*Twin Research and Human Genetics*

**The identification of hereditary and environmental determinants of frailty in a cohort of UK twins**

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**Table S1.** Questionnaires items used to derive variables

| **Questionnaire** | **Item** |
| --- | --- |
| Q2 Twins questionnaire | * At what age did you finish full time education? |
|  | * Please indicate all the qualifications you have: * University * Higher vocational * Teaching * Nursing * A-level * Middle vocational * 5+ O-levels * Low vocational * 1 to 4 O-levels * Clerical * Other * None |
| Q10 Twins Questionnaire 2005 | * Occupation \ Using the Table below as a guide, please tick one circle (1-8) for each person (i-iv)\* to show which best describes the sort of work you/your family member did:  |  | | --- | | * Clerical and intermediate occupations | | * Middle/junior managers | | * Modern professional occupations | | * Never worked | | * Routine manual and service occupations | | * Semi-routine manual and service occupations | | * Senior managers/administrators | | * Technical and craft occupations | | * Traditional professional occupations   ( \*yourself, spouse, mother, father) | |
| Q11A Twins UK: Baseline Health Questionnaire | * At what age did you finish or stop full time education? |
|  | |  | | --- | | * Are you currently living with a spouse or partner | | * In your life, how many different spouses and partners have you lived with   for more than 1 month? Please provide the total number , including  current live-in spouse/partner (If you have one ) | | * Have you ever been married? | | * Are you currently married? | | * Are you currently separated from your spouse although not divorced? | | * How many times have you been married? | | * Have you ever been divorced? | | * Have you ever been widowed? | |
|  | * In the past 30 days, on how many days did you drink at least on unit of alcohol * In the past 30 days, approx. how many units of alcohol did you drink per week * On how many days during the past 30 days did you drink 6 or more units of alcohol over the course of one drinking sessions? |
| Q17D (Health Ageing Twins Study [HATS]) | In the past ten years were you widowed? |
|  | * What is your current marital status?  |  | | --- | | * Divorced | | * Invalid entry | | * Married (and living together) | | * Married (but living apart) | | * Separated | | * Single (whether in a relationship or not) | | * Widowed | |
|  | * Are you currently in a relationship? * Do you live together? * Is your relationship status different from ten years ago? * In the past ten years did you get married? * In the past ten years did you get divorced/ separated? * In the past 10 years were you widowed? |
|  | * Have you ever smoked cigarettes? * Do you currently smoke cigarettes? * How long has it been since you gave up smoking? * For how long did you smoke in total? * When you used to smoke, what type of smoker were you?  |  |  | | --- | --- | | * Social/light * heavy smoker | | | * moderate smoker | | | * On average how many cigarettes do you smoke a day? * How long have you smoked for in total? * Please tick the statement that most accurately describes your current level of smoking. | |
|  | During the last week, how many hours did you spend on each of the following physical activities?   * Physical exercise such as swimming, jogging, aerobics, football, tennis, gym workout, power walking etc. * Cycling, including to work and during leisure time * Gentler exercise, Yoga and Pilates * Walking, including walking to work, shopping for pleasure etc. * Housework/Childcare/Carer * Gardening/DIY  |  | | --- | | * Between 1 and 3 hours | | * Less than 1 hour | | * More than 3 hours | | * None | |
|  | * How would you describe your usual walking pace? |
|  | Please tick the statement that best describes how much alcohol you drink per week on average:   * One small glass of white wine * One small glass of red wine * Half a pint of beer, lager or cider * One pub measure of port, sherry, vermouth, liqueurs * One pub measure of spirits, e.g. gin, brandy, whisky, vodka  |  | | --- | | * Once a day | | * Once a week | | * 2–3 per day | | * 2–4 per week | | * 4–5 per day | | * 5–6 per week | | * 6+ per day | | * Invalid entry | | * None / Less than once a week | |

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**Table S2**. Items from Healthy Ageing Twin Study used to create the frailty index

| **Domain** | **Specific questionnaire item** | **Scoring of original variables** | **New operationalized variable** |
| --- | --- | --- | --- |
| **Co-morbidity** | * Respiratory\Chronic bronchitis\Diagnosed by a doctor? * Respiratory\Chronic Obstructive Pulmonary Disease (e.g emphysema)\Diagnosed by a doctor? | No=0  Yes=1 | *Respiratory*  Binary  Absent=0; present=1 |
|  | * Bone\Hip fracture\Diagnosed by a doctor? * Bone\Spine fracture\Diagnosed by a doctor? * Bone\Wrist fracture\Diagnosed by a doctor? | No=0  Yes=1 | *Skeletal*  Binary  absent=0; present=1 |
|  | * Cardiovascular\Myocardial Infarction (heart attack)\Diagnosed by a doctor? * Cardiovascular\Angina (chest pain due to heart problems but not a heart attack)\Diagnosed by a doctor? * Cardiovascular\Coronary bypass (heart bypass)\Diagnosed by a doctor? * Cardiovascular\Angioplasty\Diagnosed by a doctor? * Cardiovascular\Stroke\Diagnosed by a doctor? | No=0  Yes=1 | *Cardiovascular*  Binary  absent=0; present=1 |
|  | * Cardiovascular\High cholesterol\Diagnosed by a doctor? * Cardiovascular\Hypertension (high blood pressure)\Diagnosed by a doctor? | No=0  Yes=1 | *Cardiovascular risk factors*  Binary  absent=0; present=1 |
|  | * Cardiovascular \ Deep vein thrombosis \ Diagnosed by a doctor? | No=0  Yes=1 | *Venous*  Binary  absent=0; present=1 |
|  | * Cancer\Breast\Diagnosed by a doctor? * Cancer\Colon\Diagnosed by a doctor? * Cancer\Skin – melanoma\Diagnosed by a doctor? * Cancer\Skin – basal cell\Diagnosed by a doctor? * Cancer\Skin – squamous\Diagnosed by a doctor? * Cancer\Skin – other (please specify) | No=0  Yes=1 | *Cancer*  Binary  absent=0; present=1 |
|  | * Eye\Cataract \ Diagnosed by a doctor? * Eye\Visual impairment (difficulty seeing even with glasses <6/12 acuity)\Diagnosed by a doctor? | No=0  Yes=1 | *Vision*  Binary  absent=0; present=1 |
|  | * Do you have any other chronic (on-going) conditions, diagnosed by a doctor and not listed here? eg glaucoma, multiple sclerosis, diabetes, osteoporosis, osteoarthritis etc * Other ongoing chronic conditions (1–4)\Please specify * Other ongoing chronic conditions (1–4)\Please specify\Diagnosed by a doctor? | No=0  Yes=1 | *Other1*  *Other2*  *Other3*  Binary  absent=0; present=1 |
| **Physical measures** | * Grams of Lean Tissue in Left Leg Region * Grams of Lean Tissue in Right Leg Region |  | *Lean\_leg*  (take bigger leg)  Binary  (≥5500g=0; else=1 |
|  | * Average SBP | Continuous measurement (mmHg) | *Hypertension\_sbp*  Binary  Normal=0; out of range=1 |
|  | * Average DBP | Continuous measurement (mmHg) | *Hypertension\_dbp*  Binary  Normal=0; out of range=1 |
|  | * Grip strength | Continuous measurement (kg) | *Strength*  Binary  >17 kg=0; ≤17 kg=1 |
|  | * Dexa total hip t-score† | Continuous measurement  Normal t-score >–1.0  Osteopenia t-score <–1.0 and >–2.5  Osteoporosis t-score <–2.5 | *Osteopenia\_porosis\_total\_hip*  Nominal score  Normal=0; osteopenia=0.5; osteoporosis=1 |
|  | * BMI | Continuous variable calculated from weight and height in kg/m2 | *Obesity*  Binary  Obese=0 not obese=1  with BMI ≥18.5 kg/m2 defined as obese |
| **Biochemistry** | * Measuredfev1‡ * Measuredfvc¶ | Continuous measurements (L) | *Spirometry\_fev*  Binary  Healthy=0; else=1  Where healthy =fev1/fvc≥74% |
|  | * White blood cell count | Continuous measurement of white blood cells/µL | *Wcc*  Binary  Normal=0; else=1 where normal is ≥4000 white blood cells/µL |
|  | * HDL cholesterol * LDL cholesterol * Haemoglobin (g/dL) | Continuous measurements | *Anaemia*  Binary  Not anaemic=0; anaemic=1 where anaemic is a haemoglobin measurement of ≤11 g/dL provided total cholesterol/HDL cholesterol <4 |
|  | * Glomerular filtration rate | Continuous measurement | *eGFR*  Binary Normal=0; else =1 where normal is GFR >90mls/min/1.73m2 |
|  | * mcv\* (fL) | Continuous measurement | *Mcv*  Binary  Normal=0; else=1  where normal is 74–96 fL |
| **Mental health** | * During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of any emotional problems (such as feeling depressed or anxious)? * Cut down on the amount of time you spend on work or other activities * Accomplished less than you would like * Did work or activities less carefully than usual | All  of the time=1  Most of the time=2  Some of the time=3  A little of the time=4  None of the time=5 | *Emotion*  Binary  total score >12=0; else=1 |
|  | * These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks… * Did you feel full of life * Have you felt calm and peaceful? * Have you been happy | All of the time=1  Most of the time=2  Some of the time=3  A little of the time=4  None of the time=5 | *Happy*  Binary  total score ≥1.5=1; else=0 |
|  | * How much of the time during the past 4 weeks… * Have you been very nervous? * Have you felt so down in the dumps that nothing could cheer you up? * Have you felt downhearted and depressed? | All of the time=1  Most of the time=2  Some of the time=3  A little of the time=4  None of the time=5 | *Depressed*  Binary  total score ≥1.5=1; else=0 |
| **Self-reported general health** | * In general would you say your health is: | Excellent=5  Very good=4  Good=3  Fair=2  Poor=1 | * *Health\_self\_rating* * Ordinal score of 1, 2, 3, 4 or 5 converted to 0, 0.25, 0.5, 0.75 or 1 |
|  | * Compared to one year ago, how would you rate your health in general now? | Much better now than one year ago=1  Somewhat better now than one year ago=2  About the same as one year ago=3  Somewhat worse now than one year ago=4  Much worse now than one year ago=5 | *Health\_perceived\_change*  Binary  same or better than one year ago=0; worse than one year ago=1 |
|  | * Answer TRUE or FALSE for each of the following statements: * I seem to get sick a little easier than other people * I am as healthy as anybody I know * I expect my health to get worse * My health is excellent | Definitely true=1  Mostly true=2  Don't know=3  Mostly false=4  Definitely false=5 | *Robust health*  Ordinal score of 0, 0.25, 0.5, 0.75 or 1.0 from most positive to most negative attitudes about health |
|  | * These questions are about how you feel and how things have been with you during the past 4 weeks. For each question, please give the one answer that comes closest to the way you have been feeling. How much of the time during the past 4 weeks…   o Did you have a lot of energy?  o Did you feel worn out?  o Did you feel tired? | All of the time=1  Most of the time=2  Some of the time=3  A little of the time=4  None of the time=5 | *Fatigue*  Binary  mostly not tired=0; mostly tired=1 |
| **Disability** | * The following questions are about activities you might do during a typical day. Does your health now limit you in these activities? If so, how much? |  |  |
|  | * Moderate activities, such as moving a table, pushing a vacuum cleaner, bowling, or playing golf, scored 1, 2, 3 | Yes, limited a lot=1  Yes, limited a little=2  No, not limited at all=3 | *Heavy\_housework*  Binary  Not limited or limited a little =0; limited a lot=1 |
|  | * Bending, kneeling, or stooping 1,2 3 | Yes, limited a lot=1  Yes, limited a little=2  No, not limited at all=3 | *Bending\_kneeling\_stooping*  Binary  Not limited or limited a little =0; limited a lot=1 |
|  | * Lifting or carrying groceries 1,23 | Yes, limited a lot=1  Yes, limited a little=2  No, not limited at all=3 | *Shopping*  Binary  Not limited or limited a little =0; limited a lot=1 |
|  | * Climbing one flight of stairs 1,2 3 | Yes, limited a lot=1  Yes, limited a little=2  No, not limited at all=3 | *Stairs*  Binary  Not limited or limited a little =0; limited a lot=1 |
|  | * Walking one hundred yards | Yes, limited a lot=1  Yes, limited a little=2  No, not limited at all=3 | *Walking*  Binary  Not limited or limited a little =0; limited a lot=1 |
|  | * Bathing or dressing yourself | Yes, limited a lot=1  Yes, limited a little=2  No, not limited at all=3 | *Bathing\_dressing*  Binary  Not limited or limited a little =0; limited a lot=1 |
|  | * Diabetic | Yes=1  No=0 | *Diabetic* |
|  | * During the past 4 weeks, how much of the time have you had any of the following problems with your work or other regular daily activities as a result of your physical health? * Cut down on the amount of time you spent on work or other activities * Accomplished less than you would like * Were limited in the kind of work or other activities * Had difficulty performing the work or other activities (for example, it took extra effort | All  of the time=1  Most of the time=2  Some of the time=3  A little of the time=4  None of the time=5 | *Physical*  Binary  total score of ≤17 =1;  else =0 |
| **Social functioning** | * During the past 4 weeks, to what extent has your physical health or emotional problems interfered with your normal social activities with family, friends, neighbours, or groups? | Extremely=5  Quite a bit=4  Moderately=3  Slightly=2  Not at all=1 | *Social functioning*  Binary  total of ≥5=1, else=0 |
|  | * During the past 4 weeks, how much of the time has your physical health or emotional problems interfered with your social activities (like visiting friends, relatives, etc.)? | All  of the time=1  Most of the time=2  Some of the time=3  A little of the time=4  None of the time=5 |  |
| **Polypharmacy** | * Are you currently taking any medications/supplements prescribed by a doctor?\Name of prescribed medication that you are currently taking (and please bring with you for visit) - Please specify |  | *Polypharmacy*  Binary  ≤5 medications=0; >5 medications=1 |
| **Pain** | |  | | --- | | * How much bodily pain have you had during the past 4 weeks? | | None=1  Very mild=2  Mild=3  Moderate=4  Severe=5  Very severe=6 | *Pain*  Binary  Moderate to very severe pain=1; else =0 |
|  | * During the past 4 weeks, how much did pain interfere with your normal work (including both work outside the home and housework)? | Not at all=1  A little bit=2  Moderately=3  Quite a bit=4  Extremely=5 |  |

BMI, body mass index; Dexa, dual-energy x-ray absorptiometry; dbp, diastolic blood pressure; fev1, forced expiratory volume in 1 second; fvc, forced vital capacity; HDL, high density lipoprotein; LDL, low density lipoprotein; mcv, mean corpuscular volume; sbp, systolic blood pressure

†densitometric technique for assessing bone mineral density to identify osteopenia and osteoporosis

‡FEV1 is the volume of air that can forcibly be blown out in one second, after full inspiration

¶FVC is the volume of air that can forcibly be blown out after full inspiration measured in litres

(The FEV1/FVC ratio is a calculated ratio used in the diagnosis of obstructive and restrictive lung disease which represents the proportion of a person's vital capacity they are able to expire in the first second of forced expiration.)

\*mcv (expressed in femtolitres [fL]) is a measure of the average volume of a red blood corpuscle obtained by multiplying a volume of blood by the proportion of blood that is cellular and dividing that product by the number of red blood cells in that volume