DATA NOTE

Self-reported Anxiety Sensitivity Index in the TwinsUK cohort
[version 1; peer review: 1 approved, 1 approved with reservations]

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Abstract
The anxiety sensitivity (AS) construct has received considerable attention in anxiety research and is considered to be a cognitive vulnerability factor for the study of anxiety related disorders. The Anxiety Sensitivity Index (ASI) is the most widely used instrument for the study of AS. The present Data Note provides an overview of all the 16-item ASI questionnaires filled and returned by the twins in the TwinsUK registry. This work does not provide any multidimensional or factor structure analysis of the responses provided. TwinsUK registry encompasses a wide range of clinical and self-reported data that can be used as confounding factors in the study of cognitive and mental health.

Keywords
TwinsUK, Anxiety sensitivity, ASI, Mental Health, Anxiety, Stress disorder, Anxiety Sensitivity Index

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Introduction
The Department of Twin Research and Genetic Epidemiology at St. Thomas’ Hospital, King’s College London (KCL), hosts the UK’s largest adult twin registry (or TwinsUK)\(^1\). TwinsUK is a cohort of volunteer adult twins currently consisting of 14,575 monozygotic (MZ) and dizygotic (DZ) twins with ages between 18 to 101 years. The Registry includes self-reported and clinical data that has been measured longitudinally for majority of volunteers through comprehensive visits, annual questionnaires, and several project-led studies.

Over 69% of the registered twins have attended at least one comprehensive clinical assessment and about half of those undergone at least two follow up health visits. The primary aim of TwinUK studies have been the genetic basis of complex diseases, such as cardiovascular, metabolic, musculoskeletal, and ophthalmologic diseases. Between 1992 and 2004, active twins were invited and attended a comprehensive ‘baseline’ visit, that was followed by a 1-day clinical visit (first follow-up visit). The first follow up visit aimed to discover the genetics of common disease and complex traits. The focus of the study then broaden to include the complex healthy ageing process and the genetic and lifestyle factors that influence aging over time (the Healthy Aging Twin Study (HATS))\(^2\). The second follow-up visits were part of the HATS study. The third cycle of follow-up visits were carried out between 2012 and 2017 as part of the Biomedical Research Centre (BRC) study, with the aim of understanding genetic and environmental interactions in the development and progression of disease. During the BRC study 5286 volunteers from the TwinsUK registry attended the clinics and over 6300 questionnaires were returned.

All visits followed a similar layout. Prior to each visit, participants were asked to complete a general questionnaire focused on recent self-reported clinical findings as well as behavior, and lifestyle related question. Blood and urine samples were also collected during the visits. Furthermore, a number of other tests such as weight, height, blood pressure, grip strength, and biochemical levels were measured. Cognitive tests such as Cambridge Neuropsychological Test Automated Battery (CANTAB)\(^3\) were also performed in a subset of visits. As well as the self-reported and measured phenotypes mentioned above, TwinsUK also benefits from a number of genotyping and ‘omics’ data for a subset of the cohort. The following sections of this document will provide the overlap number between the participants with both ‘omics’ and Anxiety Sensitivity Index (ASI) data.

Here, we present an overview of 16-item ASI questionnaires\(^4\) that were completed and returned by the volunteers in the TwinsUK cohort over time. The registry incorporates a wide range of other longitudinal data including different self-reported and clinical cognitive data such as the Hospital Anxiety and Depression Scale (HADS)\(^5\), and self-reported anxiety and depression diagnosis. These can be used by the scientific community, where relevant, to provide a more comprehensive research outcome.

We collected data on depression, anxiety, and anxiety sensitivity in the TwinsUK cohort in order to understand the genetic epidemiology of these traits and their link to other health related phenotypes available on the registry. These data are intended to enhance the health phenotyping in this population for the benefit of the scientific community and the public.

Method
As conceptualized by Reiss and his colleagues\(^6\), anxiety sensitivity (AS) refers to the fear of anxiety-related physical sensations, which arise from the belief that these sensations can have harmful physical, psychological, or social consequences. The 16 item Anxiety Sensitivity Index (ASI) questionnaire is the most widely used assessment for anxiety sensitivity (AS).

A total of 8328 ASI questionnaires have been collected at the department of TwinsUK from which 57.6% (N=4802) were sent and completed in 2005 as part of the TwinsUK annual questionnaire (Twins Questionnaire (2005)), while 42.4% (N=3526) were sent to the twins and returned between 2007 and 2010 as part of the HATS personality questionnaire included in the visit packs. The age of response ranged from 18 to 87, with 93.6% of respondents female.

The questionnaires were administered on paper and they were manually entered by data operators. More than half of the participants (N= 4912; 58.8%) have two time points in which they have completed and returned ASI questionnaire, across a 5-year time frame. The ASI items are listed below, alongside their TwinsUK variable code.

**Table 1. DN00001. It is important to me not to appear nervous (Table 1).**

| Frequency | Percent | Cumulative Percent |
|-----------|---------|--------------------|
| 0 Very Little | 1615 | 19.5 | 19.5 |
| 1 A Little | 1764 | 21.3 | 40.8 |
| 2 Some | 2135 | 25.8 | 66.6 |
| 3 Much | 1745 | 21.1 | 87.7 |
| 4 Very much | 1017 | 12.3 | 100.0 |
| Total | 8276 | 100.0 |
Table 2. DN00002. When I cannot keep my mind on a task, I worry that I might be going crazy.

| Frequency | Percent | Cumulative Percent |
|-----------|---------|--------------------|
| 0 Very Little | 6276 | 75.6 | 75.6 |
| 1 A Little | 1151 | 13.9 | 89.5 |
| 2 Some | 603 | 7.3 | 96.7 |
| 3 Much | 178 | 2.1 | 98.9 |
| 4 Very much | 94 | 1.1 | 100.0 |
| Total | 8302 | 100.0 | |

Table 3. DN00003. It scares me when I feel “shaky” (trembling).

| Frequency | Percent | Cumulative Percent |
|-----------|---------|--------------------|
| 0 Very Little | 4707 | 56.9 | 56.9 |
| 1 A Little | 2265 | 27.4 | 84.3 |
| 2 Some | 806 | 9.8 | 94.1 |
| 3 Much | 327 | 4.0 | 98.1 |
| 4 Very much | 159 | 1.9 | 100.0 |
| 999905* | 2 | 0.0 | 100.0 |
| Total | 8265 | 100.0 | |

*999905= Unable to determine the response given. (E.g. more than one option selected).

Table 4. DN00004. It scares me when I feel faint.

| Frequency | Percent | Cumulative Percent |
|-----------|---------|--------------------|
| 0 Very Little | 3710 | 45.2 | 45.2 |
| 1 A Little | 2618 | 31.9 | 77.0 |
| 2 Some | 1008 | 12.3 | 89.3 |
| 3 Much | 601 | 7.3 | 96.6 |
| 4 Very much | 279 | 3.4 | 100.0 |
| 999905* | 1 | 0.0 | 100.0 |
| Total | 8217 | 100.0 | |

*999905= Unable to determine the response given.

Table 5. DN00005. It is important to me to stay in control of my emotions.

| Frequency | Percent | Cumulative Percent |
|-----------|---------|--------------------|
| 0 Very Little | 1066 | 12.9 | 12.9 |
| 1 A Little | 1653 | 20.0 | 32.9 |
| 2 Some | 2253 | 27.2 | 60.1 |
| 3 Much | 1958 | 23.7 | 83.7 |
| 4 Very much | 1345 | 16.2 | 100.0 |
| 999905* | 2 | 0.0 | 100.0 |
| Total | 8277 | 100.0 | |

*999905= Unable to determine the response given.

Table 6. DN00006. It scares me when my heart beats rapidly.

| Frequency | Percent | Cumulative Percent |
|-----------|---------|--------------------|
| 0 Very Little | 3050 | 36.8 | 36.8 |
| 1 A Little | 2652 | 32.0 | 68.8 |
| 2 Some | 1518 | 18.3 | 87.1 |
| 3 Much | 674 | 8.1 | 95.3 |
| 4 Very much | 389 | 4.7 | 100.0 |
| 999905* | 2 | 0.0 | 100.0 |
| Total | 8285 | 100.0 | |

*999905= Unable to determine the response given.

Table 7. DN00007. It embarrasses me when my stomach growls.

| Frequency | Percent | Cumulative Percent |
|-----------|---------|--------------------|
| 0 Very Little | 3753 | 45.3 | 45.3 |
| 1 A Little | 2525 | 30.5 | 75.7 |
| 2 Some | 1196 | 14.4 | 90.2 |
| 3 Much | 496 | 6.0 | 96.2 |
| 4 Very much | 317 | 3.8 | 100.0 |
| 999905* | 1 | 0.0 | 100.0 |
| Total | 8288 | 100.0 | |

*999905= Unable to determine the response given.

Table 8. DN00008. It scares me when I am nauseous.

| Frequency | Percent | Cumulative Percent |
|-----------|---------|--------------------|
| 0 Very Little | 4574 | 55.4 | 55.4 |
| 1 A Little | 2110 | 25.6 | 80.9 |
| 2 Some | 934 | 11.3 | 92.3 |
| 3 Much | 410 | 5.0 | 97.2 |
| 4 Very much | 228 | 2.8 | 100.0 |
| 999905* | 1 | 0.0 | 100.0 |
| Total | 8257 | 100.0 | |

*999905= Unable to determine the response given.
When I notice that my heart is beating rapidly, I worry that I might have a heart attack.

| Frequency | Percent | Cumulative Percent |
|-----------|---------|-------------------|
| 0 Very Little | 5009 | 60.6 | 60.6 |
| 1 A Little | 1847 | 22.3 | 82.9 |
| 2 Some | 795 | 9.6 | 92.5 |
| 3 Much | 372 | 4.5 | 97.0 |
| 4 Very much | 244 | 3.0 | 100.0 |
| 999905* | 2 | .0 | 100.0 |
| Total | 8269 | 100.0 |

*999905= Unable to determine the response given.

It scares me when I become short of breath.

| Frequency | Valid Percent | Cumulative Percent |
|-----------|---------------|--------------------|
| 0 Very Little | 3827 | 46.2 | 46.2 |
| 1 A Little | 2492 | 30.1 | 76.3 |
| 2 Some | 1119 | 13.5 | 89.8 |
| 3 Much | 535 | 6.5 | 96.3 |
| 4 Very much | 307 | 3.7 | 100.0 |
| 999905* | 1 | .0 | 100.0 |
| Total | 8281 | 100.0 |

*999905= Unable to determine the response given.

When my stomach is upset, I worry that I might be seriously ill.

| Frequency | Percent | Cumulative Percent |
|-----------|---------|-------------------|
| 0 Very Little | 6033 | 72.7 | 72.7 |
| 1 A Little | 1454 | 17.5 | 90.2 |
| 2 Some | 545 | 6.6 | 96.8 |
| 3 Much | 173 | 2.1 | 98.9 |
| 4 Very much | 92 | 1.1 | 100.0 |
| 999905* | 1 | .0 | 100.0 |
| Total | 8298 | 100.0 |

*999905= Unable to determine the response given.

It scares me when I am unable to keep my mind on a task.

| Frequency | Percent | Cumulative Percent |
|-----------|---------|-------------------|
| 0 Very Little | 4890 | 58.9 | 58.9 |
| 1 A Little | 2193 | 26.4 | 85.4 |
| 2 Some | 806 | 9.7 | 95.1 |
| 3 Much | 279 | 3.4 | 98.4 |
| 4 Very much | 129 | 1.6 | 100.0 |
| Total | 8297 | 100.0 |

Unusual body sensations scare me.

| Frequency | Percent | Cumulative Percent |
|-----------|---------|-------------------|
| 0 Very Little | 4498 | 54.6 | 54.6 |
| 1 A Little | 2576 | 31.3 | 85.8 |
| 2 Some | 806 | 9.8 | 95.6 |
| 3 Much | 259 | 3.1 | 98.8 |
| 4 Very much | 102 | 1.2 | 100.0 |
| Total | 8241 | 100.0 |

Researchers use a variety of factor-based approaches in the analysis of ASI data. These are not summarized here, though the overall characteristics of the sample are presented in Table 18 as a total ASI score.

Table 17 provides the total number of valid and missing responses for each of the variables. As shown, we have a maximum of 99.7% and a minimum of 98.7% valid responses amongst all the returned questionnaires.

Scoring system

The respondent is required to rate each item by selecting one of five responses. Each item is rated on a five-point Likert scale ranging from 0 (very little) to 4 (very much). An individual’s AS score is the sum of the scores on the 16 items.

Researchers use a variety of factor-based approaches in the analysis of ASI data. These are not summarized here, thought the overall characteristics of the sample are presented in Table 18 as a total ASI score.
Anxiety sensitivity has been linked to different forms of psychopathology, such as anxiety disorder, chronic pain, and substance abuse. TwinsUK has collected data on some of the potential confounding factors such as age, BMI, smoking, alcohol consumption, and chronic pain that can be provided to the research community by following the instructions listed in the Data availability section below. Furthermore, TwinsUK holds a wide range of ‘omics’ data for subsections of its samples. Table 19 provides the overlap number of participants with available ‘omics’ data.

### Table 15. DN00015. When I am nervous, I worry that I might be mentally ill.

| Frequency    | Percent | Cumulative Percent |
|--------------|---------|--------------------|
| 0 Very Little| 7064    | 85.3               |
| 1 A Little   | 727     | 94.1               |
| 2 Some       | 296     | 97.6               |
| 3 Much       | 102     | 98.9               |
| 4 Very much  | 93      | 100.0              |
| Total        | 8282    | 100.0              |

### Table 16. DN00016. It scares me when I am nervous.

| Frequency   | Valid Percent | Cumulative Percent |
|-------------|---------------|--------------------|
| 0 Very Little| 5518          | 66.6               |
| 1 A Little  | 1804          | 88.3               |
| 2 Some      | 624           | 95.9               |
| 3 Much      | 197           | 98.2               |
| 4 Very much | 147           | 100.0              |
| Total       | 8290          | 100.0              |

### Table 17. Valid and missing responses.

| Dataset        | Mean | Valid (%) | Missing (%) |
|----------------|------|-----------|-------------|
| DN00001        | 1.85 | 8276 (99.4)| 52 (0.6)    |
| DN00002        | .39  | 8302 (99.7)| 26 (0.3)    |
| DN00003        | .76  | 8265 (99.2)| 63 (0.8)    |
| DN00004        | 1.01 | 8217 (98.7)| 111 (1.3)   |
| DN00005        | 2.29 | 8277 (99.4)| 51 (0.6)    |
| DN00006        | 1.31 | 8285 (99.5)| 43 (0.5)    |
| DN00007        | 1.02 | 8288 (99.5)| 40 (0.5)    |
| DN00008        | .84  | 8257 (99.1)| 71 (0.9)    |
| DN00009        | .86  | 8269 (99.3)| 59 (0.7)    |
| DN00010        | 1.01 | 8281 (99.4)| 47 (0.6)    |
| DN00011        | .51  | 8298 (99.6)| 30 (0.4)    |
| DN00012        | .62  | 8297 (99.6)| 31 (0.4)    |
| DN00013        | .58  | 8234 (98.9)| 94 (1.1)    |
| DN00014        | .65  | 8241 (99.0)| 87 (1.0)    |
| DN00015        | .24  | 8282 (99.4)| 46 (0.6)    |
| DN00016        | .51  | 8290 (99.5)| 38 (0.5)    |

### Table 18. ASI total scores.

|              | N   | Min | Max | Mean | StdD. |
|--------------|-----|-----|-----|------|-------|
| ASI_score    |     |     |     |      |       |
| Female       | 7783| 0   | 64  | 12.99| 9.963 |
| Male         | 535 | 0   | 62  | 13.82| 9.910 |
| age          | 8318| 18  | 87  | 55.25| 12.317|

### Omics data

Anxiety sensitivity has been linked to different forms of psychopathology, such as anxiety disorder, chronic pain, and substance abuse. TwinsUK has collected data on some of the potential confounding factors such as age, BMI, smoking, alcohol consumption, and chronic pain that can be provided to the research community by following the instructions listed in the Data availability section below. Furthermore, TwinsUK holds a wide range of ‘omics’ data for subsections of its samples. Table 19 provides the overlap number of participants with available ‘omics’ data.

| Novel Molecular and Genetic Phenotypes                  | Number of overlap |
|--------------------------------------------------------|-------------------|
| Genome-wide association study (Gwas)                    | 3926              |
| Exome sequencing                                       | 2327              |
| Epigenetic Methylated DNA immunoprecipitation sequencing (MeDIP-seq) | 3067              |
| Metabolomics (Fasting Serum) non-targeted metabolomic analysis using Metabolon Inc., platform. | 2020              |
| Glycomics                                              | 3400              |
| Microbiome gut (Gut flora DNA analysed with 16s sequencing technology.) | 1949              |
| Plasma Metals                                          | 3338              |
| Salivary Metabolomics                                  | 1864              |
| Faecal Metabolomics                                    | 930               |

### Ethical approval

All the data provided on this paper have been collected through questionnaires that had ethical approval as parts of Twins UK (EC04/015) or Healthy Ageing Twin Study (H.A.T.S) (07/H0802/84) studies from Local Research Ethics Committee at the Department of Twin Research and Genetic Epidemiology, King’s College London. A written informed consent was obtained from all the TwinUK volunteers upon registration and also during their clinical visits. All study members hold the right to withdraw their consent partially or entirely upon their request.

### Data availability

TwinsUK facilitates and encourages the sharing of data with the scientific community to further scientific research. Researchers can follow the below steps to request and access the datasets provided on this data note as well as other TwinsUK data. All the datasets included in this data note can be accessed by quoting the data note name or specific variable codes provided within this report.

1. Please search for your required phenotype using the TwinsUK Phenotype spreadsheet containing a list of all TwinsUK phenotypes.
2. Please read the TwinsUK Data Access Policy document which describes the process of accessing the data and samples as well as the costs associated.

3. Please submit your Proposal Form to the TwinsUK Resource Executive Committee (TREC) for consideration. You will be notified of the outcome of the review within three weeks and advised on the next stage.

The proposal form should specify the data and/or samples required including individual variables with an appropriate justification describing the aims/hypothesis of the project for which the data is requested. Further information can also be found on the TwinsUK website (www.twinsuk.ac.uk/data-access). If you have any other enquiries related to data access please email Collaborations and Data Access Manager, Victoria Vazquez (victoria.vazquez@kcl.ac.uk).

Grant information
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The funders had no role in study design, data collection and analysis, decision to publish, or preparation of the manuscript.

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Open Peer Review

Current Peer Review Status: ✔️ 💥

Version 1

Reviewer Report 21 October 2019

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Bronwyn K. Haasdyk Brew
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It is encouraging to see some descriptive data regarding anxiety sensitivity in such a large cohort with a lot of omics data. I hope there will be many interesting papers following this article. However I have some suggestions and some concerns. Firstly, could the authors please provide more information on how and when the twins were recruited and if there is a similar bias of women participating in the cohort as there is in those who actually completed the AS questionnaires. Could the authors please provide some thoughts on why there is such an low percentage of men who have responded and the possibility of bias when looking at AS and omics regarding these men, given that there may be distinct selection bias.

Secondly, could the authors please provide more specific information about the validity of the AS questionnaire and the exact purpose of it’s use in this cohort. I understand that you are planning to look at association with diseases using OMICS data, but my understanding of the AS questionnaire is that it is unidimensional and therefore I wonder how much it is of relevance to apply to specific diseases which are multidimensional. I think some comment on the usefulness of AS is definitely warranted as further reading suggests, e.g. Taylor et al. (2007)¹, that this is not the best measure to use.

One other suggestion is that a figure or two with the questions on the x-axis and the responses in clusters of columns would be a better way of displaying the data quickly and effectively compared to multiple tables.

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Is the rationale for creating the dataset(s) clearly described?
Yes
Are the protocols appropriate and is the work technically sound?
Partly

Are sufficient details of methods and materials provided to allow replication by others?
Partly

Are the datasets clearly presented in a useable and accessible format?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Respiratory and mental health epidemiology.

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 08 April 2019

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Samuel Jurado Cardenas
Faculty of Psychology, National Autonomous University of Mexico, Mexico City, Mexico

This is a well-conceived highly relevant research addressed to advance knowledge between genetic and environmental relations in the development and progression of disease.

The research fills a void in the existing literature showing that behavior and lifestyle related questions are important correlates to the genetic basis of disease. In particular the research informs the overlap number between the participants with “omics” and Anxiety Sensitivity Index (ASI) data.

It makes a meaningful contribution to the field providing data that advance the understanding of the genetic epidemiology of anxiety depression and anxiety sensitivity traits and their link to other health related phenotypes available in the TwinsUK registry.

It is worth to mention that TwinsUK offers facilities and encourages the sharing of data with the scientific community to further scientific research.

Is the rationale for creating the dataset(s) clearly described?
Yes

Are the protocols appropriate and is the work technically sound?
Yes
Are sufficient details of methods and materials provided to allow replication by others?
Yes

Are the datasets clearly presented in a useable and accessible format?
Yes

**Competing Interests:** No competing interests were disclosed.

**Reviewer Expertise:** Health, Psychology, Behavioral Cognitive Therapy

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard.