, n=862, 55-64 years in 2012-13) and Great Britain (MRC National Survey of Health and Development, n=2987, 53 years in 1999). Cross-sectional and prospective associations of 42 potential risk factors with self-reported falls in the past year were examined separately by cohort and gender using logistic regression. In the absence of differences between cohorts, estimates were pooled using meta-analysis.

Results: In cross-sectional models, nearly all risk factors were associated with fall risk in at least one cohort. Poor mobility (pooled OR=1.71, CI=1.34-2.07) and urinary incontinence (OR range=1.53-2.09) were consistently associated with falls in all cohorts. Findings from prospective models were consistent. Statistically significant interactions with cohort and sex were found for some of the risk factors.

Conclusion: Risk factors known to be associated with falls in older adults, were also associated with falls in middle-age. Compared with findings from previous studies of older adults, there is a suggestion that specific risk factors, for example musculoskeletal conditions, may be more important in middle-age. These findings suggest that available preventive interventions for falls in older adults may also benefit middle-aged adults, but tailoring by age, sex and country are required.

Keywords: accidental falls; mobility; middle aged; population health

Mini abstract: We identified demographic, health and lifestyle factors associated with falls in adults aged 50-64 years from Australia, The Netherlands, Great Britain and Ireland. Nearly all factors were associated with falls, but there were differences between countries and between men and women. Existing falls prevention programs may also benefit middle-aged adults.

Introduction

Falls in older adults are a major public health challenge; they are an important cause of injuries and impact on social participation, fear of falling again and health service utilisation [1-3]. However, falls among middle-aged adults are largely ignored. This is despite the fact that the estimated annual prevalence of falls triples from 9% in 40-44 year old adults to 28% in 60-64 year old adults [4], suggesting that middle-age may be a critical life stage for preventive interventions.

Current evidence-based guidelines for the prevention of falls focus on adults aged 65 and over and recommend assessment and targeting of contemporaneous risk factors, including demographic, health, lifestyle and environmental related factors [5-10]. However, less evidence is available on risk factors for falls in adults under the age of 65. The current generation of middle-aged adults differs from previous generations with regards to important demographic and health indicators including greater educational attainment and higher obesity prevalence [11]. Greater educational attainment contributes to higher adult socio-economic position, healthier lifestyles and better health [12-14], while in contrast high BMI predisposes to conditions such as diabetes and osteoarthritis, which are associated with increased fall risk [9]. As such, the current generation of middle-aged adults are therefore not necessarily healthier than their parents' generation. These generational differences, together with the lower prevalence of health problems in middle-age than in older age, likely translate to different risk factor profiles for falls in middle-aged adults than in older adults.

In a cohort of over 4000 Australian women aged 50-55 years, being overweight or obese, having poor physical functioning and vision problems were consistently associated with an increased fall risk throughout middle-age [15]. That study identified 15 other risk factors (e.g. urinary incontinence, depression and assistance with daily activities) that were associated with an increased fall risk at some but not all time points throughout middle-age [15]. While the sample was large, the prevalence for some of the risk factors was low, which may explain the inconsistent findings. Studies of middle-aged adults from Finland and New Zealand identified alcohol consumption and medication use as risk factors of fall-related injury requiring hospital admissions [16-18], but did not find evidence that being overweight or obese was a risk factor [18]. Verification of these findings in a large sample that includes men and women is required to obtain better insight into the risk factors for falls in middle-aged adults.

The prevalence of falls is higher in women than in men, both in middle-age and later life [4,9]. Research by our consortium has shown substantial variation in the prevalence of falls, even within

age- and sex-groups, between representative samples from Australia, The Netherlands, Great Britain and Ireland.[4] For example, in adults aged 60-64 years, the prevalence ranged from 20% in Irish women to 31% in Australian women and from 14% in British men to 24% in Dutch men. Differences between countries have been found in the prevalence of falls, prevalence of risk factors for falls and associations between risk factors and falls in adults aged 65 years and older in SHARE including data from 18596 participants from 12 European countries [19]. That study also found that the differences in associations between countries were largely explained by differences in the prevalence of risk factors. Hence, risk factor profiles may differ by sex and country.

This study aimed to identify demographic, health and lifestyle risk factors for falls in middle-aged adults in Australia, The Netherlands, Great Britain and Ireland. Associations of potential risk factors with falls were examined separately by (a) country, and (b) sex. The focus was on demographic, health and lifestyle factors that have been found to be associated with falls in older adults [9,10], and have informed development of recommended preventive strategies in the community setting [5-8]. If the same risk factors are important in middle-age as at older ages, this would support earlier commencement of interventions that address these risk factors, with potential benefits sustained into older age. If different risk factors are important in middle-age, different strategies may need to be developed for the prevention of falls in midlife.

Methods

Study design and participants

The STrategies for Early Prevention of falls (STEP) consortium uses data from four cohort studies in Australia, The Netherlands, Great Britain and Ireland. The cohorts were selected based on the following criteria: (i) representative, population-based sample of adults aged 50-64 years; (ii) available data on falls in the previous year at one or more data collection waves; and (iii) available data on the majority of potential risk factors. The selection of the data collection waves for each cohort and procedures for data harmonisation are described in detail in Appendix 1. Although we have previously used these data to estimate prevalence of falls from ages 40 to 64 [4], the current analyses were limited to ages 50 to 64 as only one study recorded falls comparably between ages 40 and 50 and this was in a relatively small sample. Moreover, as the primary focus of current efforts to reduce falls risk is among adults aged 65 and older, we decided that it was most appropriate to focus on the next oldest age group in these analyses. Below we describe the design and participants for each of the cohorts.

The Australian Longitudinal Study on Women's Health (ALSWH) is a prospective study of the health and well-being of four generations of women [20,21]. Samples were randomly drawn from the national Medicare health insurance database, which includes all Australian citizens and permanent residents, with intentional over-sampling of women from rural and remote areas [20]. The study was approved by Ethics Committees of the Universities of Newcastle and Queensland. All participants provided informed consent. Data were collected through self-completed surveys either completed in paper form or electronically. In 1996, 13714 participants from the 1946–51 cohort (aged 45-50 years at baseline) returned the baseline survey (estimated response rate 54%). Follow-up surveys have been completed at approximately 3-year intervals. Falls data were available from the 2004 survey onward. For the current analysis, data were used from surveys completed in 2004 (n=10641, aged 52-58), 2007 (n=10525, aged 55-61), 2010 (n=9887, aged 58-64) and 2013 (n=4883, aged 62-64) with complete data on age and falls.

The Longitudinal Ageing Study Amsterdam (LASA) is an ongoing interdisciplinary cohort study on predictors and consequences of changes in physical, cognitive, emotional, and social functioning in men and women aged 55-85 years at baseline in 1992-93. A random sample stratified for age, sex, and expected 5-year mortality was drawn from the population registries of 11 municipalities in the Netherlands [22]. In 2012-13, the original sample was replenished with 1023 participants aged 55-65 years. Data were collected through self-completed surveys and structured interviews with clinical assessment conducted by trained interviewers. The VU University Medical Centre Ethical Review Board approved the study. All participants provided informed consent. As falls data were available in the correct age-range for participants in the 2012-13 cohort only, data from this cohort were used for the current analyses. In total, data were used from 862 participants aged 55-64 years with complete data on age and falls.

The MRC National Survey of Health and Development (NSHD) is an ongoing cohort study of a nationally representative sample of 5,362 males and females born in England, Scotland and Wales during one week in March 1946 [23,24]. The sample have now been followed up prospectively 24 times across life since birth. Falls data for these analyses were ascertained from nurse interviews during two of the most recent waves of data collection; at age 53 (in 1999), 3035 participants were successfully contacted, of whom 2984 received a home visit from a trained nurse; at age 60–64 (in 2006-2010), 2856 eligible participants were invited for assessment at one of six clinical research facilities or to be visited by a research nurse at home of whom 2229 were assessed. Relevant ethical approval was received from the North Thames Multi-Centre Research Ethics Committee (MREC

98/1/121) for the 1999 assessment and from the Central Manchester Local Research Ethics Committee (07/H1008/245) and the Scottish A Research Ethics Committee (08/MRE00/12) for the 2006-2010 assessment. All participants provided informed consent. In total, data were used from 2987 participants with complete data on falls at age 53 and 2210 participants at age 60-64.

The Irish Longitudinal Study on Ageing (TILDA) is an ongoing cohort study designed to achieve a representative sample of community-dwelling people aged 50 years or older in Ireland [25]. A random sample of 25600 residential addresses in Ireland were selected with stratification for socioeconomic status, age and geography. All persons aged 50 years and over (primary respondents) and their spouses or partners of any age (secondary respondents) were eligible. Each address was visited by field staff. Participants completed an interviewer-led computer-assisted questionnaire, a self-completed questionnaire and a research nurse-led health assessment. All participants signed informed consent. Ethical approval has been obtained from the Trinity College Dublin Research Ethics Committee. Baseline data from the 8504 primary and secondary participants were collected between October 2009 and July 2011. Follow-up waves were completed in 2012/13 and 2014/15. For the current analyses, data were used from participants aged 50-64 years with complete data on age and falls in 2010 (n=4663), 2012 (n=3825) and 2014 (n=3035).

Falls

In LASA, TILDA and NSHD, participants who responded 'yes' to the question "Have you fallen in the last year?" were classified as having had a fall. In ALSWH, participants who responded 'yes' to any one of the following three questions were classified as having had a fall: "In the last 12 months, have you: (i) had a fall to the ground? (ii) been injured as a result of a fall? and (iii) needed to seek medical attention for an injury from a fall?"

Demographic, health and lifestyle factors

Variables were selected based on known associations with fall risk in older adults. Variables were harmonised and included in the current analyses only if data were available for at least three of the cohorts. For a description of how each factor was measured in each cohort and how the variables were harmonised across the cohorts, please refer to Appendix 1. Data harmonisation was undertaken following a standardised approach to ensure that similar measures from different studies were as comparable as possible. The variables include:

- Demographics: age, sex, education, marital status, number of people in the household, retirement status, urbanisation grade;

- Health: osteoarthritis, rheumatoid arthritis, cancer, anxiety, depression, diabetes, heart disease, hypertension, lung disease, stroke, number of chronic conditions (range 0-4), benzodiazepine use, number of medications, polypharmacy, self-rated health, diastolic and systolic blood pressure, body mass index (BMI), dizziness, functional limitations (range 0-4), hearing problems, vision problems, pain, sleeping problems, urinary incontinence, immediate recall, delayed recall, verbal fluency, grip strength, mobility, use of a walking aid.
- Lifestyle: alcohol use, smoking status, level of leisure time physical activity.

Statistical analyses

Cross-sectional associations between each of the potential risk factors and fall status were examined using logistic regression adjusted for age and sex. To examine whether associations differed by cohort and sex, the models were initially run in the total sample including product terms for cohort (cohort × risk factor) and sex (sex × risk factor). For each product term, models with and without that product term were compared using the likelihood ratio test. The final univariate models were run for each of the cohorts separately, and the results were combined using fixed effect meta-analyses. The I^2 statistic was used as a measure of heterogeneity between cohorts. Combined results were only presented if there was no evidence for interaction by cohort (p-value for interaction with cohort>0.01) and low to moderate heterogeneity (I^2<70%, while acknowledging that the confidence interval around the I^2 is likely wide due to having a maximum of 4 data points). Given the low prevalence of some of the risk factors, it was not feasible to stratify by both cohort and sex. Therefore, in case of a statistically significant interaction with sex, models were additionally run for the total sample after stratification by sex as a post hoc analysis. To reduce the risk of type I error given the multiple comparisons, the significance level was set at 0.01 and 99% confidence intervals (CI) were presented. To ensure maximum coverage of the 50-64 year age-range within each of the cohorts, data were used from multiple waves where available (ALSWH, NSHD, TILDA). Robust standard errors were used to account for within-person variation due to repeated measures within cohorts.

To examine potential reverse causality, prospective models were run in which risk factors assessed at one data collection wave were associated with fall status measured at the subsequent wave. These models were included as confirmatory analyses of the cross-sectional models rather than described as the main models, because (i) data from the LASA study could not be included in the prospective models (falls were measured at baseline only), and (ii) some risk factors were measured at the last data collection wave only and no follow-up data on falls were available. The prospective

models were built up in the same way as described for the cross-sectional analyses, with the exception that results were not pooled across the cohorts because of the greater degree of heterogeneity between studies expected due to variation in the length of intervals between data collection waves: 3 years in ALSWH, 10 years in NSHD and 2 years in TILDA. All analyses were done using Stata version 14.2 (StataCorp LP, US).

Results

In ALSWH, all participants were women and the average age was 55.0 years (SD=1.5) in 2004, 58.0 (SD=1.5) in 2007, 61.1 (SD=1.5) in 2010 and 63.1 (SD=0.8) in 2013. In LASA, half the sample were women, and the average age was 59.7 (SD=2.8) in 2012. In NSHD, half the sample were women and the average age was 53.5 (SD=0.2) in 1999 and 63.4 (SD=1.1) in 2006-10. In TILDA, just over half the sample were women and the average age was 56.7 (SD=43.3) in 2010, 57.6 (SD=3.9) in 2012 and 58.6 (SD=3.4) in 2014. Other characteristics of the four samples are described in Table 1.

In cross-sectional models, statistically significant interactions with cohort were found for: sex, urbanisation grade, heart disease, hypertension, anxiety, BMI, dizziness, sleeping problems and urinary incontinence (Table 2). For all but two risk factors (i.e. heart disease, hypertension), the heterogeneity in associations across the cohorts was high (I^2>70%) and the results were presented for each cohort separately. While nearly all factors were statistically significantly associated with fall risk in at least one of the cohorts, only mobility was consistently associated with falls in all cohorts that measured it (poor vs good mobility: pooled OR=1.71, CI=1.34-2.07). Demographic factors that were associated with falls in at least two of the cohorts, included age, sex, marital status, number of other people in the household and urbanisation grade. Health factors that were associated with falls in at least two of the cohorts, included self-rated health, number of chronic conditions, osteoarthritis, rheumatoid arthritis, heart disease, lung disease, stroke, number of medications, polypharmacy, benzodiazepine use, use of a walking aid, functional limitations, dizziness, pain, hearing problems, sleeping problems and urinary incontinence. Of the lifestyle factors, only level of physical activity was associated with a fall risk in at least two of the cohorts (inactive vs high: pooled OR=1.30, CI=1.19-1.41).

In prospective models, statistically significant interactions with cohort were found for: age, sex, number of other people in the household, urbanisation grade, self-rated health, heart disease, anxiety, BMI, dizziness and urinary incontinence (Table 3). For all but one risk factor (i.e. number of others in household), the heterogeneity in associations across the cohorts was high. In ALSWH and

TILDA, but not in NSHD, the findings from the prospective models were consistent with the findings from the cross-sectional models (i.e. the ORs were in the same direction and range).

The risk factors for which statistically significant interactions with sex were found differed between the cross-sectional and prospective models. Cross-sectionally, significant interactions with sex were found for the risk factors number of other people in the household, number of chronic conditions, heart disease, BMI, and urinary incontinence (Table 2). For urinary incontinence, stronger associations with falls were found in men than in women (Table 4). For number of chronic conditions and heart disease, stronger associations with falls were found in women than in men. Prospectively, significant interactions with sex were found for the risk factors cancer, heart disease and verbal fluency (Table 3). For heart disease, a strong association was found in women, but not in men. For cancer and verbal fluency, the ORs suggested different associations in men and women, but in neither group did the associations reach statistical significance.

Discussion

Many of the demographic, health and lifestyle risk factors known to be associated with falls in older adults were also associated with falls in middle-aged adults. Poor mobility and urinary incontinence were consistently associated with a higher fall risk in all cohorts that measured it. For the other risk factors, associations with falls varied between cohorts. Overall, the associations found in the cross-sectional models were supported by the findings from the prospective models in the Australian and Irish cohorts. Statistically significant interactions with sex suggest differences in risk factors for falls among middle-aged men and women.

Demographic risk factors

Similar to older adults [26], middle-aged women have a higher fall risk than men. In line with findings from a meta-analysis of 7 studies in older adults [9], we found no statistically significant association between level of education and fall risk. Consistent with findings from a study based on hospital admission records of 19518 adults aged 20-92 in Finland, being single, widowed, divorced or separated was associated with an higher fall risk than being married [18]. The association between number of other people in the household and fall risk appeared consistent across the four cohorts.

To our knowledge, no other study has examined the association between retirement status and fall risk. Being retired was associated with an increased risk of falls in the British cohort, but not in the Dutch and Irish cohorts. The prevalence of retirement was much higher in the British cohort (61.7%)

than in the Dutch (16.0%) and Irish (13.0-15.0%) cohorts, which reflects the higher average age and lower age of eligibility for retirement for women in this birth cohort in Great Britain. Differences between countries may also relate to different primary reasons for retirement; early and late retirement are influenced by financial circumstances and health [27-29], which relate differently to fall risk.

Health factors

In all four cohorts included in our study, participants with poor self-rated health (SRH) were found to have elevated odds of falling when compared with those reporting excellent SRH (pooled OR: 3.20 (95% CI: 2.55-3.84)). This estimate is substantially higher than that reported in a meta-analysis of 6 studies of older adults (pooled OR=1.50, 95% CI=1.15-1.96) [9]. Likewise, the OR for number of chronic conditions (including diabetes, heart disease, lung disease and cancer) was somewhat higher in our study (re-analysed as a continuous variable, range 0-4: pooled OR=1.37, CI=1.31-1.43) than in a meta-analysis of 10 studies in older adults (pooled OR=1.23, CI=1.16-1.30).[9] Similarly, associations with fall risk were stronger for osteoarthritis, rheumatoid arthritis, diabetes, stroke, pain and urinary incontinence in the current sample of middle-aged adults, than in the meta-analyses of studies conducted in older adults [9]. These findings indicate a stronger contrast in fall risk between those with and without chronic conditions in midlife than between those with and without chronic conditions at older ages. This may be explained by the higher prevalence of multimorbidity at older ages and by the age-related decline in balance and mobility independent of chronic conditions that reduces the contrast between those with and without multimorbidity at older ages. At younger ages people with these conditions are a more select, higher risk group who may benefit from targeted falls prevention strategies.

The findings for medication use and fall risk were similar across the cohorts (Table 2). Compared with findings from a meta-analysis in older adults, the ORs suggest stronger associations in the middle-aged adults than in the older adults. For each additional medication, the OR was 1.13 (CI=1.11-1.15) in the current middle-aged sample, whereas the unadjusted OR pooled across data from 10 studies was 1.06 (CI=1.04-1.08) in older adults [9]. For benzodiazepine use, the OR was 1.86 (CI=1.53-2.19) in the current sample, compared with 1.38 (CI=1.15-1.66) in older adults [9]. These findings suggest that medication-related interventions to prevent falls recommended for older adults, such as medication review and avoidance of benzodiazepine use [5-8], may also be relevant for younger adults.

Along with a history of falls, poor gait and balance are generally regarded as the most important risk factors of falls in older adults [30]. We found that use of a walking aid was a strong predictor for falls, even though very few people in the sample reported using a walking aid. Correspondingly, poor mobility as measured with a walking test was associated with a greater fall risk, but only in the cross-sectional models. However, the prospective models for mobility were based on data from the Irish cohort only and given the fluctuations between cohorts, verification in a different cohort is required. The ORs for functional limitations were of a similar magnitude to those previously reported in older adults [9].

In a previous paper using ALSWH data only, obesity was identified as an important risk factor for falls in middle-age [15]. In the current analyses, a statistically significant prospective association was found in the Australian cohort again, but not in the other three cohorts. However, we did find a significant interaction with sex, and after stratification found that the association between obesity and falls was stronger in women than in men (Table 4). The Australian cohort included women only, which may explain the differences in findings between the cohorts.

Systematic reviews of observational studies in older adults that examined associations between measures of cognitive function and fall risk, found stronger evidence for associations with fall risk for executive function than for memory [31,32]. In contrast, in the British cohort we found fairly strong cross-sectional associations with fall risk for immediate and delayed recall, but not with verbal fluency, a measure of executive function. However, these associations with recall tests were not found in the Dutch cohort and, while statistically significant, the effect estimate for delayed recall was much lower in the Irish cohort than in the British cohort. Moreover, the cross-sectional associations were not confirmed in the prospective models. One study examining associations between cognitive functions and fall risk used data from the LASA study, but included participants over the age of 65 only. In that study, a significant association was found between immediate recall and fall risk, but only in adults over the age of 75 [33]. In a study among 1947 adults aged 70 years and older, immediate recall was not associated with fall risk, but *decline* in immediate recall over 8 years follow-up was associated with an increased fall risk [34]. Hence, cognitive risk factors may be more important at older ages when the prevalence of cognitive decline is higher.

The association between hearing problems and fall risk in middle-aged adults was similar in the cross-sectional and prospective models , and in line with findings in older adults [9]. The associations between vision problems and fall risk varied across the cohorts. Reviews of studies

conducted in older adults also describe inconsistencies in findings between studies examining associations between objective measures of vision and fall risk [35,36]. These inconsistencies may partly be explained by differences in sample characteristics and measurement of vision. It may also be that it is the accumulation of sensory problems that is important for fall risk rather than problems with specific sensory modalities [37,38], In the current study, no data were available on other sensory modalities, such as proprioception, depth perception and contrast sensitivity [39,40]. Hence, further research is required to gain a better understanding of the role of sensory functions and fall risk in middle-aged adults.

Lifestyle factors

Similar associations between lifestyle factors and fall risk were found in middle-age as in older adults. Both never drinking alcohol and high-risk drinking may increase fall risk [41,42], although in the current sample the association was significant in the Australian cohort only. Inactivity, measured either with questionnaires [43] or accelerometers [44], has been associated with increased fall risk in older adults. This is consistent with our findings in middle-aged adults and highlights the potential benefits of extending targeted physical activity interventions which reduce inactivity with the aim of preventing or delaying functional decline in older adults to include middle-aged adults [45]. There is little evidence for an association between smoking and fall risk in middle-aged or older adults [46]. Our findings suggest that ex-smokers may have a higher fall risk than never smokers, but this was statistically significant in the Australian cohort only and was modest.

There were substantial differences in the risk factor profiles between the four cohorts. This is in line with findings from SHARE, which found substantial differences in the risk factors associated with falls in older adults across 12 European countries. That study also demonstrated that between-country differences in the prevalence of falls strongly attenuated after adjusting for differences in risk factors [19]. Country differences may reflect true differences between countries due to differences in demographics, health, lifestyle and health care systems, but may also be an artefact of differences in study design (e.g. selection criteria, sample size, measurement of risk factors), which cannot be fully removed by harmonisation. In LASA, only poor mobility was associated with a statistically significant increased fall risk. While the LASA sample was substantially smaller than the other three samples, a sample of 862 participants with 25% fallers should be large enough to detect statistically significant associations. For some risk factors with a low prevalence, for example benzodiazepine use (4.7% in LASA), the OR was of a similar magnitude to that in the other cohorts (LASA: OR=1.77, CI=0.74-4.23; other cohorts: ORs=1.68-2.39), but with wider confidence intervals. However, for many risk factors,

the ORs were substantially lower in LASA than in the other three cohorts, which cannot be explained by a lack of statistical power. Therefore, replication of these analyses in a different Dutch cohort is recommended.

The findings in the cross-sectional and prospective models in the Australian and Irish cohorts were remarkably consistent. This makes reverse causation less likely, although it cannot be ruled out. There were substantial differences in the findings from the cross-sectional and prospective models in the British cohort. This contrast is likely explained by the longer duration between data collection waves (10 years) in the British than in the Australian (3 years) and Irish (2 years) cohorts. A proportion of participants classified as not having chronic conditions at the first assessment may have developed chronic conditions such as diabetes or lung disease during follow-up. This may have reduced the contrast between the groups and diluted the association with fall risk. As middle-age is a life stage during which many changes in lifestyle and health occur, a 10-year interval may be too long to detect meaningful associations with fall risk without appropriately taking into account changes in risk factor profiles.

Risk factors known to be associated with falls in older adults, were also associated with falls in middle-aged adults. This suggests that evidence-based preventive interventions developed for older adults may also be of benefit to middle-aged adults. However, as discussed above, there are differences in the strength of associations between middle-aged and older adults. Moreover, there are differences in risk factor profiles by country and sex. Existing preventive interventions may therefore be more effective if tailored to age, sex and country. Future research is required to examine the (cost-)effectiveness of preventive interventions targeting the identified risk factors.

Strengths include using data from 20257 participants from four cohorts based in different countries. This allowed us to examine differences in associations between a comprehensive range of different risk factors and falls between cohorts and between women and men. Moreover, the large sample gave us sufficient statistical power to examine risk factors with a low prevalence in middle-age, but with a potentially large impact on fall risk, such as stroke and benzodiazepine use. However, results need to be interpreted with caution as we did not test whether the risk factors identified are independent of each other. Other limitations of our study include that not all cohorts had data available on all potential risk factors of interest. For example, we were unable to conduct meaningful comparisons of environmental factors. In addition, while we were able to investigate some objective measures of physical performance i.e. grip strength and mobility, there are other

potentially important measures of performance such as standing balance which we were unable to study and which may therefore warrant investigation in future studies. Another potential limitation is that for some variables, details in the data were lost due to data harmonisation. Although our data harmonisation approach was valid and feasible, it is also possible that some differences in the observed findings between the studies may still be due to differences in measures. Bias may also have been introduced as data on falls and many of the risk factors were self-reported. However, this would not be expected to have impacted greatly on the findings and their comparison with studies of older adults as falls in community-based samples are usually ascertained via self-report.

In conclusion, many of the demographic, health and lifestyle risk factors known to be associated with falls in older adults, were also associated with falls in middle-aged adults. However, there are differences in the strength of the associations between middle-aged and older adults with some factors such as musculoskeletal conditions being potentially more important at younger ages. Poor mobility and urinary incontinence were the only risk factors that were consistently associated with a higher fall risk across the four countries. Country differences in risk factor profiles may reflect differences in the prevalence of both the risk factors and falls and/or be driven by differences in study design. Statistically significant interactions with sex were found for five of the risk factors, suggesting that there are some differences in risk profiles for men and women. Future research should verify whether available preventive interventions that target the identified risk factors are also beneficial for middle-aged adults, and whether tailoring by age, sex and country is required.

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Table 1. Sample characteristics for each cohort and at each data collection wave.

	Australia (ALSWH)				Netherlands (LASA)	Great Britain (NSHD)		Ireland (TILDA)		
Year of data collection	2004	2007	2010	2013	2012	1999	2006-10	2010	2012	2014
N	10641	10525	9887	4883	862	2987	2210	4663	3825	3035
Age[1]	55.0 (1.5)	58.0 (1.5)	61.1 (1.5)	63.1 (0.8)	59.7 (2.8)	53.5 (0.2)	63.4 (1.1)	56.7 (4.3)	57.6 (3.9)	58.6 (3.4)
Sex (% women)	100	100	100	100	51.6	50.9	52.1	55.5	56.2	57.3
Education (% tertiary)	35.0	35.3	36.1	38.9	32.1	9.9	11.3	34.1	n/a	41.9
Married or partnered (%)	80.5	78.5	76.9	76.4	74.1	77.9	79.1	76.7	77.3	77.7
≥2 others in household (%)	27.2	18.7	15.1	15.3	19.1	44.3	16.8	47.2	48.0	46.8
Retired (%)	n/a	n/a	n/a	n/a	16.0	n/a	61.7	13.0	14.3	15.0
Living in urban areas (%)	76.8	76.8	77.8	78.5	59.4	n/a	n/a	51.2	50.9	49.9
SRH (% good-excellent)	85.8	86.3	86.1	87.2	87.5	n/a	86.1	85.3	85.7	86.1
≥2 chronic conditions (%)	2.5	3.5	4.4	5.2	6.4	3.1	10.1	4.5	2.9	3.3
Osteoarthritis (%)	n/a	15.9	18.6	25.9	40.1	n/a	n/a	9.3	12.5	12.5
Rheumatoid arthritis (%)	n/a	4.7	5.0	5.0	8.2	n/a	n/a	6.1	5.7	5.5
Cancer (%)	3.2	3.8	4.1	4.6	9.9	3.1	11.6	4.8	1.4	2.0
Diabetes (%)	4.6	6.7	7.9	8.4	7.7	2.9	8.0	5.6	5.5	5.8
Heart disease (%)	3.1	4.0	4.4	5.1	11.0	4.5	12.8	11.1	9.3	10.0
Hypertension (%)	20.7	28.0	30.5	32.7	28.3	n/a	33.6	29.2	27.4	27.7
Lung disease (%)	13.4	14.1	15.1	16.9	10.2	19.0	18.8	11.6	10.3	10.6
Stroke (%)	0.5	4.0	1.0	0.8	2.1	0.8	1.7	0.8	0.8	0.2
Depression (%)	20.8	19.7	18.7	16.6	12.0	15.6	11.6	10.6	9.9	8.5
Anxiety (%)	25.8	19.5	17.9	16.4	23.3	27.8	25.2	28.7	n/a	15.5
N° medications (0-6)[1]	n/a	3 [1-4]	4 [2-6]	n/a	1 [0-3]	0 [0-2]	2 [0-4]	1 [0-3]	1 [0-3]	1 [0-3]
Polypharmacy[1]	n/a	22.7	40.2	n/a	14.0	4.6	20.8	11.9	15.8	13.3
Benzodiazepine[1]	n/a	4.2	4.0	n/a	4.7	1.5	1.7	3.9	4.1	3.9

Immediate recall (% <11)	n/a	n/a	n/a	n/a	4.5	4.3	3.2	2.2	1.0	1.0
Delayed recall (% <4)	n/a	n/a	n/a	n/a	10.6	2.8	2.4	9.5	8.4	7.8
Verbal fluency (0-62)[1]	n/a	n/a	n/a	n/a	22.5 (5.9)	n/a	23.6 (6.9)	21.7 (7.1)	20.6 (6.0)	20.5 (5.9)
Grip strength - women (kg)[1]	n/a	n/a	n/a	n/a	25.9 (6.1)	28.0 (7.8)	26.2 (7.3)	22.6 (5.1)	24.78 (6.0)	24.2 (5.0)
Grip strength - men (kg)[1]	n/a	n/a	n/a	n/a	45.5 (8.5)	47.7 (12.2)	44.7 (11.5)	38.5 (8.0)	40.8 (8.7)	39.7 (7.9)
Mobility (% poor/unable)	n/a	n/a	n/a	n/a	14.2	n/a	26.8	12.6	n/a	17.9
Use of a walking aid (%)	n/a	n/a	n/a	n/a	3.3	n/a	1.4	0.4	0.4	0.2
Functional limitations (% ≥1)	48.8	51.0	53.8	56.0	29.2	n/a	23.5	18.7	18.8	17.1
Diastolic Bp (per 10 mmHg)	n/a	n/a	n/a	n/a	83.5 (11.1)	84.4 (12.3)	77.8 (10.0)	82.4 (11.3)	n/a	80.7 (10.5)
Systolic Bp (per 10 mmHg)	n/a	n/a	n/a	n/a	137.3 (19.0)	136.1 (20.1)	136.4 (18.3)	129.5 (18.4)	n/a	127.1 (17.2)
Body mass index[1]	27.2 (5.5)	27.4 (5.6)	27.6 (5.6)	27.7 (5.8)	27.1 (4.7)	27.4 (4.8)	27.9 (4.9)	28.6 (5.1)	27.3 (4.8)	27.4 (5.0)
Waist circumference	n/a	n/a	n/a	n/a	96.8 (13.2)	91.7 (13.3)	96.5 (12.9)	94.5 (14.0)	n/a	95.6 (14.1)
Dizzy (%)	n/a	n/a	17.7	16.3	6.6	14.5	22.6	n/a	n/a	n/a
Pain (%)	50.7	51.6	53.9	54.6	28.1	n/a	23.6	35.2	33.6	34.0
Hearing problems (%)	17.9	20.0	20.5	22.8	7.1	17.2	23.8	11.7	12.3	12.8
Vision problems (% near and/or far)	n/a	n/a	n/a	n/a	21.0	n/a	8.7	15.8	n/a	n/a
Sleeping problems (% any)	62.2	67.5	66.7	66.5	31.2	n/a	n/a	57.4	56.2	58.6
Urinary incontinence (%)	45.6	46.0	46.5	59.0	16.7	n/a	32.2	10.5	12.6	10.3
Level of alcohol intake (%)										
Low risk	54.1	56.7	55.4	54.5	55.7	54.2	61.4	49.3	43.6	58.9
Never/rarely drinks	39.2	37.0	37.9	39.1	14.2	27.2	15.5	30.7	27.1	26.7
Risky/high risk	6.7	6.3	6.7	6.4	30.1	18.7	23.2	20.0	29.3	14.5
Smoking status (%)										
Never smoked	59.1	60.0	60.7	61.9	25.9	29.3	32.3	43.5	44.2	44.4
Ex-smoker	27.4	29.0	30.4	30.0	55.9	47.5	56.4	35.0	36.6	39.5
Current smoker	13.5	11.0	8.9	8.2	18.1	23.2	11.3	21.6	19.2	16.1
Level of physical activity (%)										

Inactive	16.4	16.1	16.7	17.4	3.4	n/a	7.3	7.0	5.7	15.4
Low	25.4	22.7	23.4	21.0	16.8		15.2	13.1	12.5	3.8
High	58.3	61.2	59.8	61.5	79.8		77.4	80.0	81.7	80.8
Faller (%)	22.1	31.6	30.3	26.1	25.1	17.4	18.3	17.6	18.6	19.0

SRH Self-rated health

n/a Data not available, not reliably measured, or not possible to harmonise available variables in a comparable way to the other cohorts

[1] Presented are the mean (standard deviation)

[2] Presented are the median [interquartile range]

Table 2. Cross-sectional associations between each of the risk factors and fall status in each of the cohorts and pooled across the cohorts

	ALSWH Australia OR (99%)	LASA Netherlands OR (99%)	NSHD Great Britain OR (99%CI)	TILDA Ireland OR (99%)	Pooled estimates OR (99%)	I^2 (p-value) for heterogeneity between cohorts	p-value for interaction with cohort	p-value for interaction with sex
Demographic factors								
Age								
50-54 years	1	n/a	1	1		n/a[3]	n/a[3]	0.005
55-59 years	1.43 (1.29-1.59)	1	n/a	1.22 (1.03-1.43)				
60-64 years	1.56 (1.41-1.74)	1.14 (0.76-1.71)	1.05 (0.87-1.27)	1.36 (1.15-1.60)				
Sex						84.5% (0.002)	0.002	n/a
Male	n/a	1	1	1				
Female		1.27 (0.84-1.90)	1.90 (1.57-2.31)	1.23 (1.08-1.39)				
Education						41.1% (0.10)	0.59	0.78
Tertiary	1	1	1	1	1			
Secondary	0.92 (0.86-0.99)	1.10 (0.70-1.73)	1.19 (0.83-1.69)	0.88 (0.74-1.04)	0.94 (0.88-1.01)			
Primary/none	1.07 (0.98-1.17)	0.92 (0.43-1.96)	1.05 (0.72-1.52)	1.05 (0.84-1.30)	1.06 (0.97-1.15)			
Marital status						40.3% (0.05)	0.04	0.03
Married	1	1	1	1	1			
Registered partnership[1]	1.04 (0.90-1.19)	0.94 (0.28-3.21)	n/a	1.44 (1.04-1.99)	1.13 (0.98-1.29)			
Single (never married)	1.14 (0.95-1.37)	1.19 (0.63-2.25)	1.78 (1.21-2.64)	1.20 (0.96-1.49)	1.21 (1.04-1.38)			
Separated/divorced	1.29 (1.18-1.41)	1.05 (0.52-2.14)	1.46 (1.11-1.92)	1.74 (1.43-2.11)	1.40 (1.29-1.51)			
Widowed	1.18 (1.03-1.35)	1.47 (0.62-3.49)	1.07 (0.67-1.72)	1.06 (0.78-1.43)	1.15 (1.01-1.29)			
N° other people in household						0% (0.60)	0.71	0.009
0	1	1	1	1	1			
1	0.77 (0.71-0.84)	1.02 (0.60-1.72)	0.67 (0.50-0.90)	0.76 (0.63-0.91)	0.92 (0.54-1.30)			
2	0.76 (0.68-0.85)	0.62 (0.27-1.44)	0.65 (0.46-0.92)	0.79 (0.65-0.97)	0.66 (0.26-1.05)			
3+	0.75 (0.65-0.87)	0.73 (0.28-1.89)	0.71 (0.48-1.03)	0.69 (0.56-0.85)	0.71 (0.17-1.26)			
Retirement status						62.6% (0.07)	0.37	0.55
Not retired	n/a	1	1	1	1			

Retired		0.77 (0.41-1.45)	1.58 (1.13-2.22)	0.98 (0.82-1.18)	1.05 (0.89-1.22)			
Urbanisation grade						94.5% (<0.001)	<0.001	0.20
Urban	1	1	n/a	1				
Rural/remote	1.11 (1.03-1.19)	1.08 (0.72-1.63)		0.74 (0.65-0.84)				
Health factors								
Self-rated health						96.0% (<0.001)	0.03	0.30
Excellent	1	1	1	1	1			
Very good	1.16 (1.03-1.30)	1.14 (0.63-2.06)	1.20 (0.71-2.02)	1.07 (0.88-1.30)	1.14 (1.03-1.25)			
Good	1.67 (1.49-1.88)	0.90 (0.44-1.84)	1.49 (0.88-2.53)	1.42 (1.17-1.72)	1.59 (1.44-1.75)			
Fair	2.60 (2.28-2.96)	0.80 (0.34-1.89)	2.34 (1.28-4.28)	2.11 (1.69-2.65)	2.45 (2.17-2.72)			
Poor	3.18 (2.49-4.06)	3.27 (0.92-11.5)	5.19 (2.04-13.2)	2.85 (2.04-4.00)	3.19 (2.54-3.84)			
N° chronic conditions						87.7% (<0.001)	0.02	0.004
0	1	1	1	1	1			
1	1.40 (1.30-1.50)	0.97 (0.60-1.58)	1.37 (1.10-1.71)	1.26 (1.09-1.46)	1.36 (1.28-1.44)			
2+	2.03 (1.75-2.36)	1.66 (0.77-3.57)	1.95 (1.33-2.86)	1.64 (1.22-2.20)	1.93 (1.69-2.17)			
Osteoarthritis[2]	1.74 (1.60-1.90)	1.37 (0.90-2.08)	n/a	1.42 (1.18-1.71)	1.63 (1.50-1.76)	61.5% (0.07)	0.04	0.92
Rheumatoid arthritis[2]	1.72 (1.47-2.00)	1.35 (0.67-2.69)	n/a	1.50 (1.18-1.91)	1.64 (1.43-1.86)	0% (0.54)	0.34	0.97
Cancer[2]	1.13 (0.97-1.32)	1.01 (0.51-1.99)	1.07 (0.73-1.56)	1.09 (0.76-1.56)	1.11 (0.96-1.27)	0% (0.98)	0.59	0.76
Diabetes[2]	1.46 (1.30-1.64)	1.13 (0.54-2.38)	1.43 (0.95-2.14)	1.27 (0.99-1.64)	1.41 (1.26-1.56)	0% (0.70)	0.18	0.03
Heart disease[2]	1.78 (1.54-2.05)	1.28 (0.68-2.40)	1.46 (1.04-2.05)	1.30 (1.08-1.58)	1.64 (1.45-1.82)	67.8% (0.03)	<0.001	<0.001
Hypertension[2]	1.29 (1.20-1.37)	1.43 (0.92-2.21)	1.07 (0.79-1.44)	1.06 (0.92-1.22)	1.23 (1.16-1.30)	63.2% (0.03)	<0.001	0.62
Lung disease[2]	1.53 (1.41-1.66)	1.29 (0.68-2.44)	1.54 (1.23-1.94)	1.38 (1.15-1.66)	1.48 (1.37-1.59)	0% (0.67)	0.22	0.17
Stroke[2]	2.20 (1.78-2.72)	0.59 (0.11-3.03)	2.22 (1.05-4.71)	1.91 (1.00-3.63)	2.11 (1.65-2.57)	32.0% (0.22)	0.43	0.17
Depression[2]	1.93 (1.80-2.08)	1.44 (0.79-2.62)	1.81 (1.41-2.32)	1.85 (1.54-2.23)	1.89 (1.76-2.02)	0% (0.71)	0.47	0.59
Anxiety[2]	1.61 (1.50-1.73)	1.37 (0.85-2.18)	1.20 (0.95-1.52)	1.24 (1.02-1.51)		75.6% (<0.006)	<0.001	0.11
N° medications (0-6)	1.13 (1.10-1.15)	1.06 (0.96-1.17)	1.15 (1.09-121)	1.12 (1.09-1.16)	1.13 (1.11-1.15)	0% (0.50)	0.72	0.18
Polypharmacy[2]	1.54 (1.41-1.68)	1.27 (0.72-2.22)	1.99 (1.52-2.62)	1.73 (1.47-2.03)	1.66 (1.52-1.80)	47.4% (0.13)	0.01	0.70
Benzodiazepine[2]	1.68 (1.38-2.04)	1.77 (0.74-4.23)	2.39 (1.29-4.43)	1.91 (1.46-2.51)	1.86 (1.53-2.19)	0% (0.65)	0.26	0.19
Immediate recall						0% (0.68)	0.70	0.35

11-20 words	n/a	1	1	1	1			
0-10 words		1.35 (0.52-3.52)	1.76 (1.13-2.75)	1.31 (0.81-2.12)	1.44 (0.95-1.94)			
Delayed recall						62.9% (0.07)	0.50	0.12
4-10 words	n/a	1	1	1	1			
0-3 words		0.84 (0.41-1.70)	1.96 (1.10-3.49)	1.25 (1.01-1.54)	1.42 (1.05-1.78)			
Verbal fluency (0-62)	n/a	1.02 (0.99-1.06)	1.00 (0.98-1.02)	1.00 (0.99-1.01)	1.00 (0.99-1.01)	0% (0.56)	0.19	0.11
Grip strength (quintiles)						0% (0.64)	0.64	0.13
F: ≥30 M: ≥51 kg	n/a	1	1	1	1			
F: 26-<30 M: 45-<51 kg		0.98 (0.54-1.79)	1.16 (0.88-1.55)	0.93 (0.70-1.24)	1.01 (0.81-1.21)			
F: 23-<26 M: 40-<45 kg		1.30 (0.70-2.40)	1.24 (0.91-1.70)	1.09 (0.83-1.43)	1.15 (0.92-1.38)			
F: 20-<23 M: 34-<40 kg		1.44 (0.73-2.82)	1.34 (0.97-1.85)	1.15 (0.87-1.51)	1.23 (0.98-1.48)			
F: 0-<20 M: 0-<34 kg		1.36 (0.66-2.79)	1.61 (1.20-2.16)	1.29 (0.99-1.69)	1.40 (1.13-1.67)			
Mobility						60.2% (0.01)	0.65	0.57
Good	n/a	1	1	1	1			
Moderate		1.00 (0.60-1.66)	0.88 (0.55-1.40)	1.09 (0.86-1.38)	1.03 (0.83-1.24)			
Fair		0.70 (0.37-1.35)	0.91 (0.57-1.46)	1.16 (0.92-1.48)	1.06 (0.84-1.28)			
Poor/unable		1.85 (1.03-3.30)	2.04 (1.35-3.07)	1.57 (1.20-2.05)	1.71 (1.34-2.07)			
Use of a walking aid[2]	n/a	2.32 (0.84-6.39)	5.13 (1.65-16.0)	6.37 (2.71-15.0)	5.97 (0.89-11.1)	70.3% (0.04)	0.05	0.82
Functional limitations (0-4)	1.41 (1.38-1.46)	1.19 (0.97-1.45)	1.39 (1.22-1.59)	1.51 (1.40-1.64)	1.43 (1.39-1.47)	54.1% (0.09)	0.13	0.03
Diastolic Bp (per 10 mmHg)	n/a	1.09 (0.91-1.31)	0.99 (0.91-1.09)	1.00 (0.93-1.09)	1.00 (0.94-1.06)	0% (0.67)	0.81	0.77
Systolic Bp (per 10 mmHg)	n/a	1.04 (0.93-1.16)	0.99 (0.94-1.04)	0.99 (0.94-1.04)	0.99 (0.96-1.03)	0% (0.72)	0.79	0.51
Body mass index						89.3% (<0.001)	<0.001	<0.001
Under/normal weight	1	1	1	1				
Overweight	1.27 (1.17-1.36)	0.89 (0.54-1.45)	1.06 (0.84-1.34)	0.94 (0.80-1.10)				
Obese	1.65 (1.53-1.78)	1.40 (0.84-2.45)	1.30 (1.02-1.66)	1.17 (0.99-1.40)				
Dizziness[1]	2.22 (1.98-2.50)	1.36 (0.63-2.93)	1.45 (1.10-1.91)	n/a		82.5% (0.003)	<0.001	0.04
Pain[1]	2.02 (1.89-2.15)	1.10 (0.69-1.76)	2.09 (1.51-2.90)	1.98 (1.74-2.24)	2.00 (1.89-2.11)	72.8% (0.01)	0.62	0.60
Hearing problems[2]	1.42 (1.32-1.53)	1.01 (0.45-2.25)	1.51 (1.21-1.90)	1.37 (1.15-1.65)	1.41 (1.31-1.51)	0% (0.75)	0.90	0.06
Vision problems						81.4% (<0.001)	0.02	0.39
None	n/a	1	1	1	1			

Near only		1.09 (0.65-1.81)	2.41 (1.25-4.63)	0.93 (0.64-1.34)	1.37 (0.84-1.90)			
Far only		4.63 (0.44-48.5)	1.46 (0.74-2.88)	1.38 (0.89-2.14)	1.77 (0-4.49)			
Both near and far		5.89 (0.65-53.5)	3.43 (1.29-9.12)	1.59 (0.94-2.73)	2.60 (0-5.80)			
Sleeping problems								
None	1	1	n/a	1		83.6% (<0.001)	<0.001	0.09
Waking too early	1.34 (1.24-1.45)	1.41 (0.81-2.47)		1.28 (1.09-1.52)				
Difficulty falling asleep	1.50 (1.35-1.66)	0.86 (0.35-2.10)		1.29 (1.03-1.62)				
Both	1.96 (1.80-2.14)	1.37 (0.64-2.92)		1.58 (1.36-1.85)				
Urinary incontinence[2]	1.53 (1.44-1.63)	1.62 (0.95-2.78)	1.68 (1.22-2.31)	2.09 (1.75-2.49)		76.9% (0.005)	<0.001	<0.001
Lifestyle factors								
Level of alcohol intake						0% (0.73)	0.40	0.05
Low risk	1	1	1	1	1			
Never/rarely drinks	1.09 (1.03-1.17)	0.79 (0.42-1.49)	1.24 (0.97-1.57)	1.00 (0.85-1.19)	1.08 (1.02-1.15)			
Risky/high risk	1.12 (0.99-1.27)	1.10 (0.69-1.74)	1.03 (0.78-1.37)	1.18 (0.98-1.42)	1.12 (1.01-1.23)			
Smoking status						0% (0.93)	0.78	0.15
Never smoked	1	1	1	1	1			
Ex-smoker	1.14 (1.06-1.22)	1.36 (0.82-2.24)	1.12 (0.90-1.39)	1.08 (0.94-1.24)	1.13 (1.06-1.20)			
Current smoker	1.07 (0.97-1.18)	1.47 (0.78-2.77)	1.05 (0.79-1.41)	1.11 (0.94-1.32)	1.08 (0.99-1.17)			
Level of physical activity						69.2% (0.002)	0.36	0.93
High	1	1	1	1	1			
Low	1.05 (0.97-1.13)	1.21 (0.71-2.05)	1.34 (0.91-1.96)	0.94 (0.76-1.17)	1.04 (0.97-1.12)			
Inactive	1.33 (1.22-1.45)	0.66 (0.18-2.40)	1.29 (0.77-2.19)	1.26 (1.00-1.59)	1.30 (1.19-1.41)			

OR odds ratio; 99%CI 99% confidence interval; F female; M male

All models were adjusted for age and sex.

[1] Registered partnership may also include defacto relationships.

[2] Not having the condition or limitation was defined as the reference category.

[3] Interaction with cohort and I^2 cannot be estimated when the reference category differs between cohorts.

Table 3. Prospective associations between each of the risk factors and fall status in three cohorts.

	ALSWH Australia OR (99%)	NSHD Great Britain OR (99%CI)	TILDA Ireland OR (99%)	I^2 (p-value) for heterogeneity between cohorts	p-value for interaction with cohort	p-value for interaction with sex
Demographic factors						
Age						
50-54 years	1	n/a	1	80.6% (0.001)	<0.001	0.02
55-59 years	0.99 (0.90-1.09)		1.19 (0.99-1.43)			
60-64 years	0.89 (0.80-0.99)		1.34 (1.11-1.62)			
Sex				86.0% (0.008)	<0.001	n/a
Male	n/a	1	1			
Female		1.92 (1.42-2.60)	1.16 (1.00-1.35)			
Education				55.7% (0.05)	0.94	0.24
Tertiary	1	1	1			
Secondary	0.93 (0.86-1.00)	1.47 (0.84-2.59)	0.88 (0.70-1.10)			
Primary/none	1.09 (0.99-1.21)	1.16 (0.64-2.11)	1.06 (0.80-1.39)			
Marital status				39.5% (0.09)	0.01	0.02
Married	1	1	1			
Registered partnership	1.11 (0.96-1.29)	n/a	1.28 (0.85-1.92)			
Single (never married)	1.24 (1.01-1.53)	2.19 (1.19-4.04)	1.28 (0.99-1.66)			
Separated/divorced	1.22 (1.11-1.35)	1.30 (0.84-2.01)	1.80 (1.43-2.27)			
Widowed	1.23 (1.05-1.44)	0.48 (0.16-1.48)	1.22 (0.86-1.71)			
N° others in the household				0% (0.52)	0.006	0.58
0	1	1	1			
1	0.80 (0.72-0.88)	0.57 (0.35-0.91)	0.74 (0.59-0.92)			
2	0.81 (0.71-0.91)	0.62 (0.37-1.04)	0.77 (0.60-0.97)			
3+	0.81 (0.69-0.95)	0.53 (0.31-0.91)	0.59 (0.47-0.75)			
Retirement status				4.3% (0.31)	0.52	0.99
Not retired	n/a	n/a	1			

Retired			1.02 (0.82-1.27)			
Urbanisation grade				97.4% (<0.001)	<0.001	0.40
Urban	1	n/a	1			
Rural/remote	1.13 (1.04-1.22)		0.71 (0.61-0.83)			
Health factors						
Self-rated health				97.4% (<0.001)	0.007	0.23
Excellent	1	n/a	1			
Very good	1.22 (1.07-1.38)		1.23 (0.98-1.55)			
Good	1.68 (1.49-1.91)		1.51 (1.20-1.89)			
Fair	2.68 (2.32-3.10)		1.99 (1.52-2.62)			
Poor	3.67 (2.71-4.96)		3.02 (2.02-4.51)			
Nº chronic conditions				92.3% (<0.001)	0.04	0.03
0	1	1	1			
1	1.33 (1.23-1.45)	1.16 (0.82-1.66)	1.21 (1.02-1.44)			
2+	2.20 (1.84-2.64)	1.38 (0.52-3.67)	1.61 (1.13-2.28)			
Osteoarthritis[1]	1.72 (1.55-1.92)	n/a	1.33 (1.06-1.67)	78.4% (0.03)	0.03	0.17
Rheumatoid arthritis[1]	1.73 (1.43-2.09)	n/a	1.56 (1.18-2.07)	0% (0.55)	0.56	0.20
Cancer[1]	1.14 (0.94-1.37)	1.61 (0.74-3.52)	1.16 (0.78-1.72)	0% (0.79)	0.59	<0.001
Diabetes[1]	1.49 (1.30-1.71)	0.67 (0.19-2.41)	1.22 (0.90-1.66)	39.8% (0.19)	0.18	0.51
Heart disease[1]	1.85 (1.56-2.19)	1.77 (0.89-3.51)	1.25 (0.99-1.57)	81.2% (0.005)	0.002	0.003
Hypertension[1]	1.27 (1.18-1.38)	n/a	1.05 (0.89-1.24)	78.2% (0.03)	0.05	0.64
Lung disease[1]	1.42 (1.29-1.56)	0.99 (0.67-1.47)	1.30 (1.04-1.62)	52.6% (0.12)	0.11	0.09
Stroke[1]	1.79 (1.40-2.28)	3.57 (0.65-19.7)	1.60 (0.77-3.34)	0% (0.84)	0.97	0.52
Depression[1]	1.83 (1.69-1.99)	1.24 (0.83-1.86)	1.75 (1.40-2.19)	84.6% (<0.001)	0.15	0.44
Anxiety[1]	2.26 (2.07-2.46)	1.47 (1.03-2.10)	1.12 (0.85-1.47)	93.8% (<0.001)	<0.001	0.05
Nº medications (0-6)	1.12 (1.09-1.14)	1.11 (1.00-1.23)	1.09 (1.05-1.14)	0% (0.50)	0.93	0.73
Polypharmacy[1]	1.52 (1.38-1.67)	1.98 (1.01-3.86)	1.54 (1.26-1.89)	0% (0.71)	0.29	0.62
Benzodiazepine[1]	1.52 (1.22-1.89)	2.17 (0.68-6.95)	1.59 (1.13-2.24)	0% (0.85)	0.68	0.52
Immediate recall				0% (0.78)	0.87	0.37

11-20 words	n/a	1	1			
0-10 words		1.30 (0.56-2.98)	1.10 (0.62-1.95)			
Delayed recall				0% (0.47)	0.28	0.89
4-10 words	n/a	1	1			
0-3 words		0.77 (0.19-3.19)	1.25 (0.97-1.61)			
Verbal fluency (0-62)	n/a	1.01 (0.98-1.03)	1.00 (0.99-1.01)	0% (0.46)	0.37	0.004
Grip strength (quintiles)				5.2% (0.39)	0.25	0.22
F: ≥30 M: ≥51 kg	n/a	1	1			
F: 26-<30 M: 45-<51 kg		1.06 (0.72-1.57)	1.30 (0.94-1.83)			
F: 23-<26 M: 40-<45 kg		0.77 (0.47-1.27)	1.35 (0.97-1.87)			
F: 20-<23 M: 34-<40 kg		1.04 (0.62-1.75)	1.26 (0.90-1.75)			
F: 0-<20 M: 0-<34 kg		1.06 (0.66-1.71)	1.35 (0.98-1.87)			
Mobility				n/a	n/a	0.55
Good	n/a	n/a	1			
Moderate			1.06 (0.79-1.42)			
Fair			1.13 (0.83-1.54)			
Poor/unable			1.39 (0.97-2.01)			
Use of a walking aid[1]	n/a	n/a	6.92 (2.53-18.9)	n/a	n/a	0.38
Functional limitations (0-4)	1.39 (1.34-1.43)	n/a	1.48 (1.35-1.63)	42.1% (0.19)	0.03	0.01
Diastolic Bp (per 10 mmHg)	n/a	0.96 (0.85-1.09)	1.00 (0.90-1.11)	0% (0.62)	0.14	0.81
Systolic Bp (per 10 mmHg)	n/a	0.97 (0.90-1.05)	0.98 (0.92-1.05)	0% (0.84)	0.20	0.50
Body mass index				88.9% (<0.001)	<0.001	0.34
Under/normal weight	1	1	1			
Overweight	1.23 (1.14-1.34)	0.98 (0.70-1.37)	0.98 (0.80-1.20)			
Obese	1.66 (1.52-1.81)	1.04 (0.70-1.55)	1.17 (0.94-1.45)			
Dizziness[1]	1.91 (1.63-2.23)	0.99 (0.55-1.80)	n/a	86.0% (0.007)	0.005	n/a
Pain[1]	1.80 (1.68-1.93)	n/a	1.85 (1.59-2.16)	0% (0.75)	0.52	0.62
Hearing problems[1]	1.44 (1.32-1.56)	1.35 (0.92-1.97)	1.43 (1.15-1.77)	0% (0.95)	0.75	0.32
Vision problems						

None	n/a	n/a	1	n/a	n/a	0.25
Near only			0.93 (0.64-1.34)			
Far only			1.38 (0.89-2.14)			
Both near and far			1.60 (0.94-2.73)			
Sleeping problems				80.5% (<0.001)	0.04	0.18
None	1	n/a	1			
Waking too early	1.29 (1.18-1.40)		1.34 (1.11-1.63)			
Difficulty falling asleep	1.41 (1.25-1.58)		1.22 (0.93-1.61)			
Both	1.78 (1.62-1.97)		1.53 (1.27-1.84)			
Urinary incontinence[1]	1.46 (1.36-1.56)	1.38 (0.97-1.95)	1.99 (1.61-2.45)	77.8% (0.01)	<0.001	0.08
Lifestyle factors						
Level of alcohol intake				0% (0.56)	0.15	0.04
Low risk	1	1	1			
Never/rarely drinks	1.12 (1.04-1.20)	1.01 (0.71-1.45)	0.94 (0.77-1.15)			
Risky/high risk	1.15 (1.00-1.32)	1.23 (0.80-1.88)	1.08 (0.88-1.34)			
Smoking status				0% (0.95)	0.53	0.05
Never smoked	1	1	1			
Ex-smoker	1.12 (1.03-1.20)	1.11 (0.79-1.55)	1.08 (0.92-1.28)			
Current smoker	1.05 (0.94-1.17)	1.10 (0.72-1.69)	1.15 (0.95-1.41)			
Level of physical activity				69.2% (0.02)	0.05	0.74
High	1	n/a	1			
Low	1.34 (0.91-1.96)		0.94 (0.76-1.17)			
Inactive	1.29 (0.77-2.19)		1.26 (1.00-1.59)			

OR odds ratio; 99%CI 99% confidence interval; F female; M male

All models were adjusted for age and sex.

[1] Registered partnership may also include defacto relationships.

[2] Not having the condition or limitation was defined as the reference category.

[3] I^2 cannot be estimated when the reference category differs between cohorts.

Table 4. Pooled estimates of between each of the risk factors[1] and fall status, seperately for women and men

	Cross-sectional associations		Prospective associations	
	Female	Male	Female	Male
	OR (99%)	OR (99%)	OR (99%)	OR (99%)
Nº other people in household				
0	1	1	-	-
1	0.78 (0.73-0.84)	0.70 (0.55-0.88)		
2	0.73 (0.66-0.81)	0.80 (0.62-1.05)		
3+	0.66 (0.59-0.74)	0.76 (0.58-0.98)		
Nº chronic conditions				
0	1	1	-	-
1	1.37 (1.28-1.46)	1.17 (0.97-1.41)		
2+	1.96 (1.72-2.24)	1.48 (1.04-2.10)		
Cancer[2]	-	-	1.13 (0.95-1.34)	1.30 (0.70-2.40)
Heart disease[2]	1.57 (1.39-1.76)	1.14 (0.89-1.46)	1.60 (1.39-1.85)	1.00 (0.71-1.42)
Verbal fluency (range 0-62)	-	-	1.01 (1.00-1.02)	0.99 (0.97-1.00)
Body mass index				
Under/normal weight	1	1	-	-
Overweight	1.21 (1.13-1.29)	0.91 (0.74-1.13)		
Obese	1.57 (1.46-1.68)	1.24 (0.98-1.55)		
Urinary incontinence[2]	1.61 (1.52-1.70)	2.61 (1.99-3.42)	-	-

OR odds ratio; 99%CI 99% confidence interval;

All models were adjusted for age.

[1] Models were stratified by sex only if a statistically significant interaction with sex was found – see Tables 2 and 3 for results of the test for interaction with sex for each of the risk factors.

[2] Not having the condition was defined as the reference category.