

Institution: St George's, University of London		
Unit of Assessment: 1 Clinical Medicine		
Title of case study: International recommendations for ECG interpretation in young athletes to identify those at risk of exercise related sudden cardiac death.		
Period when the underpinning research was undertaken: 2010 to 2017		
Details of staff conducting the underpinning research from the submitting unit:		
Name(s):	Role(s) (e.g. job title):	Period(s) employed by submit
Sanjay Sharma	Professor of Cardiology	2010 – 2020 (present)
Michael Papadakis	Reader in Cardiology Senior Lecturer	2018 – 2020 (present) 2017 – 2018
	Senior Research Fellow	2016 – 2017
	Clinical Lecturer in Cardiology	2011 – 2015
	Clinical Research Fellow	2010 – 2010
Aneil Malhotra	Honorary Senior Lecturer in Cardiology Clinical Lecturer in Cardiology	2019 – 2020 (present) 2017 – 2019
	Clinical Research Fellow	2010 – 2017
Sabiha Gati	Clinical Research Fellow in Cardiology	2010 – 2013
Abbas Zaidi	Clinical Research Fellow in Cardiology	2010 – 2013
Nabeel Sheikh	BHF Clinical Research Fellow in Cardiology	2010 – 2014
Harshil Dhutia	Clinical Research Fellow in Cardiology	2013 – 2016
Gherardo Finocchiaro	Clinical Research Fellow in Cardiology	2014 – 2018
Period when the claimed impact occurred: 2016 to 2020		
Is this case study continued from a case study submitted in 2014? No		
1. Summary of the impact (indicative maximum 100 words)		
<p>Sudden death from heart disease in a young athlete is associated with decades of lost years of life and has a massive impact on the community. Accurate interpretation of the electrocardiogram (ECG) is crucial, as false results can have grave consequences. Research carried out by Prof Sharma's group into ECG patterns in athletes at risk of sudden death has led to the development of the first ever "International recommendations for ECG interpretation in athletes".</p> <p>The new recommendations have been applied worldwide, including to more than 210,000 athletes in United States and at least 120,000 athletes and young people active in amateur sport in the UK. They have resulted in an 86% decrease in the number of false positive results - from 22% to 3% compared with the previous recommendations - and a 21% reduction in the costs of investigations that follow an abnormal ECG. The number of athletes who go through worrying, time-consuming investigations and risk an unnecessary restriction or bar from their sport has been reduced by many thousands, while the resources required for investigation, treatment and counselling can now be focused on those truly at risk.</p>		
2. Underpinning research (indicative maximum 500 words)		

The research, funded by Cardiac Risk in the Young (CRY) and the British Heart Foundation, commenced in 2010 under the leadership of Professor Sanjay Sharma. Research was based on registry studies in over 35,000 athletes, 15,000 healthy controls, and comparative studies involving several hundred patients with cardiovascular diseases implicated in sudden cardiac death in young athletes. The group's findings were pivotal in providing information about normal and abnormal electrical manifestations in athletes, particularly among black athletes who appear to be at highest risk of sudden death.

Establishing the absence of a link between an ECG pattern previously considered to represent high risk and increased mortality rates in black athletes

Black male athletes frequently show electrical patterns in some ECG leads that are different from those seen in white athletes. The group performed clinical and genetic studies in these athletes and followed them up for 5 years. They also compared the prevalence of these anomalous patterns with black patients with cardiomyopathy and showed that they were more common in black athletes than in black patients with cardiomyopathy. The group's studies did not identify any evidence of cardiac disease or increased risk of death in athletes, and concluded that this pattern should be considered as a benign variant [1, 2].

Identifying ECG voltage criteria that are responsible for more than 40% of false positive results in athletes

The group's research challenged the notion that axis deviation, voltage criteria for atrial enlargement, and voltage criteria for right ventricular hypertrophy are abnormal ECG patterns in athletes. The group showed that these patterns represent more than 40% of all false positive results in athletes' ECGs. By investigating almost 14,000 apparently healthy people (including more than 2,500 athletes), the group identified 579 with one or more of these anomalies, further investigation of whom failed to reveal a higher prevalence of any inherited or congenital cardiac abnormality compared with individuals with a normal ECG [3, 4]. Therefore, the group suggested that patients with one of these anomalies should be considered as borderline variants, while the presence of more than one would place the athlete in the abnormal category [5]. This approach has been incorporated into international recommendations.

Redefining normal and abnormal ECG patterns

Anterior T wave inversion beyond V1 was considered an abnormal ECG pattern according to previous recommendations. However, the group have shown that among 14,500 young white individuals from their Cardiac Risk in the Young programme, 20% of whom were athletes, T wave inversion in V1-V2 is present in 2% males and up to 6% females. Further investigations in these individuals did not show any abnormalities. The group suggested that this pattern should be considered normal if they are confined to V1 and V2 and this was adopted by the international recommendations [6].

Defining ECG patterns in athletes that should always be considered abnormal

By contrast, the group showed that some ECG patterns, such as lateral T wave inversion are associated with a higher yield of cardiomyopathy (17%) and should always be considered abnormal in all athletes. This recommendation was also officially adopted [1, 5].

The group tested all the new recommendations on over 5,000 previously unscreened athletes. The results showed that compared with the previous guidelines on ECG interpretation in athletes - published in 2010 by the European Society of Cardiology (ESC), the largest cardiac scientific organisation in the world - the group's proposal improved specificity for identifying individuals with serious cardiac disease, which increased from 40.3% to 84.2% in black athletes and from 73.8% to 94.1% in white athletes [5]. The recommendations have had 631 citations on PubMed and 4,162 downloads.

3. References to the research (indicative maximum of six references)

1. Sheikh N, Papadakis M, Wilson M, Malhotra A, Adamuz C, Homfray T, Monserrat L, Behr ER, Sharma S. Diagnostic Yield of Genetic Testing in Young Athletes with T-wave Inversion. *Circulation*. 2018 May 15;138(12):1184-1194. pii: CIRCULATIONAHA.118.034208. doi:

- 10.1161/CIRCULATIONAHA.118.034208. Journal article cited 19 times in WOS (08.02.2021).
2. Michael Papadakis; Francois Carre; GaeleKervio; John Rawlins; Vasileios F. Panoulas; Navin Chandra; Sandeep Basavarajaiah; Lorna Carby; Tiago Fonseca; Sanjay Sharma. The prevalence, distribution, and clinical outcomes of electrocardiographic repolarization patterns in male athletes of African/Afro-Caribbean origin. *European Heart Journal* 2011;32(18):2304-2313 doi: 10.1093/eurheartj/ehr140. Journal article cited 179 times in WOS (08.02.2021).
 3. Gati S, Sheikh N, Ghani S, Zaidi A, Wilson M, Raju H, Cox A, Reed M, Papadakis M, Sharma S. [Should axis deviation or atrial enlargement be categorised as abnormal in young athletes? The athlete's electrocardiogram: time for re-appraisal of markers of pathology](#). *Eur Heart J*. 2013;34:3641-8. doi: 10.1093/eurheartj/eh390. Journal article cited 51 times in WOS (08.02.2021).
 4. Zaidi A, Ghani S, Sheikh N, Gati S, Bastiaenen R, Madden B, Papadakis M, Raju H, Reed M, Sharma R, Behr ER, Sharma S. [Clinical significance of electrocardiographic right ventricular hypertrophy in athletes: comparison with arrhythmogenic right ventricular cardiomyopathy and pulmonary hypertension](#). *Eur Heart J*. 2013;34: 3649-56. doi: 10.1093/eurheartj/eh391. Journal article cited 49 times in WOS (08.02.2021).
 5. Sheikh N, Papadakis M, Ghani S, Zaidi A, Gati S, Adami PE, Carré F, Schnell F, Wilson M, Avila P, McKenna W, Sharma S. Comparison of electrocardiographic criteria for the detection of cardiac abnormalities in elite black and white athletes. *Circulation*. 2014 Apr 22;129(16):1637-49. doi:10.1161/CIRCULATIONAHA.113.006179. Epub 2014 Mar 11. Journal article cited 170 times in WOS (08.02.2021).
 6. Malhotra A, Dhutia H, Gati S, Behr E, Tome M, Papadakis M, Sharma S. Anterior T wave inversion in young white athletes and nonathletes: Prevalence and significance. *JACC*. 2017; 1: 1-9. doi: 10.1016/j.jacc.2016.10.044. Journal article cited 40 times in WOS (08.02.2021).

4. Details of the impact (indicative maximum 750 words)

Alteration of the European Society of Cardiology (ESC) recommendations to improve cardiac screening in athletes

The prevalence of exercise related sudden cardiac death in young football players is approximately 1 in 15,000 athletes. The group's research has shown that the prevalence of potentially serious cardiac disease in this group is at least 1 in 300. They have also shown that by identifying those most at risk, several interventions can be implemented to treat underlying diseases and minimise risk.

Alongside the work of other investigators from Italy, the group's research has revealed that the majority of young athletes harbouring serious cardiac disease can be identified through ECG screening. Consequently, elite sporting organisations in Western Europe and North America mandate cardiovascular screening with ECG in young (12-35 years old) athletes. The international Olympic Committee and the FIFA also advocate cardiac screening which affects athletes worldwide. Many non-elite sporting clubs and senior schools are also now offering cardiac screening.

The ESC's 2010 recommendations remained the gold-standard for interpreting athletes' ECGs until they were replaced in 2017 by those derived from the Sharma group's research [A]. The advice emerged from insights into the effects of exercise on the electrical and structural features of the heart, which has been the focus of the group's work since 2012. By investigating large populations of athletes and non-athletes from the UK, members of the group were able to refine the ECG criteria by factoring in age and ethnicity and distinguishing between definitely abnormal ECG patterns and borderline anomalies. The group's findings formed the basis of the new international recommendations for ECG interpretation in athletes, replacing the ESC recommendations in 2017. These recommendations were published simultaneously in 3 journals (*The European Heart Journal*, *The Journal of the American College of Cardiology* and *The British Journal of Sports Medicine*). The papers resulted in a highly significant global impact, extending well beyond the academic domain: at the time of writing (March 2021) the recommendations had been referred to 941 times on Twitter, 43 times in Facebook accounts, 4

times in blogs and 1 time on Wikipedia, contributing to an aggregated Altmetrics score of 683, which places the publications in the top 5% of all research outputs scored by Altmetrics [B].

Use of the new recommendations to screen athletes worldwide

The recommendations have been adopted to investigate athletes worldwide and are now considered the sole authority for interpreting an athlete's ECG. They are used by all major sporting organisations in the UK including the Football Association, Rugby Football League and Union, Lawn Tennis Association, English Institute of Sport (national and Olympic squads) and the British Cycling Federation [C]. They are used by all elite football and athletic teams in Europe, and the National Collegiate athletic association in the US, which includes over 500,000 athletes. An International Olympic Committee (IOC) sponsored workshop recommended that its 'Consensus Statement on Periodic Health Evaluation of Elite Athletes' (2009) be updated in light of the new findings, and implementation of the new recommendations is now IOC policy [D]. The group's findings have been duplicated in studies of 1,004 adolescent athletes in West Asian/Arabic countries and 5,258 in the United States. The group estimate that at least 2,000,000 athletes have been assessed using the international ECG recommendations since 2017, resulting in 60,000 new diagnoses of serious disease. Moreover, the new recommendations have impacted sport beyond the elite level, being used by the charity Cardiac Risk in the Young to investigate non-elite sports people in the UK aged 14-35 years including in several schools (30,000 per annum since 2017) [E].

Real-world impact of new recommendations: improved specificity, positive predictive value and cost savings

The 2010 recommendations had been associated with a false positive diagnosis rate between 9% and 22%, resulting in substantial expenses related to secondary investigations to confirm or refute a diagnosis, and the potentially serious consequences of erroneous interpretation including unnecessary disqualification from sport. The new recommendations maintained the high (92%) sensitivity of ECG for detecting disease but resulted in an important increase in specificity from 84% to 96%, and in positive predictive value from 2.6% to 17%. Of the total assessed 42 athletes (0.38%) were diagnosed with serious disease, 75% of whom could be treated and returned to play.

Applications of the international recommendations to almost 5,000 previously unscreened athletes in the UK resulted in a decrease of 86% in the number of abnormal ECGs compared with the 2010 recommendations (from 22% vs. 3%), and consequent decreases of 66%, 29%, 17% and 25% in the number of echocardiograms, stress tests, Holter monitors, and cardiac MRI scans, respectively. The cost of screening using the new recommendations amounted to £62 per athlete and £20,570 per diagnosis, as compared with £86 and £28,042 under the 2010 recommendations – a relative cost in the number of echocardiograms, stress tests, decrease of 27%. Aggregated across the number of athletes screened in the UK thus far, this has led to a total cost saving of approximately £48 million based on NHS tariffs [F].

The recommendations were also applied to over 11,000 adolescent soccer players in the Football Association who were all investigated with an ECG and an echocardiogram. The international recommendations showed a decrease from 12.9% to 1.2% in positive ECGs in white athletes and a decrease from 16.2% to 3.6% in positive ECGs in black athletes when compared with the 2010 recommendations.

Importantly, the new international recommendations improved the selection of these athletes indicates the positive impact that the screening procedures and outcomes have had on their lives.

Positive effect of our recommendation on athletes

Apart from reducing the risk of false positive results, unnecessary investigations, and erroneous disqualification from sport, the group's own assessments of the impact of their research have revealed that 56% of young people in the community who were identified with a serious cardiac condition underwent a medical intervention (other than advice to reduce the intensity of exercise)

to prevent sudden death [G]. Three quarters of elite adolescent football players detected with a cardiac condition that might have resulted in disqualification from sport were able to be treated and return to competition.

Education of physicians to development of software to save lives

The recommendations are being used to train doctors from developed and developing countries using online modules supported by the British Medical Journal Group [H]. The recommendations have been incorporated into commercial software for ECG machines for investigating athletes specifically to reduce the burden of interpretation among sports physicians who may not be appropriately qualified [I].

5. Sources to corroborate the impact (indicative maximum of 10 references)

A. Copies of the three 2017 publications in which the new recommendations were simultaneously published.

B. Altmetrics summaries illustrating the worldwide impact, beyond academia, of the three publications mentioned in A.

C. Evidence that the new recommendations are being implemented in assessment protocols used by: FIFA (see section 4.1); Sports and Exercise Medicine organisations worldwide, and the International Olympic Committee.

D. Letters from:

- a. the Medical and Scientific Director of the international Olympic Committee and
- b. the Director of Medical Services at the English Institute of Sport concerning the use and impact of the 2017 recommendations.

E. Evidence for rollout in schools of the programme under the auspices of CRY.

F. Health economic analysis papers reporting the cost savings associated with the use of the new recommendations:

- a. Dhutia et al. (2017) Impact of the International Recommendations for electrocardiographic interpretation on cardiovascular screening in young athletes. *JACC* 70:805-808
- b. Dhutia et al. (2016) Cost implications of using different ECG criteria for screening young athletes in the UK. *JACC* 68:702-711.

G. Dhutia et al. Diagnostic yield and financial implications of a nationwide electrocardiographic screening programme to detect cardiac disease in the young. *Europace*. 2021 Feb 11:euab021. doi: 10.1093/europace/euab021. Epub ahead of print. PMID: 33570096.

H. ECG Interpretation in Athletes – link to training modules.

I. Cardea 2020 ECG for recognition of important ECG abnormalities of importance to athletes, based on the 2017 criteria.