Online-Only Supplemental Material
Cardiorespiratory fitness, muscular strength, and risk of type 2 diabetes: a systematic review and meta-analysis
Jakob Tarp, Andreas Plum Støle, Kim Blond, Anders Grøntved

Table of Contents
ESM Table 1. Search Strategy for PubMed (MEDLINE)
ESM Table 2. Search Strategy for EMBASE
ESM Table 3. Inclusion and exclusion criteria
ESM Table 4. Newcastle-Ottawa quality score of prospective cohort studies of cardiorespiratory fitness and incident type 2 diabetes
ESM Table 5. Newcastle-Ottawa quality score of prospective cohort studies of muscular strength and incident type 2 diabetes
ESM Table 6. List of publications excluded from systematic review because of overlapping information with other cohorts
ESM Table 7. Assumptions, calculations and unpublished data provided by contact with study authors used when harmonizing cardiorespiratory fitness data
ESM Table 8. Assumptions, calculations and unpublished data provided by contact with study authors used when harmonizing muscular strength data
ESM Table 9. Potential impact fractions (PIF) and population attributable fractions (PAF) for counterfactual cardiorespiratory fitness distributions in 40-59-years-old U.S. men and women.
ESM Table 10. Characteristics of studies included in systematic review of cardiorespiratory fitness
ESM Table 11. Characteristics of studies included in systematic review of muscular strength
ESM Table 12. Risk difference associated with a 1-MET increase in cardiorespiratory fitness or a 1-SD increase in muscular strength in age-strata and for the total U.S. adult population
ESM Table 13. Omitting, in turn, one study at a time from linear dose-response meta-analysis of cardiorespiratory fitness estimates including control for adiposity.
ESM Table 14. Omitting, in turn, one study at a time from linear dose-response meta-analysis of cardiorespiratory fitness estimates excluding control for adiposity.
ESM Table 15. Omitting, in turn, one study at a time from linear dose-response meta-analysis of muscular strength estimates including control for adiposity.
ESM Table 16. Omitting, in turn, one study at a time from linear dose-response meta-analysis of muscular strength estimates excluding control for adiposity.
ESM Figure 1. Study-specific relative risks per 1-MET increase in cardiorespiratory fitness in models not controlling for adiposity
ESM Figure 2. Relative risk of type 2 diabetes with increasing cardiorespiratory fitness level modelled using restricted cubic splines using categorical estimates not controlled for adiposity
ESM Figure 3. Study-specific relative risks per standard deviation increase in muscular strength in models not controlling for adiposity

ESM Figure 4. Risk of small-study bias visualized by funnel-plot of cardiorespiratory fitness estimates including control for adiposity.

ESM Figure 5. Risk of small-study bias visualized by funnel-plot of cardiorespiratory fitness estimates excluding control for adiposity.

ESM Figure 6. Risk of small-study bias visualized by funnel-plot of muscular strength estimates including control for adiposity

ESM Figure 7. Risk of small-study bias visualized by funnel-plot of muscular strength estimates excluding control for adiposity
**ESM Table 1. Search Strategy for PubMed (MEDLINE)**

| Exposure | Outcome | Study design |
|----------|---------|--------------|
| "muscular strength" (ti/ab) | diabetes mellitus, type 2 (mesh) | prospective studies [mesh] |
| "muscle strength" (ti/ab) | "type II diabetes" (ti/ab) | longitudinal studies [mesh] |
| muscle strength (MeSH) | "type 2 diabetes" (ti/ab) | observational study [publication type] |
| "muscle power" (ti/ab) | "diabetes mellitus" (ti/ab) | predic* (ti/ab) |
| hand strength (MeSH) | diabet* (ti/ab) | Risk (ti/ab) |
| "grip strength" (ti/ab) | | Longitudinal (ti/ab) |
| "handgrip strength" (ti/ab) | | observational study (ti/ab) |
| "cardiovascular fitness" (ti/ab) | | follow-up (ti/ab) |
| "aerobic fitness" (ti/ab) | | cohort (ti/ab) |
| cardiorespiratory fitness (MeSH) | | prospective study (ti/ab) |
| "cardiorespiratory fitness" (ti/ab) | | longitudinal study (ti/ab) |
| physical fitness (mesh) | | longitudinal (ti/ab) |
| "aerobic capacity" (ti/ab) | | risk factor (ti/ab) |
| "exercise tolerance" (ti/ab) | | risk factor (ti/ab) |
| "exercise test" (ti/ab) | | risk factor (ti/ab) |
| "maximal oxygen consumption" (ti/ab) | | risk factor (ti/ab) |
| "maximal oxygen uptake" (ti/ab) | | risk factor (ti/ab) |
| vo2max (ti/ab) | | risk factor (ti/ab) |

Total hits December 12, 2018: 1951

**ESM Table 2. Search Strategy for EMBASE**

| Exposure | Outcome | Study design |
|----------|---------|--------------|
| "muscle strength".af. | "type 2 diabetes".af. | "prospective study".af. |
| "muscle power".af. | "type II diabetes".af. | "observational study".af. |
| "hand strength".af. | "non insulin dependent diabetes mellitus".af. | "longitudinal study".af. |
| "grip strength".af. | "diabetes mellitus".af. | "risk factor".af. |
| "aerobic fitness".af. | | |
| "cardiorespiratory fitness".af. | | |
| "aerobic capacity".af. | "fitness".af. | |
| "exercise tolerance".af. | | |
| "exercise test".af. | | |
| "maximal oxygen consumption".af. | | |
| "maximal oxygen uptake".af. | | |
| vo2max.af. | | |
| "hand strength".af. | | |

Total hits December 12, 2018: 2437
**ESM Table 3. Inclusion and exclusion criteria**

| Component      | Inclusion criteria                                                                                                                                                                                                 | Exclusion criteria                                                                                                                                 |
|----------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|-----------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Population     | Studies that include human subjects free of type 2 diabetes at baseline. Cohorts will be included if they consist of participants with conditions that are associated with type 2 diabetes (e.g. obesity, metabolic syndrome, cardiovascular diseases) | Studies not excluding subjects with type 2 diabetes at baseline, studies with a population that consists exclusively of individuals with a chronic disease (e.g. cancer).                                     |
| Exposure       | Cardiorespiratory fitness* assessed by a maximal or sub-maximal stress test of any form. Muscular strength** measured as peak score or mean score. Composite scores including >1 unique test will be included. Both isotonic, isometric and isokinetic tests will be included. There are no criteria regarding muscle groups tested. Tests should allow few (<3) repetitions of a task before reaching momentary muscular fatigue | Muscular power*** or endurance****                                                                                                                                                                       |
| Outcome        | type 2 diabetes                                                                                                                                                                                                     | Not type 2 diabetes (also excluding pre-diabetes).                                                                                                                                                        |
| Study design   | Cohort studies                                                                                                                                                                                                      | Experimental studies, case-control studies, cross-sectional studies, meta-analyses, reviews, reports                                                                                                         |
| Other          | Published in English or Scandinavian language. Any publication year                                                                                                                                                 | Other languages                                                                                                                                                                                          |
| For meta-analysis | Results should be provided with relative risk, hazard ratio or odds ratio, and corresponding confidence intervals or information to calculate variance associated with estimates. Estimates should be convertible to the unit size found most appropriate for harmonization | Insufficient information/not possible to convert estimates to chosen unit for harmonization                                                                                                                   |

*Cardiorespiratory fitness is the ability to perform large muscle, dynamic, moderate-vigorous intensity activity for prolonged periods [1].

**Muscular strength is the ability of a muscle to exert maximal force [1].

***Muscular power is the muscle’s ability to exert force per unit of time [1].

****Muscular endurance is the ability of a muscle to continue to perform without fatigue [1]
| Study Selection | Comparability of cohorts | Outcome | Stars awarded |
|----------------|-------------------------|---------|---------------|
| Selection of the non-exposed cohort | Ascertainment of exposure | Demonstration that outcome was not present at start of study | Adiposity | Multivariate adjustment | Assessment of outcome | Length of follow-up | Adequacy of follow up |
| Lynch et al., 1996 [2] | A* | A* | A* | A* | B | A* | B | C | 5 |
| Katzmarzyk et al., 2007 [3] | A* | C | C | B | B | C | A* | C | 2 |
| Sui et al., 2008 [4] | A* | B* | A* | A* | B | A* | A* | B* | 7 |
| Carnethon et al., 2009 [5] | A* | B* | A* | A* | B | A* | A* | B* | 7 |
| Sieverdes et al., 2010 [6] | A* | B* | A* | A* | B | C | A* | C | 5 |
| Skretteberg et al., 2013 [7] | A* | B* | A* | B | B | B* | A* | B* | 6 |
| Kuwahara et al., 2014 [8] | A* | C | A* | A* | B | A* | A* | B* | 6 |
| Juraschek et al., 2015 [9] | A* | B* | B* | B | B | B* | A* | A* | 6 |
| Zaccardi et al., 2015 [10] | A* | A* | A* | A* | B | A* | A* | A* | 7 |
| Bantle et al., 2016 [11] | A* | B* | A* | A* | B | A* | A* | C | 6 |
| Crump et al., 2016 [12] | A* | B* | B* | A* | B | B* | A* | A* | 7 |
| Holtermann et al., 2017 [13] | A* | C | C | A* | B | B* | A* | A* | 5 |
| Kokkinos et al., 2017 [14] | A* | B* | B* | A* | B | B* | A* | A* | 7 |
### Selection of the non-exposed cohort

- **Ascertainment of exposure**
- **Demonstration that outcome was not present at start of study**
- **Adiposity**
- **Multivariate adjustment**
- **Assessment of outcome**
- **Length of follow-up**
- **Adequacy of follow-up**
- **Stars awarded**

| Study                  | Selection of the non-exposed cohort | Ascertainment of exposure | Demonstration that outcome was not present at start of study | Adiposity | Multivariate adjustment | Assessment of outcome | Length of follow-up | Adequacy of follow-up | Stars awarded |
|-----------------------|-------------------------------------|---------------------------|-------------------------------------------------------------|-----------|------------------------|-----------------------|---------------------|----------------------|---------------|
| Momma et al., 2017 [15] | A*                                  | C                         | A*                                                          | A*        | B                      | A*                     | A*                  | B*                   | 6             |
| Kawakami et al., 2018 [16] | A*                                  | C                         | A*                                                          | A*        | B                      | A*                     | A*                  | B*                   | 6             |
| Ohlson et al., 1988 [17] | A*                                  | B*                        | A*                                                          | A*        | B                      | A*                     | A*                  | B*                   | 7             |
| Williams 2008 [18]    | A*                                  | D                         | D                                                           | A*        | B                      | C                      | A*                  | C*                   | 3             |
| Kinney et al., 2014 [19] | A*                                  | D                         | D                                                           | Unclear  | Unclear                | C                      | A*                  | C*                   | 2             |
| Someya et al., 2014 [20] | A*                                  | D                         | D                                                           | A*        | B                      | C                      | A*                  | C*                   | 3             |
| Jae et al., 2016 [21]  | A*                                  | A*                        | A*                                                          | A*        | B                      | A*                     | A*                  | C*                   | 6             |
| Sydo et al., 2016 [22] | A*                                  | Unclear                   | D                                                           | B*        | B                      | B*                     | A*                  | A*                   | 4             |
| Wu et al., 2018 [23]   | A*                                  | D                         | A*                                                          | A*        | B                      | A*                     | B*                  | A*                   | 5             |

We chose not to include the “Representativeness of the exposed cohort” item of the original Newcastle-Ottawa Scale [24] since we find this irrelevant for the evaluation of the internal validity of the studies. Thus, a total of 8 stars were achievable. Study quality reflects assessments in relation to the estimates for which we extracted data and not the study per se.
Newcastle-Ottawa Score key cardiorespiratory fitness

Selection

Selection of the non-exposed cohort
A. Drawn from the same community as the exposed cohort*
B. Drawn from a different source
C. No description of the derivation of the non-exposed cohort

Ascertainment of exposure
A. Directly measured VO2 by gas exchange kinetics to stress-limited max*
B. Treadmill- or ergometry to stress-limited max*
C. Submaximal graded test
D. Other submaximal tests

Demonstration that outcome was not present at start of study
A. Clinical assessment*
B. Medical records, medication status of the patient*
C. Self-report
D. No description

Comparability

Comparability of cohorts on the basis of the design or analysis
A. Study adjusts for BMI or other adiposity index*
B. Study does not adjust for BMI or other adiposity index

Comparability of cohorts on the basis of the design or analysis
A. Study adjusts for (in addition to age, sex and ethnicity if relevant);
   Muscular fitness, smoking, family history of diabetes, dietary intake (any measure), alcohol consumption, TV-viewing, socioeconomic status (any index) - (4 out of 7)*
B. Study does not adjust for these factors

Outcome

Assessment of outcome
A. Clinical assessment*
B. Medical records, records linkage or medication status of the patient*
C. Self-report
D. No description

Was follow-up long enough for outcomes to occur
A. Yes (> 5 years)*
B. No (< 5 years)

Adequacy of follow up of cohorts
A. Complete follow up (>99%)*
B. Subjects lost to follow up unlikely to introduce bias > 80% subjects followed up or description of those lost suggests unlikely to introduce bias*
C. Follow up rate < 80% and no description of those lost
D. No statement on follow up
## ESM Table 5. Newcastle-Ottawa quality score of prospective cohort studies of muscular strength and incident type 2 diabetes

| Study Selection | Comparability of cohorts | Outcome | Stars awarded |
|----------------|--------------------------|---------|---------------|
| Selection of the non-exposed cohort | Ascertainment of exposure | Demonstration that outcome was not present at start of study | Adiposity | Multivariate adjustment | Assessment of outcome | Length of follow-up | Adequacy of follow up | |
| Kutzmarzyk et al., 2007 [3] | A* | B* | C | B | B | C | A* | C | 3 |
| Wander et al., 2011 [25] | A* | B* | A* | A* | B | A* | A* | B* | 7 |
| Leong et al., 2015 [26] | A* | B* | C | A* | A* | B* | B | B* | 6 |
| Li et al., 2016 [27] | A* | B* | A* | A* | B | A* | B | C | 5 |
| Crump et al., 2016 [12] | A* | A* | B* | A* | B | B* | A* | A* | 7 |
| Cuthbertson et al., 2016 [28] | A* | B* | C | A* | B | C | A* | C | 4 |
| Larsen et al., 2016 [29] | A* | B* | A* | A* | B | A* | A* | C | 6 |
| Marquez-Vidal et al., 2017 [30] | A* | B* | A* | A* | B | A* | A* | C | 6 |
| Karvonen-Gutierrez et al., 2018 [31] | A* | B* | A* | A* | B | A* | A* | B* | 7 |
| Lee et al., 2018 [32] | A* | A* | A* | A* | B | A* | A* | A* | D | 6 |
| Momma et al., 2018 [33] | A* | A* | A* | A* | B | A* | A* | B* | 7 |
| McGrath et al., 2017 [34] | A* | B* | C | A* | B | C | A* | Unclear | 4 |
| Zhang et al., 2018 [35] | A* | B* | A* | Unclear | B | A* | B | B* | 5 |

We chose not to include the “Representativeness of the exposed cohort” item of the original Newcastle-Ottawa Scale [24] since we find this irrelevant for the evaluation of the internal validity of the studies. Thus, a total of 8 stars were achievable. Study quality reflects assessments in relation to the estimates for which we extracted data and not the study per se.
Newcastle-Ottawa Score key muscular strength

Selection

Selection of the non-exposed cohort
A. Drawn from the same community as the exposed cohort*
B. Drawn from a different source
C. No description of the derivation of the non-exposed cohort

Ascertainment of exposure
A. Several major muscle groups measured by dynamometer, 1RM or isokinetic/isometrics/isotonic device*
B. One major muscle groups measured by dynamometer, 1RM or isokinetic/isometrics/isotonic device *
C. No description

Demonstration that outcome was not present at start of study
A. Clinical assessment*
B. Medical records, medication status of the patient*
C. Self-report
D. No description

Comparability

Comparability of cohorts on the basis of the design or analysis
A. Study adjusts for BMI or other adiposity index*
B. Study does not adjust for BMI or other adiposity index

Comparability of cohorts on the basis of the design or analysis
A. Study adjusts for (in addition to age, sex and ethnicity if relevant); Cardiorespiratory fitness, smoking, family history of diabetes, dietary intake (any measure), alcohol consumption, TV-viewing, socioeconomic status (any index) - (4 out of 7*  
B. Study does not adjust for these factors

Outcome

Assessment of outcome
A. Clinical assessment*
B. Medical records, records linkage or medication status of the patient*
C. Self-report
D. No description

Was follow-up long enough for outcomes to occur
A. Yes (> 5 years)*
B. No (< 5 years)

Adequacy of follow up of cohorts
A. Complete follow up (>99%)*
B. Subjects lost to follow up unlikely to introduce bias > 80% subjects followed up or description of those lost suggests unlikely to introduce bias*
C. Follow up rate < 80% and no description of those lost
D. No statement on follow up
### ESM Table 6. List of publications excluded from systematic review because of overlapping information with other cohorts.

| The Coronary Artery Risk Development in Young Adults Study (CARDIA) – Carnethon et al., 2009 [5] & Bantle et al., 2016 [11] included |
|----------------------------------|
| Carnethon et al., 2003 [36]  | Fewer cases and shorter follow-up. |

| Aerobics Center Longitudinal Study (ACLS) – Sui et al., 2008 [4] & Sieverdes et al., 2010 [6] included |
|----------------------------------|
| Wei et al., 1999 [37]  | Fewer cases and participants. Shorter follow-up. Only ascertains cases from clinical assessment. |
| Le et al., 2008 [38]  | Fewer cases and participants. Shorter follow-up. More women included in Sui 2008. Only ascertains cases from clinical assessment. |
| Lee et al., 2009 [39]  | Fewer cases and participants. Shorter follow-up. Only ascertains cases from clinical assessment. |
| Goodrich et al., 2012 [40]  | Fewer participants and shorter follow-up. More women included in Sui 2008. Only ascertains cases from clinical assessment. |
| Radford et al., 2015 [41]  | Fewer cases and participants. Shorter follow-up. More women included in Sui 2008. Only ascertains cases from clinical assessment. |
| Sloan et al., 2016 [42]  | Fewer cases and participants. Shorter follow-up. Only ascertains cases from clinical assessment. |

| Tokyo Gas Company Study - Momma et al., 2017 [15] & Kawakami et al 2018 [16] included |
|----------------------------------|
| Sawada et al., 2003 [43]  | Fewer cases and participants. Shorter follow-up. |
| Sawada et al., 2010a [44]  | Fewer cases and participants. Shorter follow-up. |
| Sawada et al., 2010b [45]  | Fewer cases and participants. Shorter follow-up. |
| Kawakami et al., 2014 [46]  | Fewer cases and participants. Shorter follow-up. |
| Sloan et al., 2018 [47]  | Fewer cases and participants. Shorter follow-up. |

| Veterans Affairs Medical Center Study - Kokkinos et al., 2017 [14] included |
|----------------------------------|
| Narayan et al., 2016 [48]  | Conference abstract. |

| Oslo Ischemia Study – Skretteberg et al., 2013 [7] included |
|----------------------------------|
| Bjørnholt et al., 2001 [49]  | Fewer cases and participants. Shorter follow-up. |
Table 7. Assumptions, calculations and unpublished data provided by contact with study authors used when harmonizing cardiorespiratory fitness data.

| Author                      | Assumptions/calculations                                                                                                                                                                                                 |
|-----------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Lynch et al., 1996 [2]      | Categorical data:  
  - Individuals in quartiles of CRF unclear  
    - Assigned 187 individuals to most fit quartile, 187 to other quartiles  
  - MET-level in quartiles unclear  
    - Assigned dose as mid-point (e.g. 28.35 for category 25.8 to 31.0) for two middle categories  
    - Assigned doses as 2.55 from upper/lower cut-off in outer categories  
    - Divided oxygen uptake in ml/kg/min by 3.5                                                                                                           |
| Zaccardi et al., 2015 [10]  | No transformations applied                                                                                                                                                                                             |
| Katzmarzyk et al., 2007 [3] | Linear models:  
  - Estimate presented per standard deviation increase in CRF  
    - Calculated pooled standard deviation of CRF*  
    - Converted estimate in standard deviations to per 1-MET [50]                                                                                      |
| Sui et al., 2008 [4]        | Categorical data:  
  - MET-level in tertiles unclear  
    - Pooled “No diabetes” and “diabetes” MET-values in Table 1* and assigned this value as METs-values in middle tertile  
    - Assumed normal-distribution of CRF and subtracted/added 1 MET for dose in outer tertiles under the assumption that the standard deviation of CRF was 2 METs [51]  
Linear models:  
  - GLST applied on categorical estimates                                                                                                                                                                |
| Sieverdes et al., 2010 [6]  | Data provided by personal communication                                                                                                                                                                                |
| Group | Cases | Total participants | Person-years | Dose (METs) |
|-------|-------|---------------------|--------------|-------------|
| Ref   | 307   | 5754                | 114,320      | 9.0         |
| 1     | 142   | 5718                | 107,293      | 11.3        |
| 2     | 94    | 5900                | 101,551      | 12.6        |
| 3     | 46    | 6072                | 101,196      | 14.4        |

Linear models:  
- GLST applied on categorical estimates
| Author                        | Assumptions/calculations                                                                                                                                                                                                 |
|------------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Carnethon et al., 2009 [5]  | Linear models:                                                                                                                                                                                                            |
|                              |   Estimates presented per standard deviation decrease in treadmill-time                                                                                                                                                  |
|                              |     o Calculated sex-ethnicity specific METs [52] associated with a 1 standard deviation (using sex-ethnicity based standard deviation) increase in treadmill time using the difference in METs from the mean treadmill time to mean + 1 standard deviation of treadmill time based on reported data. |
|                              |     o Convert sex-ethnicity specific estimate to per 1-MET [50]                                                                                                                                                           |
|                              |     o Invert estimate from decrease to increase CRF by: exponentiate(-log(estimate))                                                                                                                                     |
|                              |     o Using fixed-effects meta-analysis to pool ethnicity-stratified data                                                                                                                                                |
| Skretteberg et al., 2013 [7] | Linear models:                                                                                                                                                                                                            |
|                              |   Estimate presented per standard deviation increase in CRF                                                                                                                                                              |
|                              |     o Assumed standard deviation of 2 METs [51]                                                                                                                                                                             |
|                              |     o Converted estimate in standard deviations to per 1-MET [50]                                                                                                                                                         |
| Kuwahara et al., 2014 [8]   | Data provided by personal communication                                                                                                                                                                                   |
|                              |   Linear models:                                                                                                                                                                                                            |
|                              |     o GLST applied on categorical estimates                                                                                                                                                                              |
| Juraschek et al., 2015 [9]   | Categorical models:                                                                                                                                                                                                       |
|                              |   BMI-adjusted models                                                                                                                                                                                                     |
|                              |     o Cases in four CRF categories unclear                                                                                                                                                                                |
|                              |     o Estimated cases based on unadjusted 5-year unadjusted cumulative incidence scaled to match total diabetes incidence (from low-fit; 1296, 2330, 2396, 828).                                                             |
|                              | Excluding BMI from models                                                                                                                                                                                                 |
|                              |     o Total participants and cases in four CRF categories unclear                                                                                                                                                         |
|                              |     o Calculated total participants and cases based on assumption of identical distribution of participants and cases as in full cohort (participants: from low-fit; 1290, 2898, 4471, 3091. Cases: from low-fit; 324, 583, 599, 207). |
| Bantle et al., 2016 [11]    | Categorical data:                                                                                                                                                                                                          |
|                              |     MET-level in tertiles unclear                                                                                                                                                                                          |
|                              |     o Calculated MET from time on treadmill using CARDIA formula [52]                                                                                                                                                      |
|                              |     o Diabetes cases in tertiles unclear                                                                                                                                                                                   |
|                              |     o Data provided by personal communication (from low-fit; 204, 105, 84).                                                                                                                                             |
|                              | Linear models:                                                                                                                                                                                                            |
|                              |     o GLST applied on categorical estimates                                                                                                                                                                              |
| Author                  | Assumptions/calculations                                                                                                                                                                                                 |
|------------------------|------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Crump et al., 2016 [12] | Categorical data:  
  - MET-level in tertiles unclear  
    o Median watt/kg in tertiles provided by personal communication (from low-fit: 3.21, 3.84, 4.62)  
    o Estimated METs in tertiles from watt/kg by formula: $\text{ml O}_2/\text{min/kg} = 8.0697 \times \text{watt/kg} + 9.042817$  
      ▪ Formula derived by (unpublished) linear regression of maximal oxygen uptake on watt/kg in 278 Danish men aged 20-28 years from the general population participating in the European Youth Heart Study [53]. Watt/kg explained 71% of the variance in maximal oxygen uptake as measured by indirect calorimetry  
    o Divided maximum oxygen uptake by 3.5  
  - Reference group is most fit tertile  
    o Converted reference group to least fit tertile by Hamling-method implemented in Microsoft Excel macro [54]  
Linear models:  
  - Estimate presented per 1 watt/kg  
    o Estimated per MET from watt/kg by formula: $\text{ml O}_2/\text{min/kg} = 8.0697 \times \text{watt/kg} + 9.042817$  
    o Converted estimate to per 1-MET [50] |
| Holtermann et al., 2017 [13] | Data provided by personal communication  
|                          |                                                                                                                                                    |
| Group | Cases | Total participants | Person-years | Dose (METs) |                          |                                                                 |
|------|-------|---------------------|--------------|-------------|--------------------------|-------------------------------------------------------------------|
| Ref  | 178   | 1389                | 34,531       | 7.1         |                          |                                                                   |
| 1    | 137   | 1181                | 32,904       | 8.6         |                          |                                                                   |
| 2    | 102   | 1226                | 35,154       | 10.0        |                          |                                                                   |
| 3    | 101   | 1192                | 37,008       | 12.0        |                          |                                                                   |
Categorical data:  
  - MET-level in tertiles unclear  
    o Divided oxygen uptake in ml/kg/min by 3.5  
Linear models:  
BMI-adjusted:  
  - Estimates presented per 10 ml O$_2$/kg/min  
    o Divided by 3.5 to obtain estimate in METs  
    o Converted estimate in standard deviations to per 1-MET [50]  
Excluding BMI from models  
  o GLST applied on categorical estimates
| Author                  | Data provided by personal communication | Assumptions/calculations |
|------------------------|------------------------------------------|---------------------------|
| Kokkinos et al., 2017 [14] |                                          |                           |
| Group | Cases | Total participants | Person-years | Dose (METs) |
| Ref    | 336    | 954               | 15,915       | 7.8         |
| 1      | 328    | 1201              | 17,713       | 8.3         |
| 2      | 288    | 1242              | 18,529       | 9.2         |
| 3      | 123    | 695               | 14,881       | 11.2        |
| Linear models: | | | | |
| o GLST applied on categorical estimates | | | | |
| Momma et al., 2017 [15] | Categorical data: |                           |
| MET-level in quartiles unclear | | | | |
| Divided oxygen uptake in ml/kg/min by 3.5 | | | | |
| Linear models: | | | | |
| o GLST applied on categorical estimates | | | | |
| Kawakami et al., 2018 [16] | Categorical data: |                           |
| MET-level in quartiles unclear | | | | |
| Divided oxygen uptake in ml/kg/min by 3.5 | | | | |
| Linear models: | | | | |
| o GLST applied on categorical estimates | | | | |

*Using formula provided by the Cochrane Handbook for Systematic Reviews of Interventions, table 7.7.a [55]. CRF: cardiorespiratory fitness, MET: metabolic equivalent, GLST: generalized least-squares trend-estimation, CARDIA: Coronary Artery Risk Development in Young Adults*
### ESM Table 8. Assumptions, calculations and unpublished data provided by contact with study authors used when harmonizing muscular strength data

| Author                  | Models and assumptions/calculations                                                                                                                                                                                                 |
|-------------------------|--------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------------|
| Katzmarzyk et al., 2007 [3] | No transformations applied                                                                                                                                                                                                                |
| Wander et al., 2011 [25] | - Results presented per 10 pounds increase in muscular strength  
  - Assumed variance estimate in table 1 are standard error of the mean  
  - Calculated pooled standard deviation of muscular strength from table 1*  
  - Converted estimates to per standard deviation increase [50]                                                                                                           |
| Leong et al., 2015 [26]  | - Results presented per 5 kg decrease in muscular strength  
  - Assumed identical standard deviation as reported in table 1 in sample excluding individuals with prevalent cancer and cardiovascular disease  
  - Converted estimates to per standard deviation increase [50]  
  - Invert estimate from decrease to increase in muscular strength using: exponentiate(-log(estimate))                                                                      |
| Li et al., 2016 [27]     | Data provided by personal communication                                                                                                                                       |
|                         | **Group** | **Cases** | **Total participants** | **Person-years** | **Dose (kg / kg body-weight)** |                                                                                          |
|                         | Ref       |           |                         |                  |                             |                                                                                          |
|                         | 1         | 63        | 408                     | 1893             | 0.43                        |                                                                                          |
|                         | 2         | 37        | 408                     | 1920             | 0.54                        |                                                                                          |
|                         | 3         | 29        | 408                     | 1946             | 0.62                        |                                                                                          |
|                         | 4         | 17        | 408                     | 1977             | 0.72                        |                                                                                          |
|                         | - GLST applied on categorical estimates  
  - Converted estimates to per standard deviation increase [50]                                                                                                           |
| Crump et al., 2016 [12] | Results presented per 1 N/kg body-weight increase in composite muscular strength score  
  - Median Newtons/kg body-weight in tertiles provided by personal communication (from low-fit; 25.33, 30.17, 34.03)  
  - Calculated pooled standard deviation of muscular strength from table 1*  
  - Converted estimates to per standard deviation increase [50]  
  - Moved upper confidence limit from 0.97 to 0.98 to achieve symmetry around point-estimate                                                                            |
| Cuthbertson et al., 2016 [28] | Data provided by personal communication                                                                                                                                                                                                 |
| Larsen et al. 2016 [29] | No transformations applied                                                                                                                                                                                                                 |
| Author                      | Assumptions/calculations                                                                 |
|----------------------------|------------------------------------------------------------------------------------------|
| Marques-Vidal et al., 2017 [30] | – Results presented per 5 kg increase in muscular strength                             |
|                            |   o Calculated pooled standard deviation of muscular strength from table 1*             |
|                            |   o Converted estimates to per standard deviation increase [50]                        |
| Karvonen-Gutierrez et al., 2018 [31] | – Results presented per 0.1 kg/kg body-weight increase in muscular strength            |
|                            |   o Converted estimates to per standard deviation increase [50]                        |
| Lee et al., 2018 [32]      | Data provided by personal communication                                                 |
| Momma et al., 2018 [33]    | Data provided by personal communication                                                 |

*Using formula provided by the Cochrane Handbook for Systematic Reviews of Interventions, table 7.7.a [55]
ESM Table 9. Potential impact fractions (PIF) and population attributable fractions (PAF) for counterfactual cardiorespiratory fitness distributions in 40-59-years-old U.S. men and women.

| Intervention                                           | Sex     | Observed CRF distribution [56] | RR per 1-MET | Counterfactual CRF distribution | PIF |
|--------------------------------------------------------|---------|--------------------------------|--------------|---------------------------------|-----|
| 1-MET CRF increase achieved in the least fit 50%       | Men     | FRIEND database (US)<sup>a</sup> Mean: 10.37 SD: 2.76 | 0.80 (non-adiposity-controlled) | Mean: 10.82 SD: 2.38             | 13.4% |
|                                                        | Women   | FRIEND database (US)<sup>a</sup> Mean: 7.45 SD: 2.05 | 0.80 (non-adiposity-controlled) | Mean: 7.86 SD: 1.68              | 11.3% |
| 1-MET CRF increase achieved irrespective of initial CRF | Men     | FRIEND database (US)<sup>a</sup> Mean: 10.37 SD: 2.76 | 0.80 (non-adiposity-controlled) | Mean: 11.37 SD: 2.76             | 19.7% |
|                                                        | Women   | FRIEND database (US)<sup>a</sup> Mean: 7.45 SD: 2.05 | 0.80 (non-adiposity-controlled) | Mean: 8.45 SD: 2.05              | 19.5% |
| Achieve same CRF distribution as age-matched Norwegian population-based sample<sup>b</sup> | Men     | FRIEND database (US)<sup>a</sup> Mean: 10.37 SD: 2.76 | 0.80 (non-adiposity-controlled) | Norwegian HUNT study [57] (men aged 40-59 years) Mean: 12.69 SD: 2.31 | 43.4% |
|                                                        | Women   | FRIEND database (US)<sup>a</sup> Mean: 7.45 SD: 2.05 | 0.80 (non-adiposity-controlled) | Norwegian HUNT study [57] (women aged 40-59 years) Mean: 10.24 SD: 1.92 | 46.6% |
| Achieve same CRF distribution as most active tertile of age-matched individuals from a Norwegian population-based sample<sup>c</sup> | Men     | FRIEND database (US)<sup>a</sup> Mean: 10.37 SD: 2.76 | 0.80 (non-adiposity-controlled) | Norwegian HUNT study [57] (men aged 40-59 years) Mean: 14.09 SD: 2.31 | 58.4% |
| Achieve same CRF distribution as most active tertile of age-matched individuals from a Norwegian population-based sample<sup>c</sup> | Women | FRIEND database (US)<sup>a</sup> | Mean: 7.45 | SD: 2.05 | 0.80 (non-adiposity-controlled) | Norwegian HUNT study [57] (women aged 40-59 years) | Mean: 11.19 | SD: 2.08 | 55.9 |
|---|---|---|---|---|---|---|---|---|---|
| Elimination of “unfit” category (bottom 25% of CRF) | Men | FRIEND database (US)<sup>a</sup> | Mean: 10.45 | SD: 2.77 | 0.80 (non-adiposity-controlled) | - | PAF<sup>d</sup> 15.3 % |
| Elimination of “unfit” category (bottom 25% of CRF) | Women | FRIEND database (US)<sup>a</sup> | Mean: 7.45 | SD: 2.05 | 0.80 (adiposity-controlled) | - | PAF<sup>d</sup> 11.4 % |

<sup>a</sup>Age-groups combined via The Cochrane Collaboration. Higgins J & Green S (Editors). Cochrane Handbook for Systematic Reviews of Interventions. Table 7.7.a: Formulae for combining groups [55].<sup>b</sup>Feasible minimum risk<sup>c</sup>Plausible minimum risk.<sup>d</sup>PAFs [58] for low cardiorespiratory fitness were calculated by defining the bottom 25% of the population CRF distribution as unfit (<8.4 METs would be classified as unfit for men whereas women with a CRF <6.0 METs would be classified as unfit) based on the U.S. FRIEND database at 40-59 years of age. We then estimated the proportion of total diabetes cases which could theoretically be prevented by changing the cardiorespiratory fitness level of all unfit adults to the fitness level matching the distribution of the population of “fit” individuals (≥25th percentile). RR’s were based on a contrast between the fitness level of the sex-specific 12.5th percentile (the midpoint of the 1st to 25th percentile interval) and the 62.5th percentile (the midpoint of the 25th to 99th percentile) estimated from the restricted cubic spline model. This analysis is comparable to conventional PAF calculations based on eliminating the exposure and “shifting” exposed individuals into matching the distribution of the “non-exposed” reference category (above the sex-specific MET cut-points as specified above). As the PIF is calculated based on a distributional change, rather than complete elimination, it may be preferable over PAFs in the case of a continuous exposure were the minimum risk is achieved at a non-zero exposure level [59]. CRF; cardiorespiratory fitness, PIF; potential impact fraction, PAF; population attributable fraction.
| Study | Country (study name) | Numbers analysed, description and recruitment period of cohort | Men (%) Ethnicity (%) | Age at baseline (years) | Follow-up (years) | Outcome assessment | Cumulative type 2 diabetes incidence | CRF assessment | Estimates from manuscript used in meta-analysis (RR/OR/HR with 95% CI) | Model control |
|-------|----------------------|---------------------------------------------------------------|-----------------------|------------------------|-------------------|-------------------|-----------------------------------|----------------|-----------------------------------------------|----------------|
| Lynch et al., 1996 [2] | Finland Kuopio Ischemic Heart Disease Risk Factor Study | 751 Population-based random sample (78.1 % consenting to study) of men from the town of Kuopio, Finland 1984-1989 | 100% Caucasian | Mean (SD): 51.2 (6.7) Median: 4.2 Range: 3.8 – 5.2 | Clinical assessment | 5.2 % | Maximal graded exercise test on bicycle ergometer | Multivariable + BMI | 0.77 (0.32 – 1.85) 0.26 (0.08 – 0.82) 0.15 (0.03 – 0.79) | Age, baseline FPG, triglyceride, systolic BP, parental history of diabetes, alcohol consumption, BMI |
| Zaccardi et al., 2015 [10] | Finland Kuopio Ischemic Heart Disease Risk Factor Study | 2520 Population-based random sample (78.1 % consenting to study) of men from the town of Kuopio, Finland 1984-1989 | 100% Caucasian | Mean (SD): 53.0 (5.2) Range: 42-60 | Clinical assessment + records linkage | 6.1 % | Maximal graded exercise test on bicycle ergometer | Multivariable + BMI | 0.95 (0.86 – 1.04) | Age, systolic BP, HDL-c, family history of diabetes, smoking, education, socioeconomic status, BMI |
| Katzmarzyk et al., 2007 [3] | Canada Canadian Physical Activity Longitudinal Study | 852 Participants in the Canada Fitness Survey and/or Campbell’s Survey of Well-being in Canada. Sampled to be 46 % Caucasian | Mean (SD): 37.1 (12.2) Range: 18 – 69 | Mean: 15.5 | Self-report | 5.0 % | Sub-maximal graded step-test (modified Canadian Aerobic Fitness Test) | Multivariable - BMI | 0.30 (0.14 – 0.60) | Age, sex, smoking, alcohol intake, parental history of diabetes |
| Study | Location | Population | Sample Size | % Caucasian | Age (Mean, SD) | Maximal graded treadmill test | HR relative to least fit tertile according to age-specific distributions of treadmill time | Other Variables |
|-------|----------|------------|-------------|-------------|---------------|-------------------------------|---------------------------------------------------------------|---------------|
| Sui et al., 2008 [4] | USA Aerobics Center Longitudinal study | 6249 Women participating in a preventive medical evaluation at the Cooper Clinic, Texas. 1971-2004 | 0% Caucasian | Mean (SD): 43.8 (10.0) | Up to 17 | Self-report + Clinical assessment | 2.3% (143 / 6249) | Age, smoking, alcohol intake, hypertension, family history of diabetes, survey-response pattern, BMI |
| Sieverdes et al., 2010 [6] | USA Aerobics Center Longitudinal study | 23,444 Men participating in a preventive medical evaluation at the Cooper Clinic, Texas. 1970-2003 | 100% Caucasian | Mean (SD): 45 (9.8) | 19 (median) | Self-report | 2.5% 589 / 23,444 | Age, examination year, survey response pattern, physical activity, smoking, alcohol consumption, hypercholesterolemia, hypertension, family history of diabetes, family history of CVD, BMI |
| Carnethon et al., 2009 [5] | USA Coronary Artery Risk Development in Young | 3989 Recruitment aimed to obtain a representative sample of | 46% 54% Caucasian 46% | Mean: 24.9 | Up to 20 | Clinical assessment | 6.8% 271 / 3989 | Age, smoking, family history of diabetes, fasting glucose |

**USA Aerobics Center Longitudinal study**

- Sui et al., 2008 [4]
- Sieverdes et al., 2010 [6]
- Carnethon et al., 2009 [5]
| Study | Country | Recruitment Aim | Ethnicity | Age | Maximal Graded Exercise Test | HR per SD Increase | Multivariable + BMI | OR Relative to Least Fit Tertile | Notes |
|-------|---------|-----------------|-----------|-----|----------------------------|-------------------|----------------------|-------------------------------|-------|
| Bantle et al., 2016 [11] | USA | Recruitment aimed to obtain a representative sample of population in four communities 1985-1986 | Black | 44% | Clinical assessment | 25 | 1.06 (0.88 – 1.27) | 1.06 (0.88 – 1.27) | Age, sex, ethnicity, field-center, physical activity, education, smoking, energy intake, diet-quality, BMI |
| Skretteberg et al., 2013 [7] | Norway | Healthy men of five governmental agencies in Oslo 1972-1975 | Caucasian | 100% | Records linkage | 12.1% | 0.71 (0.58 – 0.86) | 0.71 (0.58 – 0.86) | Age, fasting whole-blood glucose, family history of maternal diabetes |
| Kuwahara et al., 2014 [8] | Japan | Employees at a company in Japan participating in an annual health-examination 2003-2005 | Asian | 100% | Clinical assessment | 5.6% | 0.94 (0.65 – 1.35) | 0.94 (0.65 – 1.35) | Age, baseline year, smoking, alcohol consumption, sleep duration, family history of diabetes, hypertension, BMI |
| Juraschek et al., 2015 [9] | USA | | | 52% | Maximal graded | 14.6% | 1.10 (0.76 – 1.59) | 1.10 (0.76 – 1.59) | Age, sex, ethnicity, history of |
| Study                        | Country          | Cohort Description                                                                 | Sample Size | Sex % Distribution | Mean Age (SD) | Records Linkage | Maximal Exercise Test | HR Relative to Most Fit Tertile | Additional Factors Considered                                                                 |
|------------------------------|------------------|-----------------------------------------------------------------------------------|-------------|--------------------|---------------|------------------|-----------------------|---------------------------------|-------------------------------------------------------------------------------------------|
| The FIT (Henry Ford Exercise Testing project) | (11,750 in BMI-subsample) Patients referred to exercise stress-test at Henry Ford Health System Affiliated Subsidiaries in Detroit 1991-2009 | 66 % Caucasians 27 % Black 7 % Other | 52.5 (12.6) | 5.2 (2.6-8.3)      | 6851 / 46,979 | Assumed identical incidence in BMI-subsample | treadmill test (Bruce protocol). | based on distribution of data | Multivariable - BMI 1 0.96 (0.89 – 1.03) 0.77 (0.71 – 0.83) 0.46 (0.41 – 0.51) Multivariable + BMI 1 0.99 (0.88 – 1.11) 0.90 (0.79 – 1.02) 0.64 (0.54 – 0.75) RR per 1-MET increase Multivariable - BMI 0.92 (0.91 – 0.93) RR per 1-MET increase Multivariable + BMI 0.96 (0.94 – 0.97) Hypertension, hypertension medication use, ACE inhibitor use, ARB use, β-blocker use, diuretic use, history of hyperlipidemia, lipid-lowering medication use, statin use, history of obesity, family history of CHD, smoking, physical activity, pulmonary disease medication use, depression medication use, indication for stress testing + BMI in sub-sample |
| Crump et al., 2016 [12] | Sweden | Swedish Military Conscriptio n Registry Study 1,534,425 Men participating in military conscription examination (97-98% of Swedish men) 1969 - 1997 | 100% Caucasians | All 18 Mean: 25.7 Up to 40 | 2.2 % 34,008 / 1,534,425 | Maximal exercise test on bicycle ergometer | HR relative to most fit tertile | Multivariable - BMI 1 1.15 (1.11 – 1.20) 1.72 (1.65 – 1.79) Multivariable + BMI 0.65 (0.64 – 0.67) | Year of military conscription examination, muscular strength, family history of diabetes, education, neighbourhood socioeconomic status, BMI |
| Holtermann et al., 2017 [13] | Denmark | Copenhagen Male Study 4988 Employees at 14 workplaces 1970-1971 | 100 % Caucasians | Mean (SD): 48.7 (5.4) Mean (SD): 28.0 (11.2) | 10.4 % 518 / 4988 | Sub-maximal graded exercise test on bicycle ergometer | HR relative to least fit quartile (additional estimates provided following personal communication ) | Multivariable - BMI 1 0.83 (0.66 – 1.05) 0.61 (0.47 – 0.78) | Age, smoking, status, grams of tobacco per day, systolic BP, diastolic BP, physical activity, alcohol consumption, social class, BMI |
| Study                        | Country     | Sample Size | Participants | Age (Mean ± SD) | Race | Sex (%) | Clinical Assessment | Exercise Test          | HR Relative to Least Fit Quartile | Covariates                                                                                   |
|------------------------------|-------------|-------------|--------------|-----------------|------|---------|--------------------|------------------------|----------------------------------|---------------------------------------------------------------------------------------------|
| Momma et al., 2017 [15]     | Japan       | 7158        | Employees at Tokyo Gas Company participating in law-required health-examinations 1986 | Median (IQR): 37 (32-45) Range: 20-60 | Asian | 100 %   | Clinical assessment | Sub-maximal graded exercise test on bicycle ergometer | 0.86 (0.75 – 0.98)                | Age, systolic BP, family history of diabetes, smoking, alcohol intake, desk work, frequency of CRF measurement, BMI |
| Kawakami et al., 2018 [16]  | Japan       | 7804        | Employees at Tokyo Gas Company participating in law-required health-examinations 1986 | Mean (SD): 38 (10) Range: 19-60 | Asian | 100 %   | Clinical assessment | Sub-maximal graded exercise test on bicycle ergometer | 0.86 (0.75 – 0.98)                | Age, systolic BP, family history of diabetes, smoking, alcohol intake |
| Kokkinos et al., 2017 [14]  | USA         | 4092        | Veterans participating in the ETHOS or VETS studies who are treated with statins 1986-2014 | Mean (SD): 59 (10.8) | Caucasian | 96 % | Black | 26.2 % | Maximal graded treadmill test (Bruce protocol) or individualized ramp protocol | 0.86 (0.75 – 0.98)                | Age, ethnicity, sex, β-blockers, calcium channel blockers, diuretics, ACE inhibitor use, ARB use, smoking, hypertension, sleep apnea, alcohol/drug abuse, BMI |
| Study | Country | Study Details | Participants | Measurement Details | Analysis | Results |
|-------|---------|---------------|--------------|---------------------|----------|---------|
| Ohlson et al., 1988 [17] | Sweden | Gothenburg Male Population study | 766 Individuals born in 1913 with date of birth divisible by 3 and living in the city of Gothenburg (88% of invited participating in study I 1963, 94% of these agreeing in 1967) | 100% Caucasian | Mean: 54 | Clinical assessment 6.1% 47/766 | Multivariable + BMI 1 0.82 (0.70 – 0.95) 0.76 (0.65 – 0.90) 0.66 (0.53 – 0.82) |
| Williams 2008 [18] | USA | National Runners' Health Study | 33,574 Subscribers to a running magazine and participants in running races in the US (approx. 15% of targeted individuals participating in study) | 73% Ethnicity not stated | Approx Mean (SD): 43.1 (10.7) | Self-report Men: 0.68% 197/24,517 Women: 0.23% 28/9057 | Self-reported best 10-km race during previous 5 year Data not harmonizable for inclusion in meta-analysis OR per m/s Multivariable - BMI 0.23 (0.16 – 0.33) Multivariable + BMI + BMI-squared 0.46 (0.31 – 0.67) | Age, follow-up time, intake of red meat, fish, fruit, alcohol intake, physical activity (running distance/week), BMI, BMI-squared |
| Kinney et al., 2014 (abstract only) [19] | USA | COPD Genetic epidemiology study | 7080 Smokers with and without chronic obstructive | Unclear | Approx Mean: 3.2 | Unclear 5.5% 302/7080 | 6 Minute Walk Distance Data not harmonizable for inclusion in meta-analysis HR per 100 feet lower walk distance 0.94 (0.91 – 0.97) | Unclear |
| Study                                                                 | Country          | Participants | Ethnicity | Count | Age | Test Type                                      | Adjusted HR (95% CI)                                      | Additional Factors                                                                 | Other Parameters                                                                 |
|----------------------------------------------------------------------|------------------|--------------|-----------|-------|-----|-----------------------------------------------|----------------------------------------------------------|---------------------------------------------------------------------------------|----------------------------------------------------------------------------------|
| Someya et al., 2014 [20]                                             | Japan            | Male alumni  | Asian     | 570   | 23  | Self-report                                   | 3.9% (22/579)                                             | Multivariable + BMI                                                             | Age, year of graduation, smoking, college sports-club participation, BMI          |
| Department of Physical Education Juntendo University Study 1971-1991 |                  |              |           |       |     | 1500 meters endurance run                     | Data not harmonizable for inclusion in meta-analysis     |                                                                                  |                                                                                  |
| Jae et al., 2016 [21]                                                | South Korea      | Participants | Asian     | 3770  | 47  | Clinical assessment                           | 4.5% (170/3770)                                           | Multivariable - BMI                                                             | Age, FPG, systolic BP, total cholesterol, HDL-c, LDL-c, triglycerides, uric acid, resting heart rate, smoking, alcohol intake, BMI |
| Samsung Medical Center Study                                          |                  |              |           |       |     | Maximal graded treadmill test (Bruce protocol) | Data not harmonizable for inclusion in meta-analysis     |                                                                                  |                                                                                  |
| Study of Past Smokers with an exercise test from the Mayo Clinic, Rochester 1993 - 2010 | USA              | Past smokers | Unclear   | 7090  | 54  | Records linkage                               | 8.0% (567/7090)                                          | Multivariable + BMI                                                             | Age, sex                                                                         |
| Sydo et al., 2016 (abstract only) [22]                                |                  |              |           |       |     | “Exercise test”                                | Data not harmonizable for inclusion in meta-analysis     |                                                                                  |                                                                                  |
| Wu et al., 2018 [23] | Taiwan Armed Forces Study | 27,287 | Member of Taiwan military forces without severe chronic medical conditions or disability participating in annual compulsory health examinations | 85 % Asian | Mean (SD): 33 (6) | All 2 | Clinical assessment | Unclear | 3000 meters endurance run | Data not harmonizable for inclusion in meta-analysis | Significant association observed for men without MetS only. No significant association for men with MetS or for women irrespective of MetS status |

Abbreviations: CRF; cardiorespiratory fitness, RR; relative risk, OR; odds ratio, HR; hazard ratio, SD; standard deviation, BMI; body-mass index, CVD; cardiovascular disease, IQR; inter-quartile range, BP; blood pressure, ACE: angiotensin-converting enzyme inhibitor. ARB: angiotensin II- receptor blocker, CHD; coronary heart disease, MET; metabolic equivalent, FPG; fasting plasma glucose, HDL-c; high-density lipoprotein cholesterol, LDL-c; low-density-lipoprotein cholesterol, FAC; functional aerobic capacity, Mets; metabolic syndrome.
## ESM Table 11. Characteristics of studies included in systematic review of muscular strength

| Study | Country (study name) | Numbers analysed, description and recruitment period of cohort | Men (%) Ethnicity (%) | Age at baseline (years) | Follow-up (years) | Outcome assessment | Cumulative type 2 diabetes incidence | Muscular strength assessment | Estimates from manuscript used in meta-analysis (RR/OR/HR with 95% CI) | Model control |
|-------|----------------------|---------------------------------------------------------------|-----------------------|------------------------|-------------------|-------------------|------------------------|-------------------------------|--------------------------------|-------------------|
| Katzmarzyk et al., 2007 [3] | Canada Canadian Physical Activity Longitudinal Study | 865 Participants in the Canada Fitness Survey and/or Campbell's Survey of Well-being in Canada. Sampled to be representative of the Canadian population 1988 | 46 % Caucasian | Mean (SD): 37.1 (12.2) Range: 18 – 69 | Mean: 15.5 | Self-report | 5.0 % 43 / 865 (calculated based on assumption of identical incidence in sample with data) | Maximal HGS Dynamometer | OR per SD increase (kg) Multivariable - BMI 0.62 (0.33 – 1.20) | Age, sex, smoking, alcohol intake, parental history of diabetes |
| Wander et al., 2011 [25] | USA Japanese-American Community Diabetes Study | 394 Second- and third-generation Japanese Americans of 100% Japanese ancestry Unclear | 53 % Asian | Mean: 51.9 Range: 34-75 | Range: 10-11 | Clinical assessment | 18.5 % 73 / 394 | Maximal HGS Dynamometer | OR per 10-pound increase Multivariable + BMI 1.00 (0.96 – 1.04) | Age, family history of diabetes, sex, BMI |
| Leong et al., 2015 [26] | International Prospective Urban-Rural | 139,691 Representative samples of communities from 17 | 42 % Participant from North America, | Median (IQR): 50 (42-58) | Median (IQR): 4 (2.9 – 5.1) | Records linkage and self-report | 2.1 % 2939 / 139,691 | Maximal HGS Dynamometer | HR per 5-kg decrease Multivariable + BMI 1.04 (1.01 – 1.08) | Age, sex, education level, employment status, physical activity, tobacco use, alcohol use, energy intake, % energy from |
| Study Location | Study Name | Sample Size | Sample Characteristics | Maximal HGS Measurement | HGS Units | Effect Size (95% CI) | Covariates Adjusted For |
|---------------|------------|-------------|------------------------|--------------------------|-----------|----------------------|-------------------------|
| Sweden | Swedish Military Conscript Registry Study | 1,534,425 | Men participating in military conscription examination (97-98% of Swedish men) | 100% Caucasian | All 18 | Mean: 25.7 | 2.2% | Records linkage | HR per 1 N/kg increase | Year of military conscription examination, CRF, family history of diabetes, education, neighbourhood socioeconomic status, BMI |
| UK | English Longitudinal study of Ageing | 5953 | Nationally representative sample of the English population born on or before 1952 | 45% Caucasian | Mean: 66 (9.4) | Median: 5.9 | Self-report | 3.6% | Maximal HGS Dynamometer | HR per SD increase (kg/ kg body-weight) (additional estimates provided following personal communication) | Age, sex, physical activity, smoking, alcohol, depressive symptoms, prevalent CVD |
| USA | The Health, Aging, and Body Composition Study | 2166 | Random sample of Caucasian Medicare beneficiaries and all age-eligible black community residents in selected Pittsburgh and | 47% Caucasian 39% Black | Approx Mean (SD): 73.8 (2.9) | Median: 11.3 | Clinical assessment + self-report | 12.2% | Maximal HGS Dynamometer | HR per SD increase (kg) | Age, ethnicity, clinical site, physical activity, smoking, lipids, hypertension, visceral fat (DXA), total body fat (DXA), BMI |
| Study | Country | Sample Size | Ethnicity | Mean (SD) or Median (IQR) | Follow-up | Clinical Assessment | Maximal HGS Dynamometer | HR or HR per kg increase | Adjusted Variables |
|-------|---------|-------------|-----------|----------------------------|-----------|---------------------|--------------------------|-------------------------|-----------------------|
| Li et al., 2016 [27] | Australia | 1632 | 100% Caucasian | Mean (SD): 54.1 (11.4) | 1st follow-up: 5.5 years (n=2318) 2nd follow-up: 10.7 years (n=1802) | Clinical assessment | Maximal HGS Dynamometer | HR relative to least fit quartile of kg / kg body-weight (additional estimates provided following personal communication) | Multivariable-- BMI 1 0.58 (0.37 – 0.90) 0.45 (0.27 – 0.73) 0.28 (0.15 – 0.50) | Age, sub-cohort, income, physical activity, family history of diabetes, hypertension, BMI |
| Marquez-Vidal et al., 2017 [30] | Switzerland | 2318 | 42% Caucasian | Mean (SD): 60.2 (6.7) | 1st follow-up: 5.5 years (n=2318) 2nd follow-up: 10.7 years (n=1802) | Clinical assessment | Maximal HGS Dynamometer | HR per 5-kg increase | Multivariable + BMI 0.87 (0.78 – 0.97) |
| Karvonen-Gutierrez et al., 2018 [31] | USA | 424 | 0% Caucasian, 40% Black, 60% Black | Mean (SD): 46.4 (2.8) | Median: 8.7 | Clinical assessment | Maximal HGS Dynamometer | HR per 0.1 kg/kg body-weight increase | Multivariable – waist/hip ratio 0.75 (0.65 – 0.86) | Age, race/ethnicity, difficulty paying for basics, smoking status, menopausal status, exogenous hormone use, physical activity (waist/hip ratio) |
| Study | Country | Sample Size | Percentage | Age Range | Method | Follow-up Period | Effect Size (95% CI) | Model Adjusted Variables | Additional Information |
|-------|---------|-------------|------------|-----------|---------|-----------------|----------------------|------------------------|------------------------|
| Nation (SWAN) | USA | 30 | | | Hormones and at least one menstrual period in last 3 months. Black women were oversampled | 1996 | | | |
| Lee et al., 2018 (abstract only) [32] | USA | 4681 | | 1980 - 2006 | Unclear | ACLS is predominantly white males | 4.9% 229 / 4681 | Combined 1-RM leg and bench press | HR per SD increase (kg/ kg body-weight) (additional estimates provided following personal communication) | Age, sex, smoking, alcohol consumption, parental history of diabetes, hypertension, hypercholesterolemia, abnormal electrocardiogram, glucose levels, physical activity, CRF, BMI |
| Momma et al., 2018 [33] | Japan | 21,784 | 69% Asian | 2001-2008 | Individuals participating in annual law-required health-examinations by the Niigata Association of Occupational Health in Niigata, Japan | 4.0% 861 / 21,784 | Maximal HGS Dynamometer | HR per SD increase (kg/ kg body-weight) (additional estimates provided following personal communication) | Age, smoking, alcohol consumption, breakfast skipping, hypertension, dyslipidemia, BMI |
| McGrath et al., 2017 [34] | USA | 1383 | 41% | Up to 19 years | Self-report | Unclear | Maximal HGS | Data not harmonizable for | Education, Employment, |
| Study | Region | Sample Size | Sample Characteristics | Mean (SD) | Clinical Assessment | Maximal HGS | Dynamometer | Additional Information |
|-------|--------|-------------|------------------------|------------|---------------------|-------------|-------------|------------------------|
| Zhang et al., 2018 [35] | China National Physical Education Program, Tianjin | 328 | 48% Asian | 68 (6.1) | Clinical assessment | 56 / 328 | Maximal HGS Dynamometer | Data not harmonizable for inclusion in meta-analysis OR for T2D per unknown increase (kg/kg body-weight) Unadjusted 0.97 (0.93 – 1.00) Multivariable (unknown)-adjusted 0.88 (0.82 – 0.94) Unclear |

**Notes:**
- HGS: handgrip strength
- RR: relative risk
- OR: odds ratio
- HR: hazard ratio
- SD: standard deviation
- BMI: body-mass index
- IQR: inter-quartile-range

Hispanic Established Population for the Epidemiological Study of the Elderly (using data from sensitivity analysis)
Representative sample of non-institutionalized elderly Mexican Americans in five southern US states 1993-1994

| Mean (SD): 73.3 (6.5) | | | Dynamometer | inclusion in meta-analysis HR for T2D for “weak” relative to “strong” Men (weak: ≤0.46 kg/kg): 1.05 (1.02 – 1.09) Women (weak: ≤0.30 kg/kg): 1.38 (1.35 – 1.41) |

Instrumental Activities-of-the-daily living disability, Interview language, marriage status, obesity
| Age Group  | Risk difference per 100,000 people per year | 95% Confidence Interval* |
|------------|--------------------------------------------|-------------------------|
| 18+ years  |                                            |                         |
| Cardiorespiratory fitness (adiposity-controlled) | 54                         | 40 to 68                |
| Cardiorespiratory fitness (non-adiposity controlled) | 134                        | 100 to 170              |
| Muscular strength (adiposity-controlled) | 87                         | 27 to 129               |
| Muscular strength (non-adiposity controlled) | 161                        | 60 to 244               |
| 18-44 years |                                            |                         |
| Cardiorespiratory fitness (adiposity-controlled) | 25                         | 18 to 34                |
| Cardiorespiratory fitness (non-adiposity controlled) | 62                         | 42 to 84                |
| Muscular strength (adiposity-controlled) | 40                         | 12 to 62                |
| Muscular strength (non-adiposity controlled) | 74                         | 3 to 117                |
| 44-64 years |                                            |                         |
| Cardiorespiratory fitness (adiposity-controlled) | 87                         | 64 to 112               |
| Cardiorespiratory fitness (non-adiposity controlled) | 218                        | 150 to 280              |
| Muscular strength (adiposity-controlled) | 142                        | 43 to 211               |
| Muscular strength (non-adiposity controlled) | 262                        | 98 to 399               |
| 65+ years  |                                            |                         |
| Cardiorespiratory fitness (adiposity-controlled) | 75                         | 54 to 98                |
| Cardiorespiratory fitness (non-adiposity controlled) | 188                        | 127 to 246              |
| Muscular strength (adiposity-controlled) | 122                        | 37 to 184               |
| Muscular strength (non-adiposity controlled) | 226                        | 8 to 348                |

Background incidence based in 2015 U.S. [60] *Calculated based on Excel-macro described in Newcombe et al., 2014 [61].
**ESM Table 13.** Omitting, in turn, one study at a time from linear dose-response meta-analysis of cardiorespiratory fitness estimates including control for adiposity

| Study omitted                     | RR  | 95% Confidence interval |
|-----------------------------------|-----|-------------------------|
| Sui et al., 2008 [4]              | 0.92| 0.90 to 0.95            |
| Sieverdes et al., 2010 [6]        | 0.93| 0.91 to 0.95            |
| Kuwahara et al., 2014 [8]         | 0.92| 0.90 to 0.94            |
| Juraschek et al., 2015 [9]        | 0.91| 0.89 to 0.94            |
| Zaccardi et al., 2015 [10]        | 0.92| 0.90 to 0.94            |
| Bantle et al., 2016 [11]          | 0.92| 0.89 to 0.94            |
| Crump et al., 2016 [12]           | 0.92| 0.89 to 0.95            |
| Holtermann et al., 2017 [13]      | 0.92| 0.89 to 0.94            |
| Kokkinos et al., 2017 [14]        | 0.92| 0.90 to 0.95            |
| Momma et al., 2017 [15]           | 0.92| 0.90 to 0.95            |

**ESM Table 14.** Omitting, in turn, one study at a time from linear dose-response meta-analysis of cardiorespiratory fitness estimates excluding control for adiposity

| Study omitted                     | RR  | 95% Confidence interval |
|-----------------------------------|-----|-------------------------|
| Katzmarzyk et al., 2007 [3]       | 0.81| 0.76 to 0.86            |
| Sui et al., 2008 [4]              | 0.81| 0.76 to 0.86            |
| Sieverdes et al., 2010 [6]        | 0.82| 0.77 to 0.87            |
| Carnathon et al., 2009 (Men) [5]   | 0.82| 0.77 to 0.87            |
| Carnathon et al., 2009 (Women) [5] | 0.82| 0.77 to 0.87            |
| Skretteberg et al., 2013 [7]      | 0.80| 0.75 to 0.86            |
| Kuwahara et al., 2014 [8]         | 0.79| 0.74 to 0.85            |
| Juraschek et al., 2015 [9]        | 0.79| 0.74 to 0.84            |
| Holtermann et al., 2017 [13]      | 0.79| 0.74 to 0.85            |
| Kokkinos et al., 2017 [14]        | 0.80| 0.75 to 0.86            |
| Kawakami et al., 2018 [16]        | 0.79| 0.73 to 0.86            |
### ESM Table 15. Omitting, in turn, one study at a time from linear dose-response meta-analysis of muscular strength estimates including control for adiposity

| Study omitted                  | RR  | 95% Confidence Interval |
|--------------------------------|-----|-------------------------|
| Wander et al., 2011 [25]       | 0.86| 0.80 to 0.92            |
| Leong et al., 2015 [26]        | 0.87| 0.80 to 0.94            |
| Crump et al., 2016 [12]        | 0.88| 0.81 to 0.95            |
| Cuthbertson et al., 2016 [28]  | 0.88| 0.80 to 0.95            |
| Larsen et al., 2016 (Men) [29] | 0.87| 0.80 to 0.94            |
| Larsen et al., 2016 (Women) [29]| 0.86| 0.80 to 0.92            |
| Li et al., 2016 [27]           | 0.88| 0.82 to 0.95            |
| Marques-Vidal et al., 2017 [30]| 0.88| 0.82 to 0.95            |
| Karvonen-Gutierrez et al., 2018[31]| 0.88| 0.81 to 0.95            |
| Lee et al., 2018 [32]          | 0.86| 0.79 to 0.92            |
| Momma et al., 2018 (Men) [33]  | 0.88| 0.81 to 0.95            |
| Momma et al., 2018 (Women) [33]| 0.88| 0.81 to 0.95            |

### ESM Table 16. Omitting, in turn, one study at a time from linear dose-response meta-analysis of muscular strength estimates excluding control for adiposity

| Study omitted                  | RR  | 95% Confidence Interval |
|--------------------------------|-----|-------------------------|
| Katzmarzyk et al., 2007 [3]    | 0.77| 0.64 to 0.92            |
| Cuthbertson et al., 2016 [28]  | 0.79| 0.65 to 0.94            |
| Larsen et al., 2016 (Men) [29] | 0.75| 0.62 to 0.90            |
| Larsen et al., 2016 (Women) [29]| 0.72| 0.61 to 0.85            |
| Li et al., 2016 [27]           | 0.79| 0.66 to 0.95            |
| Karvonen-Gutierrez et al., 2018[31]| 0.77| 0.63 to 0.93            |
| Lee et al., 2018 [32]          | 0.73| 0.62 to 0.86            |
| Momma et al., 2018 (Men) [33]  | 0.77| 0.62 to 0.95            |
| Momma et al., 2018 (Women) [33]| 0.77| 0.64 to 0.94            |
ESM Figure 1. Study-specific relative risks per 1-MET increase in cardiorespiratory fitness in model not controlling for adiposity

Study weights are from the random-effects analysis (D+L). Pooled RRs from the random-effects analysis (D+L) and the fixed-effects analysis (I-V) are shown based on 10 cohorts providing non-adiposity controlled estimates. Four of these cohorts provided per 1-MET (or ml O₂ kg⁻¹ min⁻¹, converted to METs) [3, 5, 7, 9] estimates while the linear estimate was modelled using GLST in 6 studies [4, 6, 8, 13, 14, 16]. D+L; DerSimonian and Laird (random-effects model), I-V; inverse variance (fixed effects model).
ESM Figure 2. Relative risk of type 2 diabetes with increasing cardiorespiratory fitness modelled using restricted cubic splines. Estimates are not controlled for adiposity.
ESM Figure 3. Study-specific relative risks per standard deviation increase in muscular strength in model not controlling for adiposity

Study weights are from the random-effects analysis (D+L). Pooled RRs from the random-effects analysis (D+L) and the fixed-effects analysis (I-V) are shown based on 7 cohorts providing non-adiposity controlled estimates. Six of these cohorts provided per unit estimates (harmonized to per SD) [3, 28, 29, 31, 32, 33] while the linear estimate was modelled using GLST in 1 study [27]. D+L, DerSimonian and Laird (random-effects model), I-V; inverse variance (fixed effects-model).
ESM Figure 4. Risk of small-study bias visualized by funnel-plot of cardiorespiratory fitness estimates including control for adiposity

ESM Figure 5. Risk of small-study bias visualized by funnel-plot of cardiorespiratory fitness estimates excluding control for adiposity
ESM Figure 6. Risk of small-study bias visualized by funnel-plot of muscular strength estimates including control for adiposity

ESM Figure 7. Risk of small-study bias visualized by funnel-plot of muscular strength estimates excluding control for adiposity
References

[1] American College of Sports Medicine (2018) ACSM’s guidelines for exercise testing and prescription. 10th Edition. Wolters Kluwer Health, Philadelphia, PA

[2] Lynch J, Helmrich SP, Lakka TA, et al. (1996) Moderately intense physical activities and high levels of cardiorespiratory fitness reduce the risk of non-insulin-dependent diabetes mellitus in middle-aged men. Arch Intern Med 156: 1307-1314

[3] Katzmarzyk PT, Craig CL, Gauvin L (2007) Adiposity, physical fitness and incident diabetes: the physical activity longitudinal study. Diabetologia 50: 538-544

[4] Sui X, Hooker SP, Lee IM, et al. (2008) A prospective study of cardiorespiratory fitness and risk of type 2 diabetes in women. Diabetes care 31: 550-555

[5] Carnethon MR, Sternfeld B, Schreiner PJ, et al. (2009) Association of 20-year changes in cardiorespiratory fitness with incident type 2 diabetes: the coronary artery risk development in young adults (CARDIA) fitness study. Diabetes care 32: 1284-1288

[6] Sieverdes JC, Sui X, Lee DC, et al. (2010) Physical activity, cardiorespiratory fitness and the incidence of type 2 diabetes in a prospective study of men. Br J Sports Med 44: 238-244

[7] Skretteberg PT, Grytten AN, Gjertsen K, et al. (2013) Triglycerides-diabetes association in healthy middle-aged men: modified by physical fitness? A long term follow-up of 1962 Norwegian men in the Oslo Ischemia Study. Diabetes Res Clin Pract 101: 201-209

[8] Kuwahara K, Uehara A, Kurotani K, et al. (2014) Association of cardiorespiratory fitness and overweight with risk of type 2 diabetes in Japanese men. PLoS One 9: e98508

[9] Jurakic SP, Blaha MJ, Blumenthal RS, et al. (2015) Cardiorespiratory fitness and incident diabetes: the FIT (Henry Ford Exercise Testing) project. Diabetes care 38: 1075-1081

[10] Zaccardi F, O’Donovan G, Webb DR, et al. (2015) Cardiorespiratory fitness and risk of type 2 diabetes mellitus: A 23-year cohort study and a meta-analysis of prospective studies. Atherosclerosis 243: 131-137

[11] Bantle AE, Chow LS, Steffen LM, et al. (2016) Association of Mediterranean diet and cardiorespiratory fitness with the development of pre-diabetes and diabetes: the Coronary Artery Risk Development in Young Adults (CARDIA) study. BMJ Open Diabetes Res Care 4: e000229

[12] Crump C, Sundquist J, Winkleby MA, Sieh W, Sundquist K (2016) Physical fitness among Swedish military conscripts and long-term risk for type 2 diabetes mellitus: a cohort study. Ann Intern Med 164: 577-584

[13] Holtermann A, Gyntelberg F, Bauman A, Thorsten Jensen M (2017) Cardiorespiratory fitness, fatness and incident diabetes. Diabetes Res Clin Pract 134: 113-120

[14] Kokkinos P, Fasulis C, Narayan P, et al. (2017) Cardiorespiratory Fitness and Incidence of Type 2 Diabetes in United States Veterans on Statin Therapy. Am J Med 130: 1192-1198

[15] Momma H, Sawada SS, Lee IM, et al. (2017) Consistently High Level of Cardiorespiratory Fitness and Incidence of Type 2 Diabetes. Med Sci Sports Exerc 49: 2048-2055

[16] Kawakami R, Sawada SS, Lee IM, et al. (2018) Long-term Impact of Cardiorespiratory Fitness on Type 2 Diabetes Incidence: A Cohort Study of Japanese Men. J Epidemiol 28: 266-273

[17] Ohlson LO, Larsson B, Bjorntorp P, et al. (1988) Risk factors for type 2 (non-insulin-dependent) diabetes mellitus. Thirteen and one-half years of follow-up of the participants in a study of Swedish men born in 1913. Diabetologia 31: 798-805

[18] Williams PT (2008) Relationship of running intensity to hypertension, hypercholesterolemia, and diabetes. Med Sci Sports Exerc 40: 1740-1748

[19] Kinney GL, Baker E, Klein OL, et al. (2014) Incident diabetes mellitus in heavy smokers. Diabetes 1): A365
Someya Y, Kawai S, Kohmura Y, Aoki K, Daida H (2014) Cardiorespiratory fitness and the incidence of type 2 diabetes: a cohort study of Japanese male athletes. BMC Public Health 14: 493

Jae SY, Franklin BA, Choo J, Yoon ES, Choi YH, Park WH (2016) Fitness, Body Habitus, and the Risk of Incident Type 2 Diabetes Mellitus in Korean Men. Am J Cardiol 117: 585-589

Sydo N, Sydo T, Carta KG, et al. (2016) Cardiovascular fitness reduces the risk of weight-associated comorbidities and all-cause mortality in past smokers. Journal of the American College of Cardiology 1): 1858

Wu CJ, Kao TW, Yang HF, et al. (2018) Predictability of cardiorespiratory fitness on the risk of developing metabolic syndrome and diabetes mellitus in Taiwan adults: preliminary analysis of a cohort study. Obes Res Clin Pract 12: 541–546

Wells GA, Shea B, O’Connell D, et al. (2009) The Newcastle-Ottawa Scale (NOS) for assessing the quality in nonrandomized studies in meta-analyses. Available from http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp, accessed February 2018

Wander PL, Boyko EJ, Leonetti DL, McNeely MJ, Kahn SE, Fujimoto WY (2011) Greater handgrip strength predicts a lower risk of developing type 2 diabetes over 10 years in leaner Japanese Americans. Diabetes Res Clin Pract 92: 261-264

Leong DP, Teo KK, Rangarajan S, et al. (2015) Prognostic value of grip strength: findings from the Prospective Urban Rural Epidemiology (PURE) study. Lancet 386: 266-273

Li JI, Wittert GA, Vincent A, et al. (2016) Muscle grip strength predicts incident type 2 diabetes: Population-based cohort study. Metabolism 65: 883-892

Cuthbertson DJ, Bell JA, Ng SY, Kemp GJ, Kivimaki M, Hamer M (2016) Dynapenic obesity and the risk of incident Type 2 diabetes: the English Longitudinal Study of Ageing. Diabet Med 33: 1052-1059

Larsen BA, Wassel CL, Kritchevsky SB, et al. (2016) Association of Muscle Mass, Area, and Strength With Incident Diabetes in Older Adults: The Health ABC Study. J Clin Endocrinol Metab 101: 1847-1855

Marques-Vidal P, Vollenweider P, Waerber G, Jornayvaz FR (2017) Grip strength is not associated with incident type 2 diabetes mellitus in healthy adults: The CoLaus study. Diabetes Res Clin Pract 132: 144-148

Karvonen-Gutierrez CA, Peng Q, Peterson M, Duchowny K, Nan B, Harlow S (2018) Low grip strength predicts incident diabetes among mid-life women: the Michigan Study of Women’s Health Across the Nation. Age Ageing 47: 685–691

Lee DC, Brellenthin A, Sui X, Blair S (2018) Muscular strength and type 2 diabetes prevention. Circulation 137: MP32 (Abstract)

Momma H, Sawada SS, Kato K, et al. (2018) Physical Fitness Tests and Type 2 Diabetes Among Japanese: A Longitudinal Study From the Niigata Wellness Study. J Epidemiol

McGrath RP, Vincent BM, Snih SA, et al. (2017) The Association Between Handgrip Strength and Diabetes on Activities of Daily Living Disability in Older Mexican Americans. J Aging Health 30: 1305–1318

Zhang W, Yang X, Han P, et al. (2018) Risk Factors for Developing Diabetes among Community Dwelling Elderly with Impaired Fasting Glucaemia after 3 Years. J Diabetes

Carnethon MR, Gidding SS, Nehmge R, Sidney S, Jacobs DR, Jr., Liu K (2003) Cardiorespiratory fitness in young adulthood and the development of cardiovascular disease risk factors. JAMA 290: 3092-3100

Wei M, Gibbons LW, Mitchell TL, Kampert JB, Lee CD, Blair SN (1999) The association between cardiorespiratory fitness and impaired fasting glucose and type 2 diabetes mellitus in men. Ann Intern Med 130: 89-96

Le TD, Bae S, Ed Hsu C, Singh KP, Blair SN, Shang N (2008) Effects of Cardiorespiratory Fitness on Serum Ferritin Concentration and Incidence of Type 2 Diabetes: Evidence from the Aerobics Center Longitudinal Study (ACLS). Rev Diabet Stud 5: 245-252

Lee DC, Sui X, Church TS, Lee IM, Blair SN (2009) Associations of cardiorespiratory fitness and obesity with risks of impaired fasting glucose and type 2 diabetes in men. Diabetes care 32: 257-262
Goodrich KM, Crowley SK, Lee DC, Sui XS, Hooker SP, Blair SN (2012) Associations of cardiorespiratory fitness and parental history of diabetes with risk of type 2 diabetes. Diabetes Res Clin Pract 95: 425-431

Radford NB, DeFina LF, Barlow CE, et al. (2015) Effect of fitness on incident diabetes from statin use in primary prevention. Atherosclerosis 239: 43-49

Sloan RA, Haaland BA, Sawada SS, et al. (2016) A Fit-Fat Index for Predicting Incident Diabetes in Apparently Healthy Men: A Prospective Cohort Study. PLoS One 11: e0157703

Sawada SS, Lee IM, Muto T, Matuszaki K, Blair SN (2003) Cardiorespiratory fitness and the incidence of type 2 diabetes: prospective study of Japanese men. Diabetes care 26: 2918-2922

Sawada SS, Lee IM, Naito H, et al. (2010) Long-term trends in cardiorespiratory fitness and the incidence of type 2 diabetes. Diabetes care 33: 1353-1357

Sawada SS, Lee IM, Naito H, Tsukamoto K, Muto T, Blair SN (2010) Muscular and performance fitness and the incidence of type 2 diabetes: prospective study of Japanese men. J Phys Act Health 7: 627-632

Kawakami R, Sawada SS, Matsushita M, et al. (2014) Reference values for cardiorespiratory fitness and incidence of type 2 diabetes. J Epidemiol 24: 25-30

Sloan RA, Sawada SS, L IM, et al. (2018) The Association of Fit-Fat Index with Incident Diabetes in Japanese Men: A Prospective Cohort Study. Sci Rep 8: 569

Narayan P, Faselis CC, Pittaras A, et al. (2016) Statin therapy, fitness status and risk of type 2 diabetes in hypertensive patients. Journal of the American Society of Hypertension 10 (4 Supplement): e32

Bjornholt JV, Erikssen G, Liestol K, Jervell J, Erikssen J, Thaulow E (2001) Prediction of Type 2 diabetes in healthy middle-aged men with special emphasis on glucose homeostasis. Results from 22.5 years' follow-up. Diabet Med 18: 261-267

Chene G, Thompson SG (1996) Methods for summarizing the risk associations of quantitative variables in epidemiologic studies in a consistent form. Am J Epidemiol 144: 610-621

Fletcher GF, Balady G, Froelicher VF, Hartley LH, Haskell WL, Pollock ML (1995) Exercise standards. A statement for healthcare professionals from the American Heart Association. Writing Group. Circulation 91: 580-615

Sidney S, Haskell WL, Crow R, et al. (1992) Symptom-limited graded treadmill exercise testing in young adults in the CARDIA study. Med Sci Sports Exerc 24: 177-183

Grøntved A, Ried-Larsen M, Ekelund U, Froberg K, Brage S, Andersen LB (2013) Independent and combined association of muscle strength and cardiorespiratory fitness in youth with insulin resistance and beta-cell function in young adulthood: the European Youth Heart Study. Diabetes care 36: 2575-2581

Hamling J, Lee P, Weitkunat R, Ambuhl M (2008) Facilitating meta-analyses by deriving relative effect and precision estimates for alternative comparisons from a set of estimates presented by exposure level or disease category. Stat Med 27: 954-970

The Cochrane Collaboration. Higgins J & Green S (Editors) (2011) Cochrane Handbook for Systematic Reviews of Interventions. Table 7.7.a: Formulae for combining groups. Available from http://handbook-5-1.cochrane.org/, accessed November 2017

Kaminsky LA, Arena R, Myers J (2015) Reference Standards for Cardiorespiratory Fitness Measured With Cardiopulmonary Exercise Testing: Data From the Fitness Registry and the Importance of Exercise National Database. Mayo Clin Proc 90: 1515-1523

Aspenes ST, Nilsen TI, Skaug EA, et al. (2011) Peak oxygen uptake and cardiovascular risk factors in 4631 healthy women and men. Med Sci Sports Exerc 43: 1465-1473

Lee IM, Shiroma EJ, Lobelo F, Puska P, Blair SN, Katzmarzyk PT (2012) Effect of physical inactivity on major non-communicable diseases worldwide: an analysis of burden of disease and life expectancy. Lancet 380: 219-229

Rehm J, Taylor B, Patra J, Gmel G (2006) Avoidable burden of disease: conceptual and methodological issues in substance abuse epidemiology. Int J Methods Psychiatr Res 15: 181-191
[60] Centers for Disease Control and Prevention (CDC) (2017) National Diabetes Statistics Report, 2017: Estimates of Diabetes and Its Burden in the United States. Available from https://www.cdc.gov/diabetes/pdfs/data/statistics/national-diabetes-statistics-report.pdf, accessed October 2017

[61] Newcombe RG, Bender R (2014) Implementing GRADE: calculating the risk difference from the baseline risk and the relative risk. Evid Based Med 19: 6-8