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Author(s): Yeung, Suey S.Y.; Reijnierse, Esmee M.; Trappenburg, Marijke C.; Hogrel, Jean-Yves; McPhee, Jamie S.; Piasecki, Mathew; Sipilä, Sarianna; Salpakoski, Anu; Butler-Browne, Gillian; Pääsuke, Mati; Gapeyeva, Helena; Narici, Marco V.; Meskers, Carel G.M.; Maier, Andrea B.

Title: Handgrip Strength Cannot Be Assumed a Proxy for Overall Muscle Strength

Year: 2018

Version: Accepted version (Final draft)

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Please cite the original version:

Yeung, S. S., Reijnierse, E. M., Trappenburg, M. C., Hogrel, J.-Y., McPhee, J. S., Piasecki, M., Sipilä, S., Salpakoski, A., Butler-Browne, G., Pääsuke, M., Gapeyeva, H., Narici, M. V., Meskers, C. G., & Maier, A. B. (2018). Handgrip Strength Cannot Be Assumed a Proxy for Overall Muscle Strength. *Journal of the American Medical Directors Association*, 19(8), 703-709.
<https://doi.org/10.1016/j.jamda.2018.04.019>

Handgrip strength cannot be assumed a proxy for overall muscle strength

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Running title: Measurement of muscle strength

Keywords: muscle strength; knee extension strength; aged; geriatric assessment

Funding sources: This study was supported by the seventh framework program MYOAGE (HEALTH-2007-2.4.5-10), the UK Medical Research Council (MR/K025252/1) as part of the Lifelong Health and Wellbeing initiative, the Dutch Technology Foundation STW, and The Ministry of Education and Culture, Kela-The Social Insurance Institution of Finland, Juho Vainio Foundation. This study was also supported by the PANINI program (Horizon 2020, Marie Curie, Sklodowska, Innovative Training Network, No. 675003)

1 **Abstract**

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

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

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

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

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

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

28 **Introduction**

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

37 In clinical practice, quantification of muscle strength in older individuals is
38 predominantly assessed by measuring handgrip strength (HGS) as the measurement is simple
39 and the device is portable and inexpensive.⁷ In addition to HGS, muscle strength can be
40 assessed by measurement of knee extension strength (KES) and this method is, however,
41 more technically challenging and not widely accessible.⁸ It has been shown that the decline of
42 muscle strength with chronological age is greater for the lower limb muscles than that of the
43 upper limb.⁹⁻¹¹ Previous studies showed a high association between HGS and KES among
44 healthy individuals aged 18-90 years¹²⁻¹⁴ and a low association among geriatric outpatients.¹⁵
45 Furthermore, previous studies used correlation coefficients quantifying the degree to which
46 two variables are related on a population level, but not at individual level.

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

50 **Methods**

51 *Study design*

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

54

55 MyoAge cohort

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

69

70 Manchester Metropolitan University (MMU) cohort

71 This cohort encompasses healthy young and old males aged 18 to 40 years or 60 to 90 years
72 and were recruited as part of a study investigating the nature and extent of motor unit changes
73 in the vastus lateralis of individuals.¹⁷ Young individuals were recruited from the university
74 and local communities around Manchester, United Kingdom (UK). Older individuals were

75 recruited from the local community. Exclusion criteria were: recent history of leg bone
76 fracture, diagnosis with any form of cancer or a stroke within the past two years,
77 immobilization for more than five days within the past four weeks, diagnosis of any
78 neuromuscular disease or dementia at any time, not living independently, body mass index
79 (BMI) <18 or >35 kg/m². In the present analysis, data on HGS and KES were available in 42
80 young and 108 old individuals.

81

82 DHEAge cohort

83 This cohort examining oral Dehydroepiandrosterone in older individuals (DHEAge) included
84 healthy females and males aged 60 to 80 years.¹⁸ Individuals attended geriatric consultations
85 in a geriatric outpatient clinic for various symptoms related to aging such as fatigue, memory
86 complaints, pain and anxiety. **Data was collected before the administration of DHEA.**

87 Exclusion criteria included diseases such as dementia, major depressive state, cardiovascular
88 disorder, respiratory deficiency, Parkinson disease, and endocrine disorder, and antecedent of
89 hormone-dependent cancer. In the present analysis, data on HGS and KES were available in
90 68 females.

91

92 Geriatric outpatients

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

98 ProMo cohort

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

108

109 *Characteristics of the different cohorts*

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

122 *Measurement of handgrip strength*

123 HGS was measured using an isometric hand dynamometer (MyoAge cohort and geriatric
124 outpatients: JAMAR, Sammons Preston, Inc., Bolingbrook, IL; MMU cohort: JAMAR,
125 Patterson Medical, Warrenville, IL, USA; DHEAge cohort: Baseline dynamometer; ProMo
126 cohort: Good Strength dynamometer, Metitur Ltd, Palokka, Finland). For the MyoAge
127 cohort, MMU cohort and geriatric outpatients, individuals were instructed to maintain an
128 upright standing position with their arms along the side while holding the dynamometer. For
129 the DHEAge cohort, HGS was assessed according to the American Society of Hand
130 Therapists instructions with individuals being seated and elbow flexed at 90 degrees without
131 support.²¹ For the ProMo cohort, individuals were seated with elbow being supported and
132 flexed at 90 degrees. Three trials were performed²² for left and right hands for all the cohorts
133 except in the ProMo cohort in which HGS were measured from the dominant hand. There
134 was a rest period between trials. For all cohorts, the best performance of all trials was used
135 for analysis and expressed in kilograms.

136

137 *Measurement of knee extension strength*

138 KES was measured using knee extension dynamometer chairs (MyoAge cohort: custom-built
139 devices in the UK, Estonia, and Finland; Forcelink B.V. (Culemborg, The Netherlands) in
140 The Netherlands and an isokinetic dynamometer (Biodex system 3 Pro, Biodex Medical
141 System Inc, Shirley, New York, USA) in France; MMU cohort: custom-built dynamometer;
142 DHEAge cohort: an isokinetic dynamometer (Biodex Medical Systems Inc, Shirley, New
143 York, USA); geriatric outpatients: Forcelink B.V. (Culemborg, The Netherlands); ProMo
144 cohort: a Good Strength dynamometer chair (Metitur Ltd, Palokka, Finland)).
145 For the MyoAge cohort, three trials of isometric maximal voluntary contraction (MVC)
146 strength measurements of knee extension were performed on the dominant leg with a rest of

147 90 seconds between efforts. For the MMU cohort, three trials were performed on the right leg
148 with short rest intervals. In the DHEAge cohort, a 3-second maximum isometric strength
149 measurement was performed for each leg. In geriatric outpatients, individuals were asked to
150 push with maximal effort against a cuff positioned just above the talocrural joint. Three trials
151 were performed for each leg. For the abovementioned cohorts, individuals were seated with
152 knees in 90 degrees and the best performance of all trials was used for analysis and expressed
153 in Newton meters. For the ProMo cohort, KES was measured in the fractured and non-
154 fractured side in a sitting position with a knee angle of 120 degrees. Three maximal efforts
155 were conducted separated by 30 seconds rest. The best result of the non-fractured side was
156 used for further analysis and expressed in Newton.

157

158 *Ethical approval*

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

164

165 *Statistical analysis*

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

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

172 KES, stratified by sex. Pearson correlation coefficient (r) between 0.3 to 0.5 was considered
173 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
174 ProMo cohort was excluded because KES was presented in a different unit (Newton) than the
175 other cohorts (Newton meters).

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

182 Intraclass correlation analysis was carried out to examine the relative agreement
183 between the z-scores of HGS and z-scores of KES. Intraclass Correlation Coefficient (ICC)
184 values were calculated using a two way mixed model of consistency²⁴ and interpreted as
185 excellent (0.90 or higher), good (0.75 to 0.90), moderate (0.50 to 0.75) or poor (below
186 0.50)²⁵. At individual level, Bland and Altman analysis were used to assess the agreement
187 between z-scores of HGS and z-scores of KES and to visually display the individual
188 dispersion patterns.²⁶ Differences in z-scores of HGS and z-scores of KES and the 95% limits
189 of agreement (LOA) (mean difference \pm 1.96 SD) were calculated.

190 Data were analysed using Statistical Package for the Social Sciences, version 24.0
191 (SPSS Inc. Chicago, IL, USA). Visualization of results was performed using GraphPad Prism
192 5.01.

193 **Results**

194 *Characteristics of different cohorts*

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

201

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

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

208

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

210 The 95% LOA of the differences between z-score of HGS and z-score of KES were larger in
211 MyoAge cohort, MMU cohort and DHEAge cohort compared to geriatric outpatients and
212 ProMo cohort, indicating that the agreement between HGS and KES is lower among healthy
213 individuals compared to geriatric outpatients and older individuals post hip fracture (Table 2
214 and Figure 1). For each cohort, there were individuals with low agreement between HGS and
215 KES i.e. z-score of HGS and z-score of KES outside the 95% LOA: healthy young: 0% to
216 6.1%, healthy old: 2.9% to 5.6%, geriatric outpatients: 6.1% and older individuals post hip
217 fracture 3.8%. Pooled analysis showed that there were 5.1% of individuals with z-score of

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

221 **Discussion**

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

224 Among healthy individuals, the present study showed a low correlation between HGS
225 and KES from Pearson correlation analysis. Previous studies showed strong correlations
226 among 155 individuals aged 20-90 years (males: 0.70, females: 0.82)¹² and among 164
227 individuals aged 18-85 years (0.77 to 0.96).¹³ This discrepancy may be explained by the
228 different inclusion criteria because the aforementioned studies required individuals to be able
229 to walk unaided while the cohorts encompassing healthy individuals in our study included
230 individuals who were able to walk more than 250 m with walking aid permitted¹⁶ or no
231 specific criteria regarding the use of walking aid and walking distance.^{17, 18} Another
232 explanation for the discrepancy in correlations is the varied physical activity level of the
233 study population. Studies have shown that a higher daily physical activity level was
234 significantly associated with higher KES but not with HGS in community-dwelling older
235 adults.^{27, 28} Another study included only limited number of individuals and found a moderate
236 to strong correlation in 20 healthy young aged 20-32 years (males (n=10): 0.63, females
237 (n=10): 0.83) and a low correlation in 18 healthy old aged 62-82 years (males (n=9): 0.35,
238 females (n=9): 0.05).¹⁴ For geriatric outpatients, the moderate correlation between HGS and
239 KES is in discrepancy with the low correlation (males: 0.35, females: 0.37) in a previous
240 study, which included community-dwelling older individuals with health problems in 3 or 4
241 domains in functional, somatic, mental and social domains and resulting in larger population
242 variance.¹⁵

243 As a result of different rates of decline between HGS and KES across aging,⁹⁻¹¹ it was
244 hypothesized that the agreement between HGS and KES would be weaker in healthy old
245 compared to healthy young. This hypothesis was supported by ICC values being lower and

246 the range of 95% LOA being wider in healthy old compared to healthy young. This is
247 consistent with a cross-sectional study in healthy young and healthy old men with the same
248 level of daily physical activity which revealed that lower limb muscles strength was
249 significantly lower in older men than in young men while upper limbs muscles strength was
250 similar between the age groups.²⁹ Differences may be further accelerated by using
251 compensation strategies, i.e. extensive use of arm muscles when rising from a chair.³⁰

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

261 Our findings suggested that measure of a single muscle group should not be regarded
262 as a proxy for overall muscle strength. Even within the same population of age and health
263 status, Bland-Altman analysis showed that the agreement between HGS and KES were lower
264 in some individuals compared to the others. Therefore, it may pose a challenge in using one
265 single muscle group strength measurement as a surrogate of overall muscle strength on an
266 individual basis or in clinical practices.³² Some feasibility issues such as the availability of
267 standardized protocol and the need for special equipment pose a challenge in measuring KES
268 in clinical practice. However, instrumented KES measurement such as hand-held
269 dynamometry³³ and isokinetic dynamometry³⁴ should be used instead of manual muscle
270 testing because of its subjectivity and the lack of sensitivity.³⁵

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

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

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

294 **Conclusion**

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

299 **Acknowledgements**

300 We thank Marjon Stijntjes, Jantsje Pasma, Astrid Bijlsma, Yoann Barnouin, Thomas Maden-
301 Wilkinson, Alex Ireland and Thomas Maden-Wilkinson for their contribution to collect the
302 data.

303 *Authors' contributions*

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

310 *Sponsor's role*

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

313 *Conflict of interest*

314 The authors have no conflict of interest.

315 *Funding sources*

316 This study was supported by the seventh framework program MYOAGE (HEALTH-2007-
317 2.4.5-10), the UK Medical Research Council (MR/K025252/1) as part of the Lifelong Health
318 and Wellbeing initiative, the Dutch Technology Foundation STW, and The Ministry of
319 Education and Culture, Kela-The Social Insurance Institution of Finland, Juho Vainio
320 Foundation. This study was also supported by the PANINI program (Horizon 2020, Marie
321 Curie, Sklodowska, Innovative Training Network, No. 675003).

322 **References**

- 323 1. Welsh TJ, Gordon AL and Gladman JR. Comprehensive geriatric assessment--a guide
324 for the non-specialist. *Int J Clin Pract.* 2014; 68(3):290-293.
- 325 2. Rijk JM, Roos PR, Deckx L, et al. Prognostic value of handgrip strength in people
326 aged 60 years and older: A systematic review and meta-analysis. *Geriatr Gerontol Int.* 2016;
327 16(1):5-20.
- 328 3. Taekema DG, Ling CH, Kurrle SE, et al. Temporal relationship between handgrip
329 strength and cognitive performance in oldest old people. *Age Ageing.* 2012; 41(4):506-512.
- 330 4. Bijlsma AY, Pasma JH, Lambers D, et al. Muscle strength rather than muscle mass is
331 associated with standing balance in elderly outpatients. *J Am Med Dir Assoc.* 2013;
332 14(7):493-498.
- 333 5. Bohannon RW. Hand-grip dynamometry predicts future outcomes in aging adults. *J*
334 *Geriatr Phys Ther.* 2008; 31(1):3-10.
- 335 6. Ling CH, Taekema D, de Craen AJ, et al. Handgrip strength and mortality in the
336 oldest old population: the Leiden 85-plus study. *CMAJ.* 2010; 182(5):429-435.
- 337 7. Cruz-Jentoft AJ, Baeyens JP, Bauer JM, et al. Sarcopenia: European consensus on
338 definition and diagnosis: Report of the European Working Group on Sarcopenia in Older
339 People. *Age Ageing.* 2010; 39(4):412-423.
- 340 8. Martin HJ, Yule V, Syddall HE, et al. Is Hand-Held Dynamometry Useful for the
341 Measurement of Quadriceps Strength in Older People? A Comparison with the Gold Standard
342 Biodex Dynamometry. *Gerontology.* 2006; 52(3):154-159.
- 343 9. Frontera WR, Hughes VA, Fielding RA, et al. Aging of skeletal muscle: a 12-yr
344 longitudinal study. *J Appl Physiol (1985).* 2000; 88(4):1321-1326.
- 345 10. Lynch NA, Metter EJ, Lindle RS, et al. Muscle quality. I. Age-associated differences
346 between arm and leg muscle groups. *J Appl Physiol.* 1999; 86(1):188-194.

- 347 11. Candow DG and Chilibeck PD. Differences in size, strength, and power of upper and
348 lower body muscle groups in young and older men. *J Gerontol A Biol Sci Med Sci*. 2005;
349 60(2):148-156.
- 350 12. Samson MM, Meeuwse IB, Crowe A, et al. Relationships between physical
351 performance measures, age, height and body weight in healthy adults. *Age Ageing*. 2000;
352 29(3):235-242.
- 353 13. Bohannon RW, Magasi SR, Bubela DJ, et al. Grip and Knee extension muscle
354 strength reflect a common construct among adults. *Muscle Nerve*. 2012; 46(4):555-558.
- 355 14. Samuel D, Wilson K, Martin HJ, et al. Age-associated changes in hand grip and
356 quadriceps muscle strength ratios in healthy adults. *Aging Clin Exp Res*. 2012; 24(3):245-
357 250.
- 358 15. Chan OYA, van Houwelingen AH, Gussekloo J, et al. Comparison of quadriceps
359 strength and handgrip strength in their association with health outcomes in older adults in
360 primary care. *Age*. 2014; 36(5):9714.
- 361 16. McPhee JS, Hogrel J-Y, Maier AB, et al. Physiological and functional evaluation of
362 healthy young and older men and women: design of the European MyoAge study.
363 *Biogerontology*. 2013; 14(3):325-337.
- 364 17. Piasecki M, Ireland A, Stashuk D, et al. Age-related neuromuscular changes affecting
365 human vastus lateralis. *J Physiol*. 2016; 594(16):4525-4536.
- 366 18. Baulieu EE, Thomas G, Legrain S, et al. Dehydroepiandrosterone (DHEA), DHEA
367 sulfate, and aging: contribution of the DHEAge Study to a sociobiomedical issue. *Proc Natl*
368 *Acad Sci U S A*. 2000; 97(8):4279-4284.
- 369 19. Reijnierse EM, Trappenburg MC, Leter MJ, et al. The association between parameters
370 of malnutrition and diagnostic measures of sarcopenia in geriatric outpatients. *Plos One*.
371 2015; 10(8):e0135933.

- 372 20. Salpakoski A, Tormakangas T, Edgren J, et al. Effects of a multicomponent home-
373 based physical rehabilitation program on mobility recovery after hip fracture: a randomized
374 controlled trial. *J Am Med Dir Assoc.* 2014; 15(5):361-368.
- 375 21. Fess EE. *Clinical Assessment recommendations.* 2 ed. (Chicago: American Society of
376 Hand Therapists).
- 377 22. Reijnierse EM, de Jong N, Trappenburg MC, et al. Assessment of maximal handgrip
378 strength: how many attempts are needed? *Journal of cachexia, sarcopenia and muscle.* 2017;
379 8(3): 466-474.
- 380 23. Mukaka MM. Statistics corner: A guide to appropriate use of correlation coefficient in
381 medical research. *Malawi Med J.* 2012; 24(3):69-71.
- 382 24. Shrout PE and Fleiss JL. Intraclass correlations: uses in assessing rater reliability.
383 *Psychol Bull.* 1979; 86(2):420-428.
- 384 25. Koo TK and Li MY. A guideline of selecting and reporting intraclass correlation
385 coefficients for reliability research. *J Chiropr Med.* 2016; 15(2):155-163.
- 386 26. Bland JM and Altman DG. Statistical methods for assessing agreement between two
387 methods of clinical measurement. *The Lancet.* 1986; 1:307-310.
- 388 27. Ikenaga M, Yamada Y, Takeda N, et al. Dynapenia, gait speed and daily physical
389 activity measured using triaxial accelerometer in older Japanese men. *The Journal of Physical*
390 *Fitness and Sports Medicine.* 2014; 3(1):147-154.
- 391 28. Aoyagi Y, Park H, Watanabe E, et al. Habitual physical activity and physical fitness
392 in older Japanese adults: the Nakanojo Study. *Gerontology.* 2009; 55(5):523-531.
- 393 29. Nogueira FRD, Libardi CA, Vechin FC, et al. Comparison of maximal muscle
394 strength of elbow flexors and knee extensors between younger and older men with the same
395 level of daily activity. *Clin Interv Aging.* 2013; 8:401-407.

- 396 30. Macaluso A and De Vito G. Muscle strength, power and adaptations to resistance
397 training in older people. *Eur J Appl Physiol.* 2004; 91(4):450-472.
- 398 31. Kallman DA, Plato CC and Tobin JD. The Role of Muscle Loss in the Age-Related
399 Decline of Grip Strength - Cross-Sectional and Longitudinal Perspectives. *J Gerontol.* 1990;
400 45(3):M82-M88.
- 401 32. Guadalupe-Grau A, Carnicero JA, Gomez-Cabello A, et al. Association of regional
402 muscle strength with mortality and hospitalisation in older people. *Age Ageing.* 2015;
403 44(5):790-795.
- 404 33. Stark T, Walker B, Phillips JK, et al. Hand-held dynamometry correlation with the
405 gold standard isokinetic dynamometry: a systematic review. *PM R.* 2011; 3(5):472-479.
- 406 34. Hartmann A, Knols R, Murer K, et al. Reproducibility of an isokinetic strength-testing
407 protocol of the knee and ankle in older adults. *Gerontology.* 2009; 55(3):259-268.
- 408 35. Bohannon RW. Manual muscle testing: does it meet the standards of an adequate
409 screening test? *Clin Rehabil.* 2005; 19(6):662-667.
- 410 36. Xue QL, Beamer BA, Chaves PH, et al. Heterogeneity in rate of decline in grip, hip,
411 and knee strength and the risk of all-cause mortality: the Women's Health and Aging Study
412 II. *J Am Geriatr Soc.* 2010; 58(11):2076-2084.

413 **Figure 1.** Bland-Altman plots of z-scores of HGS and z-scores KES
414 Results are stratified by cohort and age: MyoAge cohort (A: healthy young, B: healthy old),
415 MMU cohort (C: healthy young, D: healthy old), DHEAge cohort (E), geriatric outpatients
416 (F), ProMo cohort (G) and the pooled analysis (H). The solid line represents the mean
417 difference in HGS and KES, while the dashed lines represent the upper and lower 95% limits
418 of agreement (mean difference \pm 1.96 SD). Grey dots represent males and black dots
419 represent females.

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

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 ^f , 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 ≥ 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 ≥ 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. Agreement of handgrip strength (HGS) and knee extension strength (KES), stratified by cohort and age

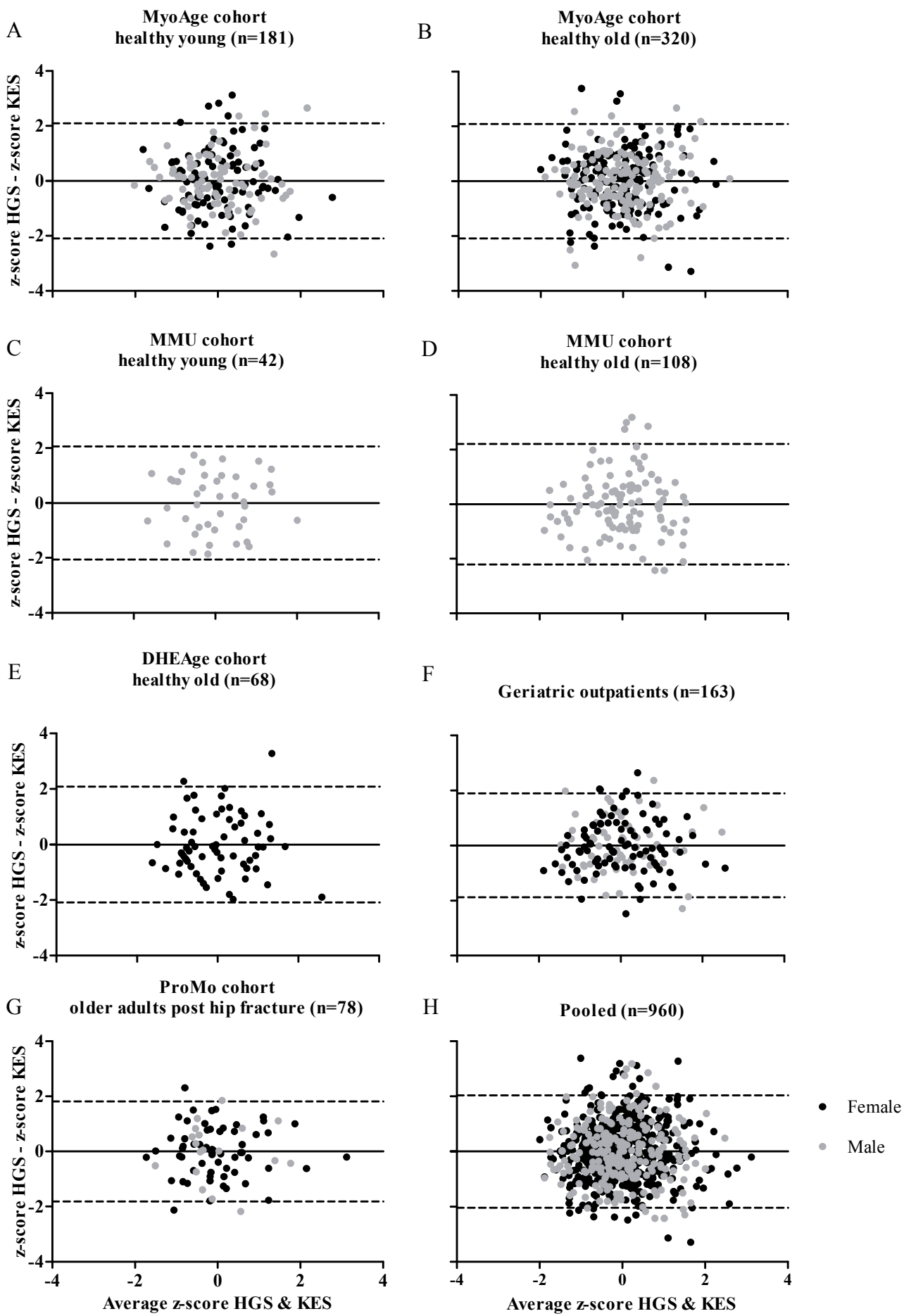
	MyoAge cohort		MMU cohort		DHEAge cohort	Geriatric outpatients	ProMo cohort	Pooled
	Young	Old	Young	Old				
	N=181	N=320	N=42	N=108	N=68	N=163	N=78	N=960
Pearson correlation^a								
<i>R</i> (Males)	0.36*	0.35*	0.45*	0.37*	NA	0.54*	0.44	0.67*
<i>R</i> (Females)	0.45*	0.44*	NA	NA	0.44*	0.54*	0.57*	0.69*
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 ± 1.96 * standard deviation. *p<0.05. ^aFor 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



Supplementary Figure 1

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