

# The association between choice stepping reaction time and falls in older adults—a path analysis model

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## Abstract

**Background:** choice stepping reaction time (CSRT) is a functional measure that has been shown to significantly discriminate older fallers from non-fallers.

**Objective:** to investigate how physiological and cognitive factors mediate the association between CSRT performance and multiple falls by use of path analysis.

**Methods:** 294 retirement-village residents, aged 62–95 years, undertook CSRT tests, requiring them to step onto one of four randomly illuminated panels, in addition to physiological and cognitive tests. Number of falls was collected during 1-year follow-up.

**Results:** 79 participants (27%) reported two or more falls during the follow-up period. Regression analyses indicated CSRT was able to predict multiple falls by a factor of 1.76 for each SD change. The path analysis model revealed that the association between CSRT and multiple falls was mediated entirely by the physiological parameters reaction time and balance (postural sway) performance. These two parameters were in turn mediated over a physiological path (by quadriceps strength and visual contrast sensitivity) and a cognitive path (cognitive processing).

**Conclusions:** this study provides an example of how path analysis can reveal mediators for the association between a functional measure and falls. Our model identified inter-relationships (with relative weights) between physiological and cognitive factors, CSRT and multiple falls.

**Keywords:** *accidental falls, aged, risk factors, physical performance, cognition, elderly*

## Introduction

In order to understand and reduce fall risk in older adults, many studies have investigated physiological performance in relation to age and falls. Compared to non-fallers, fallers have reduced lower limb strength, slow voluntary reaction time and reduced sensory acuity and balance [1–5]. Moreover, cognitive tasks requiring visuospatial skills and visuospatial working memory can affect balance control [6, 7] and can discriminate between people with and without a high risk of falls [8, 9].

Clinically, there is a need and preference for functional tests that incorporate these physiological and cognitive performances to efficiently identify people with increased fall

risk. In a previous study, we found that a functional test of stepping performance—choice stepping reaction time (CSRT)—was able to discriminate between older people who had and had not fallen [10]. In this test, subjects must step from either leg onto targets that are randomly illuminated. Body weight and balance transfers are similar to the step responses required to avoid many falls, particularly those that occur as a result of late visual detection of hazards and unanticipated changes in the gait path.

It can, however, be questioned how the relationship between this functional measure and falls is mediated by physiological and cognitive pathways. The aim of this study was therefore to use path analysis to investigate the relationship between CSRT, physiological and cognitive performance,

and multiple falls. We hypothesised that underlying physiological and cognitive impairments are primary mediators for the relationship between CSRT performance and falls. As path analysis can distinguish between direct and indirect associations, it can confirm not only the strengths of inter-relationships but also the extent to which the relationship between CSRT and multiple falls is direct or mediated via physiological and cognitive capacities.

## Methods

A total of 294 participants (46 men, 248 women) aged 62–95 years (mean 79.2, SD 6.5) comprised the study sample. The participants were residents of retirement villages in Sydney, Australia, and consisted of the control group of a randomised controlled trial of group exercise on fall risk factors [11]. For the prevalence of major medical conditions, medication use, physical activity and activities of daily living limitations in the study population, please see Appendix 1 in the supplementary data on the journal website <http://www.ageing.oxfordjournals.org>. The most common medical conditions were high blood pressure (52%) and arthritis (64%). About half of the participants used four or more medications, of which cardiovascular system medications were most common (68%). A walking aid was used by 30% of the participants, and the majority (75% or more) did not experience limitations in activities of daily living.

For the CSRT measurements, subjects stood on a non-slip black platform (0.8 × 0.8 m) that contained four rectangular panels (32 × 13 cm), one in front of each foot and one to the side of each foot [10]. One panel per trial was illuminated in a random order. Subjects were instructed to step on to the illuminated panel as quickly as possible, using the left foot only for the two left panels (front and side) and the right foot only for the two right panels. Each panel contained a pressure switch to determine the time of foot contact. After four to eight practice trials, 20 trials were conducted with five trials per panel. CSRT was measured as the time period between panel illumination and the foot making contact with it. The average time of the 20 trials was used in the analysis.

Physiological performance was assessed according to the Physical Profile Assessment [11]. ‘Visual contrast sensitivity’ was assessed using the Melbourne Edge Test. This test assessed the correct identification of the orientation of the edges in 20 circular patches containing edges with reducing contrast. ‘Proprioception’ was measured using a lower limb matching task. In this test, participants were seated with their eyes closed and asked to align their lower limbs simultaneously on either side of vertical clear acrylic sheet (60 × 60 × 1 cm) inscribed with a protractor and placed between the legs. Errors in alignment of the great toes were recorded in degrees. ‘Quadriceps strength’ was measured as the maximal isometric extension force. This test was performed while subjects were seated with hip and knee angles of 90°, with a strain gauge attached to a strap around the leg 10 cm above the ankle joint. For each leg, the subject attempted to pull

against the strain gauge with maximal force for 2–3 s, and the average of the best score for each leg was analysed. ‘Simple reaction time’ was measured using a light as the stimulus and a finger-press as the response. ‘Postural sway’ was measured using a swaymeter that recorded displacements of the body at the level of the waist. Testing was performed with subjects standing on a foam rubber mat (40 × 40 × 7.5 cm) with eyes open. The validity and reliability of these tests have been established in previous studies [11].

In addition to the physiological measures, cognitive processing performance was tested by the Trail Making Test (TMT-B). This test required subjects to draw lines connecting a number of circles alternately indicated by letters and numbers (1-A-2-B) [12]. Time in seconds taken to complete the test was measured, with less time indicating better performance.

The subjects were followed up for 1 year to determine the ‘number of falls’. A fall was defined as an event that resulted in a person coming to rest unintentionally on the ground or other lower level, not as the result of a major intrinsic event (such as a stroke) or overwhelming hazard [13]. Questionnaires were given to subjects each month, seeking details on the number of falls in the past month such as the location and cause and any injuries suffered. Subjects were classified as multiple fallers if they fell twice or more times during the follow-up period.

Statistical analyses were performed using SPSS (version 16.0) in conjunction with Analysis of Moment Structures (AMOS 7.0) Graphics. For variables with skewed distributions, data were log normalised. A missing value analysis was performed in SPSS to calculate 23 missing TMT-B values, using Expectation Maximization algorithms based on the complete variables simple reaction time, visual contrast sensitivity and age. Differences in the means of the variables between multiple fallers and non-multiple fallers were assessed using independent samples *t* tests. Univariate logistic regression analyses explored the ability of CSRT towards predicting multiple fallers. Bivariate correlations between numerical variables and point-serial correlations with the dichotomous variable multiple falls were calculated using Pearson’s correlation analysis.

Path analysis in AMOS was performed to examine the relationship between CSRT, multiple falls (multiple fallers vs non-multiple fallers) and the physiological and cognitive parameters. Path analysis has the major benefit that it can confirm to what extent predictors are mediated via underlying variables and provide estimates of the relative importance of direct and indirect factors. We constructed a model based on our hypothesis and on significant correlations. Then, as a means of investigating the model’s robustness, we compared it with an alternative model [14] as a way of questioning the hypothesised interpretation of the direction of the identified paths. We explored whether CSRT could be a result of the physiological and cognitive measures and therefore a direct cause for multiple falls. To do this, we switched the position of CSRT and the physiological and cognitive measures in the model. To compare the fit

**Table 1.** Mean (SD) test results for multiple fallers and non-multiple fallers. Note that low scores in the visual contrast sensitivity and quadriceps strength, and high scores in all other tests indicate impaired performance. Significant differences between groups are indicated with *P* values

Test	Multiple fallers ( <i>n</i> = 79)	Non-multiple fallers ( <i>n</i> = 215)	<i>P</i>
Choice stepping reaction time (ms)	1,280 (202)	1,171 (220)	<0.001
Visual contrast sensitivity (dB)	17.0 (2.5)	18.3 (3.4)	0.001
Proprioception (degrees error)	2.3 (1.6)	1.8 (1.2)	0.003
Quadriceps strength (N)	203 (84)	226 (92)	0.047
Simple reaction time (ms)	315 (80)	279 (51)	<0.001
Sway eyes open on foam (mm)	270 (147)	161 (110)	<0.001
TMT-B (s)	93.7 (64.8)	65.5 (44.0)	0.001

of the models, we examined the standard fit indices chi square ( $\chi^2$ ), adjusted goodness-of-fit index (AGFI) and root mean square error of approximation (RMSEA) [15]. The  $\chi^2$  and degrees of freedom (DF) is a conventional overall statistical test of lack of fit, resulting from over-identifying restrictions placed on a model, and should not be significant. AGFI assesses the extent to which the model provides a better fit compared to no model at all; a high value (AGFI > 0.90) is considered to reflect that the model fits the data well. RMSEA estimates lack of fit in a model compared to a perfect model, and should therefore be small (RMSEA < 0.08). Finally, standardised direct and indirect regression coefficients (rc), which are analogous to correlation coefficients, and explained variance were calculated. A Bayesian Estimation analysis, which is preferred over the standard maximum likelihood estimation when using a categorical outcome parameter (multiple falls), resulted in the same explained variance for this parameter and therefore justified the presentation of the standardised regression coefficients. Finally, model trimming [14] was used to systematically remove associations that were not significant in our initial model to obtain our final model.

**Results**

The mean CSRT for all participants was 1,200 ms (SD 220). Age was significantly correlated with CSRT (*r* = 0.35, *P* <

0.001). Men had significantly faster CSRTs than women (1,129 (SD 290) and 1,213 (SD 203) ms, respectively; *t* = -2.49, *P* = 0.019), but this difference was not significant after adjusting for quadriceps strength in an ANCOVA procedure ( $F_{1,291}$  = 0.276, *P* = 0.60).

A total of 79 subjects (27%) reported two or more falls during the follow-up period. The multiple fallers were significantly older than the non-multiple fallers (81.1 (SD 6.9) and 78.5 (SD 6.1) years, respectively; *t* = -3.04, *P* = 0.003). Table 1 shows the mean values, standard deviations and statistical test results for the CSRT and the physiological and cognitive test measures for the multiple fallers and non-multiple fallers. Multiple fallers scored worse on all cognitive and physiological measures, except for quadriceps strength. CSRT was significantly associated with multiple falls and with all test measures (Table 2). Univariate logistic regression analyses indicated CSRT was able to predict multiple falls by a factor of 1.76 (95% CI 1.30 and 2.37, *P* ≤ 0.001) for each SD change.

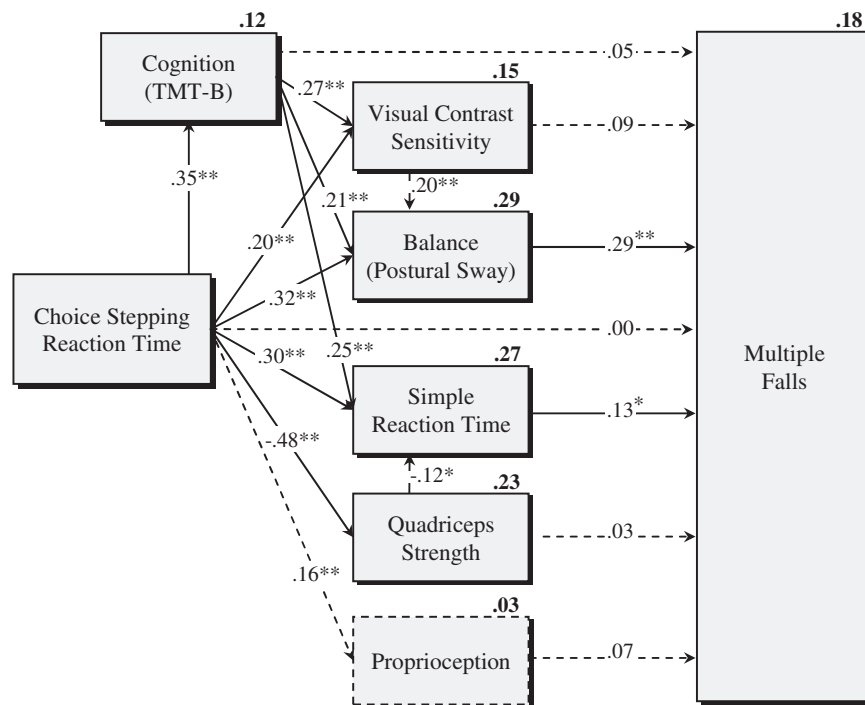
Path analysis was performed to evaluate whether the relationship between CSRT and multiple falls was mediated by physiological and cognitive measures. The initial model included the associations of CSRT and multiple falls with all variables, in addition to the associations between physiological and cognitive variables with correlation coefficients >0.30 (Table 2). Despite a significant chi square ( $\chi^2$  = 20.4, *P* = 0.026), the goodness-of-fit indicators (AGFI = 0.939 and RMSEA = 0.059) revealed that this model had a good fit, with a reasonable number of degrees of freedom (DF = 10). The solution of this model, with the standardised direct effects, is shown in Figure 1. This model showed that there was no direct effect of CSRT on multiple falls (rc = 0.004). The standardised indirect effect of CSRT on multiple falls was 0.23, mainly mediated by simple reaction time and balance (postural sway). These two parameters were in turn mediated over a physiological path (by quadriceps strength and visual contrast sensitivity) as well as over a cognitive path (cognitive processing). This initial model explained 18% of the variance in multiple falls.

The alternate model, in which the positions of CSRT and the physiological and cognitive measures were switched, had an unacceptable fit ( $\chi^2$  = 54.2, DF = 10, *P* < 0.001, AGFI = 0.834, RMSEA = 0.123), indicating that a poor CSRT performance was not a direct cause for multiple falls.

**Table 2.** Correlations between CSRT, test measures and multiple falls

	CSRT	Visual contrast sensitivity	Proprioception	Quadriceps strength	Simple reaction time	Balance (sway eyes open foam)	Cognition (TMT-B)	Multiple falls
CSRT	1.000	<b>0.292**</b>	<b>0.161**</b>	<b>-0.484**</b>	<b>0.449**</b>	<b>0.446**</b>	<b>0.346**</b>	<b>0.231**</b>
Visual contrast sensitivity		1.000	0.090	-0.196**	0.284**	<b>0.361**</b>	<b>0.336**</b>	<b>0.251**</b>
Proprioception			1.000	-0.143*	0.156**	0.229**	0.195**	<b>0.171**</b>
Quadriceps strength				1.000	<b>-0.318**</b>	-0.225**	-0.194**	<b>-0.112</b>
Simple reaction time					1.000	0.279**	<b>0.380**</b>	<b>0.260**</b>
Balance (sway)						1.000	<b>0.382**</b>	<b>0.389**</b>
Cognition (TMT-B)							1.000	<b>0.249**</b>

Significant correlations are indicated: \**P* < 0.05, \*\**P* < 0.01. Correlations in bold are included in the path analysis model.



**Figure 1.** Path analysis model and output. Direct standardised regression coefficients (analogous to correlation coefficients) between variables are shown on each arrow; significant values are indicated: \* $P < 0.05$ , \*\* $P < 0.01$ . Explained variance is provided in bold above each variable. Dashed lines indicate associations that were not significant and were therefore removed from this initial model to obtain our final model.

Finally, model trimming removed five paths that were not significant in our initial model (represented by dashed lines in Figure 1) and consequently the parameter proprioception. This improved the goodness-of-fit of our model considerably (AGFI = 0.974, RMSEA = 0.000); with  $\chi^2$  no longer significant ( $\chi^2 = 8.9$ , DF = 9,  $P = 0.451$ ). This final model also resulted in stronger direct regression coefficients for simple reaction time ( $rc = 0.16$ ) and balance ( $rc = 0.34$ ), and still explained 17% of the variance in multiple falls.

## Discussion

In a retrospective study of older people, impaired CSRT was found to be the strongest discriminator of falls status [10]. The present prospective study confirmed CSRT performance to distinguish between multiple fallers and non-multiple fallers. Path analysis was used to elucidate underlying relationships between CSRT and falls. This analysis revealed that the association between slow CSRT and multiple falls was mediated primarily by impaired balance and reaction time, with reduced strength and cognitive processing having indirect mediating roles.

Postural sway, which requires integrated reflex response to visual, vestibular and somatosensory inputs, had the strongest correlation with falls in this study. Steady standing on a compliant surface (the measure used in this study) has been shown to also require contributions from strength and reaction time [16]. In the present path analysis, however, we

found no significant path from reaction time to postural sway; instead, both parameters were independently related to falls. This suggests that reaction time may predispose to falls independently of postural control by impairing responses to balance threats in daily situations that require supraspinal processing. Indeed, slow voluntary reaction time has been reported to independently discriminate between older people who have and have not fallen [1, 17], possibly due to vitamin D deficiency [18].

The indirect cognitive path (via TMT-B) indicates that slow cognitive spatial processing can increase fall risk in frail populations by influencing reaction time and balance. This is consistent with other research that has found that balance (sway) and gait performance are impaired in people with mild cognitive impairment [9, 19]. The indirect physiological path (via quadriceps strength and visual contrast sensitivity) reinforces the importance of poor vision [3] and lower limb muscle strength [4, 20] as contributors to falls. It might be that strength has a direct association with falls in general older populations that do not have multiple chronic conditions that affect sway and reaction time.

In a recent study, Vance *et al.* [21] examined how physical, cognitive, medical or medication risk factors are interrelated and contribute to falls in a healthy older population. Their model also resulted in a physiological (lower extremity mobility) and cognitive path (i.e. TMT-B) leading to falls and explained 11% of the variance of retrospective falls. Our model builds on this work by including a greater range of

physiological measures and prospective fall data in a path analysis model, and added implications for the use of functional tasks to predict fall risk. It is acknowledged, however, that the explained variance by which physiological and cognitive performance explained multiple falls in our model is also relatively low (17%). This suggests that although the influence of medical conditions, associated medication use and daily living limitations would be manifest to a large extent in one or more of the physiological and cognitive measures included in the model [22], a more comprehensive range of medical and psychological factors [2, 5, 23, 24] are required to account for a greater proportion of variance in falls outcome.

In conclusion, this study provides an example of how path analysis can reveal mediators for the association between a functional measure and multiple falls. Our path analysis elucidated that physiological and cognitive pathways entirely mediate the association between CSRT performance and multiple falls. These findings have clinical implications, in that they provide insight into the underlying physiological and cognitive mechanisms for the functional CSRT tool. Moreover, exercise-induced improvements in functional measures such as CSRT may be due to multiple physiological and cognitive changes. Further research could examine whether greater beneficial effects in CSRT result from targeted strength and balance training, direct training of volitional and compensatory stepping responses [25–27], or a combination of both.

## Key points

- Choice stepping reaction time (CSRT) is a functional measure that is able to prospectively predict multiple fallers.
- Path analysis was used to examine the association between CSRT and multiple falls and to which extent this relationship is mediated via physiological and cognitive performance.
- Our path analysis model revealed that this relationship was mediated entirely by the physiological parameters reaction time and balance performance, which were in turn mediated over a physiological path and a cognitive path.
- These findings have clinical implications in that they provide insight in the underlying mechanisms for stepping performance and can provide guidance for designing falls prevention exercise interventions.

## Conflict of interest

The Physiological Profile Assessment is commercially available from the Prince of Wales Medical Research Institute.

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## Supplementary data

Supplementary data mentioned in the text is available to subscribers at the journal website <http://ageing.oxfordjournals.org>

## References

1. Grabiner MD, Jahnigen DW. Modeling recovery from stumbles: preliminary data on variable selection and classification efficacy. *J Gerontol A Biol Sci Med Sci* 1992; 40: 910–3.
2. de Rekeneire N, Visser M, Peila R *et al.* Is a fall just a fall: correlates of falling in healthy older persons. The health, aging and body composition study. *J Am Geriatr Soc* 2003; 51: 841–6.
3. de Boer MR, Pluijm SM, Lips P *et al.* Different aspects of visual impairment as risk factors for falls and fractures in older men and women. *J Bone Miner Res* 2004; 19: 1539–47.
4. Moreland JD, Richardson JA, Goldsmith CH, Clase CM. Muscle weakness and falls in older adults: a systematic review and meta-analysis. *J Am Geriatr Soc* 2004; 52: 1121–9.
5. Morris R. Predicting falls in older women. *Menop Internat* 2007; 13: 170–7.
6. Maylor EA, Allison S, Wing AM. Effects of spatial and non-spatial cognitive activity on postural stability. *Br J Psychol* 2001; 92: 319–38.
7. Sturnieks DL, St George R, Fitzpatrick RC, Lord SR. Effects of spatial and nonspatial memory tasks on choice stepping reaction time in older people. *J Gerontol A Biol Sci Med Sci* 2008; 63: 1063–8.
8. St George RJ, Fitzpatrick RC, Rogers MW, Lord SR. Choice stepping response and transfer times: effects of age, fall risk, and secondary tasks. *J Gerontol A Biol Sci Med Sci* 2007; 62: 537–42.
9. Liu-Ambrose TY, Ashe MC, Graf P, Beattie BL, Khan KM. Increased risk of falling in older community-dwelling women with mild cognitive impairment. *Phys Ther* 2008; 88: 1–10.
10. Lord SR, Fitzpatrick RC. Choice stepping reaction time: a composite measure of falls risk in older people. *J Gerontol A Biol Sci Med Sci* 2001; 56: M627–M632.
11. Lord SR, Castell S, Corcoran J *et al.* The effect of group exercise on physical functioning and falls in frail older people living in retirement villages: a randomized, controlled trial. *J Am Geriatr Soc* 2003; 51: 1685–92.
12. Spreen O, Strauss E. *A compendium of neuropsychological tests*. New York: Oxford University Press, 1991..
13. Gibson MJ, Andres RO, Isaacs B, Radebaugh T, Worm-Petersen J. The prevention of falls in later life. A report of the Kellogg International Work Group on the Prevention of Falls by the Elderly. *Dan Med Bull* 1987; 34: 1–24.
14. Kline RB. *Principles and practice of structural equation modelling*. Guildford Press: New York, 1998..
15. Byrne BM. Testing for multigroup invariance using amos graphics: a road less traveled. *Structural Equation Modeling* 2004; 11: 272–300.

16. Lord SR, Ward JA. Age-associated differences in sensori-motor function and balance in community dwelling women. *Age Ageing* 1994; 23: 452–60.
17. Woolley S, Czaja S, Drury C. An assessment of falls in elderly men and women. *J Gerontol A Biol Sci Med Sci* 1997; 52: M80–7.
18. Dhese J, Beame L, Moniz C *et al.* Neuromuscular and psychomotor function in elderly subjects who fall and the relationship with vitamin D status. *J Bone Miner Res* 2002; 17: 891–7.
19. Boyle PA, Wilson RS, Buchman AS *et al.* Lower extremity motor function and disability in mild cognitive impairment. *Exp Aging Res* 2007; 33: 355–71.
20. Pijnappels M, Reeves ND, Maganaris CN, van Dieën JH. Tripping without falling; lower limb strength, a limitation for balance recovery and a target for training in the elderly. *J Electromyogr Kinesiol* 2008; 18: 188–96.
21. Vance DE, Ball KK, Roenker DL *et al.* Predictors of falling in older Maryland drivers: a structural-equation model. *J Aging Phys Act* 2006; 14: 254–69.
22. Lord SR, Menz HB, Tiedemann A. A physiological profile approach to falls risk assessment and prevention. *Phys Ther* 2003; 83: 237–52.
23. Leipzig RM, Cumming RG, Tinetti ME. Drugs and falls in older people: a systematic review and meta-analysis: I. Psychotropic drugs. *J Am Geriatr Soc* 1999; 47: 30–9.
24. Pluijm SMF, Smit JH, Tromp EAM *et al.* A risk profile to identify community-dwelling elderly at high risk for recurrent falling: results of a three-year prospective study. *Osteop Internat* 2006; 17: 417–25.
25. Mansfield A, Peters A, Liu B, Maki B. A perturbation-based balance training program for older adults: study protocol for a randomised controlled trial. *BMC Geriatr* 2007; 7: 12.
26. Melzer I, Elbar O, Tsedek I, Oddsson L. A water-based training program that include perturbation exercises to improve stepping responses in older adults: study protocol for a randomized controlled cross-over trial. *BMC Geriatr* 2008; 8: 19.
27. Shigematsu R, Okura T, Nakagaichi M *et al.* Square-stepping exercise and fall risk factors in older adults: a single-blind, randomized controlled trial. *J Gerontol A Biol Sci Med Sci* 2008; 63: 76–82.

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## APOE and ACE polymorphisms and dementia risk in the older population over prolonged follow-up: 10 years of incidence in the MRC CFA Study

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### Abstract

**Background:** dementia risk conferred by *apolipoprotein-E* (*APOE*) and *angiotensin-1-converting enzyme* (*ACE*) polymorphisms have been reported for the MRC Cognitive Function and Ageing Study (CFAS) at 6-year follow-up. We concentrate on incident dementia risk over 10 years.

**Methods:** participants come from MRC CFAS, a multi-centre longitudinal population-based study of ageing in England and Wales. Three follow-up waves of data collection were used: 2, 6 and 10 years. Logistic regressions were undertaken to investigate associations between *APOE* ( $n=955$ ) and *ACE* ( $n=856$ ) alleles/genotypes and incident dementia. Two types of control groups were used: non-demented and highly functioning non-demented. Results were back-weighted.