Prevalence and factors associated with Motoric Cognitive Risk syndrome in a community-dwelling older Scottish population: a cross-sectional study

cormatrix <- cbind(FrailtyIndex\_W1,FrailtyIndex\_W2,FrailtyIndex\_W3,FrailtyIndex\_W4,FrailtyIndex\_W5,FriedPhenotype\_W1,FriedPhenotype\_W3,FriedPhenotype\_

W4,FriedPhenotype\_W5)  
cor(cormatrix, use = 'complete.obs')

correlations <- cor(cormatrix, use = 'complete.obs')  
corrplot(correlations, method="number",type="lower")

# Methods

### Study Design

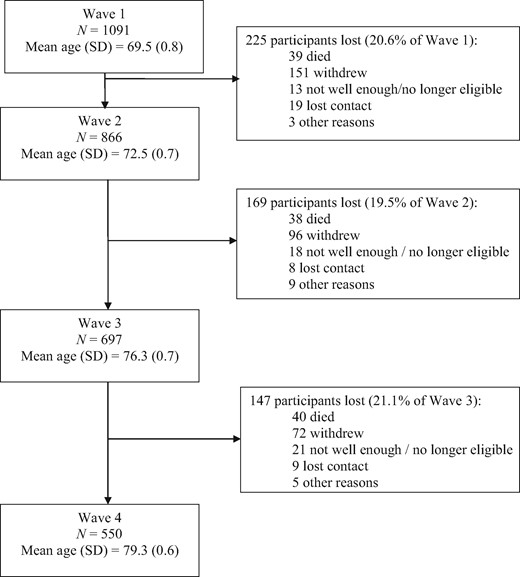
Cross-sectional design at three different time points.

### Setting

Describe the setting, locations, and relevant dates, including periods of recruitment, exposure, follow-up, and data collection

From Miles’s: <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8386587/> At Wave 1, the LBC1936 study consisted of 1091 participants, born in 1936 with a mean age of 69 (SD=0.89) years, mostly surviving members of the Scottish Mental Survey 1947.1 Wave 1 took place between 2004 and 2007, with follow-up waves approximately every 3 years thereafter at ages: 73 (n=866), 76 (n=697), 79 (n=550), and 82 years (n=431). More details on recruitment and testing procedures have been published previously.1–3 The LBC1936 study was conducted according to the Declaration of Helsinki guidelines. Ethical permission for the LBC1936 study protocol was obtained from the Multi-Centre Research Ethics Committee for Scotland (Wave 1: MREC/01/0/56), the Lothian Research Ethics Committee (Wave 1: LREC/2003/2/29), and the Scotland A Research Ethics Committee (Waves 2, 3, 4 and 5: 07/MRE00/58). Written consent was obtained from participants at each of the waves.

### Participants



Waves of testing and attrition between waves in the LBC1936 study. *Do my own version of this* (<https://academic.oup.com/ije/article/47/4/1042/4931207>)

From (<https://academic.oup.com/ije/article/47/4/1042/4931207>)

By wave, compared with those who remained in the LBC1936 study at Waves 1 to 4, participants who dropped out had: significantly lower older-age IQ scores at Wave 1 (*P* < 0.001), Wave 2 (*P* = 0.001) and Wave 3 (*P* = 0.003); lower MMSE scores at Wave 1 (*P* = 0.04), Wave 2 (*P* < 0.001) and Wave 3 (*P* = 0.001); lower socioeconomic status, represented by less professional occupational types, at Wave 1 (*P* = 0.001), Wave 2 (*P* = 0.04) and Wave 3 (*P* < 0.001); and lower physical fitness, as assessed by lung function at Wave 1 (*P* < 0.001), Wave 2 (*P* = 0.02) and Wave 3 (*P* = 0.005) and by grip strength at Wave 1 (*P* = 0.003).

### Variables

Outcomes

Exposures

Predictors:

Identification of MCR

From <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC8386587/>: Using data previously collected in the LBC1936, an algorithm was created which identifies participants who fulfil the MCR criteria as originally defined by Verghese et al.4 Variables necessary to conduct MCR coding were collected from Wave 3 (age 76) onwards. To be classified in the MCR category, participants must have met all 4 criteria reported below:

1. Slow gait measured over 6 metres: scores ≥ 1 SD slower than sex and age-matched mean speed.
2. Self-reported cognitive complaint: answering “yes” to the question “do you currently have any problems with your memory?”
3. Preservation of independence in functional abilities: scores <= 1.5 SD above the mean on the Townsend Disability Scale overall score (ie add 1.5 SD to the mean score at each wave, then take everyone below this, higher score equals greater disability). *(Townsend P. Poverty in the United Kingdom: A Survey of Household Resources and Standards of Living. Oakland, California: University of California Press; 1979.* [*Cited Here*](https://journals.lww.com/alzheimerjournal/Fulltext/2021/07000/Prevalence_of_Mild_Cognitive_Impairment_in_the.6.aspx#JCL-P-16) *note data of adl\_w1 was not normally distributed. Doing SD / 1.5SD didn’t make much sense. Mean was 3.1666 and one SD was 2.918 therefore anyone scoring even a 1 (which means not functionally impaired) would have been ruled out. As such, better to select anyone with adl\_w1 <= 1.*
4. No diagnosis of dementia: does not self-report or have a formal diagnosis of dementia *and* scores at least 24 on the Mini-Mental State Examination (MMSE) *(Folstein MF, Folstein SE, McHugh PR. “Mini-mental state”: a practical method for grading the cognitive state of patients for the clinician. J Psychiatr Res. 1975;12:189–198.*)

LBC contains three different measures of subjective cognitive complaint, with different wave coverage for each. We coded 2 other subtypes of MCR; MCRipip and MCRwembs. Creation of these subtypes followed the same procedure as for the general MCR; however, for MCRipip the subjective cognitive complaint measure was determined by answering “moderately” or “very accurate” to the question: how accurate is the statement “I often forget to put things back in their proper place”, while MCRwembs was determined by answering anything other than “all of the time” to the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) question "I've been thinking clearly".

SCC measures in LBC1936, including their wave coverage:

a) memprob1\_w3/4/5 answering “yes” to the question “do you currently have any problems with your memory?”

b) ipip28\_w1/2/3/4/5 answering “moderately” or “very accurate” to the International Personal Item Pool 50-item inventory question: how accurate is the statement: “I often forget to put things back in their proper place”. This scale was previously validated in the LBC1921 (Gow et al 2005 Goldberg’s IPIP Big-Five factor markers: internal consistency and concurrent validation in Scotland)

c) wemwbs7\_w2/3/4/5 answering anything other than “all of the time” to the Warwick-Edinburgh Mental Wellbeing Scale (WEMWBS) question "I've been thinking clearly". The WEMWBS is a scale designed to capture a wide conception of well-being including cognitive-evaluative dimensions5.

Confounders/Covariates

We examined the association between a range of covariates and MCR status. Covariates included: **age, sex, years of education**, age 11 cognitive function, body mass index (calculated in the standard way of kg/m2), smoking status (current/ex/never), alcohol intake (units per week), occupational social class (professional/managerial/skilled, nonmanual/skilled manual or semiskilled/unskilled), APOE ε4 status (allele present/absent), self-reported history of cardiovascular disease, self-reported history of stroke, depression, and physical frailty level (not frail/prefrail/frail). Physical frailty was derived using the Fried Phenotype guidelines,21 for information on how this was calculated in LBC1936 see Welstead et al.22 Depression was measured using the Hospital Anxiety and Depression scale.6 Age 11 cognitive function was based on LBC1936 participant’s scores on the Moray House Test (MHT) at age 11.2 Raw scores were corrected for age in days at the time of testing and converted to an IQ scale where mean (SD) = 100 (15). For details on how social class was derived, see [Appendix B](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456784/#s0150).

### From Miles inflammation and frailty paper <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456784/>

### 2.4. Covariates

For FI and Fried phenotype analyses we included covariates: **age, sex,** smoking status (current/ex/never), alcohol intake (units per week), years of formal full-time **education**, occupational social class (professional/managerial/skilled, non-manual/skilled manual or semiskilled/unskilled), and childhood IQ (measured with the Moray House Test in the LBC1936 at age 11) ([Penrose, 1949](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456784/#bb0135)). Childhood IQ was included as a covariate due to previous findings in the LBC1936 indicating that lower intelligence in childhood is associated with increased inflammation ([Luciano et al., 2009](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456784/#bb0115)) and an increased risk of frailty in older age ([Gale et al., 2016](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456784/#bb0075)). For details on how social class and Childhood IQ was derived, see [Appendix B](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456784/#s0150). Additionally, for Fried phenotype analyses we added covariates that were not included for FI analyses due to their inclusion in the composition of the measure. These included: self-reported history of various chronic diseases, depressive symptoms from the Hospital Anxiety and Depression scale (HADS) ([Zigmond and Snaith, 1983](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456784/" \l "bb0225)) and Body Mass Index (BMI). As one of the HADS questions was included in the composition of the Fried Phenotype, this question was removed when deriving the depressive symptoms covariate.

From Yuan, Jing lin 2021, EJN: Based on previous studies on MCR and risk factors for dementia, we selected several risk factors for analysis [24] including age, sex, obesity (based on body mass index calculated from participants’ height and weight obtained from the survey, with a value ≥30.0 kg/m2defined as overweight), occupation (farmer or other), marital status (married or unmarried), smoking status (smoking was defined as 1 cigarette per day for >6 months, and smoking status was classified as never/former/current), and drinking status (drinking was defined as consumption of 50 ml of an alcoholic beverage per day for >6 months, and drinking status was classified as never/former/current). We also analyzed a number of physician-diagnosed vascular diseases that have been linked to adverse health outcomes such as dementia, disability, and death in previous studies including hypertension, diabetes, coronary heart disease (including a history of myocardial infarction), and a history of stroke.

Modifiers

### Data sources/measurement

For each variable of interest, give sources of data and details of methods of assessment (measurement). Describe comparability of assessment methods if there is more than one group

### Bias

Describe any efforts to address potential sources of bias

### Study Size

Explain how the study size was arrived at

### Quantitative variables

Explain how quantitative variables were handled in the analyses. If applicable, describe which groupings were chosen and why

### Statistical Methods

**Describe all statistical methods, including those used to control for confounding**

Descriptive analyses including the number and percentages of people with MCR were used to characterize the study sample. Linear model analysis of variance (for continuous – lots of studies use independent *t* test for this) and Pearson χ2 tests (for categorical) were used to assess characteristics associated with MCR and non-MCR participants. All statistical analyses were conducted in R Version 4.0.2.7

From Verghese 2014 prevalence paper: We report MCR prevalence by age and sex. Associations with 95% confidence intervals (CIs) of MCR with medical and cognitive variables were examined using linear regression for continuous variables and logistic models for binary variables, adjusted for age, sex, and education.

From Yuan, Jing lin 2021, EJN: The risk factors for MCR was analyzed by binary logistic regression. Model 1 did not adjust for any confounding factors. Model 2 adjusted for age, sex, occupation, marital status, obesity, smoking status, drinking status, hypertension, coronary heart disease, history of cerebrovascular disease, and hospitalization. The association between falls and SMCs, slow walking speed, and MCR were also analyzed by binary logistic regression. Model 1 is adjusted for age and sex. Model 2 is adjusted for all covariates in model 1 and occupation, obesity, marital status, smoking and drinking. Model 3 is adjusted for all covariates in model 2 and hypertension, diabetes, coronary artery disease, and cerebrovascular disease. Odds ratio (OR) and 95% confidence interval (95% CI) are reported.

From Callisaya 2016: T-tests and Chi-squared analyses were used tocompare participants included in the study with thoseexcluded due to missing data. Descriptive statisticswere used to summarize the characteristics of par-ticipants. Log binomial regression was performed todetermine if MCR increased the relative risk of falls separately in each cohort. All models were adjustedfor age and sex. Further adjustment was made foreducation and the above listed medical conditions ifthe relevant variable changed the coefficient of MCRby more than 10%.

From Ayers 2020 JAGS (personality traits): Cox proportional hazards models adjusted for age, sex, education, and the multimorbidity index score were used to compute adjusted haz-ard ratios (aHRs) with 95% confidence intervals (CIs) fordeveloping MCR, MCI, or subtypes of MCI based on base-line BFI scores.

**Describe any methods used to examine subgroups and interactions**

**Explain how missing data were addressed**

Three participants who had been diagnosed with dementia by the LBC1936 study doctor before age 76 (wave 3) were excluded from this study. Additionally, participants missing data in any of the variables incorporated in the MCR construct at each wave were excluded from analyses (wave 3; n=x, wave 4; n=x, wave 5; n=x). Accordingly, MCR status was coded for x participants at wave 3 (age 76), x at wave 4 (age 79), and x at wave 5 (age 82).

O. Beauchet et al. / Motoric Cognitive Risk Syndrome and Cardiovascular Disease and Risk Factors:

For the present analysis, we excluded participants with dementia and those without cognitive or gait assessments aswell as participants without information on CVDRF. The participants’ characteristics were summarizedusing means and SD or frequencies and percentages,as appropriate. Participants were classified into twogroups: non-MCR and MCR. Between-group com-parisons were performed using an unpairedt-testor chi square test, as appropriate. Multiple logisticregression analyses were performed to examine theassociation between MCR syndrome (i.e., dependentvariable) and CVDRF (i.e., independent variable),adjusted according to the participants’ character-istics.p-values less than 0.05 were considered asstatistically significant.

From Callisaya: To accountfor the possibility that the findings may have beenbiased from missing data, we performed the analy-sis between MCR and falls using inverse propensityweighting. Complete cases are weighted by theinverse of their probability of being a complete case,with those that have a low probability of being acomplete case receiving a larger weight. Regressionmodels controlling for baseline information (age,sex, years of education, and all medical conditionsdescribed above) were used to estimate the proba-bility of response in each cohort separately, and thereciprocals of these propensities were used as weightsin the analysis of risk.

(d) Cohort study—If applicable, explain how loss to follow-up was addressed

Case-control study—If applicable, explain how matching of cases and controls was addressed

Cross-sectional study—If applicable, describe analytical methods taking account of sampling strategy

(e) Describe any sensitivity analyses

# RESULTS

TABLE 1 - Covariate Descriptive Statistics for Participants With MCR Present Versus Absent

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
|  | Wave 1 | | | Wave 2 | | | Wave 3 | | |
| Variables | MCR present (N= | MCR absent  (N=) | *P* | MCR present (N= | MCR absent  (N=) | *P* | MCR present (N= | MCR absent  (N=) | *P* |
| Age at wave 1, mean (SD) |  |  |  |  |  |  |  |  |  |
| Sex, n (%) |  |  |  |  |  |  |  |  |  |
| Male |  |  |  |  |  |  |  |  |  |
| Female |  |  |  |  |  |  |  |  |  |
| Years of education, mean (SD) |  |  |  |  |  |  |  |  |  |
| Age 11 cognitive function, mean (SD) |  |  |  |  |  |  |  |  |  |
| Missing data |  |  |  |  |  |  |  |  |  |
| Gait speed (mean, time for 6 metres in sec) |  |  |  |  |  |  |  |  |  |
| Males | 3.6211 |  |  |  |  |  | 4.4691 |  |  |
| Females | 4.0937 |  |  |  |  |  | 4.9697 |  |  |
| Slow gait cut-off (>= 1SD slower than mean) |  |  |  |  |  |  |  |  |  |
| Males | 4.6426 |  |  |  |  |  | 5.9094 |  |  |
| Females | 5.3318 |  |  |  |  |  | 6.9125 |  |  |
| Depressive symptoms, mean (SD) |  |  |  |  |  |  |  |  |  |
| Missing data |  |  |  |  |  |  |  |  |  |
| BMI, mean (SD) |  |  |  |  |  |  |  |  |  |
| Missing data |  |  |  |  |  |  |  |  |  |
| History of CVD, n (%) |  |  |  |  |  |  |  |  |  |
| No |  |  |  |  |  |  |  |  |  |
| Yes |  |  |  |  |  |  |  |  |  |
| Missing data |  |  |  |  |  |  |  |  |  |
| History of stroke, n (%) |  |  |  |  |  |  |  |  |  |
| No |  |  |  |  |  |  |  |  |  |
| Yes |  |  |  |  |  |  |  |  |  |
| Missing data |  |  |  |  |  |  |  |  |  |
| Social class, n (%) |  |  |  |  |  |  |  |  |  |
| Professorial |  |  |  |  |  |  |  |  |  |
| Managerial |  |  |  |  |  |  |  |  |  |
| Skilled nonmanual |  |  |  |  |  |  |  |  |  |
| Skilled manual |  |  |  |  |  |  |  |  |  |
| Semiskilled / unskilled |  |  |  |  |  |  |  |  |  |
| Missing data |  |  |  |  |  |  |  |  |  |
| *APOE* ε*4* status, n (%) |  |  |  |  |  |  |  |  |  |
| Absent |  |  |  |  |  |  |  |  |  |
| Present |  |  |  |  |  |  |  |  |  |
| Missing data |  |  |  |  |  |  |  |  |  |
| Fried phenotype status, n (%) |  |  |  |  |  |  |  |  |  |
| Not frail |  |  |  |  |  |  |  |  |  |
| Prefrail |  |  |  |  |  |  |  |  |  |
| Frail |  |  |  |  |  |  |  |  |  |
| Missing data |  |  |  |  |  |  |  |  |  |

Table 2 Slow Gait Cut points for each age and sex

Gait Cuts (cm/s)M≥75M<75F≥75F<75

Bullet point my criteria for MCR

Miles Welstead to Everyone (14:45)

MCIdata$dementia\_W3 <- ifelse(MCIdata$dement\_w3==0 & MCIdata$mmse\_w3>=24, 1,0)

Miles Welstead to Everyone (15:09)

LBCdata$gripstrength\_w2<- ifelse(LBCdata$sex==1 & LBCdata$bmi\_w2<=24 & LBCdata$strongestgrpstr\_w2<=29, 1,

ifelse(LBCdata$sex==1 & LBCdata$bmi\_w2>24 & LBCdata$bmi\_w2<=28 & LBCdata$strongestgrpstr\_w2<=31, 1,

ifelse(LBCdata$sex==1 & LBCdata$bmi\_w2>28 & LBCdata$strongestgrpstr\_w2<=32, 1,

ifelse(LBCdata$sex==2 & LBCdata$bmi\_w2<=23 & LBCdata$strongestgrpstr\_w2<=17, 1,

ifelse(LBCdata$sex==2 & LBCdata$bmi\_w2>23 & LBCdata$bmi\_w2<=26 & LBCdata$strongestgrpstr\_w2<=17.3, 1,

ifelse(LBCdata$sex==2 & LBCdata$bmi\_w2>26 & LBCdata$bmi\_w2<=29 & LBCdata$strongestgrpstr\_w2<=18, 1,

ifelse(LBCdata$sex==2 & LBCdata$bmi\_w2>29 & LBCdata$strongestgrpstr\_w2<=21, 1,0)))))))

(International Personal Item Pool) Ipip28 - Please use the rating scale to describe how accurately each statement describes you. Describe yourself as you generally are now, not as you wish to be in the future. Describe yourself as you honestly see yourself, in relation to other people you know of the same sex as you are, and roughly your same age

I often forget to put things back in their proper place

Scoring: 0 very inaccurate, 1 moderately inaccurate, 2 neither inaccurate nor accurate, 3 moderately accurate, 4 very accurate

From https://www.jstor.org/stable/41445076?seq=1#metadata\_info\_tab\_contents This has previously been validated in the LBC1921 [https://researchportal.hw.ac.uk/en/publications/goldbergs-ipip-big-five-factor-markers-internal-consistency-and-c] and has 10 items for each of the Big- Five personality factors: Extraversion (E), Agreeableness (A), Conscientiousness (C), Emotional Stability (ES; the same trait as Neuroticism, but named and scored from the opposite end of the continuum) and Intellect/Imagination (I; similar to Openness to experience). For each of the items, which are in sentence fragment form (e.g. 4 Am the life of the party'), 'I' was added at the beginning. Participants indicated how well each item described them, on a 5-point Likert-type scale (from very inaccurate to very accurate).

From Miles’ <https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456784/#s0150>

**Appendix B. Defining occupational social class and childhood IQ**

Occupational social class was based upon principal occupation, coded in line with the 1980 census ([General, 1991](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456784/#bb0090)). Five social class categories were used: professional, managerial, skilled non-manual, skilled manual, and semiskilled/unskilled. The women in the cohort were asked for their husband's occupation as well as their own, and they were assigned a social class based on the highest occupation of the household. This was derived from their own occupation for about half of the women, and from their husband's occupation for the remainder.

Childhood IQ was derived from Moray House Test scores at age 11 ([Penrose, 1949](https://www.ncbi.nlm.nih.gov/pmc/articles/PMC7456784/#bb0135)) as part of the LBC1936. Raw scores were corrected for age in days at time of testing and converted to an IQ scale where mean (SD) = 100 (15).