

41 **OVERVIEW**

42
43 In this Viewpoint we ask if information about the physiology, genetics, and empirical
44 history of elite endurance performance can provide insight into the question of “who” will
45 break the two-hour marathon barrier and when this might happen. We also identify
46 several physiological questions that we believe need attention.

47
48 The current world record in the men’s marathon is 2:03:58 (Gebrselassie 2007). This
49 record has fallen by more than 16 minutes since the early 1950s after high volume/year
50 round training was adopted widely. Except for the 1970s, the record has fallen by ~1-5
51 minutes per decade since 1960 when Africans entered international competition.

52 Improvements since 1980 likely also reflect increased prize money and competitive
53 opportunities that allowed top athletes to earn a living running. Figure 1 shows the
54 history of marathon times and projected improvements. Using times from 1960, the
55 open squares suggest it will take 12-13 years to break 2 hours assuming a ~20 sec
56 reduction per year. If times from 1980 are used the filled squares suggest it will take 25
57 years assuming a ~10 sec reduction per year. Consistent with the idea that marked
58 improvement is likely, empirical models of running times suggest that the men’s world
59 records for the 10,000m and half marathon are equivalent to a marathon time of ~2:02 -
60 2:03 (5,21).

61
62 Physiology of the Two-Hour Marathon

63 The physiological determinants of distance running performance (VO_2 max, lactate
64 threshold, and running economy) have been used to develop a model of marathon

65 performance (9,10). Elite marathon runners typically have VO_2 max values ranging
66 from ~70 ml/kg/min to ~85 ml/kg/min. These individuals can sustain running speeds
67 that require 85-90% VO_2 max for more than one hour, and these factors along with
68 knowledge of the oxygen cost to run a given speed (running economy) provide a
69 reasonable estimate of marathon pace (9,10). When outstanding values for these three
70 key variables are used in this model, a sub- two hour marathon seems physiologically
71 possible.

72
73 While there are many possible combinations that might lead to elite performances, it
74 appears that extremely high values for VO_2 max and outstanding running economy are
75 rarely seen in the same person (9,10). East African runners do not have particularly
76 exceptional values for VO_2 max or lactate threshold, but generally have outstanding
77 running economy (13,14,23). The classic study of Pollock showed that elite distance
78 runners who focused on the marathon had lower VO_2 max values and better running
79 economy than those who focused on shorter races (19). Based on these data and other
80 anecdotal reports, it appears that whoever breaks two hours for the marathon will have
81 exceptional running economy (2, 4).

82
83 In this context, there is clearly a need for more information about the relationship
84 between VO_2 max and running economy and the physiological explanation for the
85 relationship *if it exists*. There is evidence that VO_2 max and gross mechanical efficiency
86 are inversely related in cyclists and influenced by muscle fiber type (16). By contrast,
87 running economy seems more related to mechanical factors including vertical

88 displacement and so-called braking on foot strike (11,24). Exceptional running economy
89 might also provide two important physiological advantages. First, fuel utilization would
90 be lower and perhaps glycogen depletion delayed. Second, metabolic heat production
91 would also be lower potentially reducing thermal stress. To our knowledge these
92 potential advantages have not been studied extensively.

93

94 What will the Two-Hour Marathoner Look Like?

95 Forty-one of the 50 fastest marathons have been run by Kenyans or Ethiopians (1).
96 Importantly, the mean height and weight of the 30 runners (29 Africans) who have
97 broken 27 minutes for 10,000 m is 170 ± 6 cm, and 56 ± 5 kg, with only one runner
98 greater than 178 cm or 70 kg (12). Additionally, most of these athletes had exposure to
99 high altitude and significant physical activity early in life. In this context, small body size
100 has a favorable effect on VO_2 max; however, less is known about its influence on
101 running economy (7).

102

103 From these observations other questions emerge: (i) Does exposure to the combination
104 of high altitude and physical activity early in life lead to pulmonary adaptations that
105 reduce the incidence of arterial desaturation seen during heavy exercise in elite athletes
106 (3,5,15,16)? and (ii) would the reduction in metabolic heat production along with a
107 favorable body weight to surface area ratio have the net effect of reducing
108 thermoregulatory stress during periods of prolonged, intense exercise? While these
109 questions might be difficult to study, small differences could be decisive when races are
110 won and records set by very small margins. However, there are examples of “big”

111 runners like Paula Radcliffe, Ron Clarke and Derek Clayton who have been highly
112 successful. Importantly, Radcliffe and Clayton are known to have superb running
113 economy, and Radcliffe's running economy improved dramatically over time, providing
114 at least some evidence that this factor is "trainable" (8,19).

115

116 Genotype: Probabilistic versus Deterministic

117 Genetic factors may limit or enhance the possibility of running a very fast marathon. At
118 present much of what is known comes from association studies, with the angiotensin
119 converting enzyme (*ACE*) I/D and α -actinin-3 (*ACTN3*) R577X gene polymorphisms
120 having been studied extensively. The *ACE* I allele is theoretically associated with
121 improved cardiovascular function during exercise, and could also favor muscle
122 efficiency (26). While there is an overrepresentation of the I allele in the best Spanish
123 marathon runners (sub 2:09 marathon performance) (15), the *ACE* I/D polymorphism is
124 not associated with the success of the best elite endurance runners worldwide,
125 including Kenyans (25). The association between the *ACTN3* R577X variation and elite
126 'power' athlete status is strongly documented (27), yet this is not the case for endurance
127 running (28).

128

129 Beyond potential genotype/phenotype associations (which are yet to be clearly
130 established in elite marathoners), the task of quantifying the genetic contribution to elite
131 marathon performance is challenging. A record holders's phenotype results from the
132 combined influence of hundreds of genes, epigenetic factors, and non-hereditary
133 environmental influences. Using algorithms that take into account the combined

134 influence of several candidate gene variants associated with endurance performance
135 [i.e., the so-called 'total genotype score' (TGS), ranging from 0 to 100], it appears that
136 genetic factors increases the possibility of becoming a marathon champion (22). For
137 example, a Caucasian individual with a TGS value above 75 has ~5 times greater
138 chance of achieving elite endurance runner status compared to those with a TGS below
139 75. Yet, less than half of the best Spanish marathoners have TGS values above 75;
140 and, using this approach it is estimated there are nearly 6 million Spanish individuals
141 with the 'genetic' potential for elite marathon performance. Whether having the best
142 possible TGS (i.e. 100) increases the odds of breaking two-hours is unknown.

143

144 Summary

145 Whoever breaks two hours will likely have outstanding running economy and small body
146 size along with exposure to high altitude, and significant physical activity early in life.

147 However, neither these factors nor any specific suite of genotypes appear to be
148 obligatory for a time this fast. Current trends suggest that an East African will be the
149 first to break two hours. However periods of regional dominance in distance running are
150 not unique to the East Africans: athletes from Finland, Eastern Europe, Australia and
151 New Zealand have all had extended periods of success at a range of distances (17).

152 From a physiological perspective, more information is clearly needed on the relationship
153 between VO_2 max and running economy and the influence of running economy and
154 body size on thermoregulation and fuel use.

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261 Figure Legend

262 Figure 1. Progression of world record times in the marathon since the late 1920s. The
263 rapid fall in record time in the 50s and 60s likely reflects: i) the widespread adoption of
264 high volume/year round training after WWII; and ii) the participation of East-African
265 runners in international competition starting in the 1960s. There was limited progress
266 during the 1970s, but the record has fallen more than 5 minutes over the last ~30 years.
267 On average, there has been ~20 s reduction per year since 1960. The open squares
268 show that if this rate of improvement continues, a time under 2 hours could occur in 12-
269 13 years (by 2021-2022). The closed squares show that if only data from 1980 are
270 used, a time under 2 hours would occur in ~25 years based on an estimated
271 improvement of ~10s per year. The recent increase in the number of high profile races
272 on fast courses that offer substantial prize money may also contribute to faster world
273 records in the near future.

