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1	Performance declines are accelerated in the oldest-old track and field athletes
2	80 to 94 years of age
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4	Original investigation
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6	Bergita Ganse ^{1*} , Michael Drey ² , Frank Hildebrand ³ , Matthias Knobe ⁴ , Hans Degens ^{1,5}
7	
8	¹ Manchester Metropolitan University, Research Centre for Musculoskeletal Science & Sports
9	Medicine, Manchester, United Kingdom
10	² Department of Medicine IV, University Hospital, LMU Munich, Munich, Germany
11	³ RWTH Aachen University Hospital, Department of Orthopaedic Trauma Surgery, Aachen,
12	Germany
13	⁴ Department of Orthopaedic and Trauma Surgery, Lucerne Cantonal Hospital, Switzerland
14	⁵ Institute of Sport Science and Innovations, Lithuanian Sports University, Kaunas, Lithuania
15	
16	Word count:
17	
18	* address for correspondence and reprints:
19	PD Dr. Bergita Ganse
20	Manchester Metropolitan University
21	Research Centre for Musculoskeletal Science & Sports Medicine
22	Faculty of Science and Engineering
23	John Dalton Building

- 24 Manchester M15GD
- 25 United Kingdom
- 26 Phone: +49 1755300960
- 27 E-mail: b.ganse@mmu.ac.uk
- 28
- 29 Keywords: aging, athletics, activity, running, longevity, age

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31 **Abbreviated title:** The oldest-old track and field athletes

32 ABSTRACT

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Physical performance declines with age, even in exercising, healthy older individuals without 34 major illnesses or orthopaedic issues. Declines are often reported to accelerate after the age of 70 35 years, but almost no data are available on performance in the fittest oldest-old. The aim of the study 36 was to assess decline rates in performance at high age. The biggest dataset of track and field athletes 37 \geq 80 years (1567 results) ever published was collected from results lists of the years 1997 to 2019, 38 including 100m, 200m, long jump, shot put, discus and javelin throw. Performance at age 80 of 39 athletes still participating at age 85 was compared to those who discontinued. Only one out of every 40 41 22 athletes competing at age 80 still competed at age 90. The performance decline was more than three times as steep in athletes \geq 80 (on average 1.62%/year, p-values: men: 200m p=0.037, all 42 other disciplines p<0.001, women: shot put p=0.017, discus p=0.010) compared to athletes 30-69 43 years (0.46%/year), and this acceleration occurred at an average of 67 years. Performance at age 44 80 was similar in athletes still participating at age 85 to those who discontinued, and the variability 45 in results was decreased after age 90. Physical performance declines more than three times as fast 46 after around the age of 67 years compared to before. Declines are fastest in sprinting, indicating 47 that sprinting and running exercises are most crucial for old athletes' performance. Better 48 49 performing athletes did not compete longer.

51 INTRODUCTION

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Other than many of their sedentary peers or patients with orthopaedic constraints, master athletes continue to exercise until high age¹⁻⁴. Maintaining high levels of physical exercise throughout the life span seems to slow the multi-systemic deterioration commonly observed in inactive individuals⁵. Accelerated declines in performance after the age of 70 have been reported in many athletic disciplines^{1,6-10} and are evident even in longitudinal data¹¹⁻¹³. The age of peak performance is usually reported between 18 and 23 years, and performance starts to decline progressively after staying relatively constant in the third decade of life¹.

Factors that may contribute to this age-related decline are decreases in pulmonary function¹⁴, 60 muscle wasting and weakness¹⁵⁻¹⁶, loss of motor units¹⁷ and reductions in cardiovascular 61 function¹⁸. World records give a rough understanding of the age-related decrement in 62 performance^{8,19}, but they only reflect performance of the most exceptional individuals. While the 63 better athletes might continue to perform well into high age, motivated by their successes, lower 64 performers could show a faster drop in performance and stop competition altogether. If so, the 65 accelerated decline in performance in the normal population could in fact be even steeper than that 66 reported for world records. Until now, however, this has not been systematically investigated. 67

Rates of performance declines seem to differ between disciplines and types of events^{1,20}. In direct comparison, aging affects anaerobic power more than aerobic power²¹, but many more factors seem to determine declines in athletics performance. In a previous study comparing several athletics disciplines, we observed the steepest declines in javelin throw and 400 m (women), and in pole vault and 800 m (men)[,] while athletes seem to perform longer in the throwing disciplines than in the sprints, runs and jumps¹. Due to low numbers of participating athletes in the oldest age groups, decline rates are mainly unknown for the oldest age groups, apart from the running disciplines^{22,23}. This information would be valuable for a more specific training advice for older athletes and tobetter evaluate and compensate deficiencies in frailty and sarcopenia.

We used a dataset with a substantial number of longitudinal observations to 1) analyse patterns of performance declines in the oldest group of athletes and 2) assess whether older athletes that stop competing are indeed poorer performing individuals. The hypotheses were that 1) declines in performance are accelerated at high age, and 2) better athletes continue longer, leading to an underestimation of the actual age-related rate of decline in performance in the master athlete population.

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83 METHODS

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Ethical approval was given by RWTH Aachen University Hospital IRB (reference number EK
300/17, date of approval: October 11, 2017). Informed consent was not needed, as only data from
published result lists was used.

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89 Generation of dataset

Performance data of athletes 80 years and older were extracted from the following official ranking 90 lists of annual best results: North Rhine 2001 – 2019 (North Rhine Track and Field Association)²⁴, 91 Westfalia 2001 – 2019 (Soccer- and Track and Field Association of Westfalia)²⁵, Rheinland 1997 92 - 2019 (Rheinland Track and Field Association)²⁶ and Bavaria 2012 - 2019 (Bavaria Track and 93 Field Association)²⁷. All result lists are publicly available online. The named areas were selected, 94 as their results are publicly available online and date back a decent number of years. For master 95 athletes, annual best result lists are neither published for the world, nor for Europe or complete 96 larger countries. The selected areas within German comprise a total population of more than 35 97 million, making this a valuable data-set. 98

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100 Statistical analysis

All statistical tests were executed with IBM® SPSS® Statistics version 25. The six disciplines with 101 the most participants in the targeted age group were selected for analysis: 100m and 200m sprint, 102 long jump, shot put, discus and javelin throw. Regression analysis was performed, and regression 103 104 lines and equations with their corresponding p-values are shown when significant (regression coefficient, significance level 0.05). The decline in athlete numbers with age was compared to the 105 official population numbers in Germany (German Federal Statistical Office)²⁸. A two-sided t-Test 106 was used to compare performance of athletes who had a result at both 80 and 85 years to athletes 107 who had a result at age 80 but not at age 85. The percent annual decline was calculated for the 80+ 108 athletes by normalizing their performance to the average performance values at age 80 years. 109

For presentation purposes and to calculate the age of onset of accelerate decline, the performance for all athletes was normalized to the average performance at age 30 years. Normalisation of data is further explained in the results section. The age of onset of accelerated decline was calculated from regression equations of the younger (30–69 years) and older (\geq 80 years) athletes, based on the percent annual decline normalized to age 30 years, using the following formula (regression equation: Y = aX + b):

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Age of onset of decline = $(b_{30-69} - b_{\ge 80})/(a_{\ge 80} - a_{30-69})$

Implement weights in the throwing disciplines stay constant for athletes older than 79 years, which means that no changes in weights of javelins, discusses and shots affect absolute results. The following implements are used by athletes 80 years and older: shot put: men 3 kg, women 2 kg, discus throw: men 1 kg, women 750 g, javelin throw: men and women 400 g. In data of younger athletes, changing implement weights affect results of regression statistics.

123 **RESULTS**

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125 Characterization of data-set

A total of 1567 results of 80- to 94-year-old athletes (1422 and 145 results from men and women, respectively) from six athletic disciplines were included in the analysis (**Table 1**). In 80+-year-old athletes, throwing disciplines were the most popular track and field events. In men, shot put was the most popular discipline, followed by discus throw and javelin throw. For the women, discus throw was the most popular discipline, followed by shot put and javelin throw.

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132 Participation and performance

Figure 1 shows the decline in the number of \geq 80-year-old male (A) and female (B) participants with age and compares these numbers to official population numbers for Germany in the year 2019 (C). While the overall pattern of population and participation decline with age appears similar, the proportion of the population participating in master athletics decreases with increasing age (D).

Overall, there were 415 results of 80-year-old (women and men) and only 19 of 90-year-old athletes. This means that only one out of 22 athletes who competed at age 80 still participated at age 90. **Figure 2** shows individual longitudinal changes of performance in shot put (the most popular discipline) in absolute (**A**) values and as % of performance at age 80 years (**B**). It can be seen that the performance declined in the large majority of athletes.

Supplement Figure 1 shows results of regression analyses for 100m (A), 200m (B), long jump (C), shot put (D), discus (E) and javelin throw (F) in the 80+-year-old athletes. The three exceptionally slow 200m results were excluded from the analysis, as they were not representative for the master athlete population. In men, there was a linear decline in performance in all six disciplines. Exponential, logarithmic and polynomic regression models led to lower R² values in all disciplines compared to linear regression. In women, due to lower participation, only the discus
throw showed a significant age-related decline in performance that was similar to the rate of decline
seen in men. Regression lines are only shown when significant.

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151 The onset and rate of accelerated decline

Table 1 and **Figure 3** show the data of the present study combined with those in Ganse et al.¹. 152 Regression lines are shown for the 30- to 69-year-old athletes and the 80+-year-old athletes. In 153 each discipline, the slope of performance decline is steeper in the older athletes (≥ 80 years) 154 compared to those 30 to 69 years old. The regression equations were used to calculate the age of 155 156 onset of an accelerated decline, defined as the age at which the two regression lines cross (Table 1). The average age at which the accelerated decline started was 67 years (Table 1). Shot put 157 (Figure 3B) was the discipline with the latest onset and discus throw (Figure 3D) the earliest onset 158 of accelerated decline (see also **Table1**). In **figure 3G**, we pooled the data of all disciplines and 159 normalised the performance to the average performance at 30 years in each discipline. In Figure 160 4A it can be seen that the average performance decline after the age of 80 as a percentage of the 161 performance at the age of 80 was 2.5%. 162

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164 The end of participation is independent of performance

To answer the question whether the drop out of poorer performers affected the rate of decline, performance at age 80 of athletes who still participated at age 85 was compared to those who discontinued (**Figure 4B**). We found no difference in performance between these groups in any of the disciplines (100m: p=0.9 men; 200m: p=0.1 men; long jump: p=0.1 men; shot put: p=0.5 men and p=0.6 women; discus: p=0.9 men and p=0.9 women; javelin: p=0.9 men; due to limited numbers of athletes, women are only reported for shot put and discus throw). **Figures 4C** shows a decreased variability in performance after the age of 90 years, which may reflect that at this veryadvanced age cessation of poorer performers may play a role.

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174 **DISCUSSION**

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In the present study we analyzed 1567 competition results of 80- to 94-year-old master athletes. The main findings of the study were: 1. the performance decline was on average more than three times as steep in athletes ≥80 compared to athletes 30-69 years; 2. the onset of this accelerated decline occurred at an average age of 66.9 years; 3. only one out of 22 athletes competing at age 80 still competed at age 90; 4. performance at age 80 was similar in athletes still participating at age 85 to those who discontinued; 5. there was a decreased variability in results after age 90.

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183 Performance in athletes 80 years and older

We found a faster rate of decline in performance in athletes older than 80 years than we previously 184 reported in 30- to 69-year-old athletes¹ which is in line with previous smaller studies showing an 185 accelerated decline after the age of $70^{2,6-9}$. One potential criticism of such studies is that they may 186 underestimate the rate of performance decline in the older master athletes as particularly the weaker 187 188 athletes may stop competing. In line with this criticism is our observation that the proportion of the older population participating in master athletics decreases with age, suggesting that indeed frail 189 or ill individuals usually do not compete anymore. To clarify this point in more detail, we compared 190 191 the performance at age 80 of athletes who still participated at age 85 to those who discontinued master athletics competitions and found no difference in their performance at 80 years. This thus 192 193 indicates that performance selection does not introduce bias in the accelerated decline we observed in our 80+-year-old athletes. Further evidence supporting the decline is real, is reflected by the 194

similar coefficient of inter-individual variation in performance up to the age of 90 years and thesimilar rate of decline in the longitudinal data on shot putters.

197 Reasons for an accelerated performance decline at very high age have not been clearly identified 198 by research. A "fading integrative physiological capacity" was suggested by Lazarus and 199 Harridge⁹, and other authors indicated that a stochastic process, as seen in the accumulation of 200 DNA damage²⁹ is to be expected to deliver an accelerated decline in old age³⁰.

201

202 The onset of an accelerated decline

Our data set combined with our previous data set¹ allowed us to calculate the age at which the 203 accelerated decline occurred. Data suggest that shot put (71.6 years) was the discipline with the 204 latest, and discus throw (55.2 years) the earliest onset of accelerated decline. The early onset in 205 discus throw is certainly affected by an apparently steady performance in earlier years, caused by 206 the extensive declines in the weight of the discus with age. All disciplines require muscle power, 207 and the decrease in power with age seems to be a key factor in the decline in performance in master 208 athletes¹⁵. To a limited extent also changes in technique contribute, as we have shown in javelin 209 throwers². Another factor might be that some disciplines are more injury-prone than others³¹. A 210 factor opposing the accelerated decline and potentially making it appear less intense than it really 211 is, is the fact that athletes on average got better over the last decades. Schneider et al.²² showed a 212 minor effect of the calendar year on speed in sprinting and running disciplines. Kundert et al.²⁰ 213 showed the same for jumping and throwing events by analysing performance in the World Masters' 214 Athletic Championships 1975-2016. 215

216

217 Decreased variability from age 90 years

The similar variation in muscle mass between young adults and older people³² suggests that the 218 219 rate of muscle ageing does not differ much between individuals at population level. Similarly, we found that the variation in performance of master athletes was relatively constant up to the age of 220 90 years, but decreased to almost half the original variation in participants older than 90 years. The 221 222 cause of this decline in variation could, in contrast to the absence of selection between 80 and 85 years, be a selection of athletes with the healthiest physiology who can continue in sports until that 223 224 high age. In fact, only 1 out of 22 athletes competing at the age of 80 was still competing at the age of 90 years. These survivors deserve further study as they may reveal some factors contributing to 225 their longevity and excellent performance into old age. 226

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228 Differences between disciplines

In the present study, we found the steepest slope in percent performance decline per year in the sprint disciplines. This is a remarkable difference to the younger master athletes¹, where javelin throw and 400 m (women), and in pole vault and 800 m (men) showed the steepest declines. This finding indicates that the ability to sprint or run in particular is a very crucial limiting factor in athletic performance at high age and should be given specific priority in the attempt to counteract performance declines at high age.

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236 Sex aspects

Ten times more men participated in track and field competitions than women, even though life expectancy of women exceeds that of men. Reasons for the lower participation of women may be related to traditional role models in the generation born in the 1930's and 1940's³³. This influence of role model is also reflected by the relatively late introduction of organised female athletic competitions. For instance, the first women were allowed at the Olympic Summer Games in 1928 and other disciplines were opened for women much later: long jump, 200m and shot put in 1948,
400m in 1964, 5000m in 1996 and pole vault as late as 2000.

244

245 **Practical applications**

The present data give an indication of which performance declines to expect in the healthiest oldest-246 old. This is relevant in many fields, be it for the older people and athletes themselves, in 247 248 rehabilitation, for decision makers, for the design of infrastructure, or for insurance companies. Most people are not aware of rates of performance decline with age, and this knowledge could help 249 them plan their lives better and clarify expectations. On a practical level, as the decline rates are 250 251 steepest in the sprints, we recommend older people to put an emphasis on trying to keep their ability to sprint or at least run, and to include sprinting in their regular exercise sessions. For the general 252 population and/or athletes that intend to finish their sports career, it seems recommendable to 253 include especially running and if possible, sprinting in their exercise routine. 254

255

256 Strengths and weaknesses

The major strength of the study is the exceptionally large amount of data of athletes older than 80 257 years. It is the first study to analyse such a larger number of the oldest-old athletes. A weakness is 258 259 that the majority of the data are cross-sectional, but longitudinal data from a substantial number of older athletes followed the same pattern as the cross-sectional observations. In addition, we do not 260 have data on medical history or training volumes. Due to the anonymized analysis, we are not able 261 262 to name the total number of athletes included in the study, just the number of results. We also cannot provide information on the reasons for the individuals to stop competing at the end of their 263 active competitive career, which would be desirable to have. It would also be good to see 264

longitudinal data of individual athletes spanning 30 years and more partnered with information oninjuries and other life events to evaluate the actual aging effects on the individual participant.

267

268 CONCLUSIONS

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Our study is the biggest dataset of athletes 80 years and older ever published, and it gives new insights into the rate of decline in performance and abilities of the oldest-old athletes. Performance declines accelerated around the age of 70 years and this accelerated decline is not underestimated by drop out of the poorest performers after the age of 80 years. The performance decline was more than three times as steep in athletes \geq 80 compared to athletes 30-69 years. However, the lower inter-individual variability in performance after the age of 90 years might be related to the selection of the toughest in the very oldest-old.

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279

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REFERENCES

287	1.	Ganse B, Ganse U, Dahl J, Degens H. Linear Decrease in Athletic Performance during
288		The Human Life Span. Front. Physiol. 2018;9:1100.
289	2.	Ganse B, Degens H. Accelerated decline in javelin throwing performance in master
290		athletes 70 years and older. Sports Med Int Open. 2018;02(03):E79-E83.
291	3.	Kundert AML, Nikolaidis PT, Di Gangi S, Rosemann T, Knechtle B. Changes in Jumping
292		and Throwing Performances in Age-Group Athletes Competing in the European Masters
293		Athletics Championships between 1978 and 2017. Int J Environ Res Public Health.
294		2019;3;16(7).
295	4.	Tanaka H, Tarumi T, Rittweger J. Aging and Physiological Lessons from Master
296		Athletes. Compr Physiol. 2019 Dec 18;10(1):261-296. doi: 10.1002/cphy.c180041.
297	5.	Valenzuela PL, Maffiuletti NA, Joyner MJ, Lucia A, Lepers R. Lifelong Endurance
298		Exercise as a Countermeasure Against Age-Related Decline: Physiological Overview and
299		Insights from Masters Athletes. Sports Med. 2020 Apr;50(4):703-716.
300	6.	Rubin RT, Lin S, Curtis A, Auerbach D, Win C. Declines in swimming performance with
301		age: a longitudinal study of Masters swimming champions. Open Access J Sports Med.
302		2013;4:63-70.
303	7.	Rittweger J, di Prampero PE, Maffulli N, Narici MV. Sprint and endurance power and
304		ageing: an analysis of master athletic world records. Proc Biol Sci. 2009;276(1657):683-
305		9.
306	8.	Baker AB, Tang YQ. Aging performance for masters records in athletics, swimming,
307		rowing, cycling, triathlon, and weightlifting. Exp Aging Res. 2010;36(4):453-77.

308	9.	Lazarus NR, Harridge SDR. Declining performance of master athletes: silhouettes of the
309		trajectory of healthy human ageing? J Physiol. 2017;595(9):2941-2948.
310	10.	Dahl J, Degens H, Hildebrand F, Ganse B. Age-related changes of sprint kinematics.
311		Front Physiol. 2019;10:613.
312	11.	Berthelot G, Len S, Hellard P, Tafflet M, Guillaume M, Vollmer JC, Gager B, Quinquis
313		L, Marc A, Toussaint JF. Exponential growth combined with exponential decline explains
314		lifetime performance evolution in individual and human species. Age 2012;34(4):1001-
315		1009.
316	12.	Cheng S, Degens H, Evans M, Cheng SM, Selänne H, Rittweger J, Heinonen A,
317		Suominen H, Strandberg T, Alen M, Korhonen MT. What Makes a 97-Year-Old Man
318		Cycle 5,000 km a Year? Gerontology 2016;62(5):508-512.
319	13.	Lepers R, Cattagni T. Age-related decline in endurance running performance - an
320		example of a multiple World records holder. Appl Physiol Nutr Metab. 2018
321		Jan;43(1):98-100. doi: 10.1139/apnm-2017-0298.
322	14.	Degens H, Rittweger J, Parviainen T, Timonen KL, Suominen H, Heinonen A, Korhonen
323		MT. Diffusion capacity of the lung in young and old endurance athletes. Int J Sports Med
324		2013;34(12):1051-1057.
325	15.	Arampatzis A, Degens H, Baltzopoulos V, Rittweger J. Why do older sprinters reach the
326		finish line later? Exercise and sport sciences reviews 2011;39:18-22.
327	16.	Marty E, Liu Y, Samuel A, Or O, Lane J. A review of sarcopenia: Enhancing awareness
328		of an increasingly prevalent disease. Bone. 2017;105:276-286.
329	17.	Drey M, Sieber CC, Degens H, McPhee J, Korhonen MT, Müller K, Ganse B, Rittweger
330		J. Relation between muscle mass, motor units and type of training in master athletes. Clin
331		Physiol Funct Imaging. 2016;36(1):70-6.

332	18. DeVan AE, Seals DR. Vascular health in the ageing athlete. Exp Physiol. 2012;97:305-
333	10.
334	19. Knechtle B, Nikolaidis PT. The age of the best ultramarathon performance – the case of
335	the "Comrades Marathon". Res Sports Med. 2017;25(2):132-143.
336	20. Kundert AML, Di Gangi S, Nikolaidis PT, Knechtle B. Jumping and Throwing
337	Performance in the World Masters' Athletic Championships 1975-2016. Res Sports Med.
338	Jul-Sep 2019;27(3):374-411.
339	21. Gent DN, Norton K. Aging has greater impact on anaerobic versus aerobic power in
340	trained masters athletes. J Sports Sci. 2013;31(1):97-103.
341	22. Schneider AL, Nikolaidis PT, Knechtle B. Improved Performance in Master Runners
342	Competing in the European Championships Between 1978 and 2014. J Strength Cond
343	Res. 2019 Sep;33(9):2559-2569.
344	23. Ahmadyar B, Rosemann T, Rüst CA, Knechtle B. Improved Race Times in Marathoners
345	Older than 75 Years in the Last 25 Years in the World's Largest Marathons. Chin J
346	Physiol. 2016 Jun 30;59(3):139-47.
347	24. North Rhine Track and Field Association web site.
348	https://lvnordrhein.de/wettkaempfe/besten-und-rekordlisten/lvn-bestenlisten
349	25. Soccer- and Track and Field Association of Westfalia web site.
350	https://www.flvw.de/leichtathletik/wettkaempfe/bestenliste-und-rekorde
351	26. Rheinland Track and Field Association web site.
352	https://www.lvrheinland.de/wettkampfsport/statistik/lvr-bestenlisten
353	27. Bavaria Track and Field Association web site. https://www.blv-sport.de/index.php?id=80
354	28. German Federal Statistical Office web site.
355	https://service.destatis.de/bevoelkerungspyramide/

356	29. Cortopassi GA, Wang E. There is substantial agreement among interspecies estimates of
357	DNA repair activity. Mech. Ageing Dev. 1996;91, 211–218.
358	30. Degens, H. Determinants of skeletal muscle hypertrophy and the attenuated hypertrophic
359	response at old age. J. Sport Med. Doping Stud. 2012;S1:003
360	31. Ganse B, Degens H, Drey M, Korhonen MT, McPhee J, Müller K, Johannes BW,
361	Rittweger J. Impact of age, performance and athletic event on injury rates in master
362	athletics - first results from an ongoing prospective study. J Musculoskelet Neuronal
363	Interact. 2014;14(2):148-54.
364	32. Maden-Wilkinson TM, McPhee JS, Rittweger J, Jones DA, Degens H. Thigh muscle
365	volume in relation to age, sex and femur volume. Age (Dordr). 2014;36(1):383-93.
366	33. Toftegaard-Støckel J, Nielsen GA, Ibsen B, Andersen LB. Parental, socio and cultural
367	factors associated with adolescents' sports participation in four Danish municipalities.
368	Scand J Med Sci Sports. 2011;21(4):601-11.