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Cost Implications of Using Different ECG Criteria for Screening Young Athletes in the United Kingdom

Harshil Dhutia, MBBS, BSc,[a] Aneil Malhotra, MBBChir, MA, MSc,[a] Vincent Gabus, MD,[a] Ahmed Merghani, MBBS, BMedSci,[a] Gherardo Finocchiaro, MD,[a] Lynne Millar, MBBS,[a] Rajay Narain, MBBS,[a] Michael Papadakis, MD, MBBS,[a] Huseyin Naci, PhD,[b] Maite Tome, MD, PhD,[a] Sanjay Sharma, MD, MBChB, BSc[b]

ABSTRACT

BACKGROUND High false-positive rates and cost of additional investigations are an obstacle to electrocardiographic (ECG) screening of young athletes for cardiac disease. However, ECG screening costs have never been systematically assessed in a large cohort of athletes.

OBJECTIVE This study investigated the costs of ECG screening in athletes according to the 2010 European Society of Cardiology (ESC) recommendations and the Seattle and refined interpretation criteria.

METHODS Between 2011 and 2014, 4,925 previously unscreened athletes aged 14 to 35 years were prospectively evaluated with history, physical examination, and ECG (interpreted with the 2010 ESC recommendations). Athletes with abnormal results underwent secondary investigations, the costs of which were based on U.K. National Health Service Tariffs. The impact on cost after applying the Seattle and refined criteria was evaluated retrospectively.

RESULTS Overall, 1,072 (21.8%) athletes had an abnormal ECG on the basis of 2010 ESC recommendations; 11.2% required echocardiography, 1.7% exercise stress test, 1.2% Holter, 1.2% cardiac magnetic resonance imaging, and 0.4% other tests. The Seattle and refined criteria reduced the number of positive ECGs to 6.0% and 4.3%, respectively. Fifteen (0.3%) athletes were diagnosed with potentially serious cardiac disease using all 3 criteria. The overall cost of de novo screening using 2010 ESC recommendations was $539,888 ($110 per athlete and $35,993 per serious diagnosis). The Seattle and refined criteria reduced the cost to $92 and $87 per athlete screened and $30,251 and $28,510 per serious diagnosis, respectively.

CONCLUSIONS Contemporary ECG interpretation criteria decrease costs for de novo screening of athletes, which may be cost permissive for some sporting organizations. (J Am Coll Cardiol 2016;68:702–11) © 2016 by the American College of Cardiology Foundation.

Sudden cardiac death in sport is a rare, but devastating, event, and identification of young athletes harboring potentially serious cardiac disease is an important focus within the medical community. Pre-participation screening with a 12-lead electrocardiogram (ECG) is effective for detecting ion channel diseases and congenital accessory pathways and may also raise suspicion for the main cardiomyopathies implicated in sudden cardiac death (1-3). The 30-year-old, nationally sponsored Italian cardiac screening program with ECG reported a substantial reduction in the prevalence of sudden cardiac death in young athletes since its inception (4). Although both the European Society of Cardiology (ESC) (5) and the International Olympic Committee (6) endorse ECG screening in athletes, an important concern regarding such practice is the unacceptably high false-positive rate and the subsequent cost

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From the [a]Division of Cardiovascular Sciences, St. George's University of London, London, United Kingdom; and the [b]LSE Health, Department of Social Policy, London School of Economics and Political Science, London, United Kingdom. Drs. Dhutia, Malhotra, Finocchiaro, Millar, and Narain were funded by research grants from Cardiac Risk in the Young. Dr. Sharma has been an applicant on previous grants from Cardiac Risk in the Young and British Heart Foundation to study athletes. The authors have reported that they have no relationships relevant to the contents of this paper to disclose.

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generated by additional investigations to confirm or refute cardiac disease. The 2010 ESC recommendations for athletes generate a false-positive rate from 9% to 22% (3,4,7,8). The Seattle criteria significantly improved the specificity of ECG screening criteria for detecting cardiac disease associated with sudden cardiac death, by accounting for specific benign repolarization anomalies associated with black ethnicity and designating less conservative limits for an abnormal QT interval (2,7,8). More recent refined criteria have been associated with further reduction in false positives without compromising sensitivity (7). Whether modification of ECG interpretation criteria in young athletes significantly reduces cost has not been investigated.

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This study compared costs associated with additional investigations triggered by the 2010 ESC, Seattle, and refined ECG criteria in a large cohort of young athletes in the United Kingdom undergoing initial cardiovascular screening.

METHODS

SETTING. The United Kingdom does not support a state-sponsored screening program in athletes. However, the charitable organization Cardiac Risk in the Young established a cardiac screening program for young individuals in 1997 that also serves many U.K. professional sporting organizations (9). Up to 1,500 athletes age 14 to 35 years from numerous regional or national sporting squads are assessed annually. The screening program is overseen by the senior author. The cost of the initial screening evaluation is incurred by the athlete's sporting organization.

ATHLETES. Between 2011 and 2014, 5,374 consecutive athletes were screened as a mandatory requirement of their respective sporting organizations. Previously, 449 athletes had been assessed as part of their clubs' screening policy. In this group, 36 athletes (8%) had undergone further investigations beyond the ECG, and cardiac disease was excluded. We report data from 4,925 athletes who were previously unscreened by ECG. All athletes were initially evaluated by experienced sports cardiologists. Athletes were defined as individuals competing in organized team or individual sports at the regional, national, or international level. Ethnicity/race was determined by self-report.

PRELIMINARY INVESTIGATIONS IN ATHLETES UNDERGOING PRE-PARTICIPATION SCREENING. Preliminary screening consisted of a health questionnaire, physical examination, and ECG.

Health questionnaire. The health questionnaire inquired about cardiac symptoms, past medical history, drug history, and family history of premature (<40 years of age) cardiac disease or sudden cardiac death.

Physical examination. Physical examination included measurement of height, weight, radial and femoral pulses, brachial blood pressure measurements in the dominant arm, precordial examination at 45°, and assessment for features of Marfan syndrome (10). Abnormal findings that triggered further investigation were a blood pressure >140/90 mm Hg on 3 consecutive occasions, radiofemoral delay, stigmata of Marfan syndrome, a pathological murmur, widely split second heart sound, or a third/fourth heart sound.

Electrocardiography. A resting 12-lead ECG was performed using a Philips Pagewriter Trim III recorder (Philips, Bothell, Washington) with amplification of 0.1 mV/mm. P-, Q-, R-, S-, and T-wave voltages; ST-segments; QRS duration; PR interval and QT intervals were assessed. The longest QT interval value was considered as the absolute QT and was corrected for heart rate with Bazett's formula (11). The 2010 ESC recommendations were used initially to interpret the ECG because they were the only recommendations available at the time of initiation of the study (3). The Seattle criteria and refined criteria for ECG interpretation in athletes were applied to the cohort retrospectively (**Table 1**) (2,7).

T-wave inversion in leads V_1 to V_3 in asymptomatic athletes age >14 to <16 years was considered a normal variant in the absence of a relevant family history irrespective of the ECG criterion used (12). Such individuals were advised to have a repeat ECG at age 16 years with a view to further investigation if the juvenile pattern persisted.

FURTHER INVESTIGATIONS AND OUTCOMES. The requirement for further investigations was determined by the screening sports cardiologists on the basis of symptoms, relevant family history, abnormal physical examination, or abnormal ECG. Athletes requiring secondary investigations were referred to hospitals within their geographic vicinity with a report that specified the abnormal findings, included the ECG, diagnosis in question, and a proposed investigation protocol based on our longstanding experience of investigating athletes and patients with inherited cardiac disease (13).

Concurrent with our clinical practice, we used less conservative limits for abnormal QT intervals than those considered by the 2010 ESC recommendations when advising the need for further investigations. This decision was based on high false-positive rates

ABBREVIATIONS AND ACRONYMS

ECG = electrocardiography

ESC = European Society of Cardiology

MRI = magnetic resonance imaging

and very low predictive value for the limits imposed by the 2010 ESC recommendations (1,14,15). Specifically, we recommended further investigations in asymptomatic athletes with an isolated QT interval ≥470 ms and ≥480 ms in males and females, respectively, and an isolated QT interval ≤320 ms in all athletes.

The ultimate decision relating to the type and number of secondary investigations was made by the attending cardiologist. Investigations included echocardiography, exercise stress testing, 24-h ECG monitoring (Holter), 24-h blood pressure monitoring, signal average ECG, cardiac magnetic resonance imaging (MRI), computed tomography, pharmacological provocation testing or electrophysiological studies. Serious cardiac diseases were defined as those implicated in exercise-related sudden cardiac death (16). Data relating to further investigations and the final diagnosis were obtained from the club doctor using a questionnaire at 6-month intervals.

FINANCIAL ANALYSIS. Costs were incurred in Great Britain pounds (£), but are presented in U.S. dollars ($) with a currency exchange rate of £1 = $1.52 at the time of manuscript preparation. The initial screening tests (history, physical examination, and ECG) were performed at a subsidized cost of $53 per athlete screened. The costs of secondary investigations were calculated on the basis of the 2014/2015 U.K. National Health Service tariff payment system (**Table 2**) (17). There is currently no national rebate for pharmacological testing for Brugada syndrome, or for 24-h blood pressure monitoring or signal averaged ECG. Therefore, we used the fee for these procedures at our institute for the analysis. The fee for genetic testing was obtained from a national molecular center for clinical genetics in Oxford (United Kingdom) (18). The impact on cost after application of the Seattle and refine criteria was evaluated retrospectively.

STATISTICS. Statistical analyses were performed using the SPSS software, version 17 (SPSS, Chicago, Illinois). Variables were tested for normality using the Kolmogorov-Smirnov test. Group differences of normally distributed data were tested with the Student *t* test and expressed as mean (±SD). Group differences of proportions were tested with the use of chi-square or Fisher exact tests. Costs between ECG criteria were compared using paired rank sum testing. Significance was defined as $p < 0.05$.

ETHICS. Ethical approval was granted by the Essex 2 Research Ethics Committee. Written consent was obtained from individuals ≥16 years of age and from a parent/guardian for those <16 years of age.

TABLE 1 Definition of ECG Abnormalities in Athletes According to the 2010 ESC Recommendations (3), Seattle Criteria (2), and Refined Criteria (7)

All 3 criteria	ST-segment depression Pathological Q waves Complete left bundle branch block Wolff-Parkinson-White syndrome pattern Brugada-like early repolarization pattern Premature ventricular contractions Atrial or ventricular arrhythmia
2010 ESC recommendations	T-wave inversion Long QT interval >440 ms (male) or >460 ms (female) Short QT interval < 380 ms Right ventricular hypertrophy Right- or left-axis deviation Right- or left-atrial enlargement Complete right bundle branch block Nonspecific intraventricular delay (QRS >120 ms)
Seattle criteria	T-wave inversion beyond V_2 in white athletes T-wave inversion beyond V_4 in black athletes Long QT interval ≥470 ms (male) or ≥480 ms (female) Short QT interval ≤320 ms Right ventricular hypertrophy (in presence of right-axis deviation) Left-axis deviation Right or left atrial enlargement Nonspecific intraventricular delay (QRS ≥140 ms)
Refined criteria	T-wave inversion beyond V_1 in white athletes T-wave inversion beyond V_4 in black athletes Long QT interval ≥470 ms (male) or ≥480 ms (female) Short QT interval ≤320 ms Complete right bundle branch block Nonspecific intraventricular delay (QRS >120 ms) Borderline variants (requiring investigation if >1 present) T-wave inversion up to V_4 in black athletes Right ventricular hypertrophy Left-axis deviation Right-axis deviation Right atrial enlargement Left atrial enlargement

ECG = electrocardiogram; ESC = European Society of Cardiology.

RESULTS

DEMOGRAPHICS. Athletes were age 19.9 ± 5 years (14 to 35 years). The majority were male (n = 4,068; 83%) and white (n = 4,025; 85%); 444 athletes (9%) were of African or Afro-Caribbean origin, and 276 (5%) consisted of other ethnicities. Most athletes were ≥16 years of age (n = 4,230; 85.9%). Athletes represented 26 different sporting disciplines (predominantly rugby [53%], soccer [13%], and swimming [5%]) and exercised for 15.6 ± 7 h per week.

TABLE 2 Cost and Frequency of Additional Investigations Following Abnormality in History and Physical Examination, or ECG

	Cost ($)	History and Physical Examination	ECG Interpreted With 2010 ESC Recommendations	ECG Interpreted With Seattle Criteria	ECG Interpreted With Refined Criteria
Hospital appointment for further evaluation and additional investigations	249	79 (1.6)	502 (10.2)	295 (6.0)	210 (4.3)
Transthoracic echocardiography	112	66 (1.3)	484 (9.8)	274 (5.6)	197 (4.0)
Exercise stress test	258	12 (0.2)	73 (1.5)*	58 (1.2)*	63 (1.3)*
			10 (0.2)†	10 (0.2)†	10 (0.2)†
24-h ECG (Holter)	258	12 (0.2)	47 (1.0)*	38 (0.8)*	42 (0.9)*
			8 (0.2)†	8 (0.2)†	8 (0.2)†
Cardiac MRI	319	1 (0.02)	60 (1.1)	45 (0.9)	49 (1.0)
24-h blood pressure monitoring	258	4 (0.08)	1 (0.02)	1 (0.02)	1 (0.02)
Signal-averaged ECG	40	0 (0.0)	4 (0.08)	2 (0.04)	4 (0.08)
Electrophysiological study (± ablation)	3,026	1 (0.02)	3 (0.06)*	3 (0.06)*	3 (0.06)*
			4 (0.08)‡	4 (0.08)‡	4 (0.08)‡
Cardiac computed tomography	167	1 (0.02)	0 (0.0)	0 (0.0)	0 (0.0)
Transesophageal echocardiography	438	0 (0.0)	1 (0.02)	1 (0.02)	1 (0.02)
Provocation testing for Brugada syndrome	608	3 (0.06)	0 (0.0)	0 (0.0)	0 (0.0)
Genetic testing for long QT syndrome and hypertrophic cardiomyopathy	912	0 (0.0)	9 (0.2)	9 (0.2)	9 (0.2)

Values are n (%) unless otherwise indicated. *Diagnostic indication. †Noninvasive risk stratification indication. ‡Risk stratification and treatment for Wolff-Parkinson-White syndrome ECG pattern.

MRI = magnetic resonance imaging; other abbreviations as in Table 1.

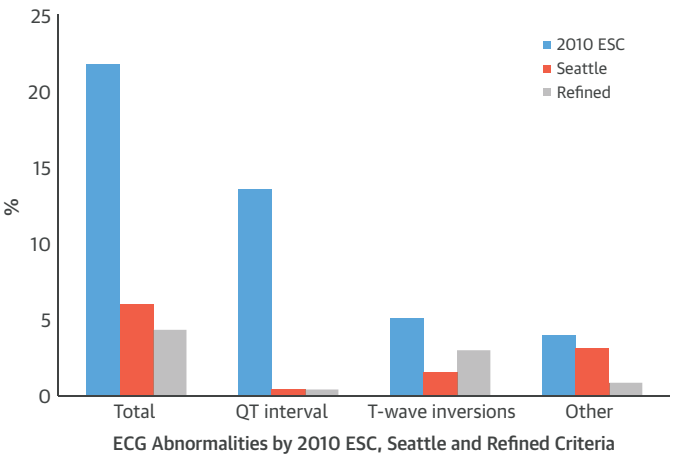
HISTORY AND PHYSICAL EXAMINATION. The health questionnaire revealed abnormalities in 61 (1.2%) athletes. Of these, 43 athletes reported symptoms consistent with cardiac disease according to the screening cardiologist (palpitations n = 18, chest pain n = 10, syncope n = 8, and dyspnea n = 7), and 18 had a significant family history (cardiomyopathy n = 6, channelopathy n = 1, unexplained premature sudden cardiac death n = 11). Physical examination was abnormal in 18 (0.4%) athletes (cardiac murmur n = 12, blood pressure >140/90 n = 4, and stigmata of Marfan syndrome n = 2).

ECG INTERPRETATION. A total of 1,072 (21.8%) athletes exhibited ≥1 ECG abnormality according to 2010 ESC recommendations (inclusive of the original criteria for an abnormal QT interval) (3); 295 (6.0%) athletes had an abnormal ECG with reference to the Seattle criteria. This represented a 73% reduction compared with the 2010 ESC recommendations ($p < 0.0001$). Application of the refined criteria reduced the number of abnormal ECGs to 210 (4.3%). Compared with the 2010 ESC recommendations and Seattle criteria, this represented an 80% ($p < 0.0001$) and 29% ($p < 0.0001$) reduction in the number of abnormal ECGs, respectively (Figure 1).

Reductions in the number of abnormal ECGs between the 2010 ESC recommendations and the Seattle and refined criteria were predominantly due to the number of athletes considered to exhibit an abnormal QT interval (13.6% vs. 0.4%) or abnormal T-wave inversion (5.1% vs. 1.6% and 3.0%, respectively).

The prevalence of abnormal T-wave inversions according to the 2010 ESC, Seattle, and refined criteria was 251 (5.1%), 81 (1.6%), and 149 (3.0%), respectively (Figure 1). The lower number of athletes diagnosed with anterior T-wave inversion (beyond V_1 for refined criteria and beyond V_2 for Seattle criteria) accounted for the difference between

FIGURE 1 ECG Abnormalities With Reference to the 2010 ESC Recommendations, Seattle Criteria, and Refined Criteria



Differences in criteria for an abnormal QT interval and abnormal T-wave inversion are responsible for the lower number of abnormal ECGs with the Seattle criteria and refined criteria compared with the 2010 ESC recommendations. ECG = electrocardiography; ESC = European Society of Cardiology.

the Seattle and refined ECG criteria (0.8% vs. 2.2%, respectively; $p < 0.0001$).

FURTHER EVALUATION. Further investigations were needed in 79 (1.6%) athletes for symptoms, family history, or abnormal physical examination, and 502 (10.2%) athletes were referred for an abnormal ECG on the basis of the 2010 ESC recommendations adapted for less conservative criteria for abnormal QT intervals. The difference in the actual number of athletes with an ECG abnormality (n = 1,072) and the number of athletes referred for further investigations for an ECG abnormality (n = 502) reflected our personal practice to not investigate asymptomatic athletes with an isolated long QT interval <470 ms (males) or <480 ms (females) (n = 300), or a short QT interval between >320 and <380 ms (n = 270). Overall, 581 (11.8%) of the 4,925 athletes were referred for further investigations after preliminary screening.

The authors received completed questionnaires relating to further investigations to confirm (or refute) diagnosis of disease in all 581 athletes. Overall, 550 (11.2%) athletes underwent transthoracic echocardiography, 85 (1.7%) underwent exercise stress testing, 59 (1.2%) underwent Holter monitoring, 61 (1.2%) underwent cardiac MRI, and 18 (0.4%) underwent a combination of 24-h blood pressure monitoring, signal averaged ECG, electrophysiological studies, transesophageal echocardiography, computed tomography, or pharmacological provocation testing for Brugada syndrome (**Table 2**).

Application of the Seattle criteria and refined criteria would result in 374 (7.6%) and 289 (5.9%) athletes requiring further investigation, a 35% and 50% reduction, respectively, compared with the 2010 ESC recommendations adapted for less conservative criteria for an abnormal QT interval (**Table 2**). None of the 449 athletes that had previously undergone cardiovascular screening required additional investigation following health questionnaire, physical examination, and ECG.

IDENTIFICATION OF CARDIAC PATHOLOGY. Following further cardiac investigation, 15 (0.3%) athletes were diagnosed with cardiac pathology implicated in sudden cardiac death in young athletes. Six were diagnosed with hypertrophic cardiomyopathy, 3 with long QT syndrome, and 6 with the Wolff-Parkinson-White syndrome ECG pattern. All 15 were asymptomatic and diagnosed following an abnormal ECG irrespective of the ECG interpretation criterion used. The 6 athletes with hypertrophic cardiomyopathy displayed T-wave inversions in the lateral or inferior-lateral leads, and were diagnosed by a combination of echocardiography and cardiac MRI. The 3 athletes with long QT syndrome were diagnosed on the basis of a prolonged QT interval (≥480 ms) and exercise stress testing (**Table 3**).

Sixteen (0.3%) athletes were diagnosed with other structural cardiac abnormalities (12 bicuspid aortic valves, 2 atrial septal defects, 2 mitral valve prolapse). Of these, 8 (50%) were diagnosed by abnormal physical examination, and 8 (50%) were detected following investigation for an abnormal ECG by the 2010 ESC recommendations. The Seattle criteria would have failed to detect 2 athletes, and the refined criteria would not have identified 5 athletes with these conditions (Online Table 1).

FINANCIAL ANALYSIS. The initial cost of screening with history, physical examination, and ECG was $53 per athlete, which equates to a total cost of $261,025 for the 4,925 athletes screened. The cost of evaluating 79 athletes with an abnormal history or examination was $39,623. The cost of secondary investigations following an abnormal ECG according to the 2010 ESC recommendations adapted for less conservative criteria for abnormal QT interval was $239,240. Therefore, the overall cost of comprehensive cardiovascular evaluation for the entire cohort of previously unscreened athletes was $539,888, or a cost of $110 per athlete screened and $17,416 per diagnosis of a cardiac condition, and $35,993 per cardiac condition associated with sudden cardiac death. Adherence to the original 2010 ESC recommendations for an abnormal QT interval would have resulted in an estimated cost of $157 per athlete on the assumption that all athletes would have had an exercise stress test and Holter monitor.

Application of the Seattle criteria reduced the cost of secondary investigations to $153,120. The overall cost for the cohort would have been $453,768, or a cost of $92 per athlete screened and a cost of $15,647 per diagnosis of a cardiac condition and $30,251 per serious diagnosis. This represents a savings of 16% compared with screening with the 2010 ESC recommendations ($p < 0.0001$). The refined criteria reduced the cost of secondary investigations to $127,009 resulting in an overall cost of $427,657, or a cost of $87 per athlete screened and a cost of $16,448 per diagnosis of a cardiac condition and $28,510 per diagnosis associated with sudden cardiac death. This represents a savings of $23 (21%) per athlete compared with the 2010 ESC recommendations ($p < 0.0001$) and $5 (5%) per athlete compared with the Seattle criteria ($p = 0.114$). Investigation for T-wave

TABLE 3 Characteristics of Athletes Diagnosed With Disease Implicated in Sudden Cardiac Death

Pathology	Age/Sex	Ethnicity	Sport	H+P Abnormality	ECG Abnormality	Diagnostics	Risk Stratification	Other	Outcome
HCM	34/male	Caucasian	Ballet	Nil	Lateral TWI	ECHO, MRI	EST, Holter	Gene test	Retired
HCM	35/male	Caucasian	Soccer	Nil	Inferior-lateral TWI	ECHO, MRI	EST	Gene test	Retired
HCM	33/male	Caucasian	Rugby	Nil	Lateral TWI	ECHO, MRI	EST	Gene test	Retired
HCM	24/male	Caucasian	Rugby	Nil	Inferior-lateral TWI	ECHO, MRI	EST	Gene test	Playing against medical advice
HCM	19 /male	Afro-Caribbean	Cricket	Nil	Inferior-lateral TWI	ECHO, MRI	–	Gene test	Playing against medical advice
HCM	14/male	Caucasian	Swimming	Nil	Inferior-lateral TWI	ECHO, MRI	EST	Gene test	Playing against medical advice
LQTS	16/female	Caucasian	Netball	Nil	QTc 480 ms T-wave notching	ECHO, EST	Holter	Gene test	Playing against medical advice
LQTS	15/male	Caucasian	Swimming	Nil	QTc 510 ms T-wave notching	ECHO, EST	Holter	Gene test	Retired
LQTS	27/male	Afro-Caribbean	Soccer	Nil	QTc 550 ms T-wave notching	ECHO, EST	Holter	Gene test	Playing against medical advice
WPW ECG pattern	14/female	Caucasian	Swimming	Nil	Short PR interval Delta wave	–	–	–	Conservative management
WPW ECG pattern	15/male	Afro-Caribbean	Soccer	Nil	Short PR interval Delta wave	–	EST, Holter, EPS	–	Treated with radiofrequency ablation
WPW ECG pattern	16/male	Caucasian	Rugby	Nil	Short PR interval Delta wave	–	EST, Holter. EPS	–	Treated with radiofrequency ablation
WPW ECG pattern	17/female	Afro-Caribbean	Cricket	Nil	Short PR interval Delta wave	–	EST	–	Conservative management
WPW ECG pattern	17/male	Caucasian	Rugby	Nil	Short PR interval Delta wave Inferior TWI	ECHO	EST, Holter, EPS	–	Treated with radiofrequency ablation
WPW ECG pattern	20/male	Caucasian	Rugby	Nil	Short PR interval Delta wave	–	EST, Holter, EPS	–	Treated with radiofrequency ablation

ECHO = echocardiogram; EPS = electrophysiology study; EST = exercise stress test; H+P = history and physical examination; HCM = hypertrophic cardiomyopathy; LQTS = long QT syndrome; QTc = QT interval corrected for heart rate; TWI = T-wave inversion; WPW = Wolff-Parkinson-White syndrome; other abbreviations as in Tables 1 and 2.

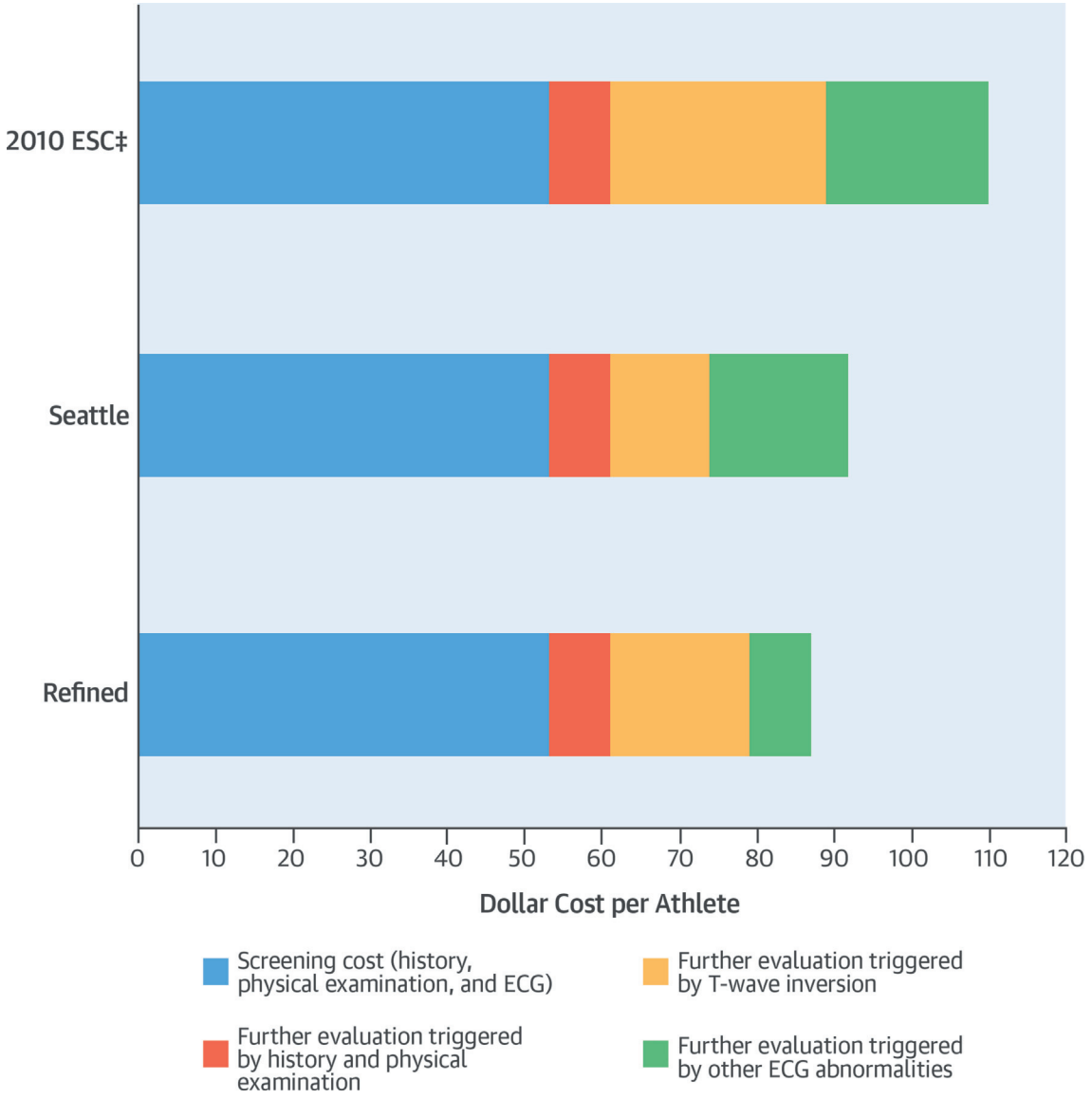
inversions accounted for 25% of the total cost of pre-participation screening with the 2010 ESC recommendations, 14% for the Seattle criteria, and 21% of the refined criteria (Central Illustration).

SENSITIVITY ANALYSIS. We performed a sensitivity analysis investigating the impact on cost per athlete screened with the refined criteria with the following variables: the initial noninvasive risk stratification tests (exercise stress test [n = 10] and Holter [n = 8]) at the time of diagnosis of serious disease, genetic testing for long QT syndrome (n = 3) and hypertrophic cardiomyopathy (n = 6), electrophysiological studies and radiofrequency ablation for 4 athletes with Wolff-Parkinson-White syndrome ECG pattern, and the inclusion of the 449 athletes who had previously undergone cardiovascular screening (Figure 2). The inclusion of noninvasive risk stratification tests would result in an additional $1 per athlete screened. Genetic testing for long QT syndrome and hypertrophic cardiomyopathy would result in a further $2 per athlete screened. Electrophysiological studies and radiofrequency ablation for Wolff-Parkinson-White syndrome ECG pattern would add a further $2 per athlete. Conversely, the inclusion of the athletes that had been previously screened would reduce the cost per athlete screened by $3.

DISCUSSION

This study evaluated the financial implications of ECG-based screening using different ECG interpretation criteria in almost 5,000 young athletes. On the basis of the diagnosis of a cardiac condition in 31 (0.6%) athletes, the overall cost of ECG screening with the 2010 ESC recommendations adapted for less conservative criteria for an abnormal QT interval equated to $110 per athlete screened and $17,416 per condition diagnosed ($35,993 per condition implicated in sudden cardiac death). The Seattle and refined criteria would reduce the cost per athlete screened by up to 21% without compromising the sensitivity for detecting athletes at risk of sudden cardiac death. The additional cost of noninvasive risk stratification at the time of diagnosis, gene testing and electrophysiological studies, and radiofrequency ablation

CENTRAL ILLUSTRATION **Costs of ECG Screening in Athletes: Comparison of the 2010 ESC Recommendations and Seattle and Refined Criteria Per Athlete**



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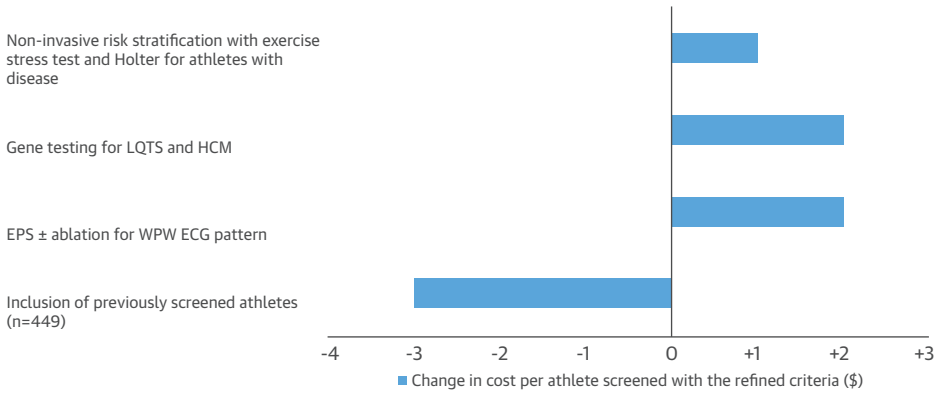
The financial impact of modification of ECG interpretation criteria in young athletes. Compared to the 2010 ESC recommendations, the costs for subsequent investigation following an abnormal ECG with the Seattle criteria and refined criteria are reduced by 21%. ‡Adapted for less conservative criteria for an abnormal QT interval. ECG = electrocardiography; ESC = European Society of Cardiology.

for Wolff-Parkinson-White syndrome ECG pattern amount to an additional $5 per athlete. This figure represents a small cost increment of 5% based on the refined criteria and is still $18 (16%) cheaper than the cost of diagnosis alone using the adapted 2010 ESC recommendations.

TRENDS IN INVESTIGATIONS. Following preliminary assessment, 11.2% of the athletes required transthoracic echocardiography, 1.7% exercise stress testing, 1.2% Holter monitoring, 1.2% cardiac MRI, and 0.4% required other tests, respectively (Table 2). To our knowledge, there are only 3 studies describing

FIGURE 2 Sensitivity Analysis Reporting the Impact of Several Variables on the Cost per Athlete Screened With the Refined Criteria



Risk stratification tests at diagnosis, genetic testing, and electrophysiological studies ± ablation for Wolff-Parkinson-White ECG pattern raise costs by $5 per athlete screened. Conversely, inclusion of previously screened athletes in the analysis reduces the cost by $3 per athlete screened. ECG = electrocardiography; EPS = electrophysiological study; HCM = hypertrophic cardiomyopathy; LQTS = long QT syndrome; WPW = Wolff-Parkinson-White syndrome.

the extent of secondary investigations following abnormalities on history, physical examination, or ECG (4,19,20). In the Veneto region of Italy, 9% of 42,386 athletes required further investigation due to an ECG abnormality; overall, further investigations included echocardiography in 9.2%, exercise stress testing in 3.1%, Holter monitoring in 1.2%, and a combination of cardiac MRI or more invasive testing such as electrophysiological studies or angiography in 0.2%. Although our cohort differs from the Italian study in that secondary investigations were not limited to a single center, the overall trend is similar. The higher rate of cardiac MRI in our study can be explained by the increasing availability and application of this test compared with the Italian study in 2006 (4).

Compared with the 2010 ESC recommendations adapted for less conservative limits for abnormal QT intervals, application of more contemporary ECG interpretation guidelines would reduce the number of athletes requiring further investigation following screening by up to 50% (**Table 2**). Specifically, the refined criteria would have resulted in 50% reduction in the number of echocardiograms, 12% reduction in the number of exercise tests, 8% reduction in Holter monitors, and 18% reduction in the number of cardiac MRI scans that would need to be performed to confirm (or refute) the diagnosis of cardiac disease.

COST ANALYSIS. Our study was intended to report the impact on the type and cost of further investigations following the modification of ECG criteria rather than assess the cost-effectiveness of cardiac screening. Our findings are comparable with a significantly smaller Swiss study of just over 1,000 athletes who were also screened by ECG that was interpreted on the basis of the 2010 ESC recommendations with several modifications similar to the Seattle criteria (19). The study reported a cost of $146 per athlete screened and $39,119 per serious condition detected. Unlike our study, all athletes self-referred and were exclusively white. Furthermore, the indications for additional investigations were consensually established by only 2 cardiologists, which does not reflect real-life practice. Another study from Qatar also reported the costs relating to ECG screening in 1,628 athletes also using recommendations resembling the Seattle criteria (20). The cost per athlete was significantly higher than our study and equated to $265. Besides a significantly smaller sample size, the study was not comparable to ours in several aspects. More than 50% of athletes were of Arabic origin, which is not representative of athletes in the Western world. All investigations were conducted in a single center and therefore not representative of nationwide screening of young athletes.

Compared with the 2010 ESC recommendations, the modifications in the Seattle and refined criteria would reduce the overall cost of screening by 16% and 21% per athlete, respectively. On the basis of our sensitivity analysis, these savings may allow organizations to afford the additional costs of noninvasive risk stratification tests at time of diagnosis, gene testing, and radiofrequency ablation for the Wolff-Parkinson-White syndrome ECG pattern. Although

the refined criteria were associated with a reduction in the number of abnormal ECGs compared with the Seattle criteria, this advantage did not translate to a significant cost saving. The discrepancy can be attributed to the differences in the interpretation of anterior T-wave inversion between the 2 criteria (2,7). T-wave inversion in the right precordial leads is associated with arrhythmogenic right ventricular cardiomyopathy, which invariably requires a plethora of cardiac investigations, including cardiac MRI, signal averaged ECG, Holter monitor, and exercise stress test for diagnosis (21). In white athletes, the refined criteria recommend investigation in athletes with anterior T-wave inversion beyond V_1, whereas the Seattle criteria recommend further investigation only if T-wave inversion extends beyond V_2 (**Table 1**). The added costs associated with investigating a greater proportion of athletes with anterior T-wave inversion negate the positive impact of a lower number of abnormal ECGs with the refined criteria.

The 2010 ESC recommendations resulted in the detection of a higher number of minor congenital abnormalities compared with contemporary criteria, but we believe this was fortuitous. Although left atrial enlargement or left-axis deviation was present on the ECG in a significant proportion of such athletes, we have previously demonstrated that there is no difference in the prevalence of minor congenital cardiac abnormalities in athletes and healthy controls with either of these ECG anomalies compared with athletes with normal ECGs (22). Even after allowance for these diagnoses, the cost of screening remained lower with contemporary criteria.

COST ISSUES AND CLINICAL IMPLICATIONS FOR THE LARGER UK ATHLETE POPULATION. Based on the Active People Survey, a national survey of sports participation, 3,245,400 young people (14 to 35 years) participated in competitive sport in 2014/15 (23). Extrapolation of our costs to these athletes means that a de novo screening program for all athletes in the United Kingdom would cost $356,994,000 and detect a substantial number (9,736 athletes) harboring conditions that are associated with exercise-related sudden cardiac death using the 2010 ESC recommendations (adapted for less conservative criteria for abnormal QT intervals). Application of the Seattle and refined criteria would cost $298,576,800 and $282,349,800, respectively, equating to a huge saving of approximately $58 to 75 million. These estimates do not take into consideration the invariable cost reduction of screening the same cohort during subsequent years.

Whether these costs provide a feasible solution for all athletes is debatable. Application of the most specific ECG interpretation criteria (refined criteria) would translate to a cost of nearly $29,000 per diagnosis of a potentially serious cardiac condition and may be acceptable for lucrative organizations. However, considering the large number of exercising young individuals and the low incidence of exercise-related sudden cardiac death, it is arguable that the cost of nationwide screening may be excessive for less financially endowed sporting organizations, and could be invested in improving training and facilities for cardiopulmonary resuscitation (24–26).

STUDY LIMITATIONS. Our cost analysis was based on subsidized amounts for preliminary assessment ($53 per athlete) and relatively modest costs of secondary investigations in the U.K. National Health Service, which may be considerably cheaper compared with other health care models. Nevertheless, the systematic methodology of investigating a large number of athletes should enable a relatively precise estimate of the number of additional investigations required by other Western populations. Secondary investigations were at the discretion of the attending cardiologist and may have been influenced by personal clinical practice as would be expected in real-life clinical situations. It is prudent to emphasize that these costs relate solely to the detection of new cardiac conditions and do not account for any downstream costs of management and on-going clinical surveillance of affected athletes.

Finally, data relating to secondary investigations in athletes with abnormal history, physical examination, or ECG relied solely on information provided by club doctors and may be subject to recall bias.

CONCLUSIONS

Contemporary ECG interpretation guidelines are associated with a cost reduction of up to 21% without compromising sensitivity to detect serious cardiac disease. These results represent a welcome saving for sporting organizations equipped with the infrastructure and expertise for cardiac screening in athletes.

REPRINT REQUESTS AND CORRESPONDENCE: Dr. Sanjay Sharma, Division of Cardiovascular Sciences, St. George's University of London, Cranmer Terrace, London, SW17 0RE, United Kingdom. E-mail: sasharma@sgul.ac.uk.

PERSPECTIVES

COMPETENCY IN SYSTEMS-BASED PRACTICE: The overall cost of screening young athletes using the 2010 ESC recommendations amounted to $110 per individual and $35,993 for each serious cardiovascular diagnosis established. Use of Seattle and refined criteria reduced the cost to $92 and $87 per athlete screened and $30,251 and $28,510 per serious diagnosis, respectively, representing a 21% cost saving per athlete screened.

TRANSLATIONAL OUTLOOK: Sequential follow-up studies are needed to evaluate the long term cost-effectiveness of modifying ECG screening criteria for competitive athletes in various health care settings.

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APPENDIX For a supplemental table, please see the online version of this article.