# Wearables in the UK Biobank


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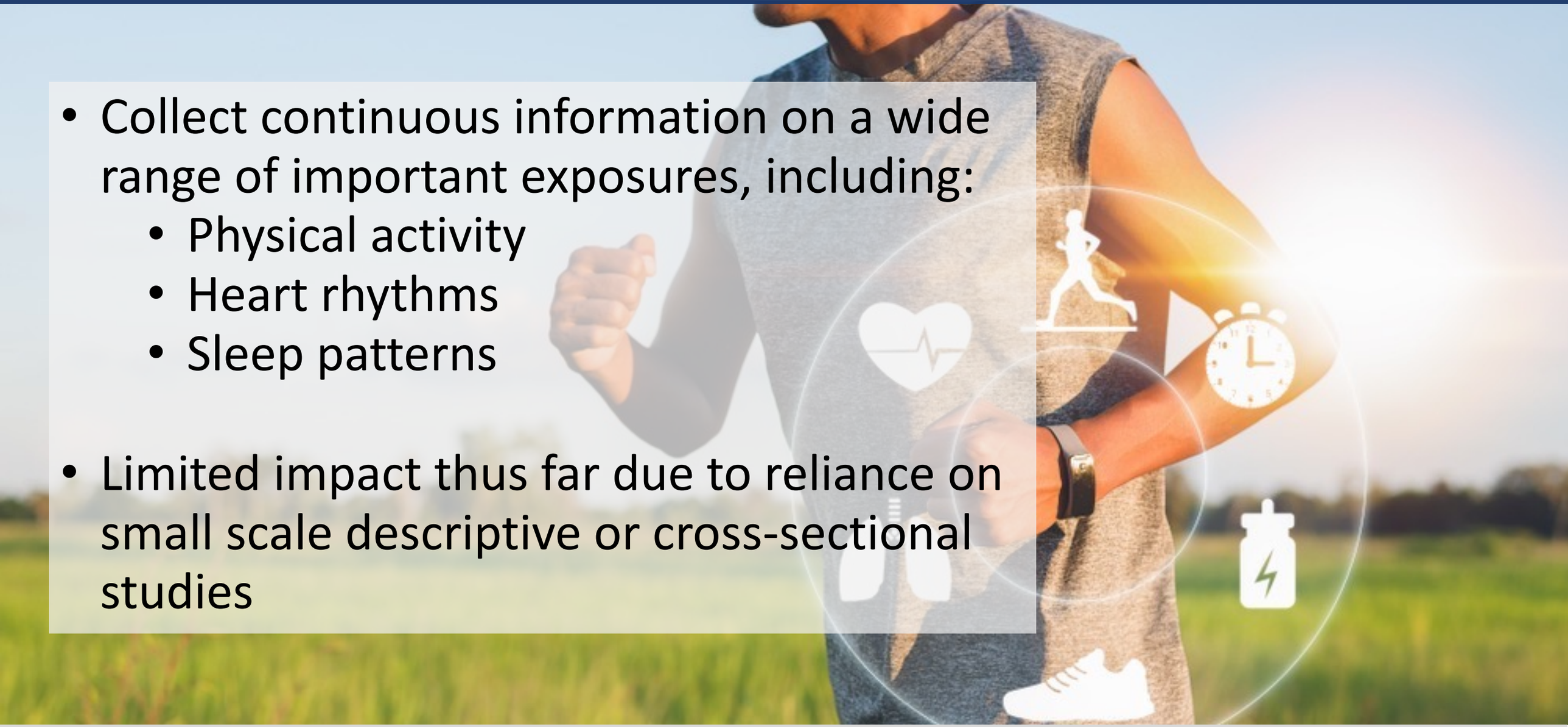
# Wearable sensors in health



- Collect continuous information on a wide range of important exposures, including:
  - Physical activity
  - Heart rhythms
  - Sleep patterns

- Limited impact thus far due to reliance on small scale descriptive or cross-sectional studies

British Heart Foundation Data Science Centre. (2022). Workshop report – How can consumer wearables transform our understanding of cardiovascular disease? https://doi.org/10.5281/zenodo.5827260

# Wearable sensors in health

nature medicine

Article

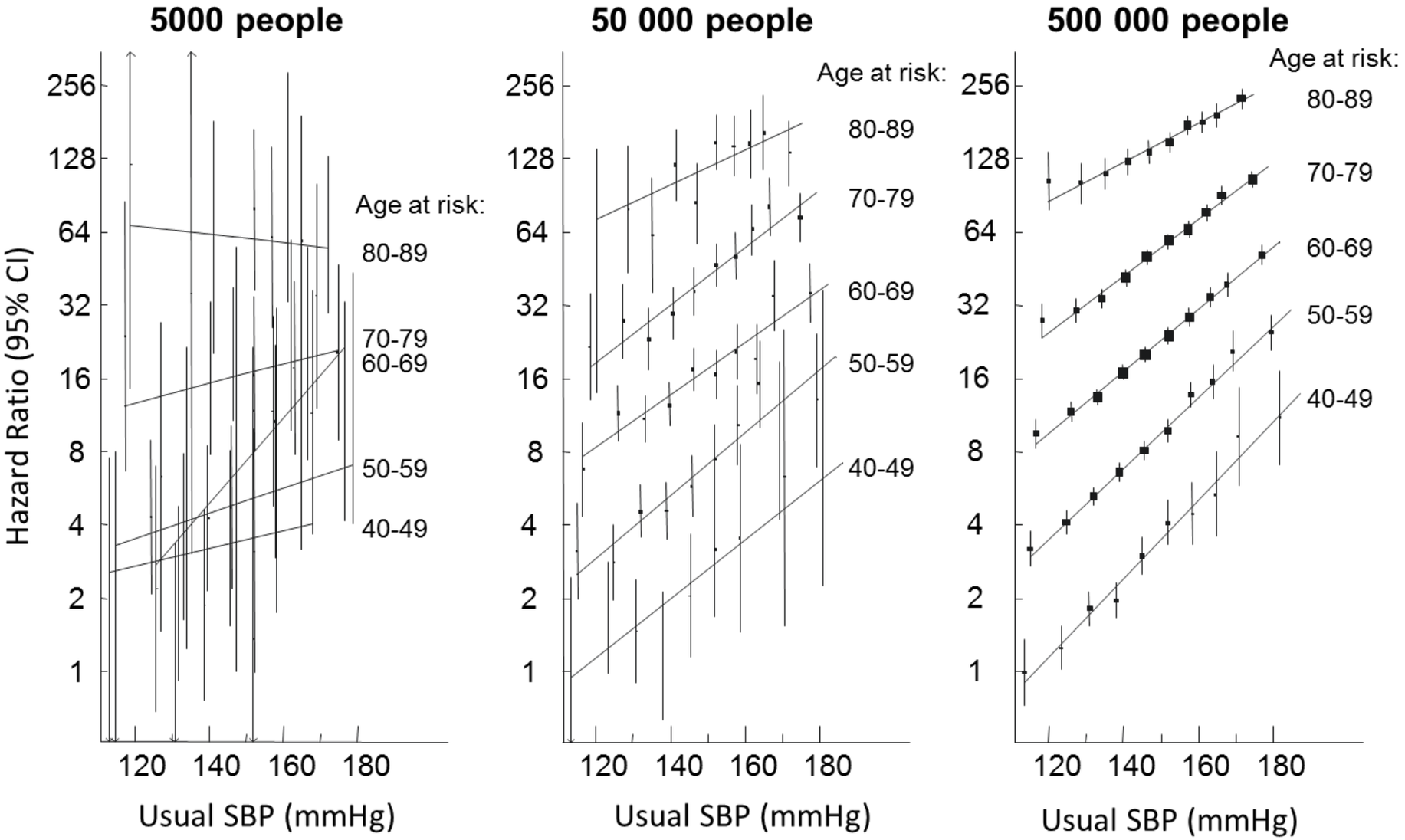
https://doi.org/10.1038/s41591-022-02012-w

## Association of step counts over time with the risk of chronic disease in the *All of Us* Research Program

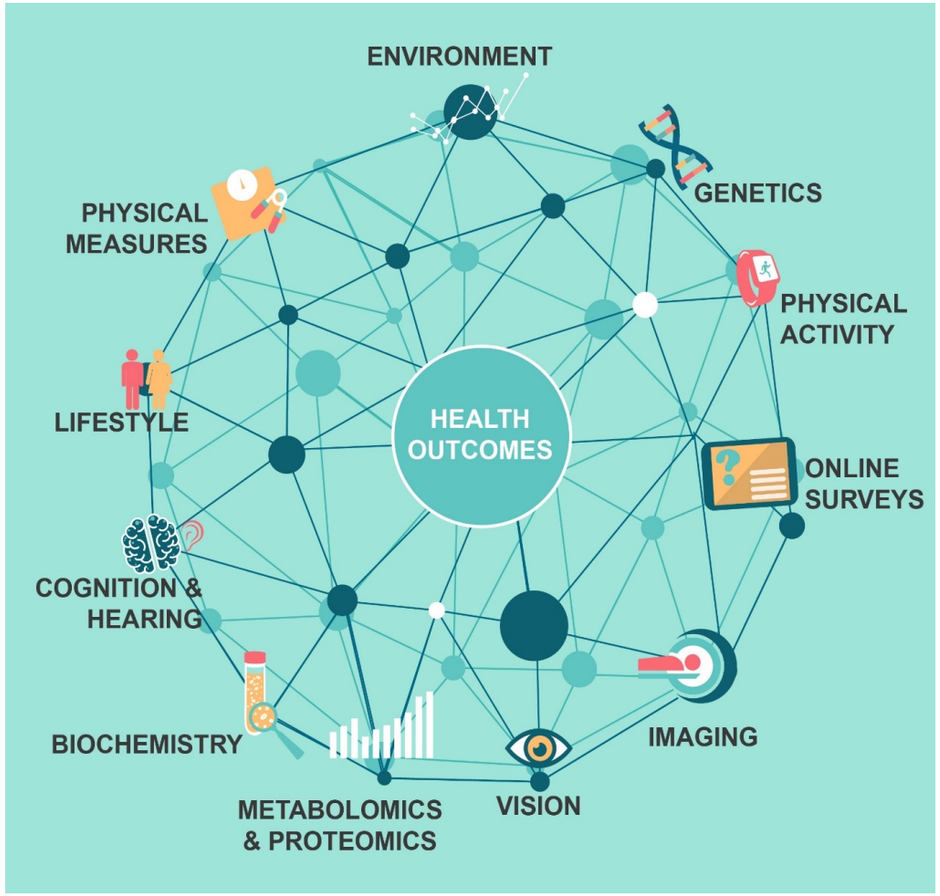
*…Using the electronic health records data from the All of Us Research Program, we show that step count volumes as captured by participants' own Fitbit devices … **6,042 participants** included in the study … walked a median of 7,731.3 (5,866.8–9,826.8) steps per day over the **median activity monitoring period of 4.0 (2.2–5.6) years** with a total of 5.9 million person-days of monitoring.*

Master et al ***Nature Medicine*** 2022;28:2301-2308

# The power of large numbers: Ischaemic heart disease ~ systolic BP



# UK Biobank: combination of 4 dimensions

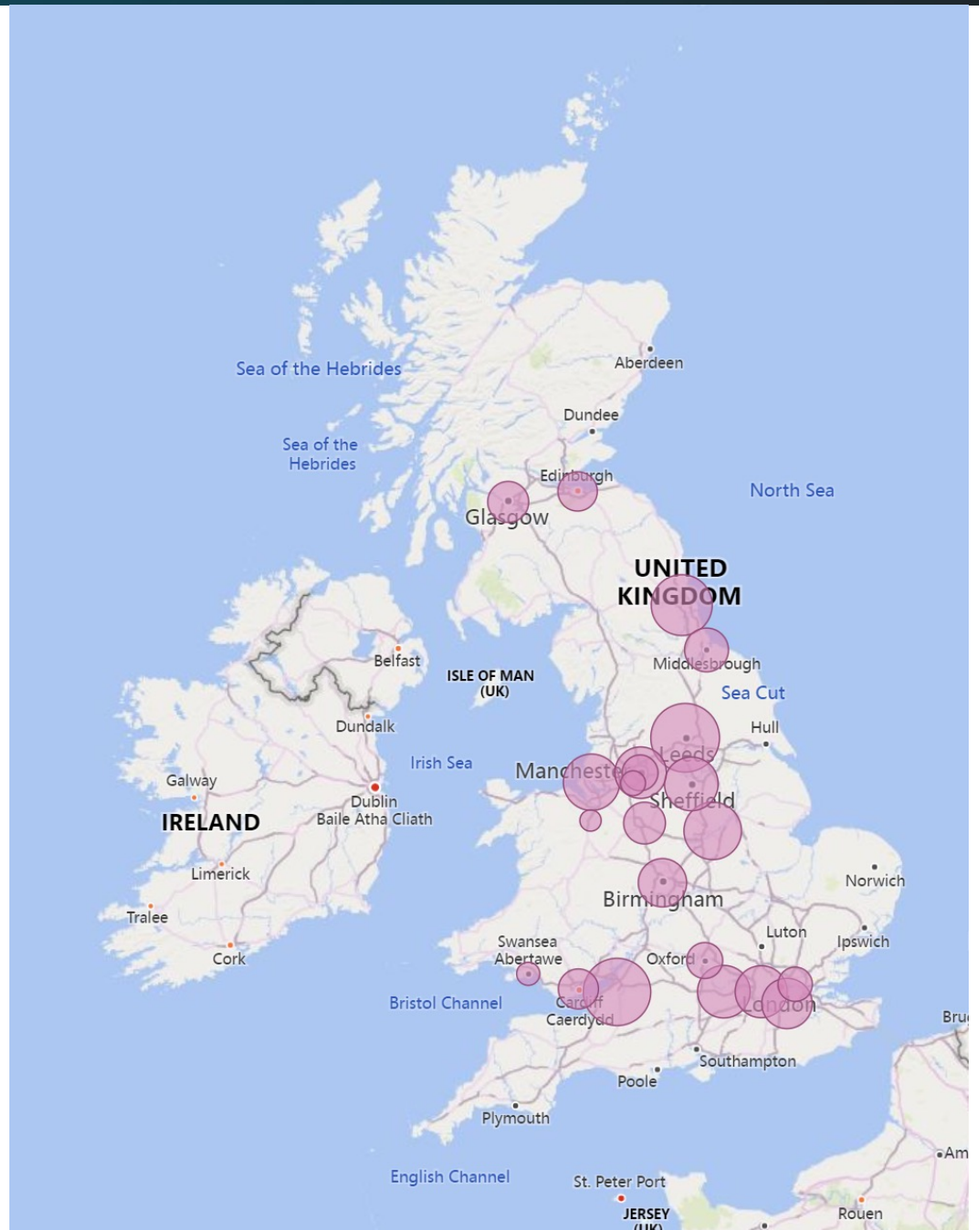



Combination of size with increasing depth x duration x accessibility enabling cutting-edge science

- SIZE: 500,000 diverse individuals
- DEPTH: Genetics with extensive detail about lifestyle, environment and medical history, and other biological assays (biochemistry, genetics, -omics) and imaging
- DURATION: ~15 years of follow-up has already yielded very large numbers of many different health outcomes
- ACCESSIBILTY: Very rapidly increasing number of different types of researcher globally using UK Biobank

# Overview of UK Biobank recruitment

- 500,000 participants
- 2006-2010
- Aged 40-69 years old
- Registered with the NHS
- Living within ~25 miles of 1 of the 22 assessment centres.



# Data collected at UK Biobank Recruitment

| | |
|---|---|
| **Touchscreen questionnaire** | Demographics, lifestyle, environment, medical history, cognitive function, hearing and vision tests etc. |
| **Verbal interview** | Occupation, medical conditions, medications, operations, etc. |
| **Physical measures** | Blood pressure, heart rate, anthropometry, spirometry etc. |
| **Sample collection** | Blood, urine and saliva |

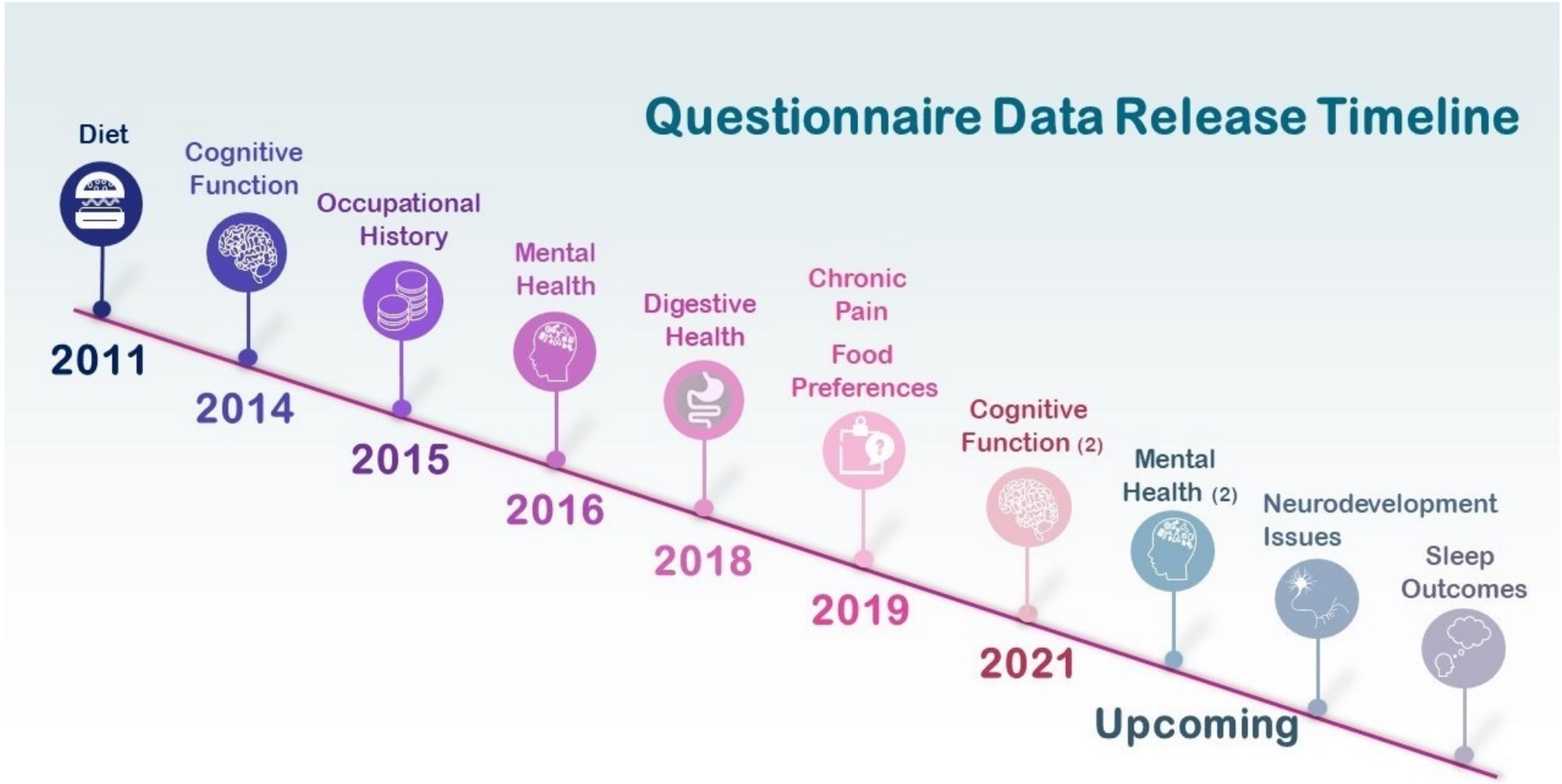
Consent to access medical and other health-related records, and to re-contact participants for further assessments

# UK Biobank baseline characteristics

| Characteristic | Category | Participants, n (%) |
|---|---|---|
| Age | 40-49 yrs | 119,000 (24%) |
| | 50-59 yrs | 168,000 (34%) |
| | 60-69 yrs | 213,000 (42%) |
| Sex | Male | 230,000 (46%) |
| | Female | 270,000 (54%) |
| Ethnicity | White | 473,000 (95%) |
| | Other | 27,000 (5%) |
| Deprivation | More | 92,000 (18%) |
| | Average | 166,000 (33%) |
| | Less | 241,000 (46%) |
| Total | | 500,000 |

Wide range of backgrounds represented

# Enhancements: Web-based questionnaires




Among 330,000 participants for whom we have an email address.

Enhanced information on selected exposures and outcomes that was not feasible to collect at baseline.

# Enhancements: Resurvey and imaging

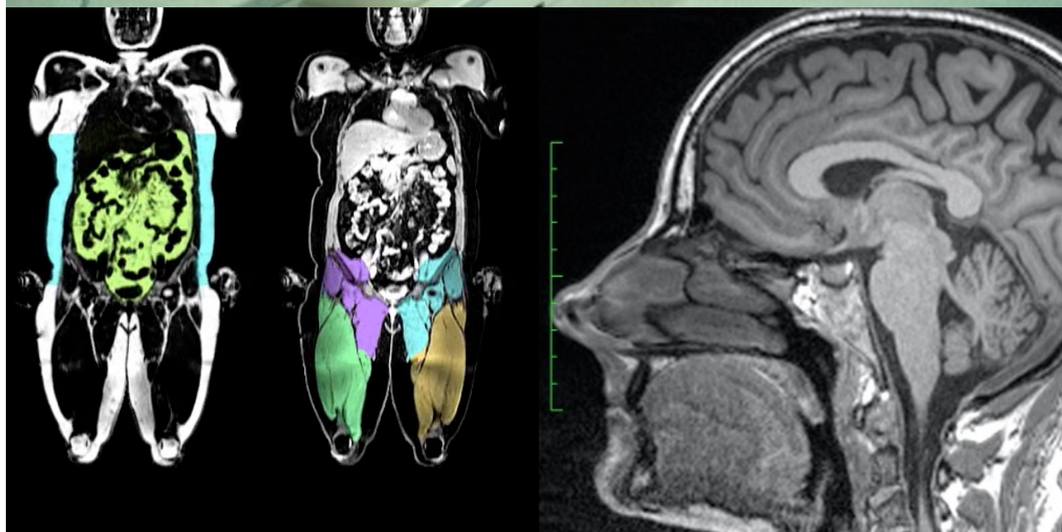
**Repeat assessment** in 20,000 participants (2012-13)

**Multi-modal imaging** (60,000 of 100,000 ppts; 2014-)

- MRI (heart, brain, abdomen)
- Full-body DEXA
- Carotid ultrasound
- 12-lead ECG

**Repeat imaging underway** (target of 60,000 ppts; 2019-)

Imaging visit includes repeat assessment of baseline survey



# Enhancements: Samples into data

## Genetics

### Genome-wide genotyping

- 850k variants directly measured; >90M variants imputed
- Full cohort made available 2017

### Whole Exome Sequencing

- Full cohort made available 2022

### Whole Genome Sequencing

- First 200,000 made available Q4 2021
- Full cohort to be made available 2023

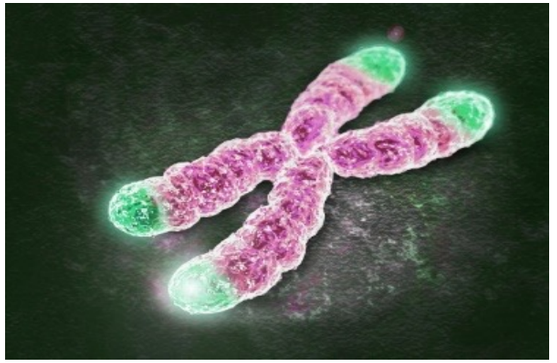
# Enhancements: Samples into data

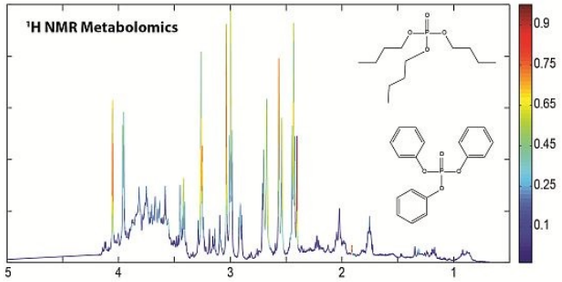
**Biochemical measures in all 500,000**
- 34 biomarkers in plasma, serum, red blood cells, and urine samples

**Telomere length in all 500,000**

**NMR-metabolomics in 120,000**
- Data released for first 120,000 in 2021
- Full cohort to be made available 2023

**Proteomics in ~60,000 (initially)**
- Pharma consortium
- ~3000 plasma proteins using Olink's assay
- First tranche of data available 2023

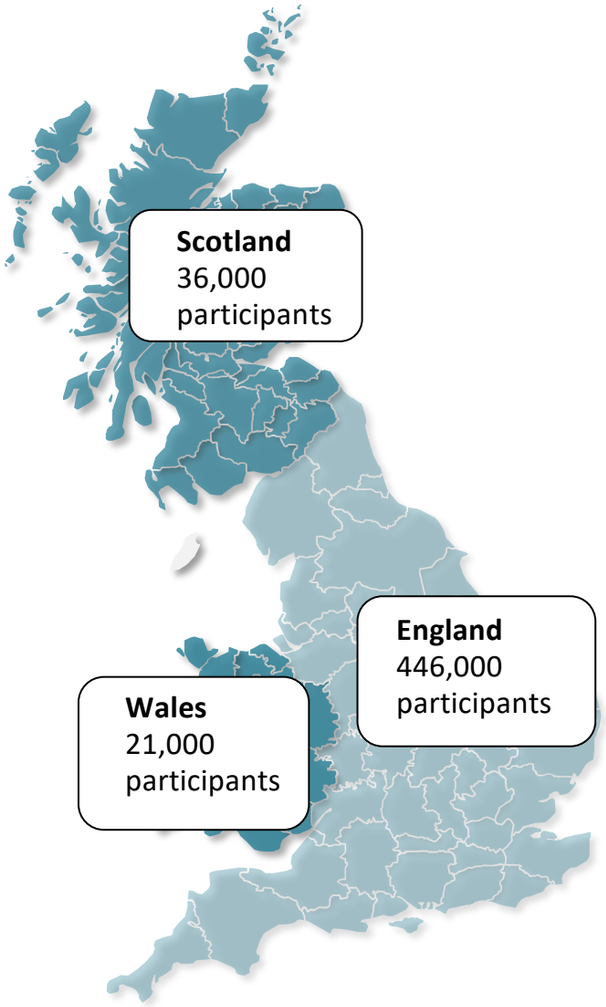





# Follow-up of health outcomes

Regularly updated information on a wide range of diseases from NHS datasets in all 3 countries:

- **Deaths**
- **Cancers**
- **Hospitalisations**
- **Primary care** (~45% of participants)
- **SARS-CoV-2 antigen tests**



# Cumulative number of incident cases over time

| Condition | Year of diagnosis | | |
|---|---|---|---|
| | Observed | Predicted | |
| | 2020 | 2027 | 2032 |
| Diabetes | 31,000 | 54,000 | 70,000 |
| Myocardial infarction | 15,000 | 30,000 | 46,000 |
| Stroke | 12,000 | 25,000 | 37,000 |
| COPD | 25,000 | 47,000 | 65,000 |
| Depression | 25,000 | 39,000 | 47,000 |
| Breast cancer | 9,000 | 14,000 | 18,000 |
| Colorectal cancer | 5,000 | 8,000 | 11,000 |
| Lung cancer | 4,000 | 6,000 | 8,000 |
| Prostate cancer | 10,000 | 16,000 | 20,000 |
| Hip fracture | 5,000 | 13,000 | 22,000 |
| Rheumatoid arthritis | 4,000 | 6,000 | 8,000 |
| Parkinson’s disease | 4,000 | 10,000 | 14,000 |
| Alzheimer’s disease | 5,000 | 17,000 | 37,000 |

# Mortality rates 50% lower compared to general population

# Principles of accessing UK Biobank data

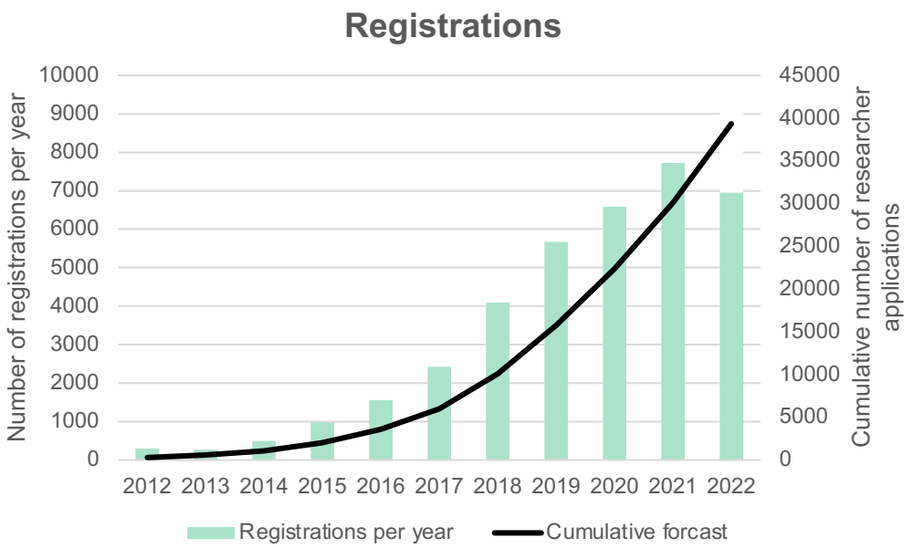
- **Open access resource**, available for bona fide researchers to conduct health-related research that is in the public interest

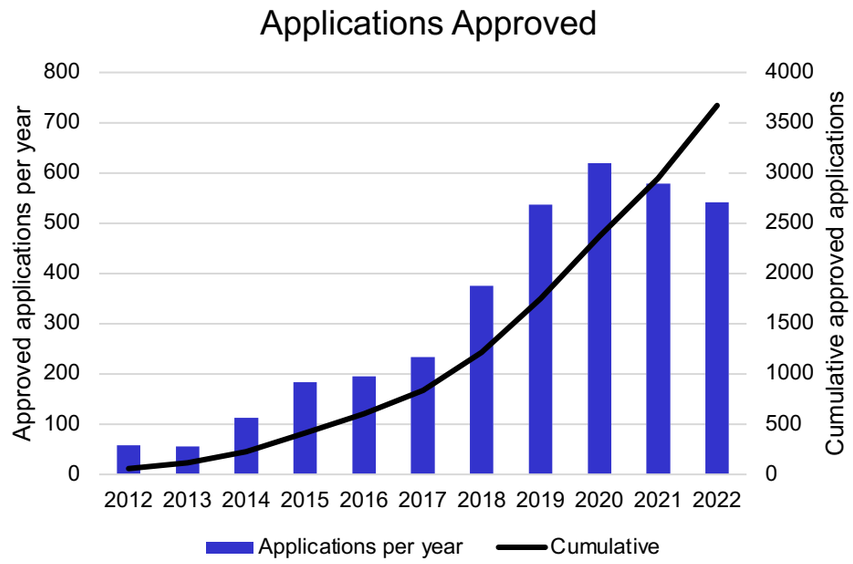
- Available for use by academia and commercial companies, both in the UK and overseas

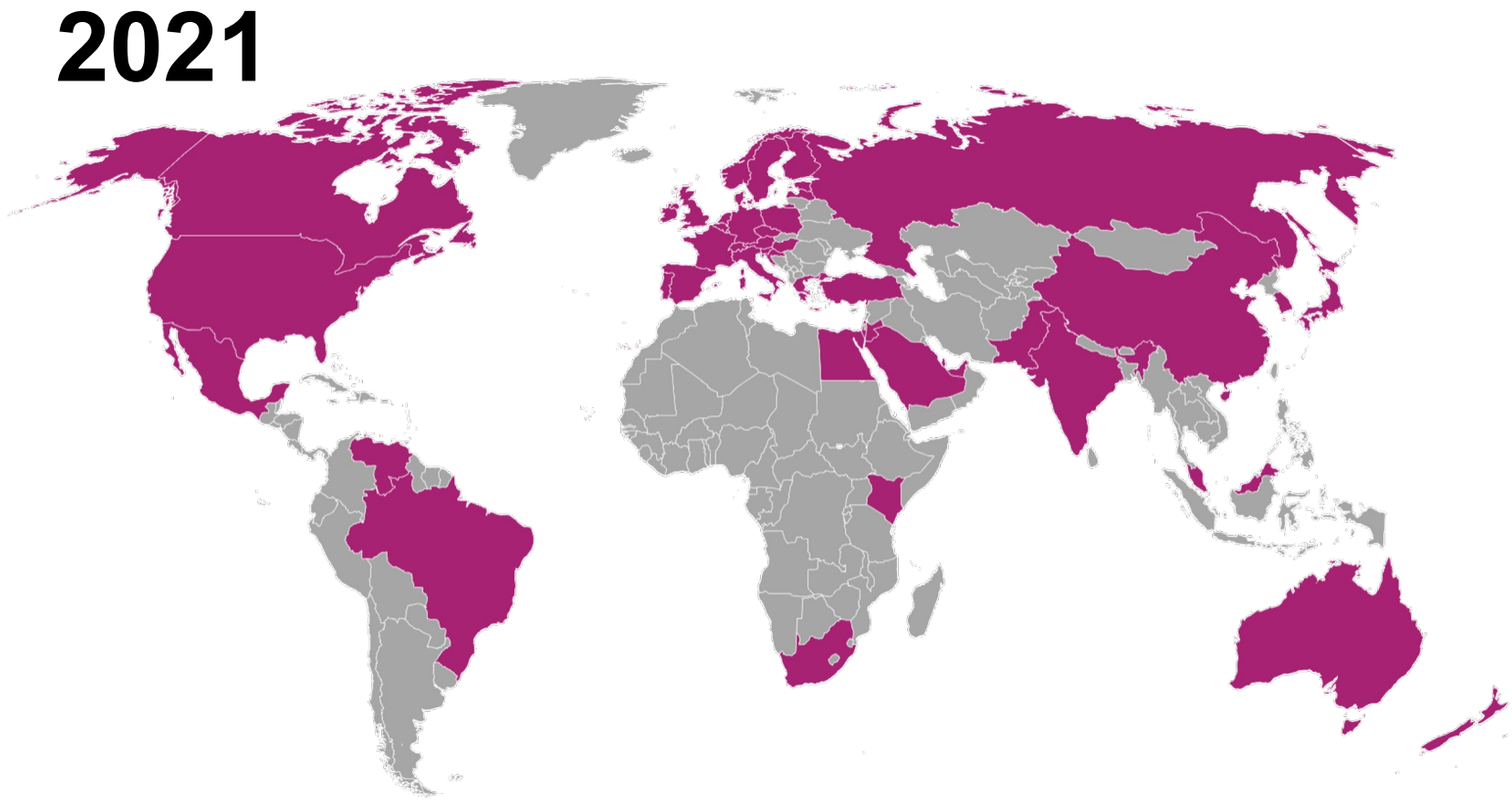
- **No preferential or exclusive access to the resource** (*and limited exclusive access for data generated by researchers*)

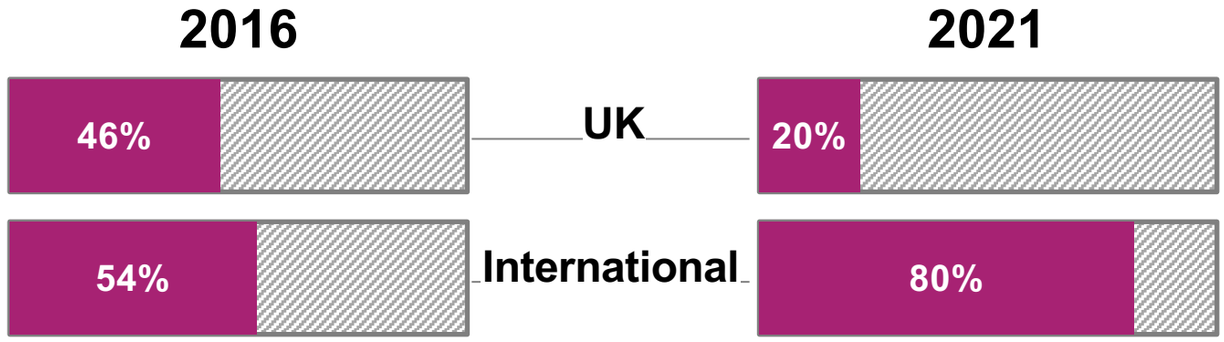
- Researchers are obliged to return their results to UK Biobank so they can be shared with others

# Who is using the resource?



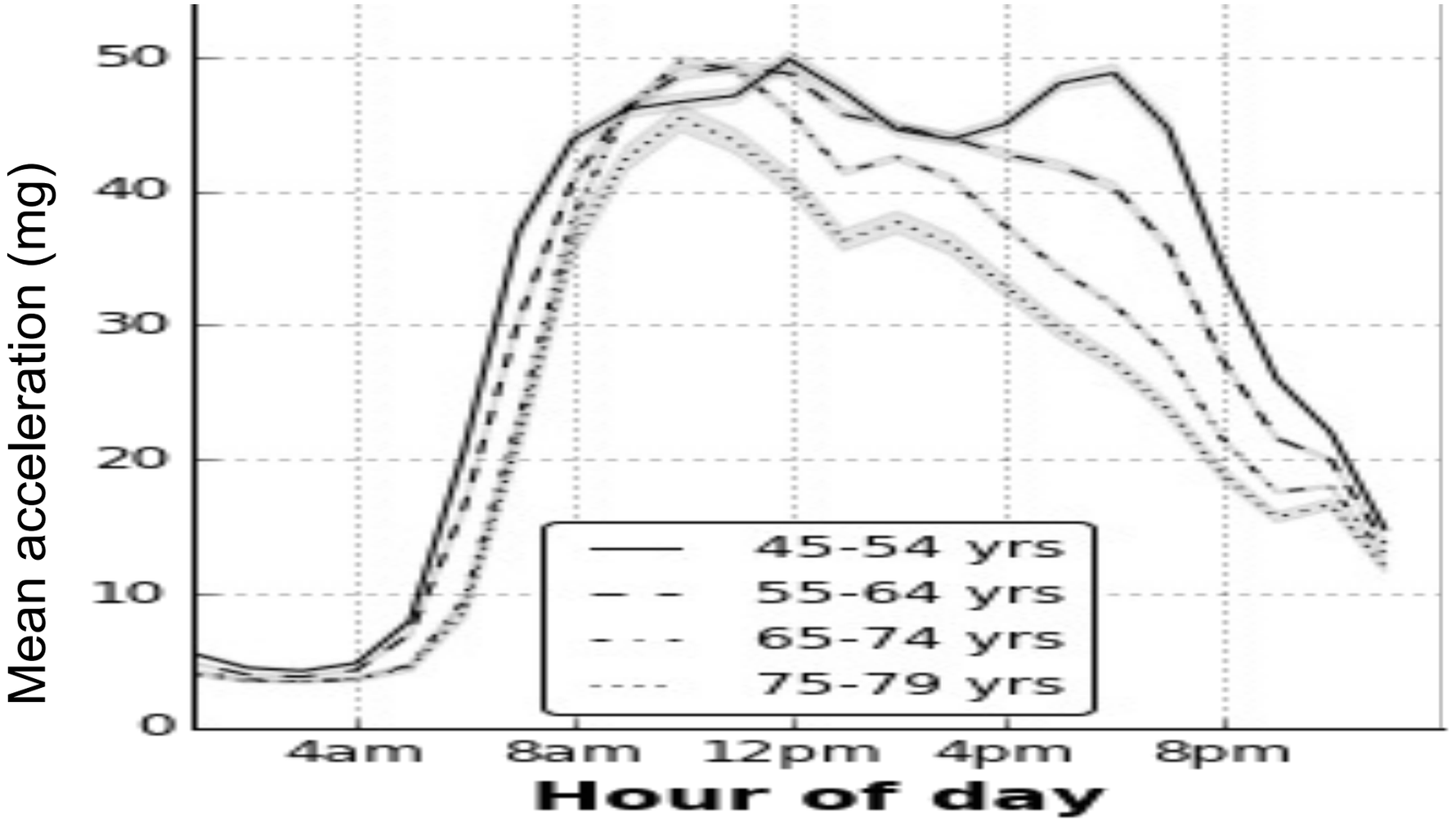
# 7 day wrist-worn accelerometer data collection in UK Biobank

**2013 – 2015**

**n = 103,712**

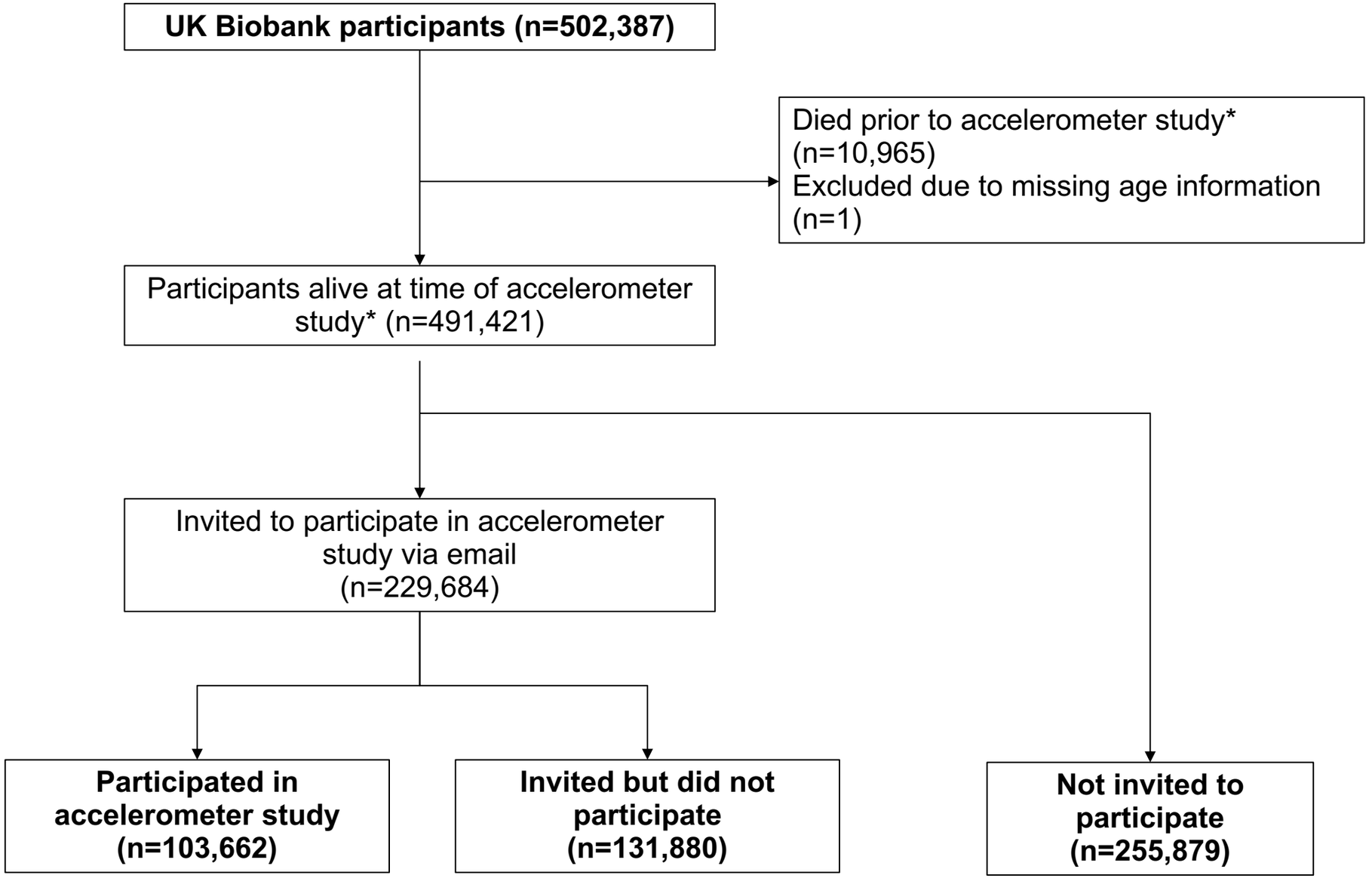
Consent = 47%

Adherence = 93%



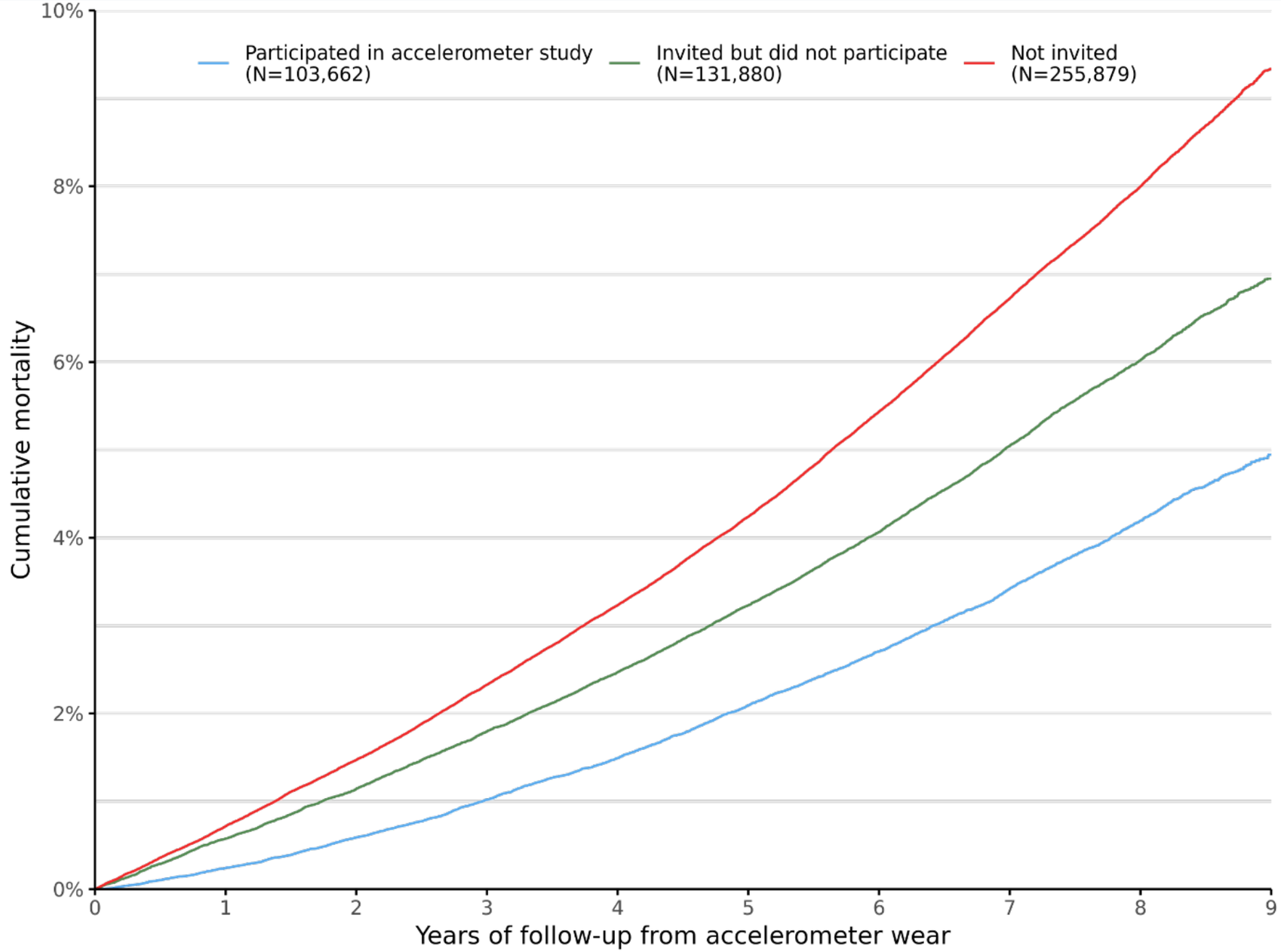

Doherty et al. ***PLoS One*** 12, (2017). 12(2):e0169649

# Who agrees to wear a device in UK Biobank?




Harper et al (in preparation)

# Survivorship by who agrees to wear a device in UK Biobank



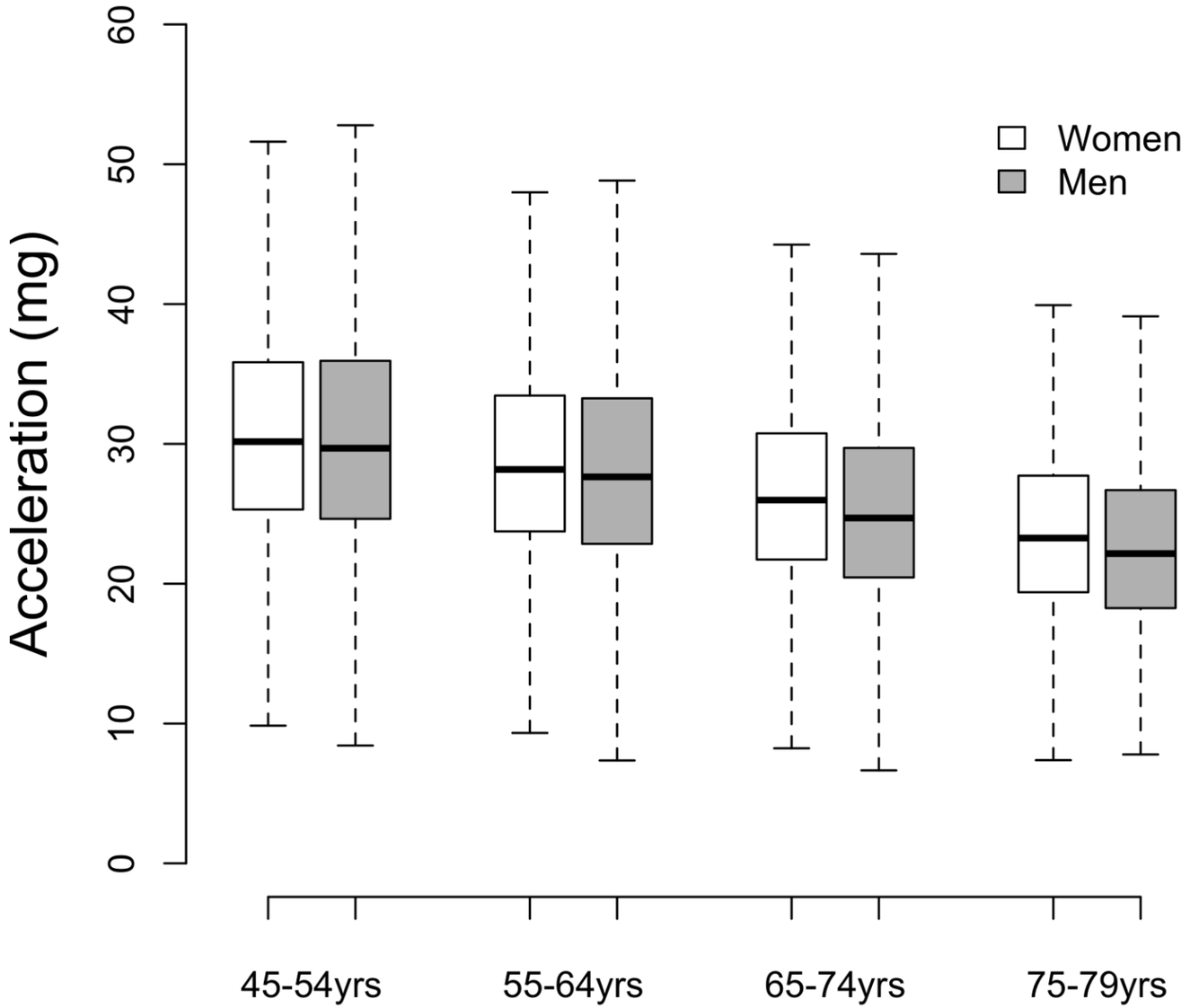

Decliner

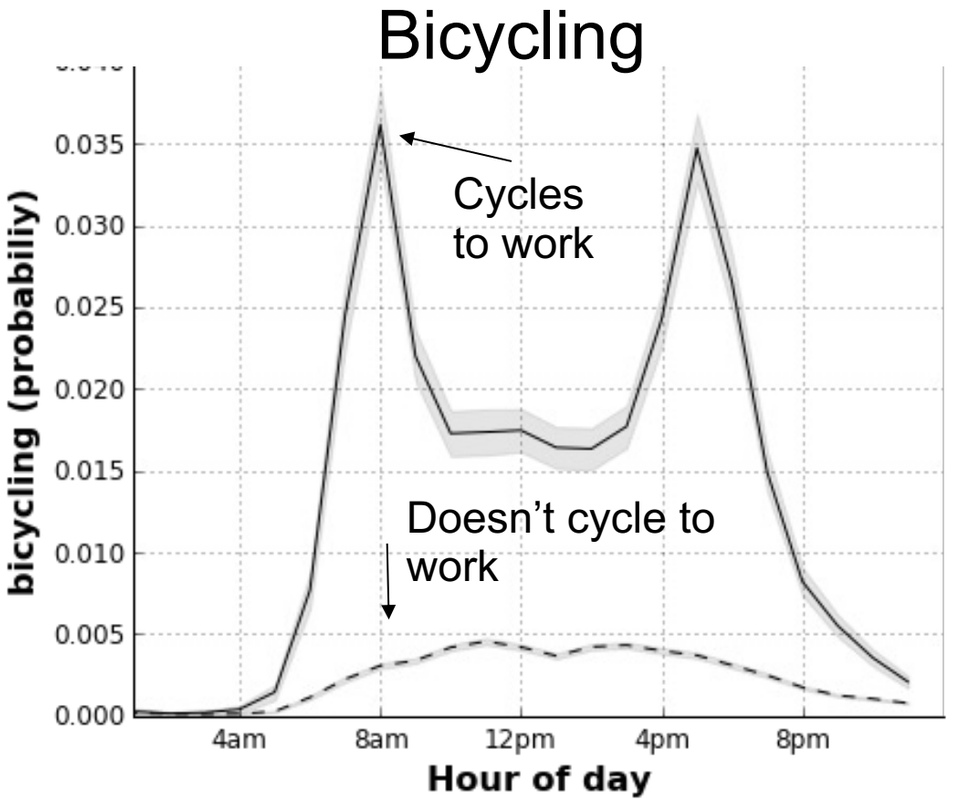
Responder

**For participants not in the accelerometer study cohort, a hypothetical study date was generated (based on the distribution of existing dates) using bootstrap sampling with replacement.*

Harper et al (in preparation)

# Does the accelerometer data in UK Biobank look believable?

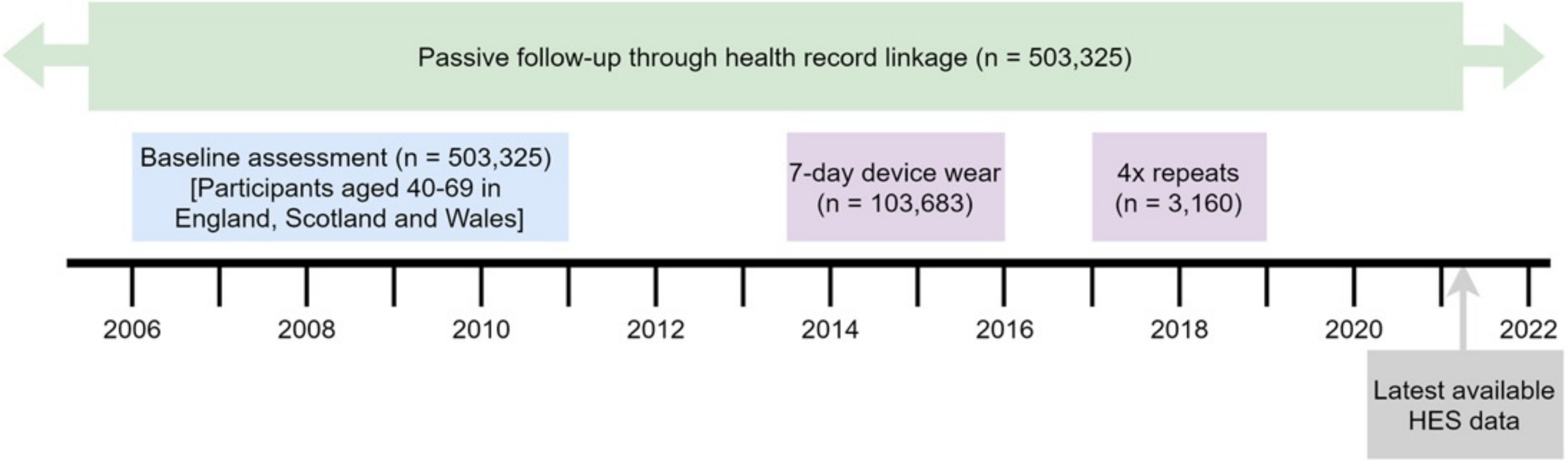



Doherty et al. ***PLoS One*** 12, (2017). 12(2):e0169649

Willetts et al **Scientific Reports 2018**

# Test – retest reliability - Is a seven-day measurement sufficient?




Within person measurement error lambda ≈ 0.70

Ramakrishnan et al ***PLOS Medicine*** 2021
Brage, Strain, Walmsley, Wijndaele, Bennett et al ***(in preparation)***

# Cross-sectional differences in activity by prior disease?

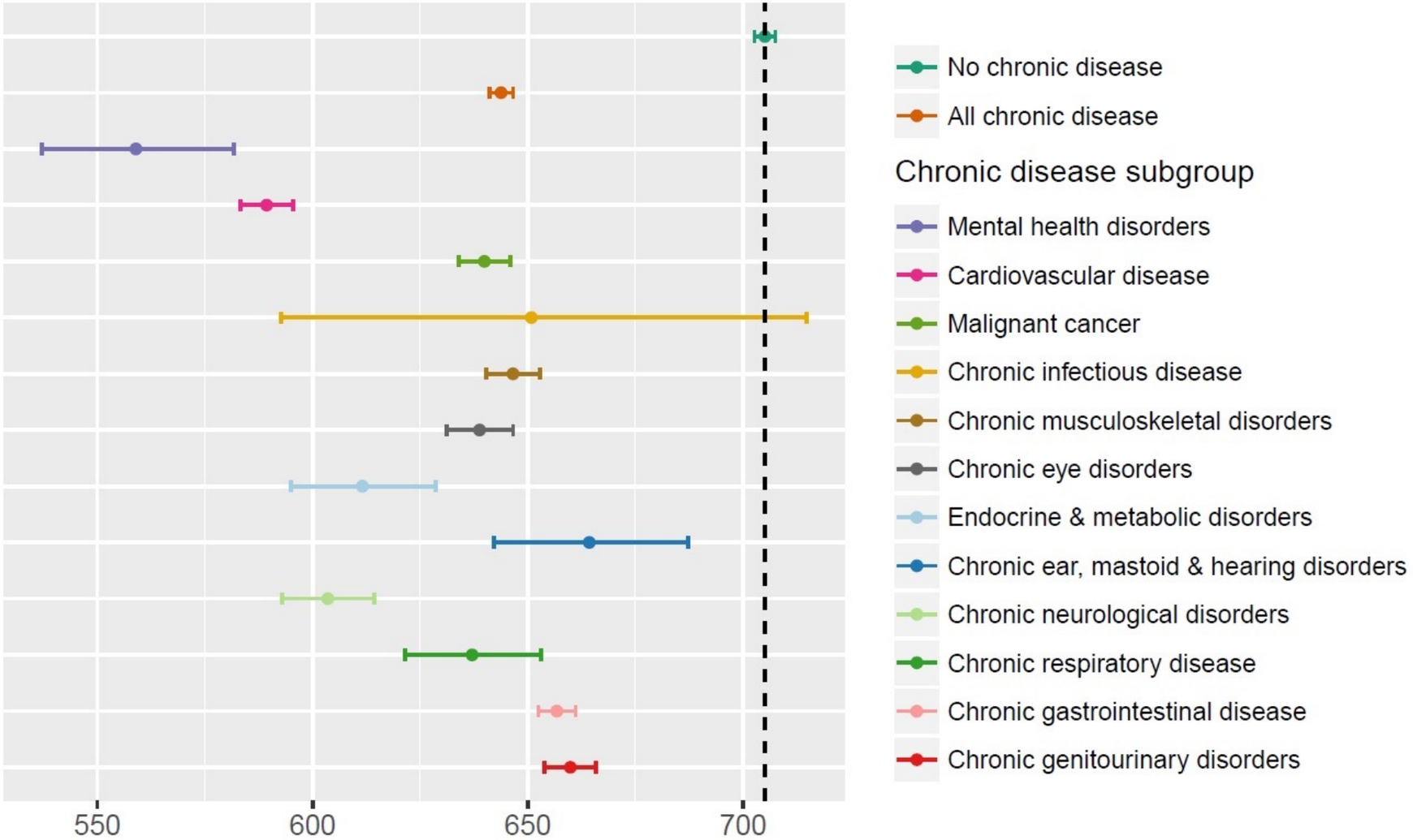
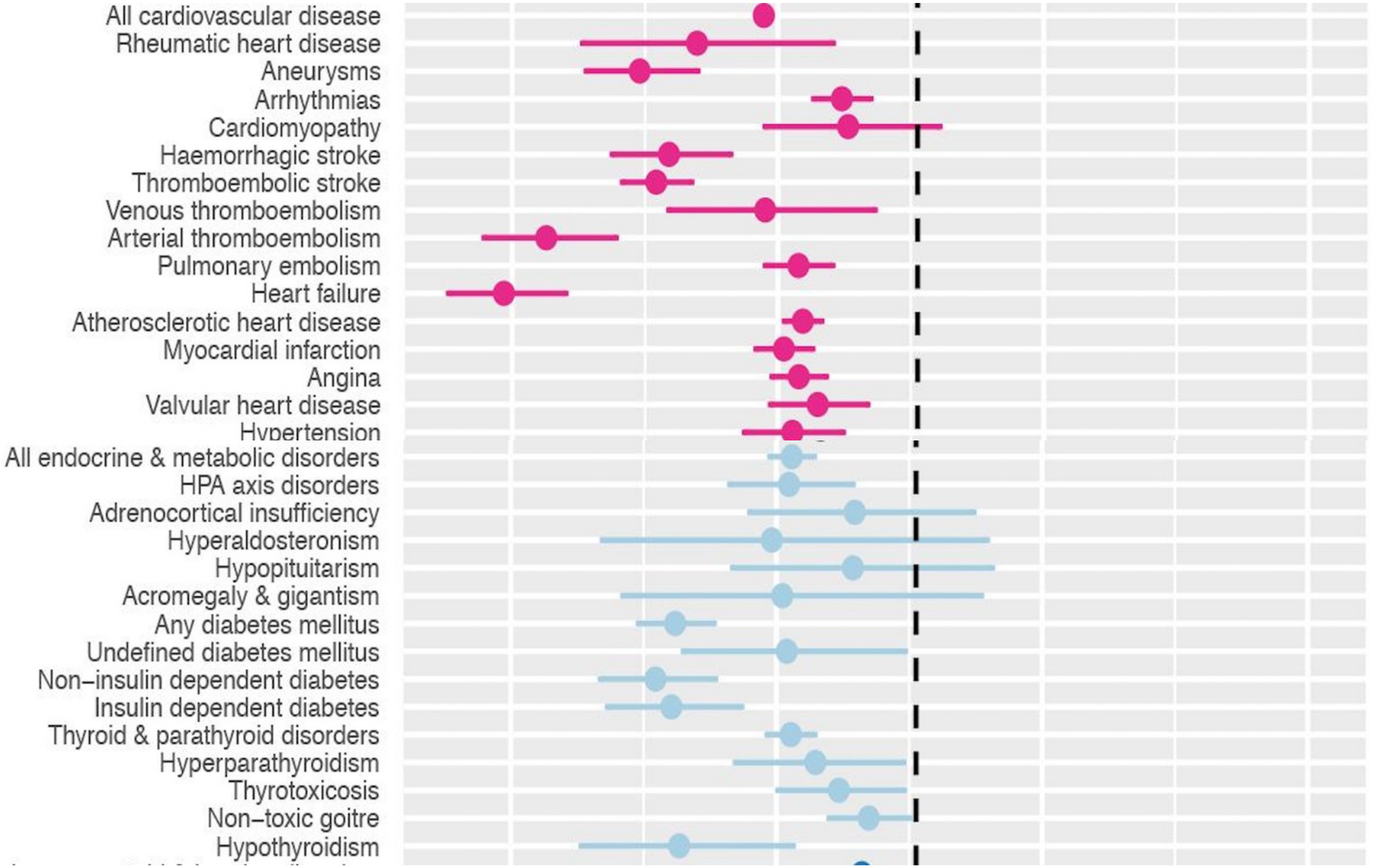



Figure 1. Geometric mean moderate activity in minutes per week for participants with and without chronic diseases

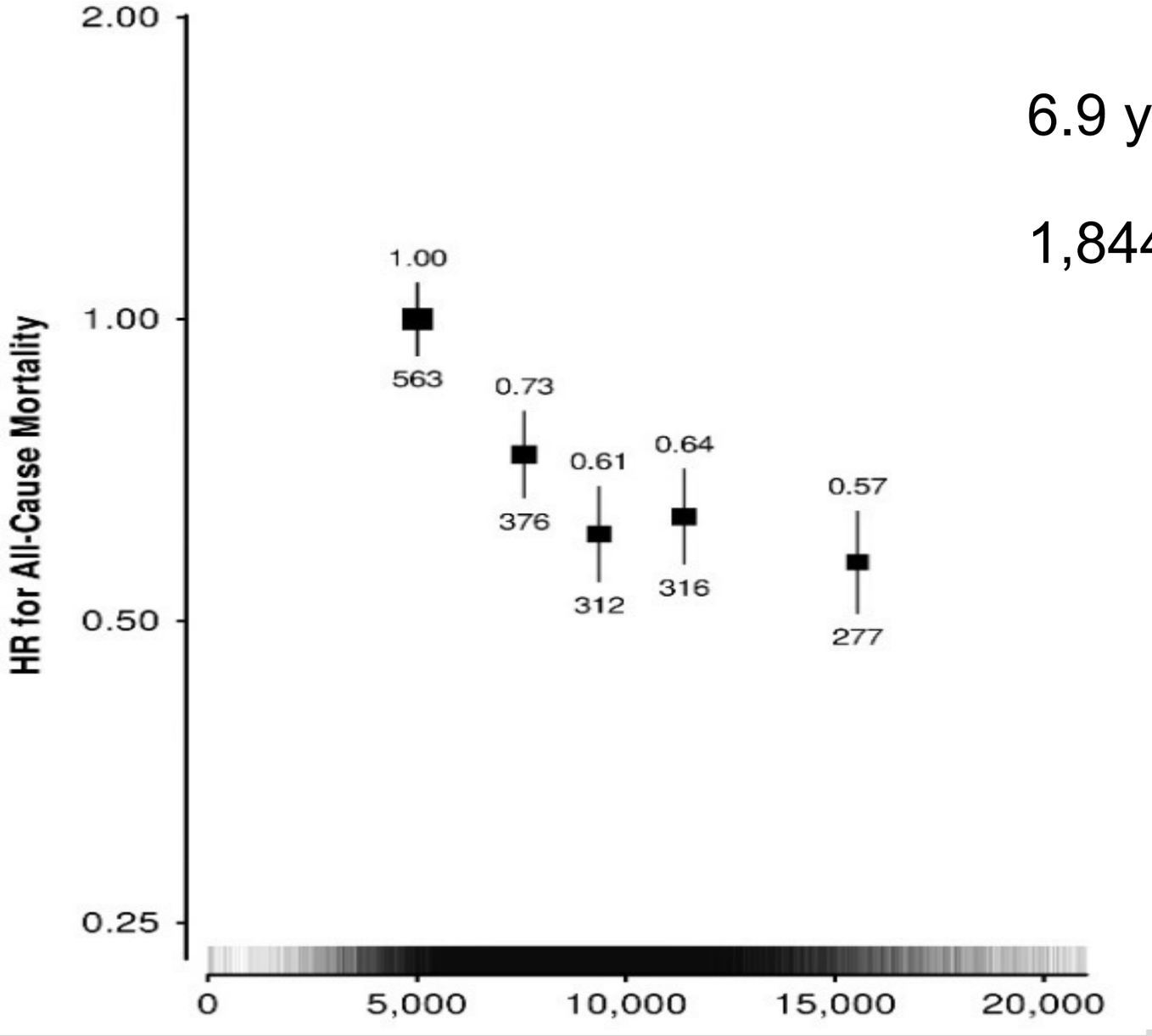
Barker, Smith-Byrne, Doherty, et al (2019***). Intl J Epidemiology*** (https://doi.org/10.1093/ije/dyy294)

# Cross-sectional differences in activity by prior disease?




Barker, Smith-Byrne, Doherty, et al (2019***). Intl J Epidemiology*** (https://doi.org/10.1093/ije/dyy294)

# Steps & all-cause mortality




6.9 years follow-up

1,844 mortality events

Using age as a timescale

Adjusted for:

- sex
- ethnicity
- education
- area deprivation
- alcohol intake
- smoking status
- Processed meat
- Fresh fruit
- Oily fish
- Added salt

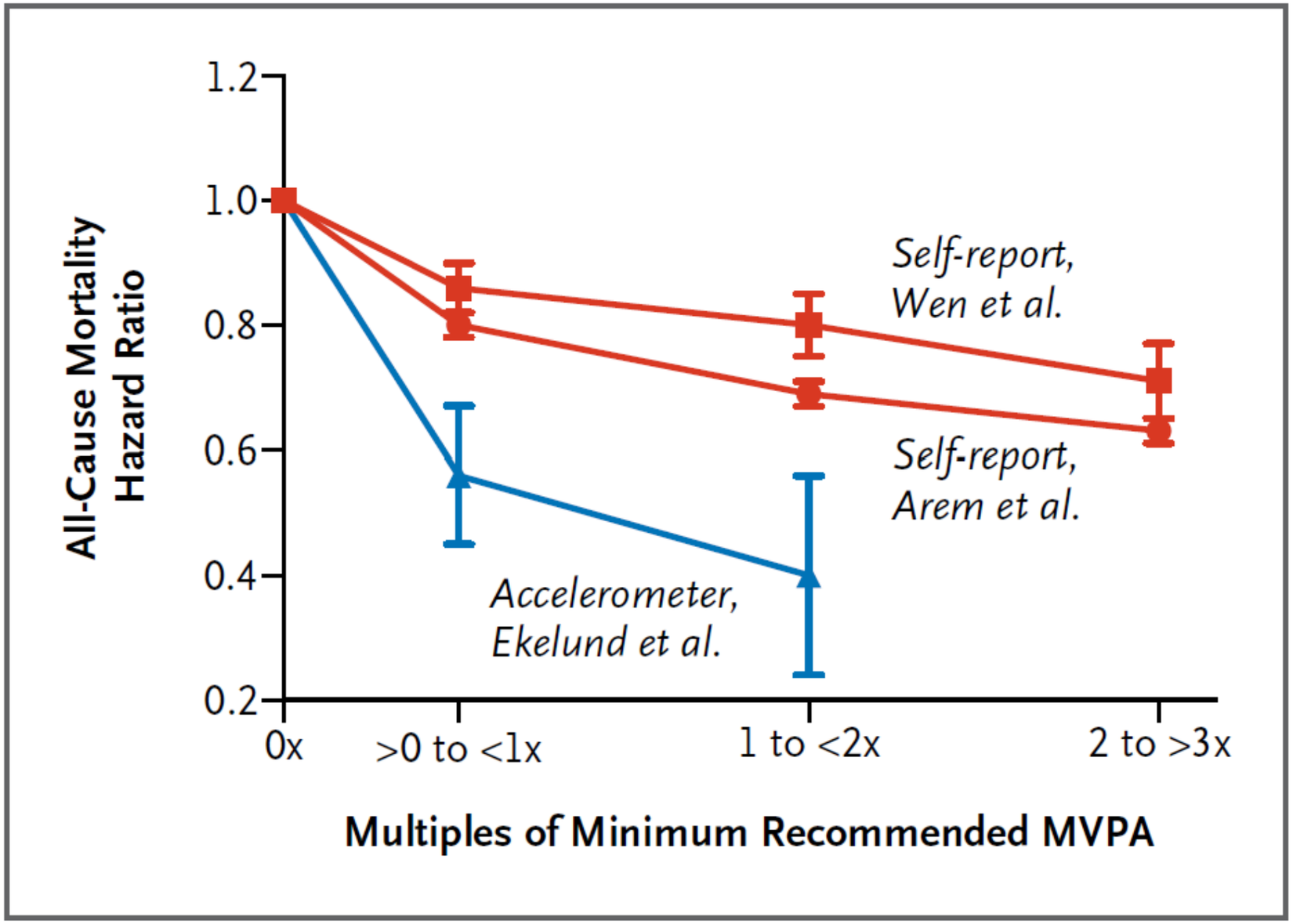
Small et al. ***medRxiv*** 2023.02.20.23285750

# Sequential adjustment (top vs bottom fourth) – activity & CVD

| | |
|---|---|
| + Age | 0.55 (0.50, 0.61) |
| + Sex | 0.58 (0.52, 0.64) |
| + Education | 0.58 (0.52, 0.64) |
| + Townsend Deprivation Index | 0.58 (0.53, 0.64) |
| + Ethnicity | 0.58 (0.53, 0.64) |
| + Smoking | 0.59 (0.53, 0.65) |
| + Alcohol consumption | 0.60 (0.54, 0.66) |
| + Hypertension | 0.60 (0.54, 0.67) |
| + Self rated health | 0.66 (0.60, 0.73) |
| + Body Mass Index | 0.71 (0.64, 0.79) |
| + Total cholesterol | 0.71 (0.63, 0.79) |
| + HDL cholesterol | 0.73 (0.65, 0.82) |
| + LDL cholesterol | 0.73 (0.65, 0.82) |
| + Triglycerides | 0.73 (0.65, 0.82) |
| + C-reactive protein | 0.74 (0.66, 0.83) |
| + HbA1c | 0.74 (0.66, 0.83) |
| + Red and processed meat intake | 0.74 (0.66, 0.83) |
| + Fresh fruit intake | 0.74 (0.66, 0.84) |

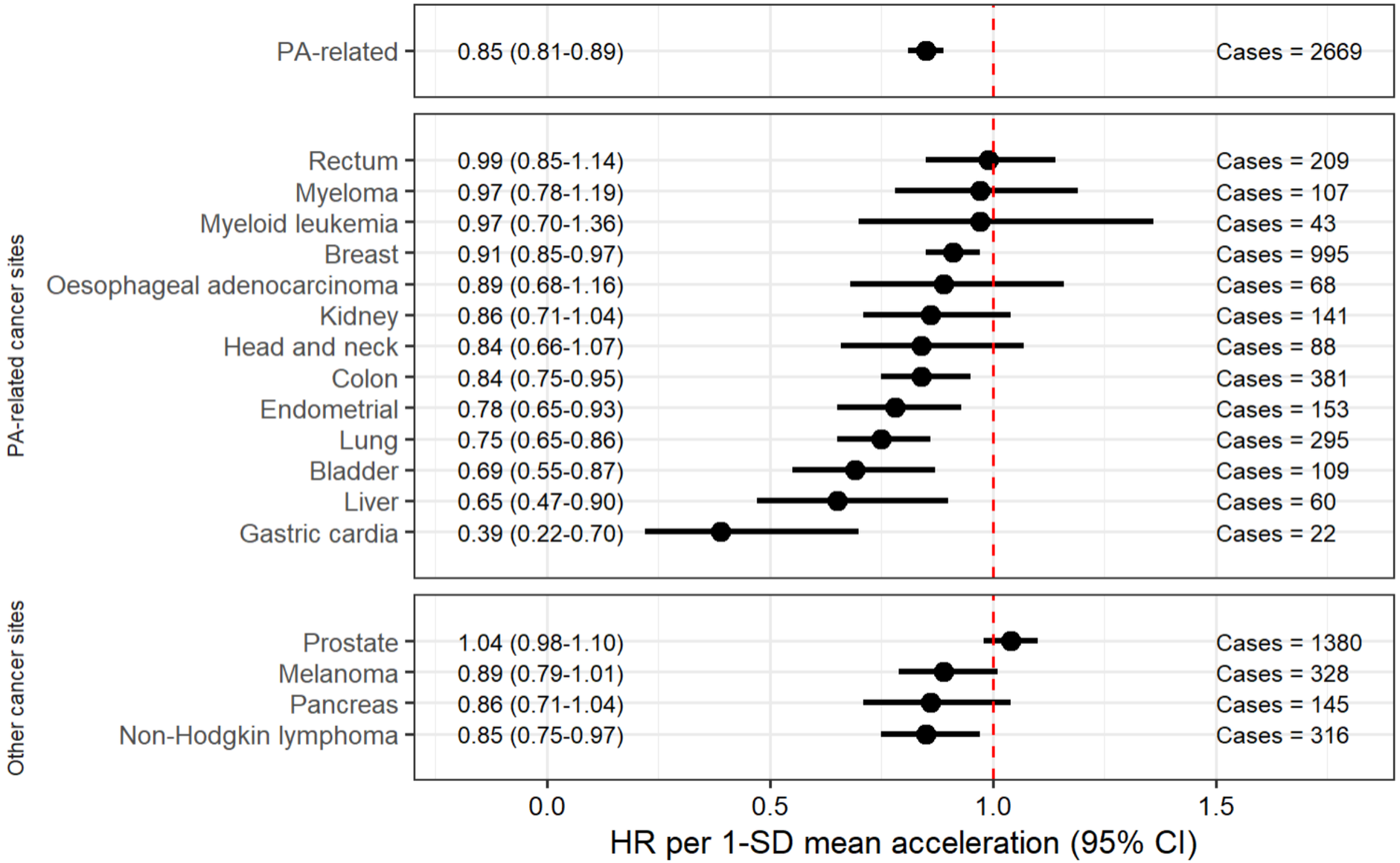
Ramakrishnan et al ***PLOS Medicine*** 2021

# Associations with all-cause mortality - device vs. self-report




Wasfy & Lee, ***NEJM*** 2022

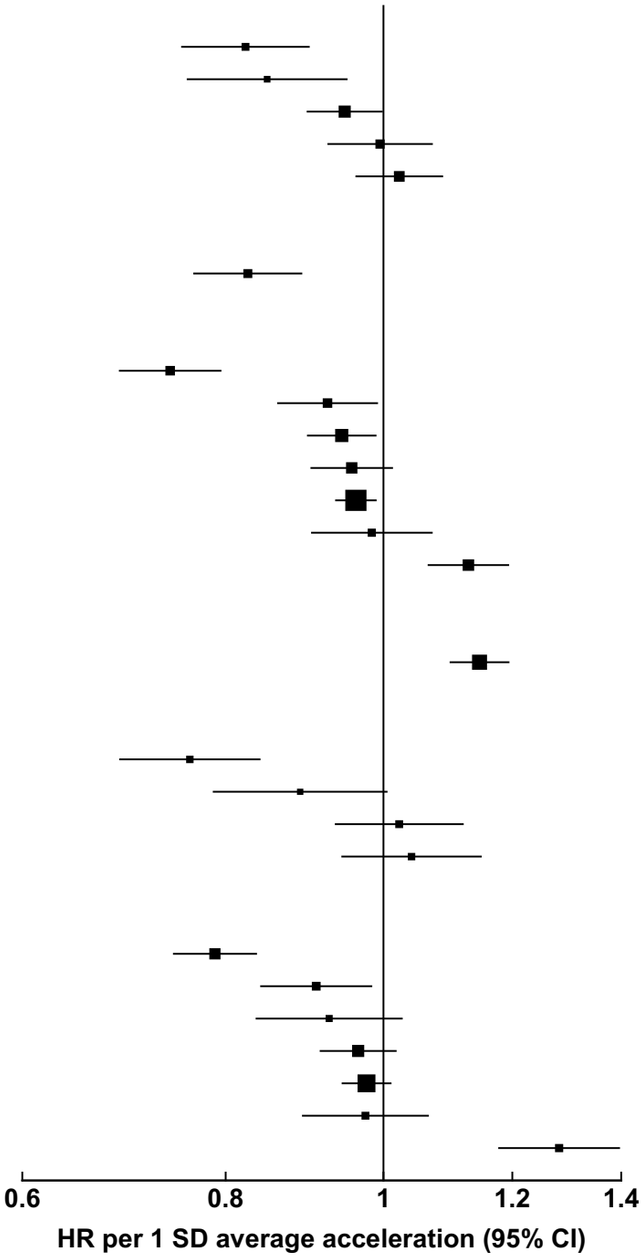
# Associations with incident cancer outcomes




Shreeves (in preparation)

# Associations with common non-cancer outcomes

| Condition | Cases | HR per 1 SD (95% CI) | Ptrend |
|---|---|---|---|
| **Circulatory disease** | | | |
| Venous thromboembolism | 673 | 0.82 (0.75, 0.90) | **<0.0001** |
| Ischemic stroke | 426 | 0.85 (0.76, 0.95) | **0.004** |
| Ischemic heart disease | 1742 | 0.95 (0.90, 1.00) | 0.04 |
| Atrial fibrilliation and flutter | 898 | 1.00 (0.92, 1.07) | 0.90 |
| Hemorrhoids | 1151 | 1.02 (0.96, 1.09) | 0.47 |
| **Respiratory disease** | | | |
| Pneumonia | 941 | 0.83 (0.77, 0.89) | **<0.0001** |
| **Digestive disease** | | | |
| Gallbladder disease | 1108 | 0.74 (0.69, 0.79) | **<0.0001** |
| Gastro-esophageal reflux disease | 969 | 0.92 (0.86, 0.99) | 0.03 |
| Diverticular disease | 2096 | 0.94 (0.90, 0.99) | **0.02** |
| Gastritis and duodentis | 1438 | 0.96 (0.90, 1.01) | 0.12 |
| Colon polyps | 5850 | 0.96 (0.94, 0.99) | **0.007** |
| Non-infective enteritis and colitis | 640 | 0.98 (0.90, 1.07) | 0.70 |
| Inguinal hernia | 1263 | 1.13 (1.07, 1.19) | **<0.0001** |
| **Joint disorder** | | | |
| Osteoarthritis | 2702 | 1.15 (1.10, 1.19) | **<0.0001** |
| **Genitourinary disease** | | | |
| Urinary tract infection | 585 | 0.76 (0.69, 0.84) | **<0.0001** |
| Kidney stones | 309 | 0.89 (0.79, 1.00) | 0.06 |
| Enlarged prostate | 542 | 1.02 (0.93, 1.12) | 0.63 |
| Female genital prolapse | 505 | 1.04 (0.94, 1.15) | 0.43 |
| **Other diseases** | | | |
| Diabetes | 1678 | 0.79 (0.74, 0.84) | **<0.0001** |
| Iron deficiency anemia | 804 | 0.91 (0.84, 0.98) | **0.02** |
| Cellulitis | 470 | 0.93 (0.84, 1.03) | 0.14 |
| Non melanoma skin cancer | 1734 | 0.96 (0.92, 1.02) | 0.19 |
| Cataracts | 4525 | 0.98 (0.94, 1.01) | 0.17 |
| Benign neoplasms of the uterus | 572 | 0.97 (0.89, 1.07) | 0.57 |
| Carpal tunnel syndrome | 576 | 1.28 (1.18, 1.40) | **<0.0001** |

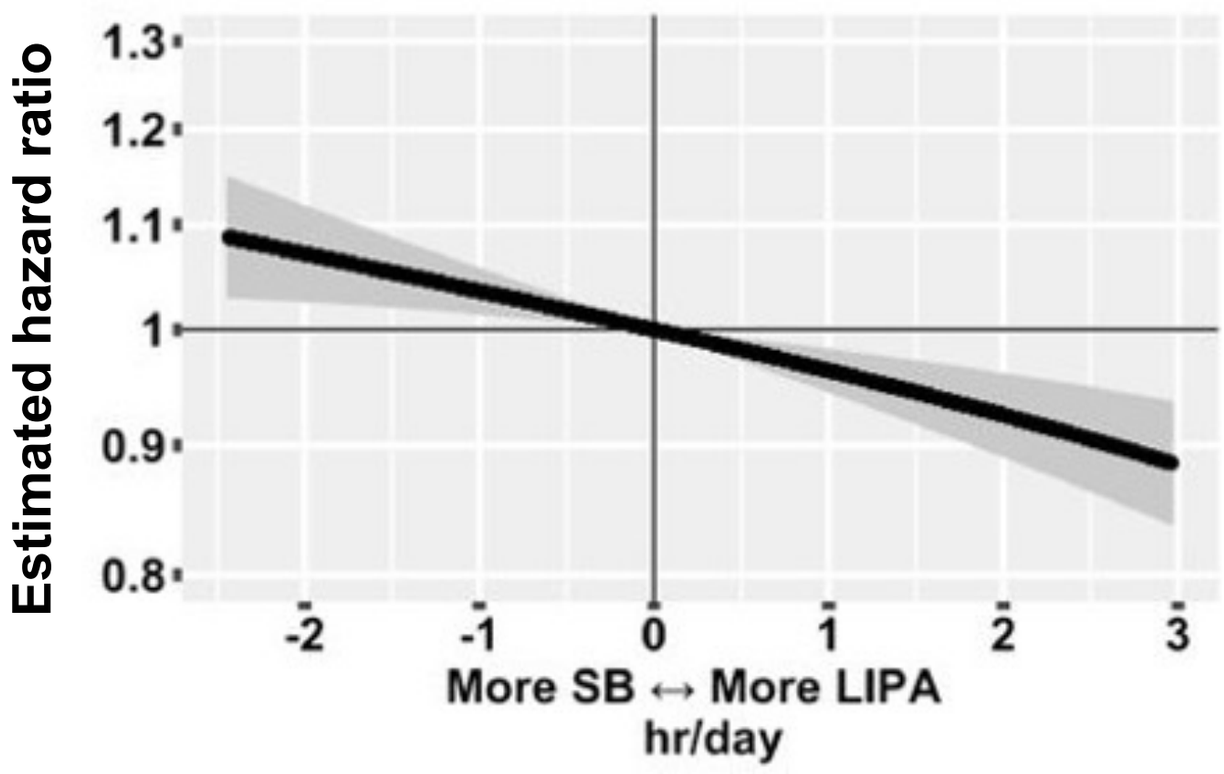


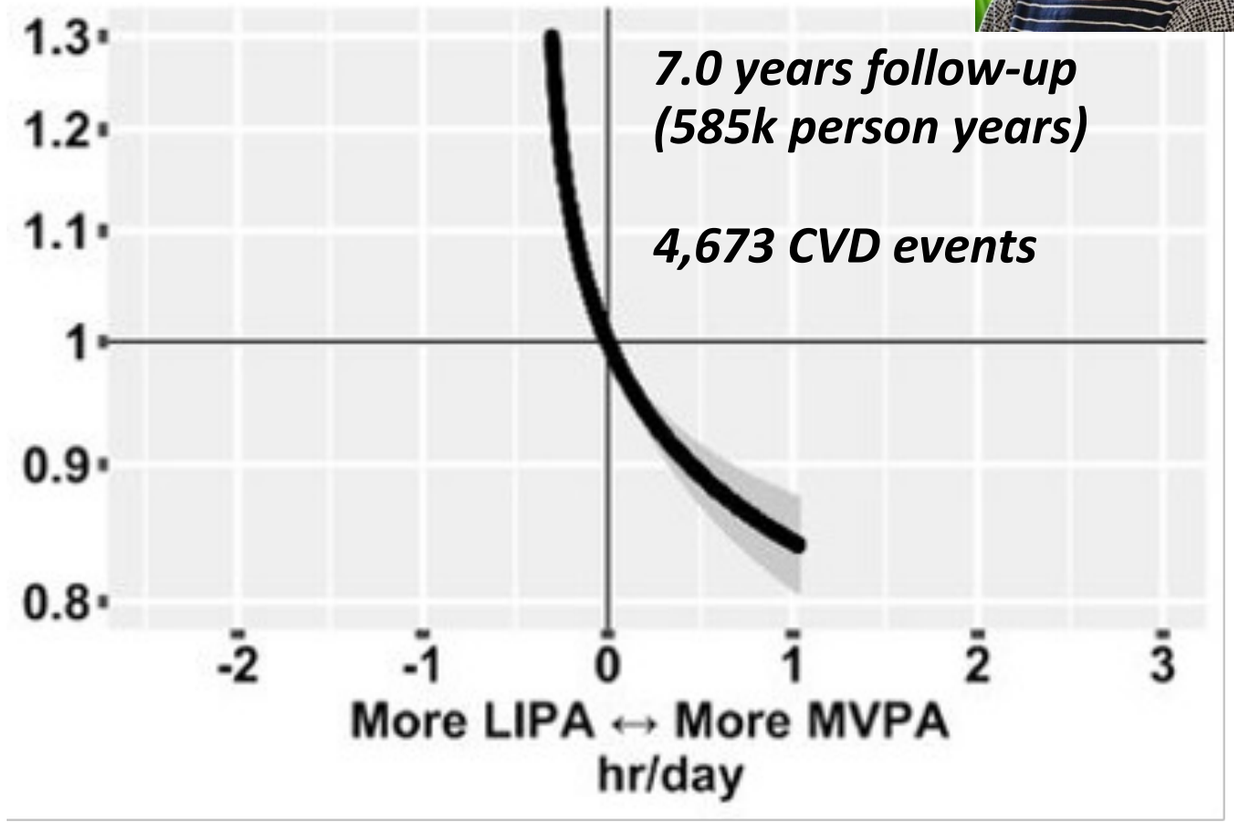

***6.8 years follow-up***

Watts et al
***JAMA Net Open*** 2023;6(2):e2256186.

# Substitution of time between behaviours - cardiovascular disease

**Hazard ratios for incident cardiovascular disease associated with balance between physical behaviours in 87,498 UK Biobank participants**



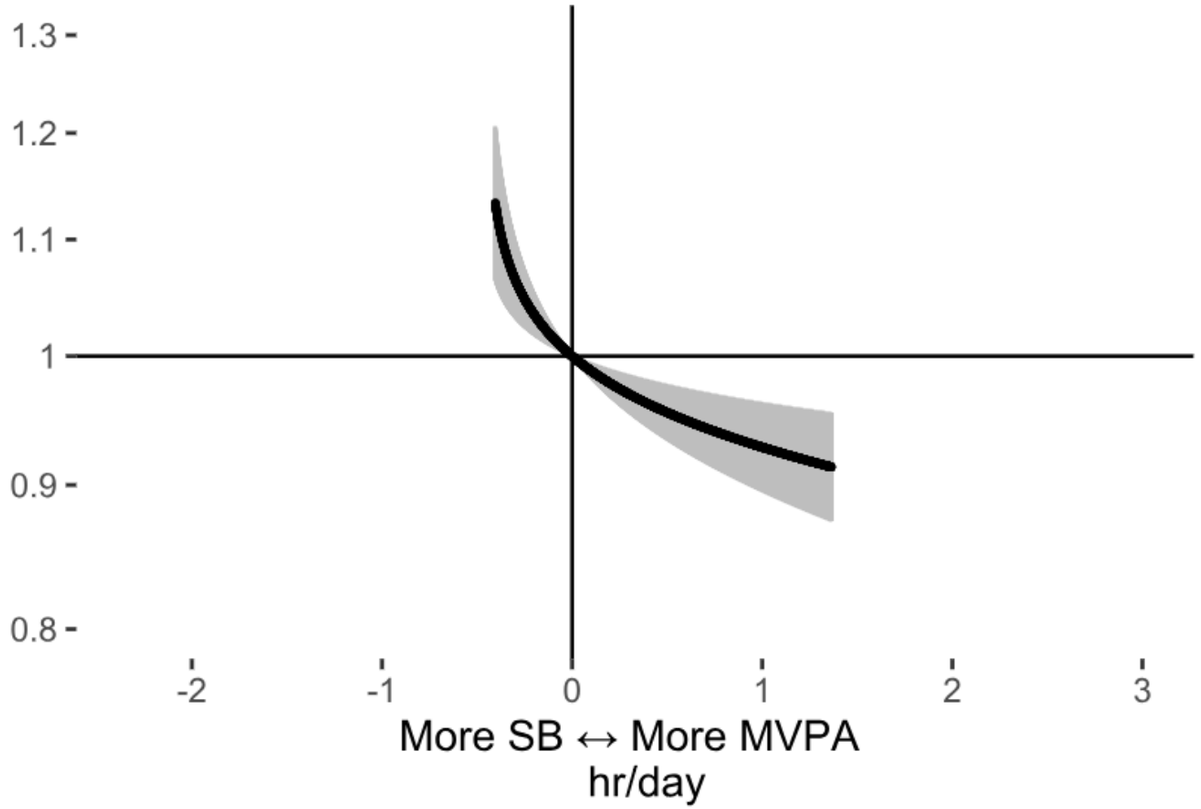

**Model based on 4,105 events in 87,498 participants.** All relative to the mean behaviour composition (8·8 hours/day sleep, 9·3 hours/day sedentary behaviour, 5·6 hours/day light physical activity behaviours, 0·35 hours/day (21 minutes/day) moderate-to-vigorous physical activity behaviours). Model used age as the timescale, was stratified by sex and was additionally adjusted for ethnicity, smoking status, alcohol consumption, fresh fruit and vegetable consumption, red and processed meat consumption, oily fish consumption, deprivation and education. 95% Confidence Intervals shown.

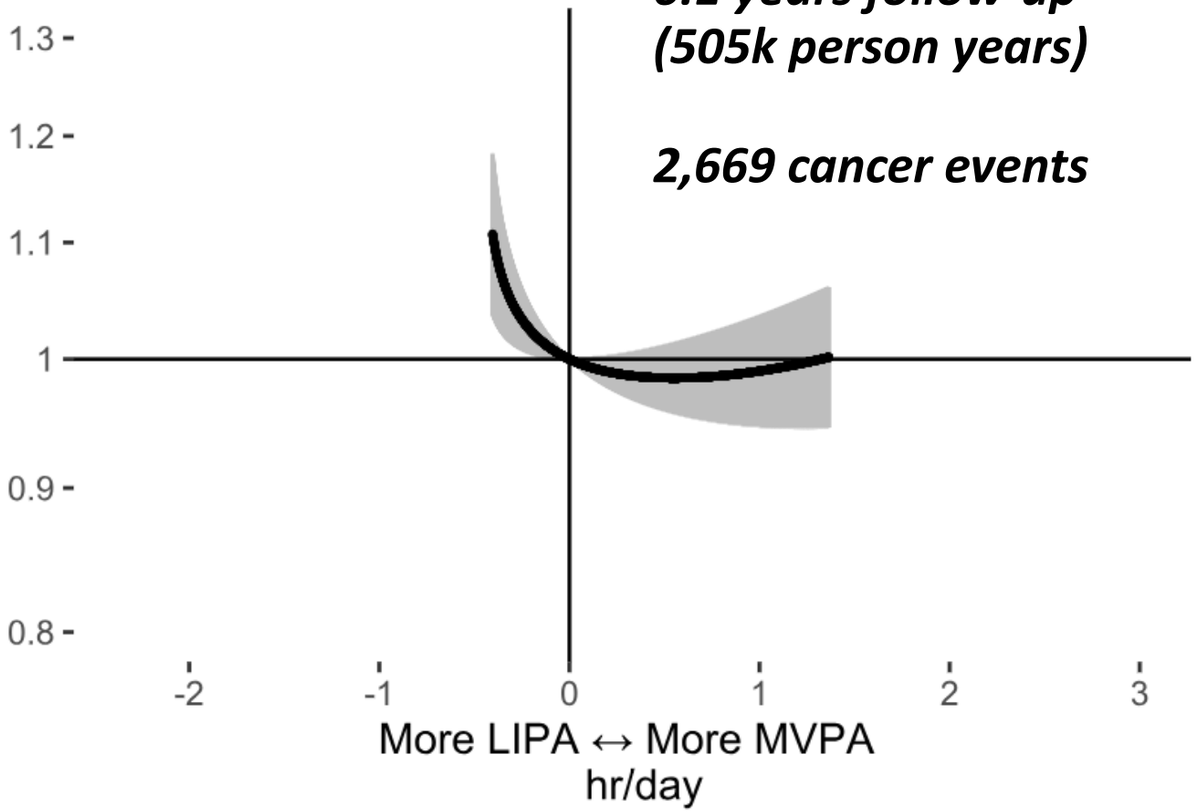
# Substitution of time between behaviours – activity-related cancers

**Hazard ratios for incident activity-related cancer associated with balance between physical behaviours in 86,556 UK Biobank participants**

***6.1 years follow-up (505k person years)***

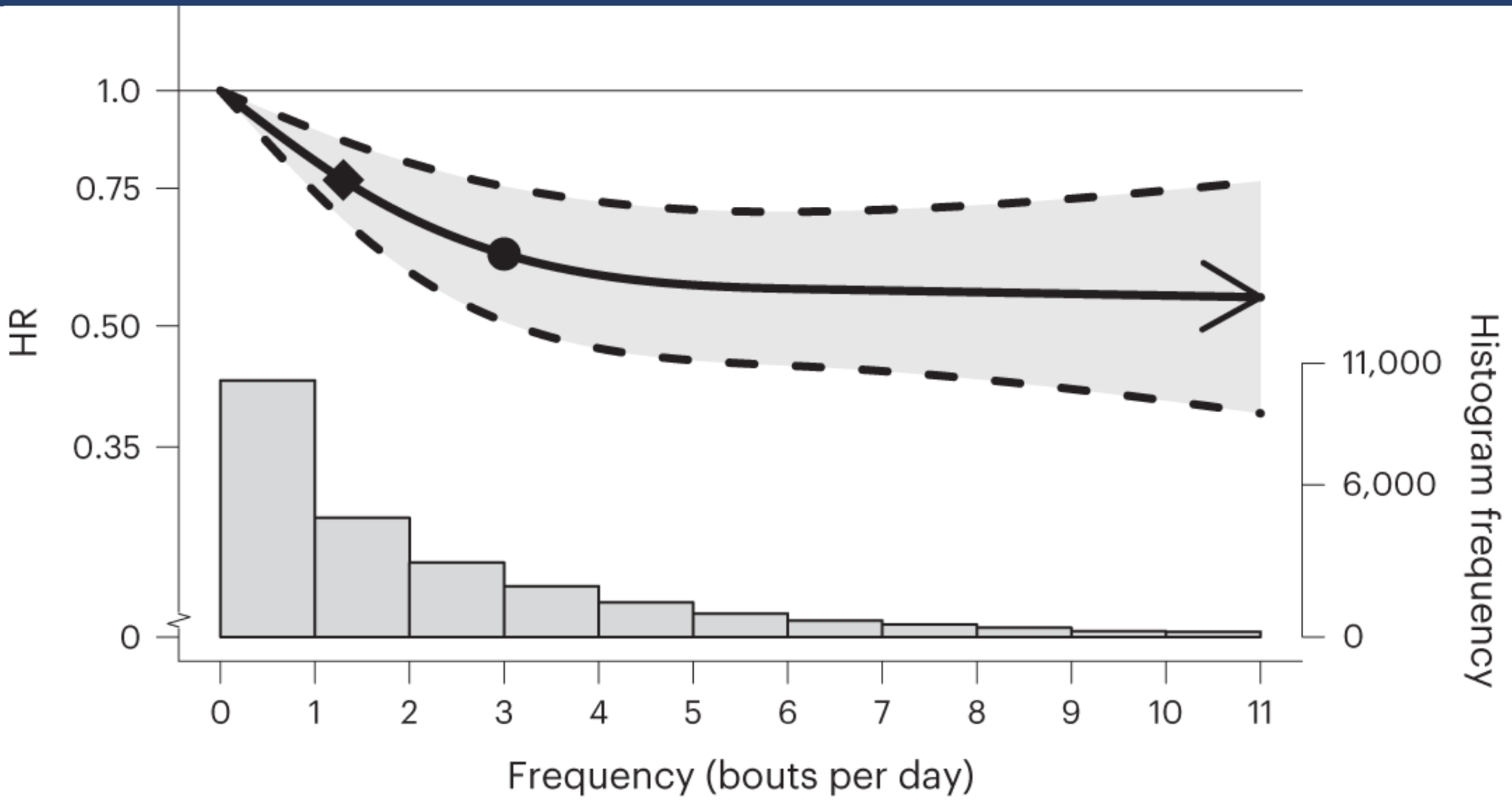
***2,669 cancer events***




Shreeves (in preparation)

# Vigorous Intermittent Lifestyle Physical Activity & all-cause mortality



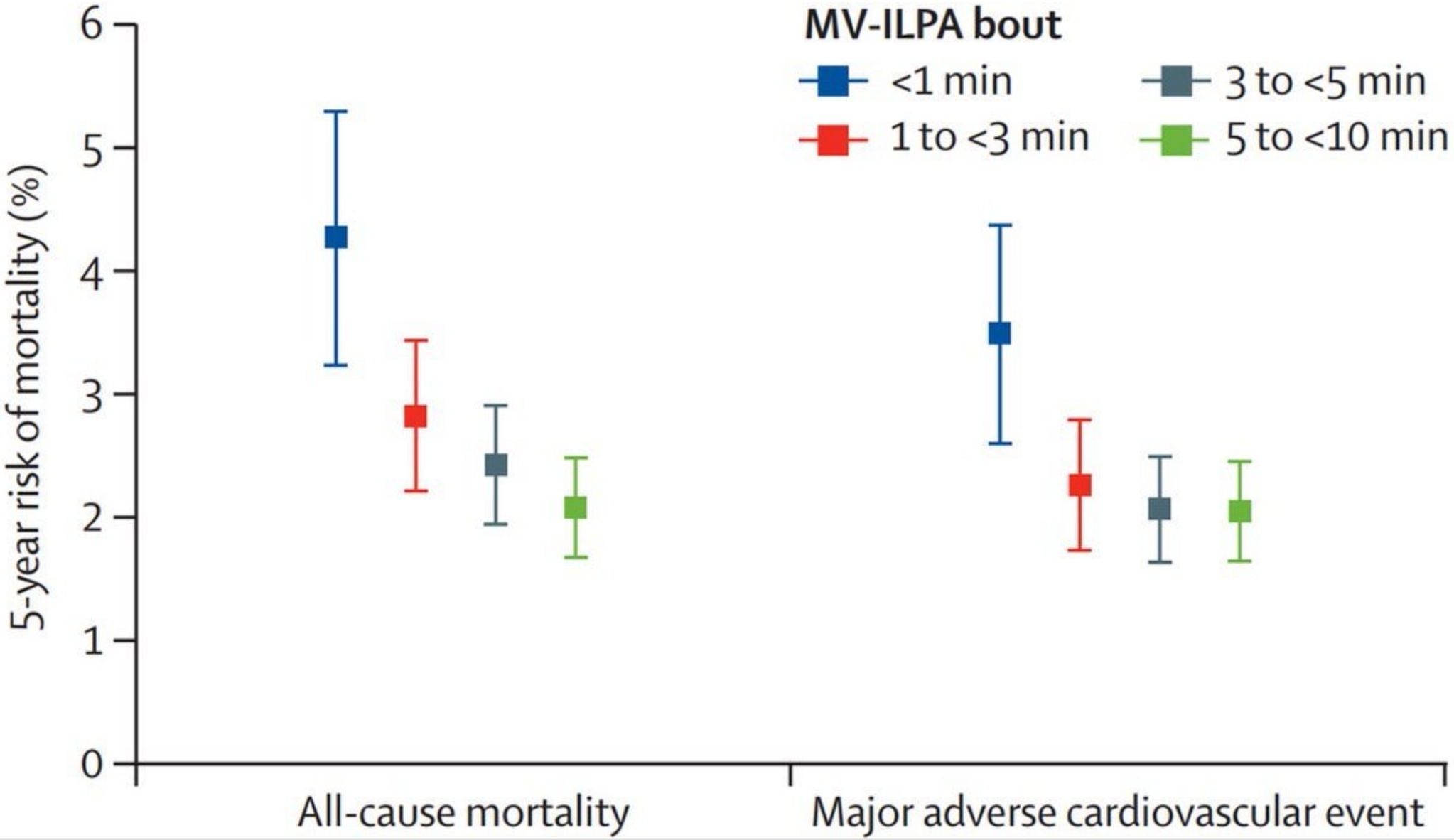

*n* = 25,241

852 events

6.9 years follow-up

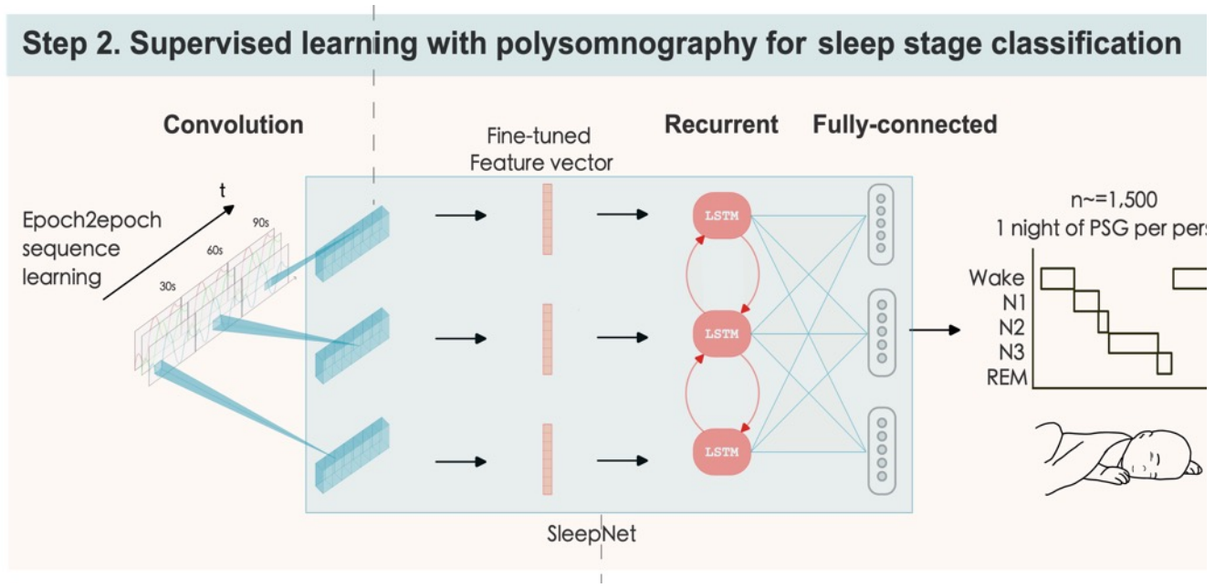
Stamatakis, et al. ***Nat Med*** 28, 2521–2529 (2022)

# Moderate intermittent lifestyle physical activity




Ahmadi, et al. ***Lancet Public Health*** 2023;8: e800–10

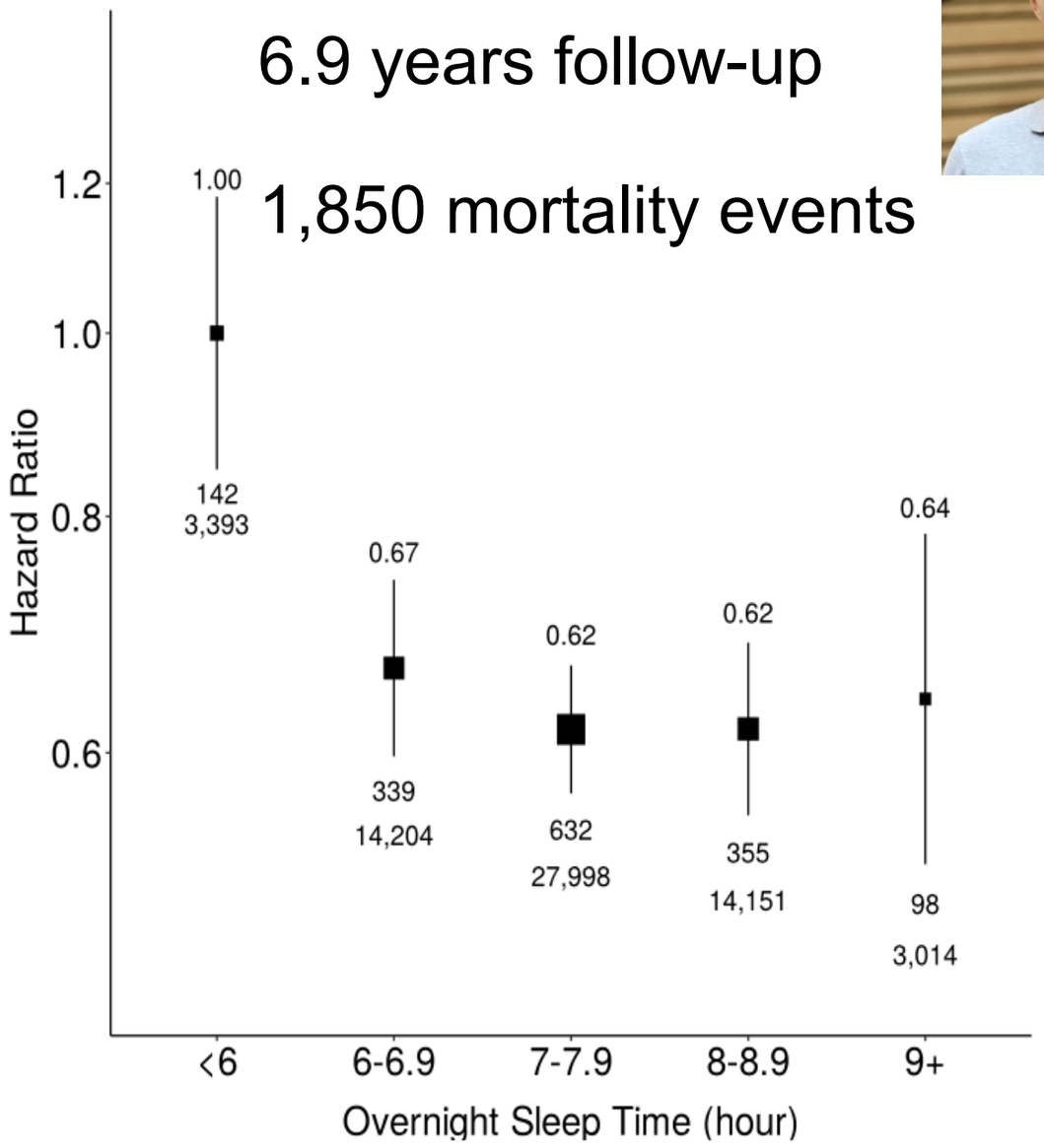
# Sleep duration & all-cause mortality




Validation versus polysomnography
n ≈ 1,500

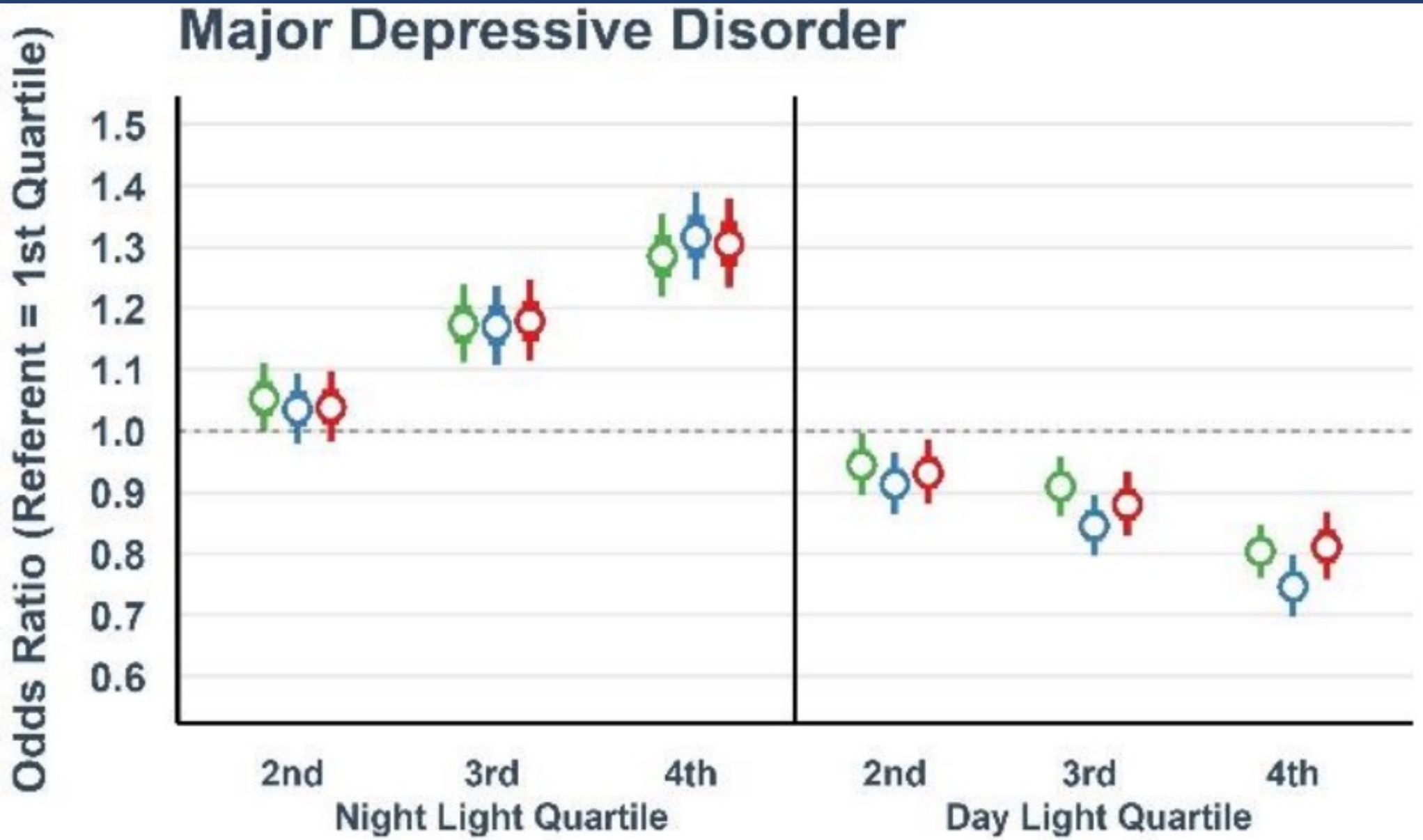
6.9 years follow-up

1,850 mortality events




Yuan et al. ***medRxiv*** 2023.07.07.23292251

# Light exposure & major depressive disorder




*n* = 86,631

2 years follow-up

Burns, et al. ***Nature Mental Health*** 2023 https://doi.org/10.1038/s44220-023-00135-8

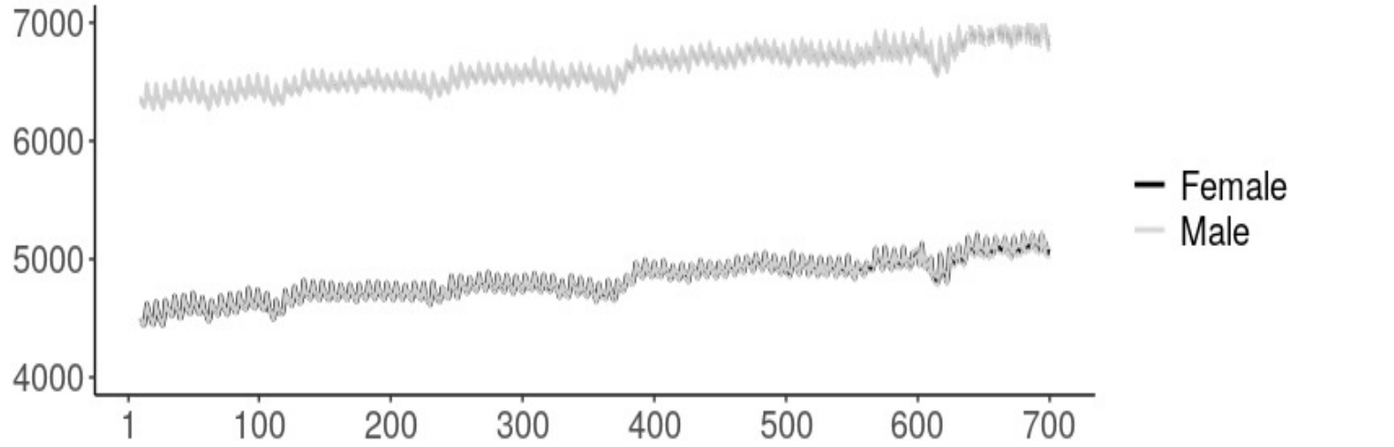
# Where next? New populations – China Kadoorie Biobank

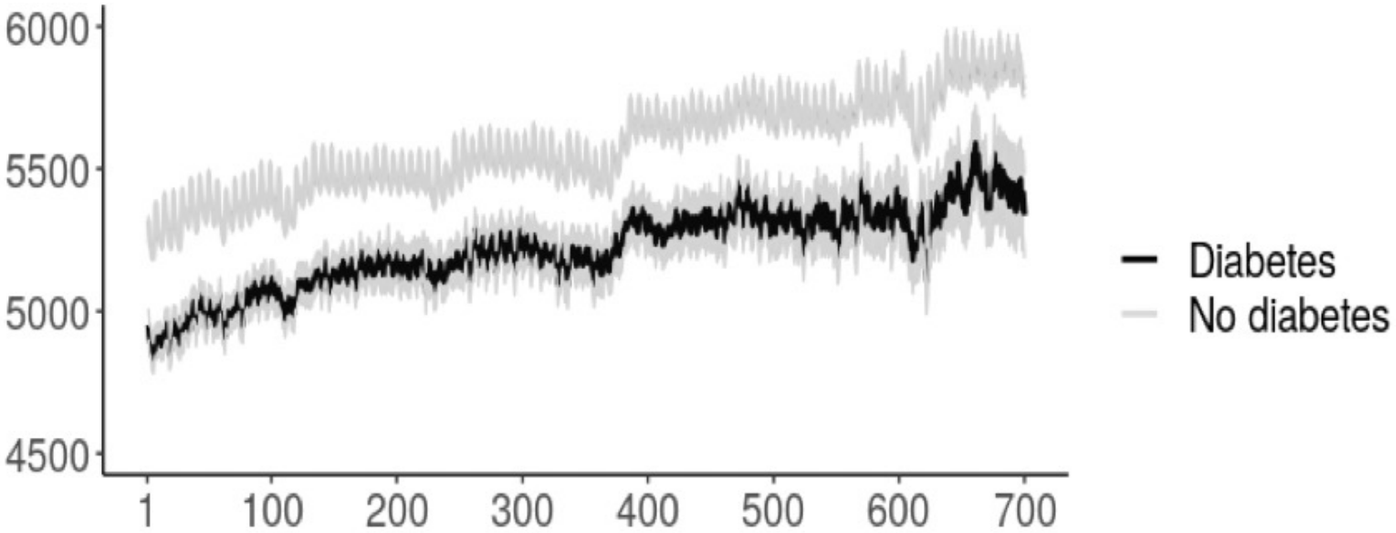
**UKB 2013 – 2015**
**n = 103,712**
Consent = 47%
Adherence = 93%

**CKB 2020 - 2021**
**n = 20,375**
Consent = 89%
Adherence = 93%


Doherty et al. ***PLoS One*** 12, (2017). 12(2):e0169649
Yu, Du, Bennett et al *(in preparation)*

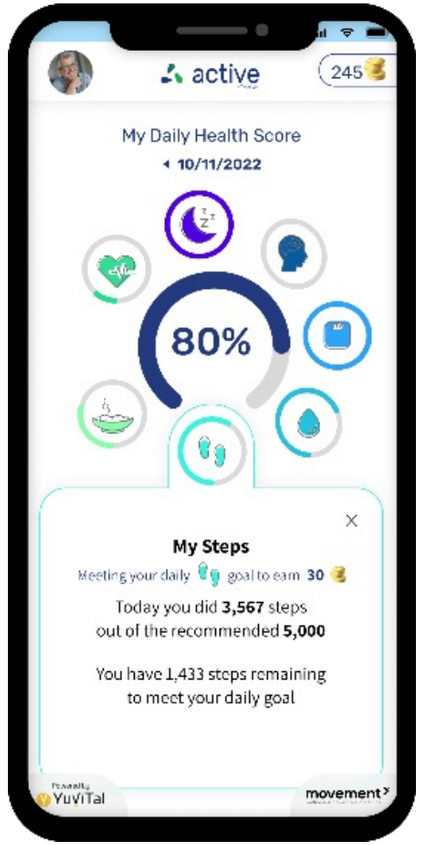
# Where next? New populations – Clalit Cohort, Israel




**n = 622,584**

Consent = ~26 %
Adherence = ?? %




Berliner et al. ***(in preparation)***

# https://www.bdi.ox.ac.uk/research/wearables-group

Integrating wearables across large-scale studies will transform our ability to answer important new questions:

- What is the impact of transitions in physical activity and sleep on future disease risk?
- Are movement behaviours causally associated with incident disease?
- What is the association between new exposures and common disease outcomes?
- Which randomised interventions improve activity and sleep?

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