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**Handgrip strength cannot be assumed a proxy for overall muscle strength**

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**Abstract**

**Objectives:** Dynapenia, low muscle strength, is predictive for negative health outcomes and is usually expressed as handgrip strength (HGS). Whether HGS can be a proxy for overall muscle strength and whether this depends on age and health status is controversial. This study assessed the agreement between HGS and knee extension strength (KES) in populations differing in age and health status.

**Design:** Data were retrieved from five cohorts.

**Setting and participants:** Community, geriatric outpatient clinics and a hospital. Five cohorts (960 individuals, 49.8% males) encompassing healthy young and old individuals, geriatric outpatients and older individuals post hip fracture were included.

**Measures:** HGS and KES were measured according to the protocol of each cohort. Pearson correlation was performed to analyse the association between HGS and KES, stratified by sex. HGS and KES were standardized into sex-specific z-scores. The agreement between standardized HGS and standardized KES at population level and individual level were assessed by Intraclass Correlation Coefficients (ICC) and Bland-Altman analysis.

**Results:** Pearson correlation coefficients were low in healthy young (males: 0.36 to 0.45, females: 0.45) and healthy old individuals (males: 0.35 to 0.37, females: 0.44), and moderate in geriatric outpatients (males and females: 0.54) and older individuals post hip fracture (males: 0.44, females: 0.57) ($p<0.05$, except for male older individuals post hip fracture ($p=0.07$)). ICC values were poor to moderate in all populations: i.e. healthy young individuals (0.41, 0.45), healthy old individuals (0.37, 0.41, 0.44), geriatric outpatients (0.54) and older individuals post hip fracture (0.54). Bland-Altman analysis showed that within the same population of age and health status, agreement between HGS and KES varied on individual level.

**Conclusion:** At both population and individual level, HGS and KES showed a low to moderate agreement independently of age and health status. HGS alone should not be assumed a proxy for overall muscle strength.

## Introduction

Measurement of muscle strength is an important part of the comprehensive geriatric assessment (CGA)[1] due to its predictive validity for decline in cognition, mobility and functional status in community-dwelling older individuals.[2-4] Low muscle strength, known as dynapenia, was also associated with an increased risk of postoperative complications, prolonged length of stay and mortality in hospitalized or postsurgical patients.[5, 6] Muscle strength is part of the diagnostic criteria for sarcopenia, which is defined as low muscle mass and low muscle function (muscle strength and/or physical performance), depending on the applied definition.[7]

In clinical practice, quantification of muscle strength in older individuals is predominantly assessed by measuring handgrip strength (HGS) as the measurement is simple and the device is portable and inexpensive.[7] In addition to HGS, muscle strength can be assessed by measurement of knee extension strength (KES) and this method is, however, more technically challenging and not widely accessible.[8] It has been shown that the decline of muscle strength with chronological age is greater for the lower limb muscles than that of the upper limb.[9-11] Previous studies showed a high association between HGS and KES among healthy individuals aged 18-90 years[12-14] and a low association among geriatric outpatients.[15] Furthermore, previous studies used correlation coefficients quantifying the degree to which two variables are related on a population level, but not at individual level.

The aim of this study was to assess the agreement between HGS and KES in various populations of individuals differing in age and health status at population and individual level.

## Methods

*Study design*

Data were derived from five cohorts including 960 individuals encompassing healthy young and old individuals, geriatric outpatients and older individuals post hip fracture.

<u>MyoAge cohort</u>

Healthy young and old individuals were derived from the European MyoAge cohort. The study rationale and design is reported in detail elsewhere.[16] The MyoAge cohort included healthy young (aged 18 to 30 years) and old individuals (aged 69 to 81 years) recruited from five centres located in the United Kingdom (Manchester), France (Paris), The Netherlands (Leiden), Estonia (Tartu) and Finland (Jyväskylä). Exclusion criteria included: inability to walk for a distance of 250 meter, being institutionalised, morbidities (neurological disorders, metabolic diseases, rheumatoid arthritis, recent malignancy, heart failure, coagulation diseases, chronic obstructive pulmonary disease), using immunosuppressive drugs, insulin and anticoagulants, fracture over the previous year, immobilisation for one week over the previous three months, orthopaedic surgery during the past two years or still causing pain or physical limitation. All study centres adopted the same standardized operation procedure to perform the measurements of muscle strength. In the present analysis, data on HGS and KES were available in 181 healthy young individuals and 320 healthy old individuals.

<u>Manchester Metropolitan University (MMU) cohort</u>

This cohort encompasses healthy young and old males aged 18 to 40 years or 60 to 90 years and were recruited as part of a study investigating the nature and extent of motor unit changes in the vastus lateralis of individuals.[17] Young individuals were recruited from the university and local communities around Manchester, United Kingdom (UK). Older individuals were recruited from the local community. Exclusion criteria were: recent history of leg bone fracture, diagnosis with any form of cancer or a stroke within the past two years, immobilization for more than five days within the past four weeks, diagnosis of any neuromuscular disease or dementia at any time, not living independently, body mass index (BMI) <18 or >35 kg/m$^2$. In the present analysis, data on HGS and KES were available in 42 young and 108 old individuals.

DHEAge cohort

This cohort examining oral Dehydroepiandrosterone in older individuals (DHEAge) included healthy females and males aged 60 to 80 years.[18] Individuals attended geriatric consultations in a geriatric outpatient clinic for various symptoms related to aging such as fatigue, memory complaints, pain and anxiety. Data was collected before the administration of DHEA. Exclusion criteria included diseases such as dementia, major depressive state, cardiovascular disorder, respiratory deficiency, Parkinson disease, and endocrine disorder, and antecedent of hormone-dependent cancer. In the present analysis, data on HGS and KES were available in 68 females.

Geriatric outpatients

This inception cohort included community-dwelling older individuals referred due to mobility problems to a geriatric outpatient clinic in a middle-sized teaching hospital (Bronovo Hospital, The Hague, The Netherlands).[19] The CGA included questionnaires and measurements of physical and cognitive function was performed by trained nurses or medical staff. In the present analysis, data on HGS and KES were available in 163 outpatients.

ProMo cohort

This cohort includes community-dwelling older individuals aged 60 years and older with a hip fracture operated at the Central Finland Central Hospital, Finland.[20] Individuals were asked to participate in a randomized controlled trial investigating the effects of a rehabilitation program aiming to restore mobility and functional capacity. Baseline measurements were performed after discharged home from hospital; on average 65±21 days after hip fracture operation. Exclusion criteria included being institutionalised or confined to bed at the time of the fracture, Mini Mental State Examination of <18 points, alcoholism, severe cardiovascular, pulmonary or progressive disease, para-or tetraplegic or severe depression. In the present analysis, data on HGS and KES were available in 78 individuals.

*Characteristics of the different cohorts*

Demographics of individuals were assessed by questionnaires in the MyoAge, ProMo and MMU cohort and by medical charts in the DHEAge cohort and geriatric outpatients. In all cohorts, body weight was measured to the nearest 0.1 kg and height to the nearest 1 mm (to the nearest centimeter for DHEAge cohort). Body composition was assessed by dual-energy X-ray absorptiometry (DXA, MyoAge, DHEAge and MMU cohorts), or by direct segmental multi-frequency bioelectrical impedance analysis (DSM-BIA, geriatric outpatients and ProMo cohort). Fat mass percentage and lean mass percentage were calculated as total fat mass and total lean mass as percentage of total body mass respectively. Appendicular lean mass percentage was calculated as the sum of lean mass in all four limbs as percentage of total body mass. Gait speed was assessed by the six-minute (MyoAge cohort), four-meter (MMU cohort and geriatric outpatients) and ten-meter walking test (ProMo cohort). Gait speed was expressed in meters per second. It was not performed in the DHEAge cohort.

*Measurement of handgrip strength*

HGS was measured using an isometric hand dynamometer (MyoAge cohort and geriatric outpatients: JAMAR, Sammons Preston, Inc., Bolingbrook, IL; MMU cohort: JAMAR, Patterson Medical, Warrenville, IL, USA; DHEAge cohort: Baseline dynamometer; ProMo cohort: Good Strength dynamometer, Metitur Ltd, Palokka, Finland). For the MyoAge cohort, MMU cohort and geriatric outpatients, individuals were instructed to maintain an upright standing position with their arms along the side while holding the dynamometer. For the DHEAge cohort, HGS was assessed according to the American Society of Hand Therapists instructions with individuals being seated and elbow flexed at 90 degrees without support.[21] For the ProMo cohort, individuals were seated with elbow being supported and flexed at 90 degrees. Three trials were performed[22] for left and right hands for all the cohorts except in the ProMo cohort in which HGS were measured from the dominant hand. There was a rest period between trials. For all cohorts, the best performance of all trials was used for analysis and expressed in kilograms.

*Measurement of knee extension strength*

KES was measured using knee extension dynamometer chairs (MyoAge cohort: custom-built devices in the UK, Estonia, and Finland; Forcelink B.V. (Culemborg, The Netherlands) in The Netherlands and an isokinetic dynamometer (Biodex system 3 Pro, Biodex Medical System Inc, Shirley, New York, USA) in France; MMU cohort: custom-built dynamometer; DHEAge cohort: an isokinetic dynamometer (Biodex Medical Systems Inc, Shirley, New York, USA); geriatric outpatients: Forcelink B.V. (Culemborg, The Netherlands); ProMo cohort: a Good Strength dynamometer chair (Metitur Ltd, Palokka, Finland)).

For the MyoAge cohort, three trials of isometric maximal voluntary contraction (MVC) strength measurements of knee extension were performed on the dominant leg with a rest of

90 seconds between efforts. For the MMU cohort, three trials were performed on the right leg with short rest intervals. In the DHEAge cohort, a 3-second maximum isometric strength measurement was performed for each leg. In geriatric outpatients, individuals were asked to push with maximal effort against a cuff positioned just above the talocrural joint. Three trials were performed for each leg. For the abovementioned cohorts, individuals were seated with knees in 90 degrees and the best performance of all trials was used for analysis and expressed in Newton meters. For the ProMo cohort, KES was measured in the fractured and non-fractured side in a sitting position with a knee angle of 120 degrees. Three maximal efforts were conducted separated by 30 seconds rest. The best result of the non-fractured side was used for further analysis and expressed in Newton.

*Ethical approval*

Each study has been approved by the local ethical committees and have been performed in accordance with the ethical standards laid down in the 1964 Declaration of Helsinki. All individuals gave written informed consent, except for geriatric outpatients for whom the need for individuals informed consent was waived by the ethical committee since the study was based on regular care.

*Statistical analysis*

Continuous variables with a normal distribution were presented as mean (standard deviation (SD)) or if not normally distributed as median (interquartile range (IQR)). Categorical variables were presented as number (*n*) and percentage (%).

Analyses were performed stratified by cohort and age, next to a pooled analysis of the five cohorts. At population level, Pearson correlation was performed to analyse the overall association between HGS and KES using the absolute values of maximal HGS and maximal

KES, stratified by sex. Pearson correlation coefficient (r) between 0.3 to 0.5 was considered as low, 0.5 to 0.7 as moderate, and 0.7 to 0.9 as high.[23] For the pooled analysis, data of the ProMo cohort was excluded because KES was presented in a different unit (Newton) than the other cohorts (Newton meters).

To allow comparison between HGS and KES due to different units, HGS and KES were standardized into sex- and country-specific z-scores for the MyoAge cohort and sex-specific z-scores for the other cohorts. Standardization of HGS and KES in each cohort allows comparison between cohorts, even with the use of different assessment methods. For the pooled analysis, cohort-sex-specific z-scores of HGS and cohort-sex-specific z-scores of KES from the five cohorts were used.

Intraclass correlation analysis was carried out to examine the relative agreement between the z-scores of HGS and z-scores of KES. Intraclass Correlation Coefficient (ICC) values were calculated using a two way mixed model of consistency[24] and interpreted as excellent (0.90 or higher), good (0.75 to 0.90), moderate (0.50 to 0.75) or poor (below 0.50)[25]. At individual level, Bland and Altman analysis were used to assess the agreement between z-scores of HGS and z-scores of KES and to visually display the individual dispersion patterns.[26] Differences in z-scores of HGS and z-scores of KES and the 95% limits of agreement (LOA) (mean difference $\pm$ 1.96 SD) were calculated.

Data were analysed using Statistical Package for the Social Sciences, version 24.0 (SPSS Inc. Chicago, IL, USA). Visualization of results was performed using GraphPad Prism 5.01.

## Results

*Characteristics of different cohorts*

Table 1 shows the characteristics of different cohorts, stratified by age. Most of the individuals were living independently (86.3% to 100%) and a low percentage of individuals had excessive alcohol use (0% to 14.0%) or were a current smoker (0% to 15.4%). The prevalence of multimorbidity and polypharmacy was higher in geriatric outpatients and individuals post hip fracture compared to healthy individuals. HGS and KES were lower in geriatric outpatients and older individuals post hip fracture compared to healthy individuals.

*Agreement of handgrip strength and knee extension strength at population level*

A low to moderate positive correlation was found between HGS and KES, stratified by cohort and age and in the pooled analysis ($p<0.05$; $p=0.067$ in male older adults post hip fracture) (Table 2 and Supplementary Figure 1). ICC values between z-scores of HGS and z-scores of KES were poor to moderate, indicating low relative agreement (below 0.8 for all cohorts) (Table 2).

*Agreement of handgrip strength and knee extension strength at individual level*

The 95% LOA of the differences between z-score of HGS and z-score of KES were larger in MyoAge cohort, MMU cohort and DHEAge cohort compared to geriatric outpatients and ProMo cohort, indicating that the agreement between HGS and KES is lower among healthy individuals compared to geriatric outpatients and older individuals post hip fracture (Table 2 and Figure 1). For each cohort, there were individuals with low agreement between HGS and KES i.e. z-score of HGS and z-score of KES outside the 95% LOA: healthy young: 0% to 6.1%, healthy old: 2.9% to 5.6%, geriatric outpatients: 6.1% and older individuals post hip fracture 3.8%. Pooled analysis showed that there were 5.1% of individuals with z-score of

HGS and z-score of KES outside the 95% LOA (Figure 1). Since HGS and KES have been standardized into z-scores, mean differences between z-scores of HGS and z-scores of KES were zero for all cohorts.

## Discussion

This study showed a low to moderate agreement between HGS and KES at population level and individual level for five cohorts differing in age and health status.

Among healthy individuals, the present study showed a low correlation between HGS and KES from Pearson correlation analysis. Previous studies showed strong correlations among 155 individuals aged 20-90 years (males: 0.70, females: 0.82)[12] and among 164 individuals aged 18-85 years (0.77 to 0.96).[13] This discrepancy may be explained by the different inclusion criteria because the aforementioned studies required individuals to be able to walk unaided while the cohorts encompassing healthy individuals in our study included individuals who were able to walk more than 250 m with walking aid permitted[16] or no specific criteria regarding the use of walking aid and walking distance.[17, 18] Another explanation for the discrepancy in correlations is the varied physical activity level of the study population. Studies have shown that a higher daily physical activity level was significantly associated with higher KES but not with HGS in community-dwelling older adults.[27, 28] Another study included only limited number of individuals and found a moderate to strong correlation in 20 healthy young aged 20-32 years (males (n=10): 0.63, females (n=10): 0.83) and a low correlation in 18 healthy old aged 62-82 years (males (n=9): 0.35, females (n=9): 0.05).[14] For geriatric outpatients, the moderate correlation between HGS and KES is in discrepancy with the low correlation (males: 0.35, females: 0.37) in a previous study, which included community-dwelling older individuals with health problems in 3 or 4 domains in functional, somatic, mental and social domains and resulting in larger population variance.[15]

As a result of different rates of decline between HGS and KES across aging,[9-11] it was hypothesized that the agreement between HGS and KES would be weaker in healthy old compared to healthy young. This hypothesis was supported by ICC values being lower and the range of 95% LOA being wider in healthy old compared to healthy young. This is consistent with a cross-sectional study in healthy young and healthy old men with the same level of daily physical activity which revealed that lower limb muscles strength was significantly lower in older men than in young men while upper limbs muscles strength was similar between the age groups.[29] Differences may be further accelerated by using compensation strategies, i.e. extensive use of arm muscles when rising from a chair.[30]

It was expected that the agreement of HGS and KES would be lower as a function of health status. However, ICC values showed higher agreement and Bland-Altman analysis showed a smaller range of 95% LOA in geriatric outpatients and older individuals post hip fracture compared to healthy old. Apart from higher population variance which results in higher ICC values, HGS weakness may increasingly link to KES weakness in lower health status; physiological "floor" effects may further contribute as both HGS and KES may approach their low limits.[31] The result might also be explained by the potentially higher variance in physical activity among healthy old compared to geriatric outpatients and older individuals post hip fracture.

Our findings suggested that measure of a single muscle group should not be regarded as a proxy for overall muscle strength. Even within the same population of age and health status, Bland-Altman analysis showed that the agreement between HGS and KES were lower in some individuals compared to the others. Therefore, it may pose a challenge in using one single muscle group strength measurement as a surrogate of overall muscle strength on an individual basis or in clinical practices.[32] Some feasibility issues such as the availability of standardized protocol and the need for special equipment pose a challenge in measuring KES in clinical practice. However, instrumented KES measurement such as hand-held dynamometry[33] and isokinetic dynamometry[34] should be used instead of manual muscle testing because of its subjectivity and the lack of sensitivity.[35]

Our findings showed a low agreement between HGS and KES, however, whether HGS, KES or both are associated with clinical outcomes was not investigated. A population-based cohort study (n=1755) showed that lower KES in females was associated with increased mortality and hospitalization while lower HGS in males was associated with increased risk of mortality alone.[32] Another study in community-dwelling older females showed that a faster rate of decline in HGS but not KES was predicted of mortality.[36] These results suggest that there were sex-specific differences in the association between HGS and KES, mortality and hospitalization. Another point to be noted is that the reliability and accuracy of measuring HGS and especially KES is not known in our study. Therefore, it remains questionable of whether it is worthwhile to measure both HGS and KES.

A strength of this study is the inclusion of different cohorts representing different age and health status, thereby making the results generalizable to the wider population differing in age and health status. However, HGS and KES was measured using different types of devices and protocols in the cohorts, resulting in the use of different units (Newton meters/Newton or kilograms), which made it necessary to use z-scores in ICC and Bland-Altman analysis. It is recommended that in future studies the measurement of HGS and KES should be conducted according to the same standardized operation procedure to ensure reproducibility and consistency across different studies.

One limitation of this study is that the reliability and accuracy of HGS and KES is unknown. It is difficult to know whether individuals truly gave a maximal voluntary effort in each trial. Different conditions of individuals including pain in joints and osteoarthritis were not registered and could have influenced the muscle strength. In addition, HGS and especially KES measurement are not gold standard to quantify muscle strength.

## Conclusion

A low to moderate agreement between HGS and KES was found as a function of age and health status at population level. Within the same population of age and health status, agreement between HGS and KES also varied on individual level. The use of one muscle group strength measure seems not justified as an indicator of overall limb muscle strength.

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*Authors' contributions*

Study concept and design: EMR, MCT, CGMM, ABM. Acquisition of data: JH, JSM, MP, SS, AS, GB, MP, HG, MVN, CGMM, ABM. Data analysis: SSYY. Contributed to data analysis: EMR, MCT, CGMM, ABM. Interpretation of data: SSYY, EMR, MCT, CGMM. Drafting of the manuscript: SSYY. Critically revision of the manuscript for important intellectual content: EMR, MCT, JH, JSM, MP, SS, AS, GB, MP, HG, MVN, CGMM, ABM. All authors read and approved the final manuscript.

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None of the funders had a role in the study design, methods, data collection, data analysis, interpretation of data or preparation of this manuscript.

*Conflict of interest*

The authors have no conflict of interest.

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**Figure 1.** Bland-Altman plots of z-scores of HGS and z-scores KES

Results are stratified by cohort and age: MyoAge cohort (A: healthy young, B: healthy old), MMU cohort (C: healthy young, D: healthy old), DHEAge cohort (E), geriatric outpatients (F), ProMo cohort (G) and the pooled analysis (H). The solid line represents the mean difference in HGS and KES, while the dashed lines represent the upper and lower 95% limits of agreement (mean difference $\pm$ 1.96 SD). Grey dots represent males and black dots represent females.

**Supplementary Figure 1.** Scatterplot illustrating the correlation between handgrip strength (HGS) and knee extension strength (KES). Results are stratified by cohort and age: MyoAge cohort (A: healthy young, B: healthy old), MMU cohort (C: healthy young, D: healthy old), DHEAge cohort (E), geriatric outpatients (F), ProMo cohort (G) and the pooled analysis (H). Grey lines represent regression line for females and black lines represent regression line for males. Grey dots represent males and black dots represent females.

Table 1

**Table 1.** Characteristics of different cohorts, stratified by age

| | MyoAge cohort | | MMU cohort | | DHEAge cohort | Geriatric outpatients | ProMo cohort |
|---|---|---|---|---|---|---|---|
| | Young | Old | Young | Old | | | |
| | N=181 | N=320 | N=42 | N=108 | N=68 | N=163 | N=78 |
| **Sociodemographics** | | | | | | | |
| Age, years | 23.4 (2.9) | 74.4 (3.2) | 26.2 (4.4) | 72.8 (6.7) | 65.7 (2.7) | 81.7 (7.2) | 79.8 (7.0) |
| Male, n (%) | 85 (47.0) | 161 (50.3) | 42 (100) | 108 (100) | 0 (0) | 64 (39.3) | 18 (23.1) |
| Independent living[a], n (%) | 181 (100) | 320 (100) | 42 (100) | 108 (100) | 68 (100) | 138 (86.3) | 78 (100) |
| **Lifestyle factors** | | | | | | | |
| Excessive alcohol use[b], n (%) | 22 (12.2) | 28 (8.8) | 1 (2.4) | 15 (14.0) | 0 (0) | 7 (4.3) | 0 (0) |
| Current smoking, n (%) | 23 (12.7) | 14 (4.4) | 0 (0) | 4 (3.7) | 0 (0) | 21 (15.4) | 7 (9.0) |
| **Health characteristics** | | | | | | | |
| Multimorbidity[c], n (%) | 0 (0) | 56 (17.5) | 0 (0) | 13 (12.3) | 0 (0) | 60 (38.2) | 68 (87.2) |
| Polypharmacy[d], n (%) | 0 (0) | 23 (7.2) | 0 (0) | 29 (27.3) | 0 (0) | 98 (61.6) | 61 (78.2) |

**Table 1.** (*continued*)

| | MyoAge cohort | | MMU cohort | | DHEAge cohort | Geriatric outpatients | ProMo cohort |
|---|---|---|---|---|---|---|---|
| | Young | Old | Young | Old | | | |
| | N=181 | N=320 | N=42 | N=108 | N=68 | N=163 | N=78 |
| **Body composition** | | | | | | | |
| Height, m | 1.73 (0.09) | 1.67 (0.09) | 1.79 (0.06) | 1.73 (0.06) | 1.61 (0.07) | 1.67 (0.10) | 1.61 (0.09) |
| BMI, $kg/m^2$ | 22.8 (3.0) | 25.6 (3.3) | 25.2 (4.4) | 25.9 (4.1) | 25.3 (3.5) | 25.8 (4.6) | 25.1 (3.5) |
| Fat mass, % | 23.7 (9.1) | 30.5 (8.1) | 17.6 (9.1) | 26.2 (9.9) | 33.6 (6.7) | 31.8 (10.1) | 31.1 (6.5) |
| Lean mass, % | 72.8 (9.1) | 66.6 (8.3) | 79.3 (8.8) | 70.8 (9.7) | 63.1 (6.6) | 63.5 (8.8) | 68.3 (8.0) |
| ALM, % | 33.1 (4.7) | 28.6 (4.1) | 38.7 (4.3) | 32.8 (5.5) | 23.8 (2.8) | 28.0 (4.6) | 28.0 (2.3) |
| **Physical performance** | | | | | | | |
| Gait speed[e], m/s | 1.85 (0.30) | 1.49 (0.23) | 1.28 (0.19) | 1.09 (0.32) | Not available | 0.75 (0.28) | 0.88 (0.26) |
| HGS, kg (Males) | 52.7 (9.3) | 40.3 (7.7) | 53.2 (9.2) | 38.7 (7.9) | Not applicable | 32.9 (5.5) | 28.5 (7.3) |
| HGS, kg (Females) | 33.0 (5.1) | 25.9 (4.9) | Not applicable | Not applicable | 26.7 (4.5) | 21.5 (4.9) | 17.1 (6.7) |
| KES, Nm (Males) | 249.0 (59.8) | 156.6 (42.2) | 249.3 (74.6) | 141.1 (44.6) | Not applicable | 111.1 (42.5) | 285.3 (91.7)[f] |
| KES, Nm (Females) | 149.4 (35.9) | 96.1 (25.0) | Not applicable | Not applicable | 118.0 (31.5) | 61.6 (21.7) | 218.9 (81.9)[f] |

All values are presented as mean (SD) unless indicated otherwise. *BMI* body mass index; *ALM* appendicular lean mass; *HGS* handgrip strength; *KES* knee extension strength

[a] Defined as living at home or serviced apartment

[b] Defined as >21 units/week of alcohol for males and >14 units/week of alcohol for females

[c] Defined as $\geq$ 2 diseases including: MyoAge cohort: hypertension, cardiovascular events, noninsulin-dependent diabetes mellitus, mild chronic obstructive pulmonary disease (COPD), osteoarthritis, arterial surgery and thyroid disease; Geriatric outpatients: hypertension, myocardial infarction, stroke, diabetes, diabetes mellitus, COPD, cancer, Parkinson's disease and rheumatoid arthritis/ osteoarthritis.

[d] Defined as $\geq$ 5 medications

[e] assessed by the six-minute (MyoAge cohort), four-meter (MMU cohort and geriatric outpatients) and ten-meter walking test (ProMo cohort)

[f] Presented as Newton

Table 2

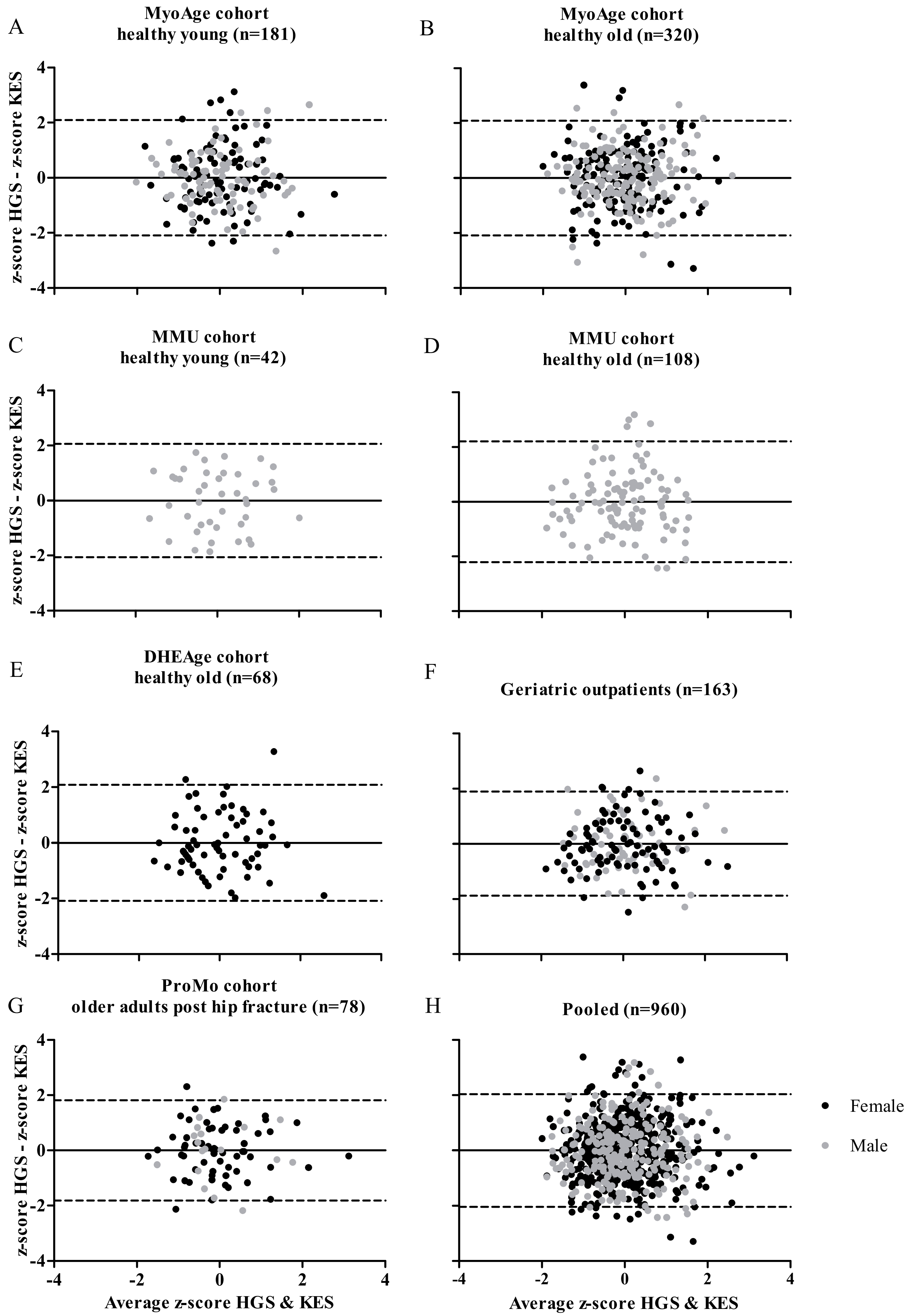
**Table 2.** Agreement of handgrip strength (HGS) and knee extension strength (KES), stratified by cohort and age

| | MyoAge cohort | | MMU cohort | | DHEAge cohort | Geriatric outpatients | ProMo cohort | Pooled |
|---|---|---|---|---|---|---|---|---|
| | Young | Old | Young | Old | | | | |
| | N=181 | N=320 | N=42 | N=108 | N=68 | N=163 | N=78 | N=960 |
| **Pearson correlation[a]** | | | | | | | | |
| *R* (Males) | 0.36* | 0.35* | 0.45* | 0.37* | NA | 0.54* | 0.44 | 0.67* |
| *R* (Females) | 0.45* | 0.44* | NA | NA | 0.44* | 0.54* | 0.57* | 0.69* |
| **Intraclass correlation** | | | | | | | | |
| ICC | 0.41 | 0.41 | 0.45 | 0.37 | 0.44 | 0.54 | 0.54 | 0.44 |
| 95% CI | 0.27-0.52 | 0.32-0.50 | 0.17-0.66 | 0.19-0.52 | 0.22-0.61 | 0.42-0.64 | 0.36-0.68 | 0.39-0.49 |
| **Bland-Altman, 95% LOA** | | | | | | | | |
| Lower | -2.09 | -2.09 | -2.06 | -2.21 | -2.08 | -1.88 | -1.87 | -2.04 |
| Upper | 2.09 | 2.09 | 2.06 | 2.21 | 2.08 | 1.88 | 1.87 | 2.04 |

*R* Pearson Correlation coefficient*; ICC* intraclass correlation coefficient*; CI* confidence interval*; LOA* limits of agreement; *NA* not applicable.

Pearson correlation was performed to analyse the overall association between HGS and KES using the absolute values of maximal HGS and maximal KES, stratified by sex. Intraclass correlation was performed for standardized HGS and standardized KES (sex- and country specific z-scores for MyoAge and sex-specific z-scores for other cohorts). Bland-and-Altman analysis was performed for standardized HGS minus standardized KES. LOA was calculated by the mean difference $\pm$ 1.96 * standard deviation. *$p<0.05$. [a]For the Pearson correlation pooled analysis, data of the ProMo cohort were excluded because KES was presented in a different unit (Newton) than the other cohorts (Newton meters).

Figure 1



A
MyoAge cohort
healthy young (n=181)
B
MyoAge cohort
healthy old (n=320)
C
MMU cohort
healthy young (n=42)
D
MMU cohort
healthy old (n=108)
E
DHEAge cohort
healthy old (n=68)
F
Geriatric outpatients (n=163)
G
ProMo cohort
older adults post hip fracture (n=78)
H
Pooled (n=960)
z-score HGS - z-score KES
Average z-score HGS & KES
Female
Male
4
2
0
-2
-4

Supplementary Figure 1