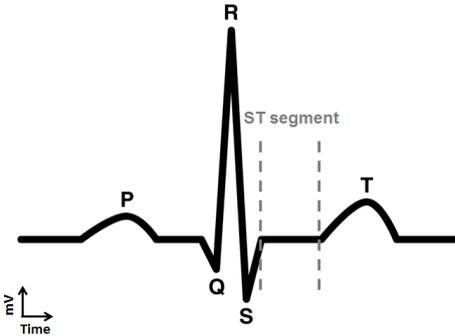


**Impact case study (REF3b)**

<p><b>Institution:</b> University of Glasgow</p>
<p><b>Unit of Assessment:</b> Unit 1; Clinical medicine</p>
<p><b>Title of case study:</b> Advancing heart disease diagnosis – influencing international guidelines and commercial adoption of automated ECG analysis software</p>
<p><b>1. Summary of the impact</b>          The electrocardiogram (ECG) is one of the most commonly used medical tests which assist in diagnosing heart disorders worldwide. However, diagnosis relies on accurate interpretation of ECG recordings. Studies by University of Glasgow researchers have led to changes to international guidelines for ECG-based diagnosis of a heart attack (myocardial infarction; MI) and have led to significant refinements to the automated ECG analysis software called the ‘Glasgow Program’. Commercialisation of the Program since 2008 has resulted in its incorporation into some of the market-leading medical devices, with approval of the Glasgow Program by the FDA and more than 40,000 devices sold worldwide, potentially aiding millions of patients around the world. The Program assists hospital doctors, family practitioners and others such as first responding emergency services, e.g. ambulance and fire services, with the reliable interpretation of ECGs, enabling rapid and accurate diagnosis and treatment of patients with a variety of heart problems.</p>
<p><b>2. Underpinning research</b>          Each heartbeat is controlled by an electrical signal which travels through the heart, causing the muscle to contract, pump blood around the body and relax in time for the next beat. By placing electrodes on a person’s chest and limbs, this electrical activity can be detected and plotted (normally in millivolts [mV] as a function of time) to form an ECG. As shown in the diagram (right), the ECG cycle representing one heartbeat consists of a series of waves (P, QRS and T) with corresponding segments and intervals, which map the electrical signal as it travels through the heart. The standard 12-lead (waveform) ECG is typically recorded over a 10-second period so that many cycles (hence heartbeats) are recorded. Alterations in the normal ECG recording (changes in the shape of waves or the length and height of segments or intervals) might indicate abnormalities and can be used to diagnose disorders associated with abnormal heart rate and rhythm, enlarged heart (hypertrophy) or heart attacks. However, accurate detection of ECG abnormalities requires a clear appreciation of the normal limits of the ECG signal in apparently healthy populations.</p>

<p><b>The Glasgow Program: key advances since 1993</b>          Professor Peter Macfarlane and his team at the University of Glasgow have an extensive track record in ECG research and pioneered the development of automated analysis and interpretation of the ECG. By the early 1980s, the team had developed a basic computer algorithm called the ‘Glasgow Program’, which could automatically detect ECG components, compare these with reference ‘normal’ values and provide an interpretation to aid the clinical diagnosis of heart problems. From 1993 onwards, the team has systematically studied the effects of age, sex and race on the normal limits of the 12 lead ECG and refined criteria so that ECG signals can be accurately interpreted in different patient subpopulations, e.g. males, females, Caucasians, Chinese, Africans. The current form of the Glasgow Program incorporates these refined criteria.</p>
<p>Heart attacks are associated with a characteristic change in the ST segment on an ECG recording and consequently the height of the ST segment is used to diagnose heart attacks. Joint guidelines issued by the American College of Cardiology (ACC) and European Society of Cardiology (ESC) in 2000 stated a common diagnostic upper limit for the ST segment height in most of the 12 leads for all adults, regardless of age, sex or race. Between 1993 and 2000, the University of Glasgow team defined age-based and sex-based criteria for evaluating the height of the ST segment in the adult 12-lead ECG. In 2001, Macfarlane reported findings obtained through the examination of ECGs from 1,338 healthy men and women (age range between 18 and 78 years). These showed that the upper limit for the normal ST segment’s height in three specific chest leads was at least 50% higher in men than in women, and for one of these leads, the upper limit was distinctly different from the other two in both men and women.<sup>1</sup> The latter finding demonstrated that this lead should be</p>

evaluated independently of the other two leads when defining the diagnostic criteria for heart attacks. Furthermore, the work revealed an age-dependent decrease in the upper limit in two of these leads, which is observed only in men. These findings were incorporated into the existing Glasgow Program to produce an enhanced version for reporting ST elevation MI (STEMI).

### **Validation of the enhanced Glasgow Program's sensitivity and specificity for diagnosing heart attack**

In a collaborative research study with the medical device manufacturer Medtronic Physio Control, the Glasgow team compared almost 3000 ECG recordings taken from Scottish and American men and women (approximate age range 20-80 years, 60% of whom had presented with chest pain) using either the enhanced Glasgow Program or the 2000 guideline criteria. The results showed that the Glasgow Program significantly improved the sensitivity and specificity of the ECG-based diagnosis of heart attacks.<sup>2</sup> In 2010, the enhanced Glasgow Program's ability to accurately diagnose a heart attack was comparable to that of specialist cardiologists and, in fact, it proved to be superior in its ability to reduce the number of false-positive diagnoses.<sup>3</sup>

The University of Glasgow researchers also provided vital data on paediatric ECGs by characterising recordings of over 1,700 healthy neonates, infants and children.<sup>4</sup> This study revealed that the components of the ECG (particularly the QRS height) change over the course of the first few days of life. These findings led to the incorporation of age-adjusted normal limits for ECG values in neonates, infants and children into the Glasgow Program.

### **Use of the Glasgow Program in large-scale clinical trials**

The Glasgow Program has been at the design core of a number of high-profile cardiovascular randomised clinical trials. The value of combining automated interpretation with automated coding, using an internationally agreed scheme, was first demonstrated in the landmark West of Scotland Coronary Prevention Study (WOSCOPS).<sup>5</sup> As part of this, the participants' ECGs were recorded annually for a minimum of 5 years in various health centres in the west of Scotland, and the recordings were transmitted electronically over the telephone network to a central computer for automated analysis using the Glasgow Program. In this way, the Glasgow Program detected heart attacks of which the participants had been unaware. In addition, the ECGs were automatically coded using an internationally agreed scheme known as the Minnesota Code. This approach is accepted worldwide by epidemiologists as a standardised method for classifying ECG waveforms. WOSCOPS highlighted the potential of this approach to control for variation in ECG-based diagnosis of heart attacks between clinicians within the same trial centre and those who are physically separated on different sites/countries thereby improving the trial outcome assessment.

**Key University of Glasgow researchers:** Peter Macfarlane (Professor in Medical Cardiology [1991-1995]; Professor of Electrocardiology, [1996-2010]; Honorary Research Fellow [2010-present]); Brian Devine (Software Development Manager [1988-present]); Elaine Clark (Software Applications Specialist [1998-present]); WOSCOPS study group members (see article for full details). **Key external collaborators:** Medtronic Physio Control

### **3. References to the research**

1. Macfarlane PW. [Age, sex and the ST amplitude in health and disease](#). *J Electrocardiol* 2001; 34 (suppl):235-41. doi: 10.1054/jelc.2001.28906
2. Macfarlane PW, Browne D, Devine B, Clark E, Miller E, Seyal J, Hampton D. [Modification of ACC/ESC criteria for acute myocardial infarction](#). *J Electrocardiol* 2004; 37 (suppl):98-103. doi: 10.1016/j.jelectrocard.2004.08.032
3. Clark EN, Sejersten M, Clemmensen P, Macfarlane PW. [Automated electrocardiogram interpretation programs versus cardiologists' triage decision making based on teletransmitted data in patients with suspected acute coronary syndrome](#). *Am J Cardiol*. 2010; 106(12):1696-702. doi: 10.1016/j.amjcard.2010.07.047.
4. Macfarlane PW, McLaughlin SC, Devine B, Yang TF. [Effects of age, sex, and race on ECG interval measurements](#). *J Electrocardiol*. 1994;27 Suppl:14-19
5. Shepherd J, Cobbe SM, Ford I, Isles CG, Lorimer AR, MacFarlane PW, McKillop JH, Packard CJ. [Prevention of coronary heart disease with pravastatin in men with hypercholesterolemia](#).

West of Scotland Coronary Prevention Study Group. *N Engl J Med.* 1995; 333(20):1301-7. doi: 10.1056/NEJM199511163332001

#### 4. Details of the impact

The ECG is used routinely in medicine to assess the health status of the heart. In addition to routine monitoring of heart function (e.g. in the general practice setting or prior to surgery), the ECG can provide critical insights into various clinical conditions, such as a heart attack, disorders of heart rhythm or an enlargement of the heart (as seen in heart failure). However, the interpretation of the ECG is complex and requires the reader to have knowledge, skill and practice to undertake the task accurately. The University of Glasgow's wealth of research on the normal ECG, showing the differences associated with age, sex and race, particularly on the height of the ST segment, has driven the revision of clinical guidelines defining the ECG criteria for diagnosing heart attacks.

##### ***Influencing international guidelines on heart attack***

An ECG is considered to be the single most important clinical test in the rapid, initial evaluation of patients experiencing chest pain due to suspected myocardial infarction (heart attack). In 2009, Macfarlane was one of 10 experts who revised the joint recommendations of the American Heart Association (AHA), the American College of Cardiology and the Heart Rhythm Society. The revised guidelines<sup>a</sup> directly adopted Macfarlane's findings published in 2001, which defined different ST-height thresholds for men and women and stipulated two sets of age-based thresholds among men.<sup>1</sup> In 2012, the AHA joined the World Heart Federation and the European Society of Cardiology (ESC) to publish the 'Third universal definition of myocardial infarction'.<sup>a</sup> In this guideline, the ST segment elevation thresholds for diagnosing heart attacks are again based directly on the University of Glasgow's work (Table 3 in the document and reference 38). This consensus guideline from the leading global cardiovascular authorities is the most powerful guidance currently available to cardiologists and standardises the diagnosis of heart attack around the world.

##### ***Commercial adoption of the Glasgow Program by the medical devices industry***

Correct interpretation of the ECG, particularly in the ambulance or the accident and emergency department, is usually the basis for immediate treatment and/or subsequent diagnostic tests. Whilst cardiologists are expert at interpreting the ECG, these specialists are not readily available in all clinical settings. Automated ECG interpretation provides a solution to this problem.

The global market for ECG monitoring systems is estimated to reach more than US\$800 million in the next few years. Coupled with the rising incidence of heart disease, there is a highly lucrative market for automated ECG interpretation software. The Glasgow Program is a major competitor in this market and remains at the cutting edge of electrocardiographic research. As such it has been adopted commercially by some of the world's leading electro-medical device manufacturers in various product formats, all of which have gained approval from the FDA.

Firstly, the Glasgow Program has been integrated into ECG machines that acquire, read out and interpret ECGs. Cardiac Science, a US-based market-leading company with customers in over 100 countries worldwide, offers this type of product through its *Burdick* brand [models 8300 & 8500]. Mindray, a leading Chinese medical device manufacturer, now uses the program in its *R3 electrocardiograph*. Secondly, the Glasgow Program has been embedded into computer software packages that accompany Holter monitor ECG systems: Teled Solutions' flagship product is the *TM-12 recorder*. Thirdly, Draeger use the software in its patient monitoring system – the *Infinity® Central Station*. Finally, the Glasgow Program has been combined with defibrillator/patient monitor devices such as the Physio-Control *Lifepak®15*.<sup>b</sup> Physio-Control states that:

*"It is important that our product use an ECG analysis program that is widely used in clinical practice and is recognized as being among best in class. The Glasgow program meets those requirements. The Glasgow program gave us an advantage over our previous generation product in that the Glasgow program adjusts its STEMI criteria based on patient gender and, for men, on patient age."* – Principal Scientist, Physio-Control Inc.<sup>c</sup>

[Text removed for publication]. Inclusion of the Glasgow Program in the above devices allows faster recording and immediate interpretation of ECGs, thereby reducing, and even eliminating, the need

## Impact case study (REF3b)

for routine manual ECG interpretation and filing. The read-out format of the Program contains headline statements (such as 'CONSIDER ACUTE STEMI' and 'SIGNIFICANT ARRHYTHMIA'), which can aid initial diagnosis. Such headline statements are especially important for emergency ambulance services, which need to decide quickly whether a patient should be taken to a heart specialist centre, for example. Furthermore, the Glasgow Program is one of the few automated systems that can accurately interpret ECGs from birth, thereby enabling clinicians to use this diagnostic tool in a paediatric setting.

Since 2008, over 40,000 devices containing the Glasgow Program have been sold worldwide to a range of end-users.<sup>d</sup> For example, Physio-Control has sold a significant number of *Lifepak@15* devices to UK ambulance services, including around 740 to the London Ambulance Service (LAS).<sup>c</sup> LAS responds to an estimated 1.5 million emergency calls per annum and has reported an increase in survival following a cardiac arrest from 12% to 32% in the last five years. It is conceivable that the rapid and reliable interpretation of ECGs with the Glasgow Program will have contributed to this improvement.<sup>e</sup> Similarly, Physio-Control Inc. has sold devices to fire services as well as other medical service vehicles, ships and hospitals.<sup>c</sup> As each of these 40,000 devices will undoubtedly be used on multiple patients, the software is estimated as being used to interpret the ECGs of millions of patients annually.

### ***Influence on practice-changing clinical trials and epidemiological studies***

The Glasgow Program has been used in a number of large multi-centre randomised controlled clinical trials and epidemiological studies. The dedicated University of Glasgow Core Lab<sup>f</sup> acts as a partner to a number of stakeholders in clinical trials by providing a standardised approach to ECG interpretation that is used in all centres. Since 2008, the Glasgow Program and Core Lab have been involved in over 12 trials and studies. These trials have established major clinical outcomes of international significance, for example the benefits of statins in preventing cardiovascular disease, which have themselves led to changes in guidelines and clinical practice.

## **5. Sources to corroborate the impact**

### **a. *International guidelines***

- Wagner GS, Macfarlane P, *et al.* [AHA/ACCF/HRS recommendations for the standardization and interpretation of the electrocardiogram](#). *J Am Coll Cardiol*. 2009; 53:1003-11. (Ref 8 is Macfarlane *J Electrocardiol* 2001, cited in ST-segment recommendations, p1005)
- Thygesen K *et al.*, [Joint ESC/ACCF/AHA/WHF Task Force for the Universal Definition of Myocardial Infarction. Third universal definition of myocardial infarction](#). *Eur Heart J*. 2012 Oct; 33:2551-67. (Ref 38 is Macfarlane *J Electrocardiol* 2001, cited in 'Electrocardiographic detection of myocardial infarction' - 'ECG manifestations' Table 3 and evidence base, p8).

### **b. *Medical device companies citing inclusion of the Glasgow Program in their product:***

Cardiac Science – *Burdick 8300 ECG* and *Burdick 8500 ECG* (until mid-2013 available directly from Cardiac Science, now sold via distributors e.g. [Moore Medical Burdick 8300 ECG](#) and [Fisher Medical Burdick 8300 ECG](#)); Mindray - [R3 electrocardiograph](#); Telemed Solutions - [TM-12 recorder](#); Draeger - [Infinity@ Central Station](#); Physio-Control - [Lifepak@15 monitor/defibrillator device](#) ('Interpretive algorithm' section, p17)

### **c. Statement from Principal Scientist, Physio-Control Inc. available on request**

### **d. *Commercial adoption of the Glasgow Program***

- Full list of medical device companies who have purchased or extended rights to use the Glasgow Program since 2008 is as follows: *Schmidt, McKesson, Cardiolex, Cardiac Science, Draeger, Epiphany, Heartlab, Spacelabs Healthcare Inc., Physio-Control Inc., Dan Medical, AMPS, Mindray Inc., Memtec Corporation (who licence to Telemed Solutions), Vitalograph Ltd., Allengers, Gestio Agfa, Mediana Co., Maestros Mediline Systems Ltd., Quinton.*

### **e. Physio-Control '[Inside Physio](#)' website. The link at the bottom of this page '[Click here to read about LAS](#)' redirects to a PDF document 'LAS NHS Trust: A model system of care' confirming enhanced survival rates (p1) and 740 devices purchased (p3).**

### **f. [ECG core lab](#), a service for large multi-centre clinical trials.**