

# **Recognition of STEMI by Paramedics and the Effect of Computer inTerpretation (RESPECT) pilot study**

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*As with many interventions intended to prevent ill health, the effectiveness of parachutes has not been subjected to rigorous evaluation by using randomised controlled trials. Advocates of evidence based medicine have criticised the adoption of interventions evaluated by using only observational data. We think that everyone might benefit if the most radical protagonists of evidence based medicine organised and participated in a double blind, randomised, placebo controlled, crossover trial of the parachute.*

CS Smith and JP Pell [1]

## *Abstract*

**Background** Timely diagnosis and appropriate management of patients with ST-segment elevation myocardial infarction (STEMI) depends on accurate interpretation of the 12-lead ECG by paramedics. Computer interpretation messages on ECGs are often provided, but the effect they exert on paramedics' decision making is not known. The pilot study objective is to assess the feasibility of conducting a trial using an online assessment tool, to determine the effect of computer interpretation messages on paramedics' diagnosis of STEMI from a 12-lead ECG.

**Methods** The RESPECT pilot study is a randomised cross-over trial utilising a bespoke, web-based assessment tool. Participants were randomly allocated 12 of 48 ECGs, with an equal mix of correct and incorrect computer interpretation messages, and STEMI and STEMI-mimics.

**Results** 254 Health and Care Professions Council (HCPC) registered paramedics in the UK consented into the study, 205 completing the first phase and 156 completing phase two; an attrition rate of 24%. The ICC for participants was 0.05 and for ECGs, 0.41. Overall, participant accuracy was 80% when the computer message was visible and 79% when hidden. In the subset of correct computer interpretations, accuracy was 84% (message hidden) and 87% (message visible). The subset of incorrect computer interpretations resulted in an accuracy of 77% (message hidden) and 71% (message visible). Overall, the unadjusted odds ratio (OR) of a correct interpretation with a computer message was 0.94 (95%CI 0.77–1.10, p=0.44) and adjusted OR, 0.92 (95%CI 0.77–1.10, p=0.38). For the subset of correct computer interpretation, the unadjusted OR was 1.31 (95%CI 1.01–1.71, p=0.04) and adjusted OR, 1.42 (95%CI 1.06–1.89, p=0.02). Incorrect computer interpretations had an unadjusted OR of 0.76 (95%CI 0.61–0.93, p=0.01) and adjusted OR, 0.70 (95%CI 0.56–0.88, p=0.00).

**Conclusion** Data from the pilot study suggests the main study is feasible, assuming the sample size calculation for the main study is not prohibitively large.

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Whoever advised me to consult a statistician during the planning of a study also deserves much praise, although I cannot recollect where I first heard those words. A seemingly simple study that recorded binary responses to a question about the presence of STEMI, turned out to have a rather complex analysis, involving clustering and cross-classified modelling, and I am indebted to Dawn Tere for assisting me through the minefield of binary logistic regression with random effects.

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# Abbreviations

<b>ACI-TIPI</b>	Acute cardiac ischaemia time-insensitive predictive instrument
<b>ACS</b>	Acute coronary syndrome
<b>AMI</b>	Acute myocardial infarction
<b>ASA</b>	Ambulance services association
<b>CAD</b>	Coronary artery disease
<b>CASP</b>	Critical appraisal skills programme
<b>CCU</b>	Coronary care unit
<b>CINAHL</b>	Cumulative index to nursing and allied health literature
<b>CONSORT</b>	Consolidated standards of reporting trials
<b>CPD</b>	Continuous professional development
<b>CSE</b>	Common standard for quantitative electrocardiography
<b>CSV</b>	Comma-separated values
<b>ECG</b>	Electrocardiogram
<b>ED</b>	Emergency department
<b>EMS</b>	Emergency medical service
<b>ESC</b>	European society of cardiology
<b>GLM</b>	Generalised linear model
<b>HCPC</b>	Health and care professions council
<b>ICC</b>	Intra-class correlation coefficient
<b>IEC</b>	International electrotechnical commission
<b>IMMEDIATE</b>	Immediate myocardial metabolic enhancement during initial assessment and treatment in emergency care
<b>IVCD</b>	Interventricular conduction delay
<b>JRCALC</b>	Joint royal colleges ambulance liaison committee
<b>LBBC</b>	Left bundle branch block

<b>LVH</b>	Left ventricular hypertrophy
<b>MEDLINE</b>	Medical literature analysis and retrieval system online
<b>MI</b>	Myocardial infarction
<b>MySQL</b>	My structured query language
<b>NAEMT</b>	National association of emergency medical technicians
<b>NHS</b>	National Health Service
<b>NIAP</b>	National infarct angioplasty project
<b>NSR</b>	Normal sinus rhythm
<b>OR</b>	Odds ratio
<b>PCP</b>	Primary care paramedic
<b>PDF</b>	Portable document format
<b>PHP</b>	PHP: Hypertext Preprocessor (a recursive acronym)
<b>PICO</b>	Population, intervention, comparison and outcome
<b>pPCI</b>	Primary percutaneous coronary intervention
<b>PRISMA</b>	Preferred reporting items for systematic reviews and meta-analyses
<b>PVC</b>	Premature ventricular contraction
<b>REC</b>	Research ethics committee
<b>RESPECT</b>	Recognition of STEMI by paramedics and the effect of computer interpretation
<b>RVH</b>	Right ventricular hypertrophy
<b>SHO</b>	Senior house officer
<b>STEMI</b>	ST-segment elevation myocardial infarction
<b>TPI</b>	Thrombolytic predictive instrument
<b>UK</b>	United Kingdom
<b>URL</b>	Uniform resource locator
<b>YAS</b>	Yorkshire ambulance service

# Chapter 1

## Introduction

### 1.1 Health burden of coronary artery disease

Worldwide, coronary artery disease (CAD) is the most common cause of death, with around seven million people dying each year [2]. In Europe, every sixth man and seventh woman will die from an acute myocardial infarction (AMI), or heart attack [3]. In developed countries, including the United Kingdom (UK), the incidence of myocardial infarction has been decreasing over the past 30 years [4], but there were still 125,245 inpatient episodes at National Health Service (NHS) facilities with a primary diagnosis of AMI in 2010/11 [5].

### 1.2 Pathophysiology of myocardial infarction

Coronary artery disease is almost always caused by atherosclerosis of the coronary arteries. This is a systemic, lipid (fat) driven immune/inflammatory disease of the medium and large arteries [6]. Over time (usually decades), atherosclerosis causes the formation of plaques; collections of lipids and cholesterol that accumulate in the intimal layer of arteries, some of which attract macrophages (a type of white blood cell). The macrophages secrete protein dissolving enzymes and engulf the lipids, leaving behind a lipid-rich ‘necrotic core’. The interface between the plaque and the lumen of the artery is known as the fibrous cap.

Ruptured plaques are the most common cause of AMI [7], and typically involve a plaque with a thin fibrous cap [8]. This rupture usually occurs during, or just after, a sympathetic nervous system trigger such as physical or sexual activity, anger, anxiety, work stress, temperature change or cocaine use [9]. The exposed necrotic core is highly thrombogenic, leading to platelet aggregation and activation of the clotting cascade [10]. Should the artery become completely occluded, blood proximal to the blockage will stagnate and may coagulate, extending the thrombosis along the artery and making subsequent reopening of the artery much more difficult [6].

An occluded coronary artery will usually lead to myocardial cell death secondary to prolonged ischaemia, i.e. cause a myocardial infarction (MI). This process can begin in under 20 minutes, but complete necrosis of myocardial cells which have had their supplying coronary artery (or arteries) occluded, typically does not occur until 2–4 hours, and sometimes longer, have elapsed, depending upon the presence of collateral circulation, the pre-morbid state of the patient, the nature of the occlusion (intermittent or permanent) and the sensitivity of the myocytes to ischaemia, for example [11]. This provides an opportunity for timely salvage of the myocardium, improving heart function and reducing mortality, if blood flow can be restored [12].

### 1.3 The electrocardiogram and AMI

The first step in the development of AMI is the onset of myocardial ischaemia, as oxygen delivery fails to meet demand. Clinically, this is typically identified from the patient history, presenting signs and symptoms, and interpretation of the 12-lead electrocardiogram (ECG). The ECG is a recording of the electrical activity generated by the cells of the heart, and is obtained by the placement of a number of electrodes around the heart, which provide different views of this electrical activity [13]. The resulting output on a screen or paper plots the voltage generated against time. Characteristic components of the ECG enable a clinician to recognise a number of medical conditions, including AMI. Figure 1.1 shows the components of the ECG, including the ST segment and T wave, which are important in the recognition of a specific type of AMI, ST-segment elevation MI (STEMI) [14]. Ordinarily, the ST-segment is level with the baseline (typically measured at the level of the PR segment), as shown in the the normal 12-lead ECG in Figure 1.2.

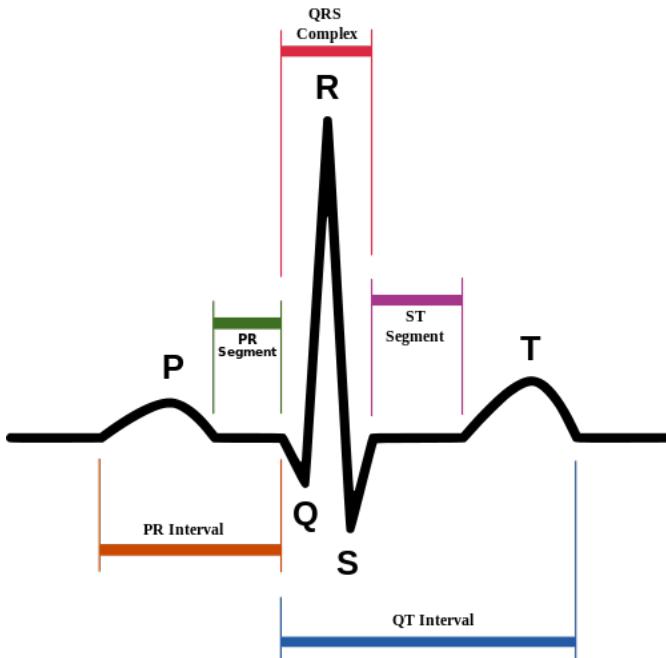


FIGURE 1.1: The components of an ECG complex

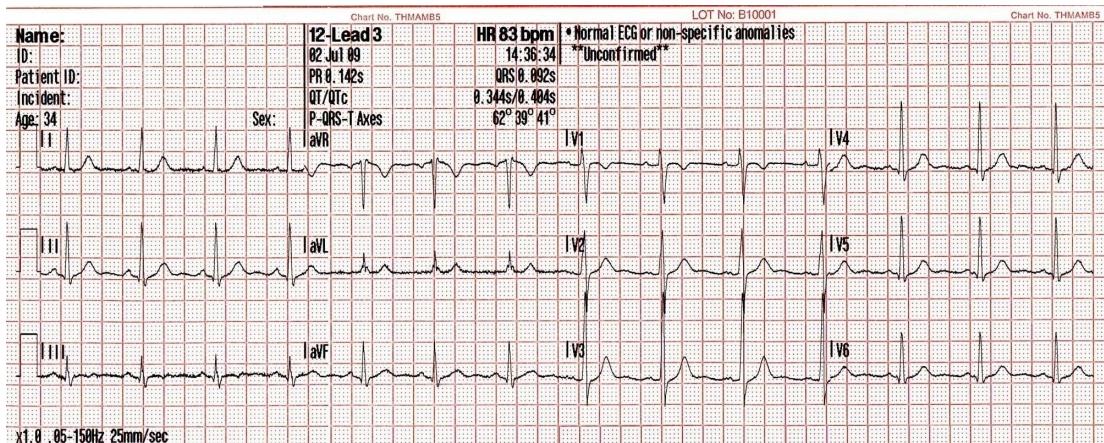


FIGURE 1.2: A normal 12-lead ECG

During a period of myocardial ischaemia, myocardial injury often produces a characteristic rise in the ST-segment from the baseline. Criteria vary, but typically if the ST-segment rises 2mm or more in two or more leads looking at the same area of the heart, then the patient is said to be having a STEMI, even if myocardial necrosis has not yet occurred [15]. Figure 1.3 shows an example of this ST-segment rise and the computer interpretation message, which is printed at the top of the 12-lead ECG.

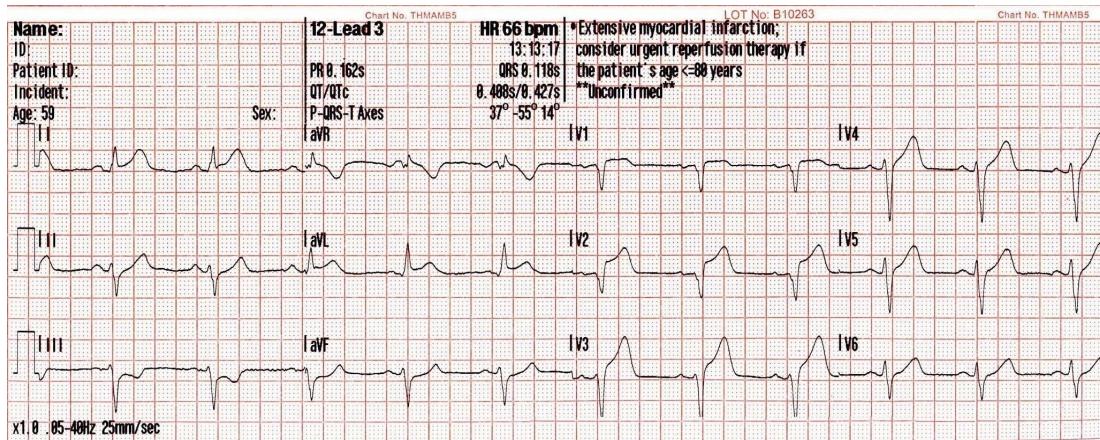


FIGURE 1.3: A 12-lead ECG with ST-segment elevation

## 1.4 Treatment of STEMI

Clinical trials have demonstrated a clear link between patient outcome and time to reperfusion in STEMI [12], which heightened interest in the prehospital recognition and treatment of STEMI. In 2001, prehospital thrombolysis was introduced, a technique previously only used in hospital, to chemically clear the blockage in the patient’s coronary arteries. Initially, diagnosis was supported by the use of telemetry, whereby the ECG would be sent to the local hospital for diagnosis. Subsequent studies demonstrated that paramedics’ diagnosis of STEMI was highly sensitive and specific [16, 17], leading some to question the need for telemetry with its associated costs and technical issues [18–20]. However, thrombolysis is associated with increased risk of bleeding, including haemorrhagic strokes, and is not always successful in clearing the affected coronary arteries. Fortunately, there is an alternative, mechanical clearance of coronary arteries with a balloon catheter and stent, collectively known as primary percutaneous coronary intervention (pPCI). In 2008, the National Infarct Angioplasty Project (NIAP) concluded that numerous international trials demonstrated reduced mortality and improved long-term outcome of pPCI compared with thrombolysis. However, this is time dependent, and delays beyond 90 minutes from when thrombolysis could have been administered, is considered to be point at which the benefit of pPCI is negated. In addition, NIAP also demonstrated that in order to achieve this, bypassing local hospitals in favour of a regional centre which had a cardiac catheter lab was the most effective (and cost-effective) method [12].

As with the early administration of thrombolysis, ambulance services now have an important role in minimising the time from a patient's call for professional help, to undergoing pPCI (the call-to-balloon time). In the UK, 95% of STEMI patients are treated with pPCI, and 77.5% of patients with STEMI are taken directly to the cardiac catheter labs by the ambulance service [21]. The current European Society of Cardiology (ESC) guidelines for the management of patients presenting with STEMI, advocate the recording of a 12-lead ECG within 10 minutes of first medical contact, and direct transfer to a pPCI capable centre, if this is possible, within 120 minutes. If this is not possible, then the administration of thrombolysis should be achieved within 30 minutes [2]. This guidance has been incorporated into the current UK ambulance service clinical guideline for the management of STEMI [15].

## 1.5 Computer interpretation of ECGs

Since Augustus Waller first demonstrated the measurement of electrical current produced by the human heart in 1887 (Figure 1.4) [22, 23], ECG recording fidelity has improved considerably, as has the portability of the hardware required to produce the waveforms.

However, recording the ECGs is just the first step, since they also require interpretation. Since skilled personnel are not universally available, computers have been seen as a possible solution. In the 1960s, computer interpretation of ECGs was introduced, although this was typically only available at larger hospitals with large, dedicated computers [24]. Today, computer interpretation of ECGs is possible at the patient's side, thanks to the increased power and reduced size of computers.

In order to interpret an ECG, a computer needs to complete five steps [13]:

1. Obtaining and filtering the signal
2. Identifying and sorting complexes in order to create an average (typically median) complex for each lead
3. Recognising the waveform and identifying the onset and offset of a single complex

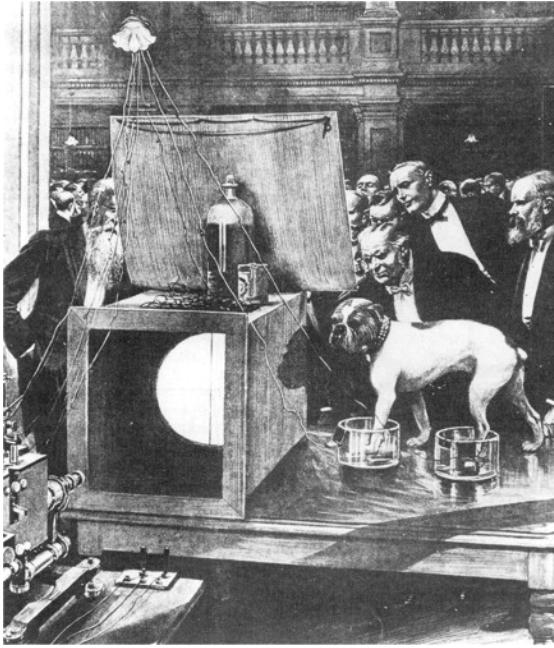


FIGURE 1.4: Waller demonstrating at the Royal London Society with his bulldog Jimmie

4. Extracting features from complexes and measuring amplitudes and intervals
5. Utilising heuristic or statistical methods to allocate diagnoses.

### 1.5.1 ECG standards

In order to introduce a standard performance benchmark for the first four steps, a Common Standard for Quantitative Electrocardiography (CSE) database was created in the late 1980s (and finalised in 1990). This consists of 1220 calibrated ECGs which are provided to manufacturers to test their ECG hardware and software [25, 26]. These ECGs were subsequently incorporated into the International Electrotechnical Commission standard IEC 60601–2–51 (superseded by IEC 60601–2–25 ed2.0 in 2011), which also includes acceptable tolerances in mean and standard deviation differences from the published measurements [27]. In addition, there are also standards relating to the messages produced by the computer interpretation algorithm. Examples of these are shown in Table 1.1 [28].

TABLE 1.1: ECG computer interpretation statements

Type	Description	Example
A	Diagnosis of an anatomical lesion relating to pathophysiological state	Interior infarct
B	Diagnosis of electrophysiological changes	Left bundle branch block
C	Descriptive ECG features	Nonspecific ST abnormality

### 1.5.2 Computer interpretation algorithms

Probably the most ubiquitous ECG interpretation algorithm in use by UK ambulance personnel is the General Electric (GE) Healthcare Marquette 12SL ECG analysis program [29]. This is a heuristic algorithm, utilising experience-based, deterministic rules that incorporate measurements from the median waveform into a decision tree and boolean combinations of criteria [13].

Other algorithms adopt alternative approaches, such as statistical methods, which generate probability statements. An example is the acute cardiac ischaemia time-insensitive predictive instrument (ACI-TIPI) [30]. At least one algorithm in use by prehospital healthcare professionals utilises algorithms trained using artificial neural networks [31], although in practice, these have been found to work better if combined with more traditional, deterministic, methods rather than as a standalone method [32].

### 1.5.3 Validation of ECG algorithms

Irrespective of the method used by the ECG interpretation algorithm, there is a need for training and testing in order to validate its use more generally. This typically consists of training the algorithm on databases containing ECGs with specific, often single, pathophysiologies, for example an MI or a specific arrhythmia. Subsequent testing usually utilises much larger ECG databases, containing a wide spectrum of ECG electrophysiologies, in order to calculate sensitivity and specificity statistics. The gold standard varies, depending on what characteristic is being tested. For example, the expert opinion of a cardiologist might be appropriate for conditions such as arrhythmias whereas, in acute coronary syndromes, it is more typical for cardiac enzymes or angiography confirmation of diagnosis to be used [33, 34].

## 1.6 Recognition of STEMI by paramedics

Timely diagnosis and appropriate management of patients with STEMI depends on accurate interpretation of the 12-lead ECG by paramedics. However, since only 4–6% of chest pain calls to emergency services are actually acute coronary syndromes, this is not always straightforward [35]. Thus, initial and ongoing training in the accurate acquisition and interpretation of 12-lead ECGs by paramedics, is important [36, 37].

There is little published literature about the training provided to UK ambulance personnel in relation to ECG interpretation. The most credible is arguably a 2001 technology appraisal process document, authored by the Joint Royal College Ambulance Liaison Committee (JRCALC) and the Ambulance Services Association (ASA), which set out a suggested syllabus for a prehospital thrombolysis course [38]. This itself, was based on existing courses being run at the time by four ambulance services and included the following topic areas:

1. ECG acquisition
2. Components of a ‘normal’ ECG
3. Arrhythmias
4. Coronary artery disease
5. The ECG in coronary artery disease
6. Management of MI including thrombolytics and other drugs.

Two courses were created by pharmaceutical companies who manufactured thrombolysis drugs, namely Fast Track to Thrombolysis by Roche, and Thrombolysis Up Front by Boehringer Ingelheim. These courses were provided free of charge to UK ambulance services, and although there are no national statistics regarding the utilisation of such course material, Thrombolysis Up Front was used by every UK ambulance service at that time [39].

In the absence of telemetry, computer aided interpretation of the 12-lead ECG is an attractive option, and is available on all ECG monitors carried by UK ambulance services (although at extra cost). Depending on the study, computer interpretation alone is

58–78% sensitive and 90–100% specific, with false positive rates varying between 19–39% [40–42]. Most studies consist of a mixture of paramedic and computer interpretation combined, either embedded in a protocol (usually requiring paramedic and computer agreement), or available for the paramedic to optionally utilise as a diagnostic tool. Sensitivities in this instance fall in the range 68–99.6%, specificities 68–97% and false positive rates 12–40% [37, 43–47]. However, with the exception of one study, in which the computer interpretation was deliberately switched off, it is difficult to unpick what effect the computer interpretation, and the paramedic’s own diagnostic skills, contribute to the figures mentioned. If it is the case that computer interpretation is adversely affecting accurate interpretation of the ECG, then it can be switched off. It may be the case, that the initial, and continuing, education of paramedics is the key. However, it is also possible that maintaining the status quo (i.e. a combination of paramedic and computer interpretation) is the best option.

## 1.7 Consequences of false negatives and positives

In contrast to early studies examining paramedics’ safe administration of thrombolysis, false-positive rates for pPCI referral, have been reported to be 20–31% [47–50], possibly due to poor ECG recording, mis-interpretation of the ECG and/or the perception that pPCI is less risky than administering thrombolytics [51]. Inappropriate referral to pPCI centres has potential cost implications, may contribute to staff burnout, particularly for hospital staff who are called in from home out-of-hours, and result in longer patient transport times to a regional pPCI centre, rather than the local emergency department (ED), which is associated with an increased risk of mortality [52].

False negatives are equally undesirable, since failure to identify and appropriately manage patients with STEMI, is more likely to result in delayed time to reperfusion, with the subsequent negative impact on mortality and morbidity [12]. However, existing research has not explored this in any detail. Work on thrombolysis perhaps unsurprisingly focussed on ensuring the patients paramedics choose to thrombolyse had been selected appropriately, ignoring those who may have been inappropriately missed [53–55]. In addition, research examining the prehospital activation of cardiac catheter labs, perhaps unsurprisingly, focussed on false positive rates and the impact this would have on pPCI services. However, only recruiting participants on a pPCI pathway meant that none of

the studies were able to identify patients who were missed (with the exception of the Ting study [46], which did record patients who had been taken to the ED at the study hospital).

## 1.8 Research focus

The Recognition of STEMI by Paramedics and the Effect of Computer inTerpretation (RESPECT) aims to answer the following research question:

Do computer interpretation messages have an effect on paramedics' diagnosis of STEMI from a 12-lead ECG?

# Chapter 2

## Literature review

### 2.1 Search strategy

In order to identify an appropriate set of key search terms for the literature review, a population, intervention, comparison and outcome (PICO) framework was utilised ([Table 2.1](#)) [56]. A brief scoping study identified that there were likely to be few studies focussing exclusively on paramedics, so the population definition was expanded to include all healthcare professionals, on the basis that although the results may not be directly applicable, they would assist in study planning. The remaining elements of the PICO framework utilised the research question as a guide.

TABLE 2.1: PICO framework for RESPECT research question

Framework element	Description
Population	Healthcare professionals who are required to interpret 12-lead ECGs and recognise STEMI.
Intervention	Computer assisted interpretation of a 12-lead ECG by healthcare professionals to determine the presence of STEMI.
Comparison	An appropriate reference standard e.g. blood cardiac enzymes, angiography, expert opinion.
Outcome	Diagnostic accuracy of healthcare professionals' diagnosis of STEMI

The medical literature analysis and retrieval system online (MEDLINE), cumulative index to nursing and allied health literature (CINAHL), Cochrane library and Google

scholar databases were searched between the 1st of December 2012 and 31st July, 2013, with no language or publication restrictions.

## 2.2 Inclusion and exclusion criteria

Full-text articles were obtained for systematic reviews and studies that were randomised, quasi-experimental, observational or diagnostic cohort in design. Consensus statements or guidelines, which related to the prehospital management of patients with acute coronary syndrome, were reviewed in order to identify further relevant studies, but excluded from the final analysis. For a study to be considered for the final analysis, it had to be randomised, quasi-experimental, observational or diagnostic cohort in design, and include a comparison between healthcare professionals and a reference standard, in the diagnosis of STEMI. Studies which only included process measures, such as door-to-balloon or door-to-needle times, were excluded. No geographical or service type (for example public versus private) restrictions were placed on the studies.

## 2.3 Assessment of quality

To aid in the evaluation of the research studies identified by the literature search, the Critical Appraisal Skills Programme (CASP) checklist was utilised [57]. This evaluates published research by asking three general questions about the study and providing additional questions under each heading, to aid critical appraisal:

1. Is the study valid?
2. What are the results?
3. Are the results applicable to my needs?

## 2.4 Data extraction

Although the literature review was not systematic, the methodology used to identify and extract information from the review was informed by a prehospital systematic literature review and the Cochrane handbook of systematic reviews [58, 59].

## 2.5 Results

A total of 147 titles and abstracts were obtained using the search strategy specified. Five full-text articles and one conference abstract met the inclusion criteria (see the Preferred Reporting Items for Systematic Reviews and Meta-Analyses [PRISMA] flow diagram in Figure 2.1) [43, 46, 60–63]. One further article was obtained, which explained the methodology used for the conference abstract study, enabling a critical appraisal of the study to be undertaken, since the lead author of the conference abstract did not reply to an email request for further information [64].

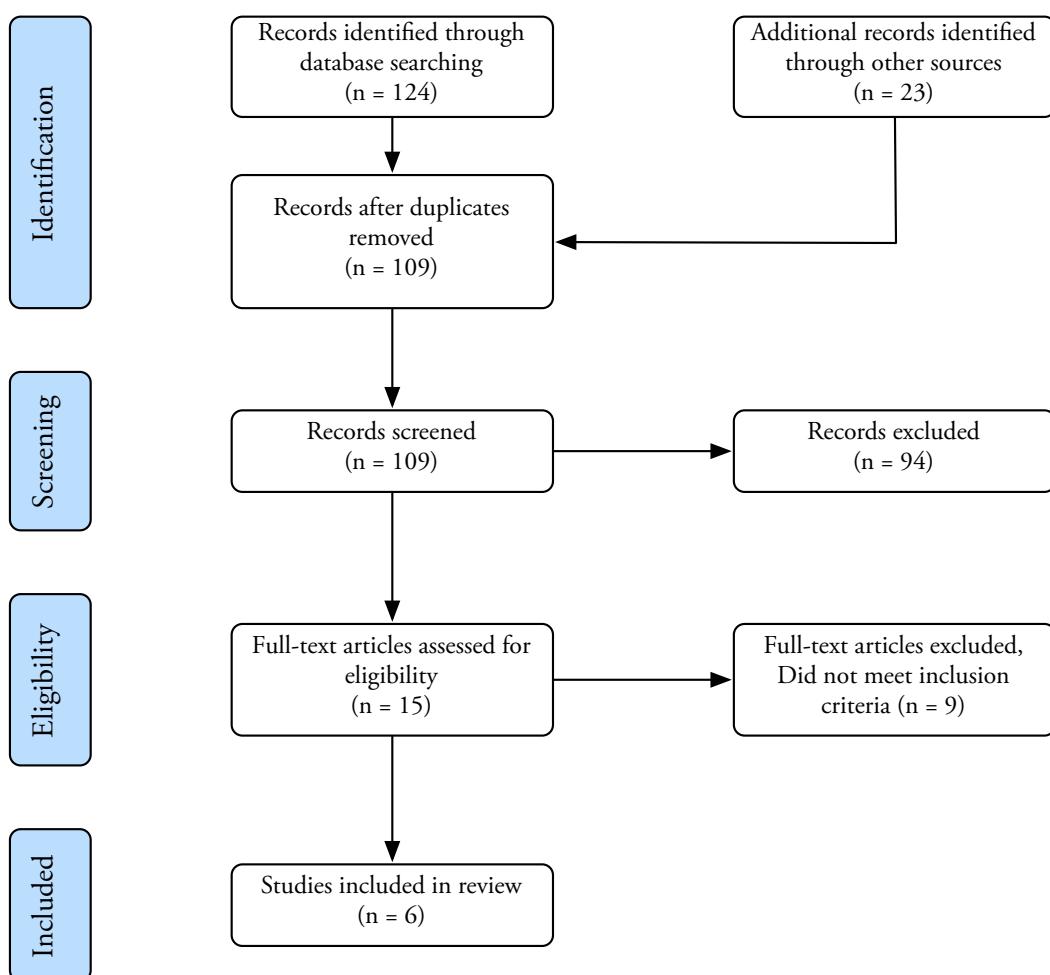


FIGURE 2.1: PRISMA flow diagram of search results

### 2.5.1 Description of studies

The six studies can be split into two groups, both in terms of their respective populations and methodologies. Three of the studies (Ting [46], Selker [63] and Cantor [43]), included paramedics as participants and were not randomised. Instead, two were prospective diagnostic studies (Ting and Cantor) and the third, a before and after, quasi-experimental design (Selker). These studies are summarised in Table 2.2.

TABLE 2.2: Summary of literature review studies (paramedic participants)

Study	Cantor 2012 [43]	Selker 2011 [63]	Ting 2009 [46]
Population	134 consecutive patients with suspected STEMI taken for pPCI.	437 patients over three phases.	2,007 patients but only 54 patients with suspected STEMI.
Intervention	New protocol for primary care paramedics. Computer interpretation of 12-lead ECG (GE Marquette 12SL).	Computer interpretation using ACI-TIPI and TPI diagnostic tools. Usual computer interpretation message provided (GE Marquette 12SL).	Prehospital ECG protocol. Computer interpretation message provided (GE Marquette 12SL).
Comparison	Blinded doctor interpretation of prehospital 12-lead ECG. Final diagnosis confirmed with angiography and cardiac biomarkers.	Blinded doctor with access to patients clinical records, ECGs and cardiac biomarkers.	Diagnosis determined by angiography.
Outcomes	Accuracy of STEMI recognition, complications during transfer and treatment times.	Percentage of true and false positive patients identified by paramedics as having ACS or STEMI.	Accuracy of STEMI recognition by paramedics.
EMS system, skill level and training	Single site in Canada. Primary care paramedics in study received 4 hours training on 12-lead ECG STEMI recognition.	11 sites throughout USA. NAEMT certified paramedics received 4 hours training in ACS and STEMI recognition and ACI-TIPI and TPI tools.	Single site in USA. 67 NAEMT certified paramedics received 3 hours training on protocol, ECG acquisition and interpretation.
Results	Doctor agreed with paramedic 121/134 (90%) participants. Final diagnosis: STEMI 106/134, false positive 28/134. 11/28 false positives could have been excluded if only computer interpretation utilised. 8 true STEMIs missed by computer interpretation.	Comparison between phase 1 and 2: STEMI identification increased from 40.8% to 68.4% ( $p<0.01$ ). Retrospective analysis of ACI-TIPI and TPI gave true positive rate for STEMI as 73%.	Prehospital recognition of STEMI: sensitivity 48.0%, specificity 99.6%, Positive predictive value 86.7%, Negative predictive value 97.4%. False negatives: 57% due to inaccurate computer interpretation, 21% due to cardiac arrest where no ECG recorded.

*Continued on next page*

Table 2.2 – *Continued from previous page*

Study	Cantor 2012	Selker 2011	Ting 2009
Notes	Primary care paramedics are equivalent to EMT-B in USA and ambulance technicians in the UK.	Training for new (to study) paramedics reduced to 1.5 hours in phase 3. Only study which utilised ACI-TIPI and TIPI tools. Analysis of phases retrospective. Patients not required to have chest pain.	Only post-implementation data usable. No record of missed STEMIs not using protocol. Not clear what demographic data recorded for patients who were not in the protocol.

The three remaining studies utilised doctors as participants and were randomised, utilising experimental survey designs rather than actual patient episodes (Goodacre [60], Massel [61] and Tsai [62]). A summary of these doctor studies is provided in Table 2.3.

TABLE 2.3: Summary of literature review studies (doctor participants)

Study	Tsai 2003 [62]	Massel 2003 [61]	Goodacre 2001 [60]
Population	30 doctors (internal medical residents) in second or third year of training.	9 doctors. 3 medical residents, 3 cardiology fellows and 3 consultant cardiologists.	10 doctors, all senior house officers.
Intervention	23 ECGs (11 in group A, 12 in group B) with computer interpretation message.	75 ECGs with typical history, checklist and computer interpretation.	25 ECGs with computer interpretation message.
Comparison	23 ECGs (11 in group A, 12 in group B) with computer interpretation message hidden.	75 ECGs with atypical history, no checklist and no computer interpretation.	25 ECGs without computer interpretation message.
Outcomes	Interpretative accuracy of the medicine residents. Secondary outcome measure: the effect of incorrect computer interpretation.	Intra- and inter-observer variability and bias measurements.	Proportion of major errors missed in each group. Secondary outcome measure: number of completely correct ECGs, without major or minor errors.
Site(s)	US university department of medicine.	Single tertiary care centre in Canada.	Single emergency department in a UK teaching hospital.

*Continued on next page*

Table 2.3 – *Continued from previous page*

Study	Tsai 2003	Massel 2003	Goodacre 2001
Results	Without computer interpretation, accuracy 48.9% (95% CI, 45.0-52.8%). With computer interpretation, 55.4% (95% CI, 51.9-58.9%; p<0.0001). When the correct computer interpretation included, accuracy 68.1% (95% CI, 63.2-72.7%; p<0.0001). Participants wrongly agreed with incorrect computer interpretation more often when visible 67.7% (95% CI, 57.2-76.7%) than when it was not 34.6% (95% CI, 23.8-47.3%; p<0.0001).	When all doctors considered as a group, improvement in inter-observer ECG interpretation when computer message provided (p=0.0001). Medical residents biased by computerised ECG (p<0.001) and less likely to recommend thrombolysis.	Major errors found in 46/250 (18.4%) ECG interpretations made by SHOs with computer interpretation visible. 56/250 (22.4%) major errors found in interpretations without computer message visible. No evidence of relationship between computer interpretation use and major errors by SHOs.
Notes	Computer algorithm not identified. ECGs not restricted to STEMI.	GE Marquette 12SL algorithm used. ECGs were not restricted to STEMI.	GE Marquette 12SL algorithm used. ECGs were not restricted to STEMI.

### 2.5.1.1 Paramedic studies

The Cantor study [43] was a prospective diagnostic study, and enrolled 134 patients who were taken directly for pPCI at one Canadian hospital. The intervention was a newly introduced prehospital protocol, allowing primary care paramedics (PCP) to bypass local EDs in order to take patients directly to the pPCI centre. Prior to the study, PCPs received three hours training relating to 12-lead ECG interpretation.

The primary outcome was accuracy of prehospital STEMI recognition, which was compared to an experienced cardiologist who had access to the prehospital ECG, but not the angiography or cardiac biomarker results, and final diagnosis, as determined by cardiac biomarker results and angiography. Secondary outcomes included the number of complications en route and various treatment timings. In addition, computer interpretative accuracy alone, was calculated.

The Selker study [63] was a three phase, before and after quasi-experimental study, to test the use of the acute cardiac ischaemia time-insensitive predictive instrument [30] and thrombolytic predictive instrument by paramedics [65], to identify suitable participants for the Immediate Myocardial Metabolic Enhancement During Initial Assessment and Treatment in Emergency Care (IMMEDIATE) trial. [66] It was conducted in multiple

sites throughout the US, with paramedics who were National Association of Emergency Medical Technicians (NAEMT) registered, and so roughly equivalent to UK paramedics. Prior to the study commencing, four hours of ECG interpretation and study tool training were provided.

The primary outcomes were proportions of patients correctly and incorrectly identified by paramedics as having an ACS, with a subsequent sub-group analysis of patients with STEMI. In addition, a retrospective analysis was conducted to determine the accuracy of the ACI-TIPI and TPI alone.

The Ting study [46] was a prospective diagnostic study conducted in the US, which collected demographic data from 2,007 patients taken by a single ambulance service to the study hospital, who were diagnosed with STEMI and underwent pPCI. The intervention was a new prehospital protocol which allowed study paramedics (NAEMT registered) to bypass the local ED and take patients directly to the study hospital's cardiac catheter lab. Prior to the start of the study, paramedics received three hours training, including familiarisation with the study protocol and 12-lead ECG acquisition and interpretation.

The primary outcome was accuracy of paramedic recognition of STEMI, which was compared to final hospital discharge diagnosis determined by ECG findings, angiography and successful reperfusion with pPCI.

#### **2.5.1.2 Doctor studies**

The Tsai study [62] was a randomised crossover controlled trial with 30 internal medicine residents from a single US university medical centre, who were in their second or third year of training. The participants were stratified according to year of training and then randomly allocated into one of two groups, which determined in which order the ECGs with computer interpretation would be viewed. Group A contained 11 ECGs and group B, 12, making a total of 23 ECGs. The study took place over a five-month period, with the ECG interpretation being conducted as a one-hour, supervised session.

The primary outcome was interpretative accuracy of the medicine residents, with a secondary outcome of the effect of incorrect computer interpretation on the participant's interpretations which were incorrect.

The Massel study [61] was a two-by-two-by-two factorial randomised control trial (RCT) with nine participants from a single tertiary teaching hospital in Canada. There were three doctors from each of the following grades:

- Medical resident
- Cardiology fellow
- Consultant cardiologist.

The participants reviewed 75 ECGs, selected from the coronary care unit (CCU) and hospital patients by the researchers. Due to the factorial design, they were required to review the ECGs eight times over an eight-month period.

The primary outcome was the reliability and accuracy of ECG interpretation and the effect of three contributing factors (clinical history, a checklist developed as part of the study and computer interpretation).

The Goodacre study [60] was an RCT with 10 participants, all junior doctors, working at a single UK teaching hospital emergency department. They reviewed 50 ECGs (half with the computer interpretation message visible and half without) at a single sitting, and under examination conditions.

The primary outcome was the proportion of major errors missed in each group, with a secondary outcome measure of the number of completely correct ECG interpretations (i.e. those without major and minor errors specified by the study design).

## 2.5.2 Methodological quality

### 2.5.2.1 Validity

All six studies had a clear research question, which conformed to the population, intervention, comparison, outcome (PICO) model. Only one of the studies [60] was conducted in the UK, with the remainder conducted in North America (three from the US [46, 62, 63] and two from Canada [43, 61]). There was a clear distinction between the studies involving paramedics, which included patients with suspected acute coronary

syndromes (ACS), and those with doctors as participants, which utilised previously obtained ECGs.

The eligibility criteria in the paramedic studies were typically two-fold, since both paramedics and patients were required. Skill levels were specified, with paramedics in the Selker and Ting studies having comparable qualifications to that of UK paramedics (i.e. NAEMT paramedic registration), whereas the Cantor study utilised Canadian primary care paramedics, equivalent to UK ambulance technicians, the tier below paramedics. The patients in the paramedics studies also had slightly differing eligibility criteria, with Selker and Cantor not stipulating an age limit, but specifying a requirement for patients to present with signs and symptoms of ACS, whereas the Ting study only considered the ECG criteria, and patients were only eligible for entry into the study if there was agreement between paramedic and computer interpretation. The Selker and Cantor studies also allowed local protocols and the paramedic's judgement to override the study criteria.

A key omission in determining the accuracy of paramedic's interpretation in all studies, was the omission of patients who did not undergo pPCI at the study hospital, or, in the case of the Selker study, were not identified as having an ACS and so not enrolled. In addition, none of the studies compared paramedics diagnoses alone. Therefore, without the benefit of computer interpretation, differentiating the effect that paramedic and computer interpretations had on the accuracy of diagnosis is difficult to determine, even when the computer interpretation accuracy rates were reported separately.

The doctor studies all involved junior doctors (defined as being 2–3 years post-graduation), although Massel also included middle and senior grades. No information was provided about how the participants were recruited, but the randomisation strategy was clearly laid out in all studies, although none included a consolidated standards of reporting trials (CONSORT) flow diagram [67]. All participants were accounted for and none were lost to follow-up.

In the paramedic studies, it was apparent that some patients did not receive the diagnostic test and/or had the reference standard applied. Nine patients in the Ting study did not have a prehospital 12-lead ECG, but were subsequently taken for pPCI and included in the results as false negatives. No two-by-two table was included, although it is possible to calculate this from the sensitivity, specificity, negative and positive predictive

values provided. Almost 3% of patients in the Selker study did not have an ACI-TIPI score calculated, leading to a risk of verification bias [68]. A two-by-two table was not provided in the results, as only the test positive results were included. There was no missing data in the Cantor study, although one patient did not receive the reference standard test (pPCI) since the patient was considered to be a false positive and so not appropriate for pPCI.

The reference standard for the doctor studies were senior cardiologists or ED consultants, who independently reviewed the study ECGs prior to the study commencing, and who were blinded to the computer interpretation result. Their responses were collated and any disagreements were resolved by discussion. When assessing the participants' responses, only the Tsai study made it clear that the marker was blinded to the participant identity and computer interpretation message. However, the marking in this study was conducted by only one researcher. The Goldacre study blinded the assessors to the computer report, but it was not clear whether they were blinded to the participant identity. However, in contrast to the Tsai study, both ED consultants independently reviewed the participants' results and their agreement was measured by the calculation of the  $\kappa$  statistic, with disagreements resolved by discussion. The Massel study provides no information about whether the researchers were blinded to the participant identity or the presence of the computer interpretation message, which could be a source of review bias [69]. However, the participants were blinded to their previous answers and those of fellow participants.

All three paramedic studies used angiography and cardiac biomarkers as the reference standard for diagnosis. In addition, two of the paramedic studies (Selker and Cantor), also used a doctor with access to the patients' notes, but blinded to the paramedic's study results as an additional reference standard. The Ting study did not specify whether the research staff accessing the patients' notes were blinded.

Four of the studies utilised the GE Marquette 12SL algorithm, with the Tsai and Massel studies failing to identify the algorithm used. In addition, the Selker study also utilised two additional novel algorithms (ACI-TIPI and TPI) in the latter phases of their study.

The study procedures were clearly outlined in all studies, although in the case of the Ting study (published as a conference abstract), it was necessary to obtain a further article to review the protocol, after the lead author failed to respond to direct communication [64].

Eligibility criteria were provided for all of the paramedic studies, but little explanation was provided in the doctor studies. Baseline characteristics of patients were provided in two of the paramedics studies, with only Cantor failing to provide any demographic or co-morbidity information, making assessment of spectrum bias impossible [69]. All of the doctor studies provided current job role and years since graduation, but only Massel provided additional data about average ECG interpretations conducted by the participant per week. This was lacking in the Goodacre and Tsai studies, making it difficult to determine whether control and intervention groups were equivalent. The Tsai study describes the design as a matched pairs crossover design, but the only matching that appears to have been conducted was years since graduation. In addition, a single participant did not see the same ECG twice, once with and without the computer interpretation, but instead saw an equivalent set of ECGs for each phase. Massel used a crossover design, and participants saw the same ECG on multiple occasions, both with and without the computer interpretation. These issues aside, all of the doctor studies did treat the intervention and control arms of the studies in the same way, except for applying the intervention.

### 2.5.2.2 Results

While all three of the paramedic studies provided information about the accuracy of computer interpretation alone, it was not possible to determine the accuracy of the paramedics alone, since all were exposed to the computer interpretation when making a diagnosis. The doctor studies in comparison, thanks to their randomised control trial design, provide responses with and without the computer interpretation.

In the Cantor study, paramedics identified 134 patients as suspected STEMI and were correct in 106 (79%) of cases. If the diagnosis had been made by computer interpretation alone, 98/106 (92%) of patients with STEMI would have been correctly identified, correctly excluding a further 11/28 (39%) of the false positives.

The three phase design of the Selker study makes analysis of the results rather more complicated. All three phases provided paramedics with computer interpretation, however in the latter phases, the criteria were amended to require an ACI-TIPI prediction of 75% or more, or a TPI prediction of STEMI. Despite this, paramedics were still able to activate their local pPCI pathway if the local emergency medical service (EMS) protocol

eligibility criteria was met. The study found a statistically significant increase in the percentage of patients with STEMI between phases 1 and 2, rising from 40.8% to 68.4%. However, since the study also included patients with ACS and not just STEMI, it makes direct comparison with the other paramedic studies difficult. A retrospective analysis by the researchers explored the ACI-TIPI and TPI across all three phases and found that, in cases of confirmed ACS, the computer correctly identified 226/284 (80%) of patients, compared with paramedics with computer interpretation, who correctly identified 296/437 (68%).

The Ting study was the only one to provide sufficient information to construct a two-by-two table. In addition, although study protocol required that paramedic and computer interpretation had to agree in order for the patient to be considered for direct admission to the cardiac catheter unit, patients who were taken to the study hospital and who had a final diagnosis of STEMI were also included. This made it possible to identify occurrences when the paramedic and computer disagreed. Paramedics agreed with the computer interpretation in 26/54 (48.1%) of STEMI cases. If only the paramedic's interpretation had been required, correct recognition would have increased to 43/54 (79.6%).

The Tsai study reported correct and incorrect results for computer interpretation alone, participants alone, and participants with the computer message. However, only 18/54 of the study ECGs could be considered to be STEMI or STEMI-mimic in morphology, which limits the results' applicability to the RESPECT study. Results were reported as average (presumably means, although this was not stated) values. In the sub-category of correct computer interpretation, 53% of participants correctly interpreted the ECG without the computer message, with a statistically significant increase to 68%, when it was visible. However, when the computer interpretation was incorrect, participants were incorrect 35% of the time when the message was hidden, rising to a statistically significant 68% when the incorrect message was shown.

The Massel study utilised a two-by-two-by-two factorial design, requiring participants to view ECGs on four separate occasions with and without the computer interpretation, and with differing combinations clinical history and the presence (or absence) of a checklist. Results were reported using inter- and intra-class reliability measures ( $\kappa$

statistics) and tendencies of bias. Mean overcalls and undercalls for thrombolysis eligibility were also reported, including 95% confidence intervals. Only the medical residents had statistically significant effects caused by the presence of the computer interpretation message. They were biased by the computer interpretation and more likely to undercall thrombolysis (the mean undercall rose from 5.4% to 8.5% in the presence of the computer interpretation message). In the sub-group of ECGs which were accompanied by a typical history of AMI, medical residents were more likely to change their decision in favour of thrombolysis if the computer interpretation was provided.

The Goodacre study consisted of 10 junior ED doctors who each interpreted 50 ECGs, 25 with a computer interpretation and 25 without. As with the Massel study, ECGs were not exclusively limited to STEMI and the breakdown of ECG findings was not reported. Interpretations were classified into three categories: completely correct, major errors and minor errors. The criteria for major errors did include ST-segment elevation of >1mm. Results were reported as proportions, with confidence intervals and p-values provided. Overall, the computer interpretation messages had no statistically significant effect on the participants. Major errors occurred in 46/250 (18%) of interpretations with the computer message, which rose to 56/250 (22%) without ( $p=0.13$ ). Participants correctly interpreted 104/250 (42%) ECGs with the computer message and 91/250 (36.4%) without ( $p=0.15$ ).

Only the Goodacre study provided a power calculation to justify the sample size chosen, but this did not account for the clustering of data in the study. In fact, none of the studies took clustering into account in the analysis of data. The Tsai study did acknowledge the multi-level nature of the data, but assumed that this would not have any effect. This is unwise, since not accounting for clustering leads to smaller standard errors (and confidence intervals), increasing the likelihood that chance findings will be considered to be statistically significant [70].

#### **2.5.2.3 Context**

The literature review has highlighted the absence of studies directly examining the effect of computer interpretation messages on paramedic's recognition of STEMI. The paramedic studies identified in the review do have a clinically relevant context, but the lack of results of paramedic interpretation alone, makes it impossible to isolate the effect

of the computer interpretation. The studies do suggest that computer interpretation has an effect, but not whether this is clinically significant.

The doctor studies are able to determine the effect of computer interpretation alone, however, this is a distinctly different population to paramedics, and the results of the studies lack generalisability, due to the small numbers of participants. In addition, ECG interpretation was not limited to STEMI or STEMI-mimics in two of the studies (Goodacre and Tsai), further reducing their applicability to the research question. This is compounded by the failure to account for the clustering effects of the data.

Only one of the studies was based in the UK (Goodacre, a doctor study), and one of the paramedic studies was conducted with paramedics who have a skill equivalent of ambulance technicians in the UK.

In conclusion, the methodology of the doctor studies provides a good indication about how this research question could be answered if the correct population is identified. Thus, a sufficiently powered randomised crossover trial with UK paramedics would provide a sound basis on which to answer the research question for this dissertation.

# **Chapter 3**

## **RESPECT study and pilot**

Given the doubt surrounding the effect of computer interpretation on paramedic accuracy in recognising STEMI, and the importance of minimising false positives and negatives, this study will focus on the effect that computer interpretation has on a paramedic's accurate recognition of STEMI. From the literature review, it is clear that the study design needs to take account of clustering. However, in the absence of existing studies to provide insight into intra-class correlation coefficients to determine design effects, a pilot study is necessary. In addition, the pilot provides an opportunity to test a customised, web-based assessment tool, which will record the paramedic participant's ability to correctly diagnose STEMI and exclude STEMI-mimics, both with and without a computer message, using a randomised crossover design [71].

### **3.1 Aims and objectives**

Pilot study aims:

- To create and test a web-based assessment tool, suitable to address the main study aim
- To determine the feasibility of the main study.

Pilot study objectives:

- Source at least 48 ECGs, with a proportional mix of STEMI and STEMI-mimic patterns, all with computer diagnostic messages
- Obtain a gold-standard diagnosis of each ECG
- Create custom database-driven website to administer the study
- Conduct the pilot study to:
  - Determine recruitment rates and identify incentives to minimise attrition in the main study
  - Check the randomisation procedure
  - Test that the assessment tool works correctly
  - Obtain preliminary estimates of the accuracy, sensitivity and specificity of paramedic's interpretation, to determine whether it is appropriate to conduct the main study
  - Estimate intra-class correlation coefficients for participants and ECGs, and the number of discordant proportions, in order to provide guidance in determining the sample size for an appropriately powered main study
  - Construct a generalised linear model to determine the odds ratios relating to paramedics accuracy in recognising STEMI, taking into account the clustering of participant responses and ECG.

Main study aim: To examine the effect of computer interpretation messages printed on ECGs on the accuracy of paramedics recognition of STEMI.

Objectives:

- Estimate an appropriate sample size to ensure the study is adequately powered, taking into account the clustering of data
- Recruit paramedics from Yorkshire Ambulance Service to take part in the study
- Obtain precise estimates of the accuracy, sensitivity and specificity of paramedic's interpretation

- Estimate the effect of computer-generated messages on paramedic interpretation (overall and stratified by correct and incorrect computer interpretation)
- Disseminate the results.

### **3.2 Value of this research**

The results from this pilot study will demonstrate whether an online assessment tool can appropriately test paramedics' accuracy in STEMI recognition. The estimation of intra-class correlation coefficients will help determine appropriate sample sizes for an adequately powered, main study. In addition, the publication of the pilot data will also assist other researchers conducting studies in this area, given the paucity of published studies relating to this topic.

Assuming that the main study is feasible, the results will provide information about the effect that computer interpretation messages has on paramedics' recognition of STEMI. This should assist ambulance services determine whether computer interpretation should continue to be provided to their paramedics and provide insight into the current interpretation accuracy of UK paramedics.

# Chapter 4

## Research methods

### 4.1 Study design

This pilot study is a randomised crossover trial, utilising a bespoke, web-based assessment tool<sup>1</sup> to enrol participants, randomise them appropriately, and track their progress through the study. The pilot has been designed to mirror the main study, enabling the testing of the assessment tool, data collection and analysis methods, and the statistical methods required for hypothesis testing.

### 4.2 12-lead electrocardiograms

A key component of the assessment tool is a database of 48 12-lead ECGs showing a STEMI or STEMI-mimic waveform morphology. These are classified into four categories, based on the computer interpretation message on the ECG: true positive, true negative, false positive and false negative, when compared to the reference standard for ECGs in this study. Note that there are 12 ECGs for each classification.

#### 4.2.1 Reference standard

In order to qualify for inclusion in the study, the ECGs had to meet the following reference standard set for the study:

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<sup>1</sup><http://respect.ambulanceresearch.co.uk>

- The ECG had to be a 12-lead ECG recorded in the out-of-hospital environment
- The ECG had to display a wave morphology consistent with either a STEMI or STEMI-mimic, and a computer diagnostic message printed on the ECG.
- The diagnosis of the ECG (i.e. STEMI or not-STEMI) had to be determined by the independent assessment and agreement of two senior doctors with specialist knowledge of ECGs. Any disagreements on diagnosis were resolved by discussion between the doctors. An option for subsequent review by an independent third party, was provided, but not required.

Information relating to the 48 ECGs that met the reference standard and were included in the pilot study, can be found in [Appendix A](#).

### 4.3 Participants

Participants for the pilot study were Health and Care Professions Council (HCPC) registered paramedics working in the United Kingdom, but not employed with Yorkshire Ambulance Service NHS Trust at the time of the study. The main study, planned to commence once the pilot data has been completed, will consist of Yorkshire Ambulance Service paramedics only. Approval has already been granted by the Service research and development department for the main study ([Appendix C](#)).

### 4.4 Recruitment

A number of strategies were employed to recruit the target number of paramedics into the study. Firstly, the study was advertised on the [College of Paramedics website](#)<sup>2</sup> (with the support of the College Research and Development Advisory Committee). In addition, paramedics were notified about the study via the [UK Ambulance Forum](#)<sup>3</sup>, an online [continuing professional development portfolio builder](#)<sup>4</sup> for ambulance staff, social media outlets such as [Twitter](#)<sup>5</sup>, email and word of mouth.

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<sup>2</sup><https://www.collegeofparamedics.co.uk/>

<sup>3</sup><http://www.ukambulanceforum.com>

<sup>4</sup><http://www.resuscitate.me.uk>

<sup>5</sup><http://www.twitter.com>

## 4.5 Ethical concerns

The confidentiality of the participants was maintained primarily through anonymity. The only potential source of personally identifiable data, the participant's email address, was encrypted on the pilot study database using a Rijndael 256-bit cypher and was not known to the researcher. In addition, there was no personal contact between participants and the researcher during the pilot study, since the website handled all communication with the participant, such as sending out reminder emails, for example. Access to the study database was limited to the chief investigator only. Once the study was completed, participants' email addresses and data were removed within one calendar month, unless express consent had been obtained from a participant to be contacted about involvement in a subsequent study.

The HCPC standards of conduct, performance and ethics, states that paramedic (and other) registrants must act in the best interests of service users, which includes reporting on the conduct, performance and health of colleagues if there is a cause for concern [72]. This raised a potential ethical issue within the RESPECT pilot study, since paramedic participants' ability to interpret ECGs was tested, and since the chief investigator is a registrant of the HCPC, a dilemma about whether to report poorly performing participants arose. In actuality, since participants' identities were anonymised, and no overall score for an individual participant was calculated, it was not possible identify poorly performing participants individually.

Since the study was not conducted on NHS patients, there was no need for NHS research ethics committee (REC) approval as this is not required for research conducted on NHS staff [73]. However, the study was approved by the University of Sheffield ethics committee ([Appendix D](#)), and the University acted as the study's research governance sponsor ([Appendix E](#)). In addition, a risk assessment was conducted, in keeping with University policy ([Appendix F](#)).

## 4.6 Informed consent

Participants in the RESPECT study consented online. Although, arguably, this raised an issue of ensuring that the participants were fully informed, comprehensive participant

information was provided on the website ([Appendix G](#)). Obtaining consent in this way, meant that no pressure to enrol in the study was exerted on the participant, which can occur in face-to-face consenting methods [74]. Participants who submitted the consent form webpage ([Figure 4.1](#)), were considered to have provided informed consent. Additional consent was also obtained for the use of anonymised data from the study to be used in subsequent research, and for participants to be contacted for potential enrolment into a subsequent, qualitative study. These were both optional and not required to participate in the pilot.

## The RESPECT Study

Recognition of STEMI by Paramedics and the Effect of Computer inTerpretation

HOME / CONSENT

**Consent Form for The Recognition of STEMI by Paramedics and the Effect of Computer Interpretation (RESPECT) Pilot study**

I understand that my participation is voluntary and that I am free to withdraw at any time without giving any reason and without there being any negative consequences. In addition, should I not wish to answer any particular question or questions, I am free to decline.

I understand that my responses will be kept strictly confidential and I give permission for members of the research team to have access to my anonymised responses. I understand that my name will not be linked with the research materials, and I will not be identified or identifiable in the reports that result from the research.

I consent to anonymised data from this study to be used in subsequent research (you will not be personally identifiable from the data).  Tick box to agree **Optional**

I consent to be contacted after this study has been completed for a follow-up study on the same topic. Note, you are only consenting to being contacted, not to be enrolled in the study.  Tick box to agree **Optional**

**Click to Consent and take part in the study**

If you would like more information about the study, you can read the [participant's information](#).

© 2012 Richard Pilbury

FIGURE 4.1: Online consent form for RESPECT pilot study

## 4.7 Research tool

Since it was anticipated that participants would be geographically dispersed, an online assessment tool was identified as the most efficient method to collect the data. Existing

services were examined, including Survey Monkey<sup>6</sup> and the forms tool in the Google Docs<sup>7</sup> suite, but none met the needs of the study. Instead, a custom website was created by the researcher, coded using a PHP<sup>8</sup> framework, cakePHP<sup>9</sup>, with a MySQL<sup>10</sup> database to record and collate the data. To ensure maximum browser and device capability, the Zurb Foundation<sup>11</sup> responsive front-end framework was used.

In an effort to make the ECGs used in the study as life-size as possible, participants were not permitted to use mobile devices, such as smart phones and tablets, to undertake the study. The study tool calculated the correct size to display the ECGs, based on the participant's computer screen size and resolution. This was achieved by asking participants to resize a virtual bank card displayed on the screen, to a real bank or ID card that they placed on the screen (Figure 4.2). Once this was submitted by the participant, the correct dimensions of the ECG image were calculated.

#### 4.7.1 Randomisation

The study website obtained random numbers from the true random number service RANDOM.ORG<sup>12</sup>, which generates random numbers from atmospheric noise. These were then utilised by the website to allocate ECGs to participants, to determine ECG and message visibility order, and determine the block randomisation sequence.

### 4.8 Procedure

The participant flow through the study is shown in Figure 4.3. Paramedics interested in taking part in the pilot study, were invited to visit the study website, read the participant information and enter a contact email address on the sign-up form. Once completed, the website created an entry for the potential participant and sent them an email containing a unique uniform resource locator (URL) web link, as well as links to the participant information sheet and webpage. When the participant clicked the link

<sup>6</sup><http://www.surveymonkey.com>

<sup>7</sup><http://docs.google.com>

<sup>8</sup><http://php.net>

<sup>9</sup><http://cakephp.org>

<sup>10</sup><http://www.mysql.com>

<sup>11</sup><http://foundation.zurb.com>

<sup>12</sup><http://www.random.org>

## Calibration

In order to show the ECGs at their actual size, we need to estimate the size of your monitor. **If you have not already done so, please maximise your browser window.** Place a credit card, or ID card over the card on the screen and use the slider to change the size of the card on the screen to match the one you are holding onto the screen. You can either click and drag the square slider or click on the square and use the arrow keys. Click the 'Submit Card Size' button when you are happy with the size of the card.

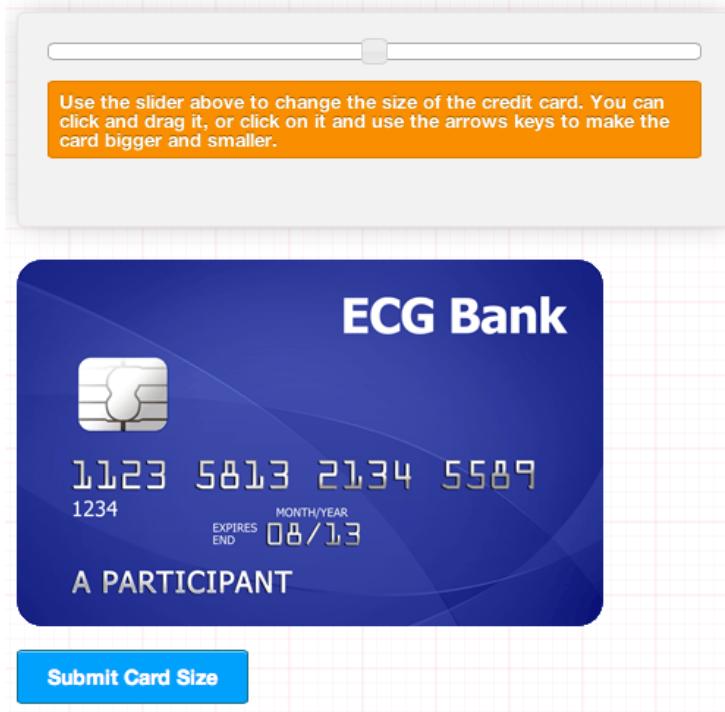


FIGURE 4.2: The RESPECT study calibration screen

within the email, they were directed to the consent page (Figure 4.1), where informed consent was considered to have been obtained once participants submitted the consent form. Participants were also asked to optionally consent to the use of their anonymised data in subsequent research, and to be contacted about becoming involved in a future, qualitative, study.

After consenting, the participants calibrated their monitor. If the website was accessed using a tablet or mobile device, participants were informed that this could not be used to complete the study, and they were advised to use a desktop or laptop computer.

The next step was to gather some basic demographic data about the participants, which took the form of four questions:

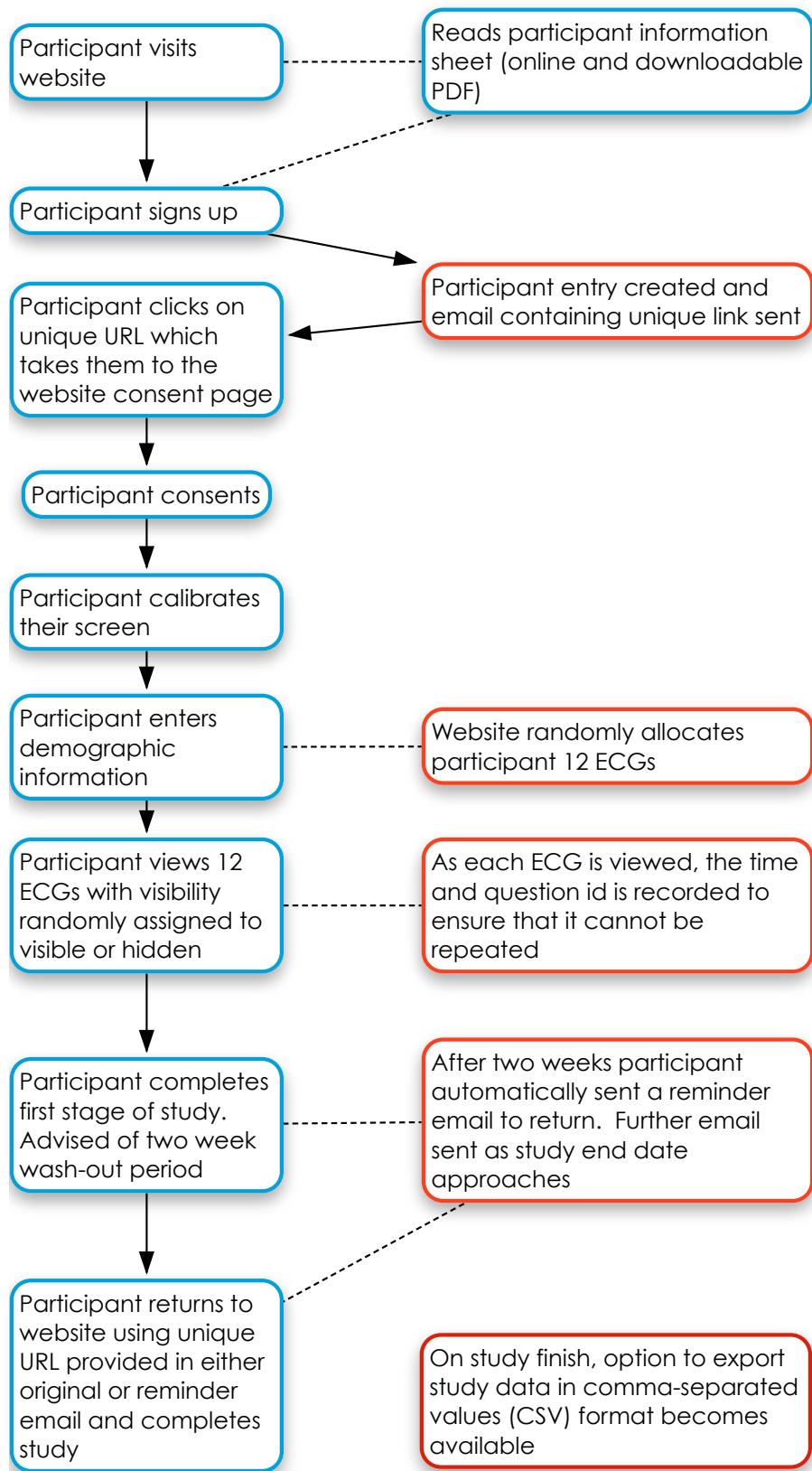


FIGURE 4.3: Flow of participant and website actions during the study

1. Which educational route did you take to become a paramedic (traditional/vocational, university)
2. How long have you been a paramedic (in years)?
3. How much time have you spent on 12-lead ECG training/continuous professional development (CPD) in the past 12 months (in hours)?
4. How many patients have you taken for primary percutaneous coronary intervention or thrombolysed in the past 12 months?

Once completed, participants were randomly allocated 12 ECGs from the study pool of 48. These included three ECGs from each of the following four sub-groups:

- Patient has a STEMI and computer interpretation states STEMI (true positive)
- Patient does not have a STEMI and computer interpretation states STEMI (false positive)
- Patient has a STEMI and computer interpretation states no STEMI (false negative)
- Patient does not have a STEMI and computer interpretation states no STEMI (true negative).

Note that the terms in brackets (e.g. true positive) refer to the computer interpretation in relation to the reference standard.

The ECGs were displayed on a pop-up webpage ([Figure 4.4](#)), complete with countdown timer and a form to record the participant responses.

Each ECG was viewed by the participant twice, once with and without the message, and the order that these ECGs were shown, was randomised. Participants were informed that the ECGs would be a mixture of STEMI and STEMI-mimic patterns, but not how many of each would be seen. In addition, they were advised that after the wash-out period, they would see the same ECGs again, but with the message visibility reversed. Incentives for completion were randomised in the pilot study, with participants either

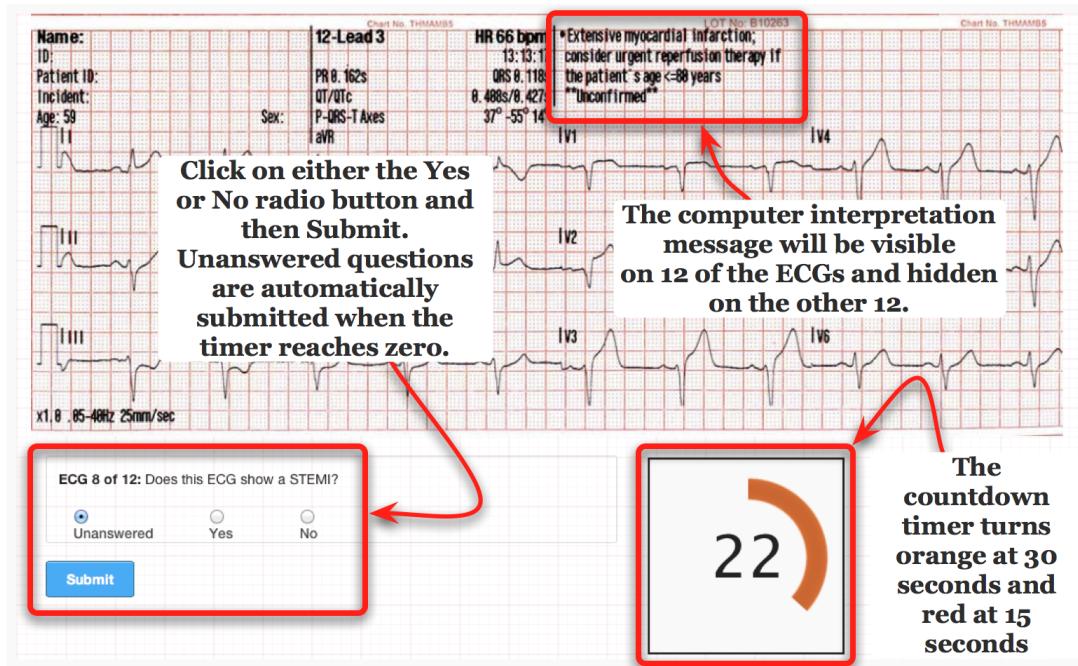


FIGURE 4.4: The RESPECT study ECG webpage

offered a CPD certificate, entered into a prize draw to win an paramedic textbook, or nothing.

To ensure that all ECGs were viewed in roughly equal numbers, block randomisation of the ECGs was used [75]. This meant that all 48 ECGs were allocated after every forth participant, assuming that they completed the study. To minimise the chance of subversion bias, allocation was completely automated and the researcher unaware of the randomisation sequence [76].

Once the allocation of ECGs was completed, participants were presented with 12, 12-lead ECGs, each having a time limit of 60 seconds to interpret the ECG and submit a response. As soon as an ECG was displayed on the participant's screen, the record for that attempt was updated and no subsequent attempt was allowed, even if the participant failed to answer the question. After 60 seconds, or on submission of the form on the page, the ECG and submission form were removed from the screen and the participant was invited to view the next ECG.

Once the first 12 ECGs had been reviewed, participants were given a two-week wash-out period and not allowed to progress until this time period had elapsed. Once the wash-out period was over, participants were contacted by email and invited to take part

in the second phase (i.e. the crossover). Participants reviewed the same 12 ECGs as before, but in a random order, and with the computer message visibility the opposite of that viewed in the first phase.

## 4.9 Analysis plan

### 4.9.1 Data checking

Prior to analysing the results, the data was checked to ensure that categorical data (training route and the ECG answers) had allowed values, and numerical variables (CPD hours, service years, number of thrombolysis/pPCI patients) were within appropriate ranges. In addition, question start and finish times were reviewed to ensure that finish times occurred after start times.

### 4.9.2 Missing data

Due to the crossover nature of the design, each ECG viewed by an individual participant should have a paired response. Where this did not occur, the responses for the specific individual were excluded. This was on the basis that the data were unlikely to be missing at random and the statistical analysis required to account for this is well beyond the capabilities of a non-statistician [77]. In addition, continuing with the analysis on the assumption that the data was missing at random would have resulted in bias [78].

Responses which timed out (i.e. were not answered within 60 seconds) were coded differently in order to differentiate them from active participants responses. However, for the analysis, these were treated as providing an incorrect answer on the basis that a delayed response reflected the participant's uncertainty regarding the interpretation.

### 4.9.3 Data description

Since the data were clustered around participants (who viewed multiple ECGs) and ECGs (which were viewed by multiple participants), a modified Consolidated Standards

of Reporting Trials (CONSORT) flow diagram [79] was created to clearly identify participant flow through the study, and provide summary information for the ECGs, including details about the characteristics of the clusters.

#### 4.9.4 Participants

As part of the consenting process, participants were asked if they were prepared to allow their anonymised data to be used in future studies, and for permission to contact them for a subsequent, qualitative study. Since the demographic-type data collected from participants was not expected to be normally distributed, it was summarised using median values.

#### 4.9.5 Electrocardiograms

Two summary tables containing participant responses for each of the ECGs was created to provide overall completion rates for individual ECGs and a descriptive analysis of the responses. These tables are best utilised alongside the summary ECG data in Appendix A, which provides the characteristics of the ECGs themselves, including the classification and the actual, and computer, interpretation.

#### 4.9.6 Data analysis

Statistical data analysis was conducted using the R<sup>13</sup> statistics package and proceeded in an incremental fashion, commencing with the calculation of participant accuracy, sensitivity and specificity values and intra-class correlation coefficients, before fitting generalised linear regression models (GLM) with and without random effects (multi-level) modelling, to take account of the clustering of data around the participants and ECGs [80]. Although it is not possible to analyse the results of these models, due the lack of *a priori* power calculations, it provided an opportunity to test the analysis methods that will be adopted in the main study. The results of the GLM analysis were verified with another statistics package, MLWin<sup>14</sup>, using the procedure described in Appendix B.

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<sup>13</sup><http://www.r-project.org>

<sup>14</sup><http://www.bristol.ac.uk/cmm/software/mlwin/>

#### 4.9.6.1 Hypotheses

The following hypotheses are to be tested in the main study, and so were tested in the pilot study, to ensure that accurate data preparation and analysis could be conducted:

Null hypothesis **1** - Computer interpretation messages have no effect on paramedics' correct diagnosis of STEMI from a 12-lead ECG

Alternative hypothesis **1** - Computer interpretation messages have an effect on paramedics' correct diagnosis of STEMI from a 12-lead ECG.

The first hypothesis includes all computer interpretation messages, irrespective of classification (true positive, false positive etc). However, the subsequent hypotheses (2 and 3), aim to examine two subsets of the data: accurate (true positive and true negative) and inaccurate (false positive and false negative) computer interpretations:

Null hypothesis **2** - *Accurate* computer interpretation messages have no effect on paramedics' correct diagnosis of STEMI from a 12-lead ECG

Alternative hypothesis **2** - *Accurate* computer interpretation messages have an effect on paramedics' correct diagnosis of STEMI from a 12-lead ECG

Null hypothesis **3** - *Inaccurate* computer interpretation messages have no effect on paramedics' correct diagnosis of STEMI from a 12-lead ECG

Alternative hypothesis **3** - *Inaccurate* computer interpretation messages have an effect on paramedics' correct diagnosis of STEMI from a 12-lead ECG.

#### 4.9.6.2 Generalised linear modelling

Regression models that require a transformation (via a link function) of the outcome are known as generalised linear models (GLM). For the binary outcome of a correct (or incorrect) diagnosis, logistic regression was used. Logistic regression is so called because the link function is the logit (or log odds) [81]. Thus the first model to be tested (which ignores the clustering of ECGs and participants) takes the form:

$$\text{logit}(\pi) = \log\left(\frac{\pi}{(1-\pi)}\right) = \beta_0 + \beta_1 \text{MESSAGE}$$

where  $\pi$  is the probability of a correct answer when the message is visible,  $\beta$ s are the regression coefficients and MESSAGE denotes whether the message is visible (1) or hidden (0) [82]. All data and sub-groups, consisting of accurate computer interpretation only and inaccurate computer interpretation only, were modelled. The Odds ratio, regression coefficient standard error and 95% confidence interval, z statistic and p-values were calculated and summarised.

#### 4.9.6.3 Generalised linear modelling with random effects

Regression modelling assumes that the outcome and parameters are independent and identically distributed [83]. However, that is not the case in this study, as each participant response is clustered around the participant and the ECG. Ignoring clustering generally leads to underestimation of regression coefficient standard errors, which in turn leads to overly narrow confidence intervals, and p-values which are too small. Ultimately, coefficients could erroneously be assumed to be significant effects, when in fact the results occurred by chance [84].

Clustering can be accounted for by adding random effects to the model. This is achieved by the inclusion of a parameter which varies randomly between clusters, and is assumed to be normally distributed with a mean zero, and a variance equal to the intra-parameter variance. Including random effects in this way, allows observations within the same cluster to be assumed to be independent. Models using random effects are often called multi-level models, since the observations (a participant's individual response to a single ECG) is nested within clusters of the participant and ECG.

The participants and the ECGs are nested within a hierarchy, with each participant response belonging to a participant and an ECG. This is known as a cross-classified structure [85] and can be expressed, using classification notation [86], as:

$$y_i \sim \text{Binomial}(1, \pi_i)$$

$$\text{logit}(\pi_i) = \beta_0 + \beta_1 \text{MESSAGE}_i + u_{\text{ecg}(i)}^{(3)} + u_{\text{participant}(i)}^{(2)}$$

$$u_{\text{ecg}(i)}^{(3)} \sim N(0, \sigma_{u(3)}^2)$$

$$u_{\text{participant}(i)}^{(2)} \sim N(0, \sigma_{u(2)}^2)$$

where  $u_{ecg(i)}^{(3)}$  is the random effect for ecg(i), and is assumed to be normally distributed with a mean of zero and variance,  $\sigma_{u(3)}^2$ . Likewise,  $u_{participant(i)}^{(3)}$  is the random effect for participant(i), and is assumed to be normally distributed with a mean of zero and variance,  $\sigma_{u(2)}^2$ .

#### 4.9.6.4 Intra-class correlation coefficients

The intra-class correlation coefficient (ICC) is a measure of the degree of similarity in ECG interpretation attempts within a cluster [87], and is used to calculate the design effect, by which sample size estimates are multiplied, in order to account for clustering [88].

Three ICCs were calculated from the random effects models. The first, examined the correlation between two randomly selected responses from the same participant:

$$\frac{\sigma_{participant}^2}{\left(\sigma_{ecg}^2 + \sigma_{participant}^2 + \frac{\pi^2}{3}\right)}$$

The second ICC, measured the correlation between two randomly selected responses from the same ECG:

$$\frac{\sigma_{ecg}^2}{\left(\sigma_{ecg}^2 + \sigma_{participant}^2 + \frac{\pi^2}{3}\right)}$$

Finally, the correlation between two randomly selected responses from the same participant, and same ECG (sometimes called the interaction ICC) was calculated:

$$\frac{\sigma_{ecg}^2 + \sigma_{participant}^2}{\left(\sigma_{ecg}^2 + \sigma_{participant}^2 + \frac{\pi^2}{3}\right)}$$

In all cases,  $\sigma_{participant}^2$  is the variance between participants,  $\sigma_{ecg}^2$  the variance between ECGs and  $\frac{\pi^2}{3}$  is the residual variance for a logit model.

#### 4.9.6.5 Incentives

Participants who consented to take part in the study were randomly assigned one of three incentive options (no incentive, a downloadable continuing professional development

certificate and a prize draw for a paramedic textbook). A participant was eligible for the incentive IF they completed both parts of the study. To determine the potential impact of offering incentives on retention, the following hypothesis was proposed:

Null hypothesis **4** - The proportion of study completion does not differ between the incentive options

Alternative hypothesis **4** - The proportion of study completion is different between the incentive options.

This was tested using a chi-squared test for independence.

## 4.10 Limitations and potential problems

Since this study is a pilot, the results, will require confirmation in a subsequent study [76]. No clinically important results were determined prior to the study commencement, which means that an appropriate sample size calculation to improve statistical rigour, was not calculated.

Recruiting participants was anticipated to be a significant problem [89]. Although there was an incentive, it could not be advertised, since 1 in 3 participants were not going to receive one. Given that there was no budget for marketing, social networking tools were utilised, including Twitter<sup>15</sup>, the UK Ambulance Forum<sup>16</sup> and personal contacts throughout the UK. In addition, support was obtained from the College of Paramedics who advertised the study on the College website<sup>17</sup>.

There was a risk that the web-based assessment tool could prove difficult to use and/or suffer from technical glitches, making data collection problematic. However, the tool was extensively tested prior to the start of the pilot to ensure it captured data reliably. Furthermore, limited usability testing on paramedics who were not taking part in the pilot study was undertaken to ensure that the instructions were clear and the assessment tool straightforward to use. These issues are precisely why conducting a pilot study is a good idea, and should ensure that the tool is robust enough for use in the main study.

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<sup>15</sup><http://twitter.com>

<sup>16</sup><http://www.ukambulanceforum.com>

<sup>17</sup><https://www.collegeofparamedics.co.uk/home/>

With a web-based assessment tool, there was a risk that the participant might have utilised a textbook or sought advice from others. In order to minimise this, a unique universal resource locator (URL) was included in the emails sent to each participant, preventing unauthorised access to the study website. In addition, each ECG, once viewed by the participant, could not be answered again, and a time limit was imposed for each question, after which the website automatically removed the ECG and the response form from view.

The study's crossover design required participants to return to the website, to repeat the assessment, two weeks after completing the first stage. This did present an issue, since if participants did not return, then there would be no paired data to analyse. In an effort to minimise this, automatically generated emails were sent to participants, reminding them to return to the study, and the aforementioned social networks were utilised in an ongoing effort not just to recruit new participants, but also to encourage existing participants to return after the wash-out period.

## 4.11 Methods of dissemination

The results of the study are presented and discussed in detail in chapter 5. Since consent was obtained from participants to use an anonymised version of the dataset in subsequent research, the data will be made publicly available online, via the study website, to promote data sharing [90]. However, in an attempt to reduce the likelihood of post-hoc data analysis (data-dredging) [91], researchers who wish to access the study data will be required to submit a study protocol to the RESPECT chief investigator. In addition, to enable the research to be reproducible, a full summary of the statistical analysis will be presented using the R statistics package knitr<sup>18</sup>, which enables a researcher to present the R scripts which conduct the analysis, and the results of that analysis, together (an example can be found in Appendix I). More conventional methods of dissemination will also be utilised, including publishing findings in a peer-reviewed journal, such as the *Emergency Medicine Journal*, presenting at conferences, and the publication of plain English summaries in the College of Paramedics newsletter and free ambulance magazines.

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<sup>18</sup><http://yihui.name/knitr/>

## 4.12 Timetable

Figure 4.5 shows the planned timeline for the RESPECT pilot study, which commenced in September 2012 and finished with the dissertation write up and submission towards the end of September, 2013. Regular meetings were scheduled with the dissertation supervisor. In addition, a statistician was periodically consulted during the design and analysis stages.

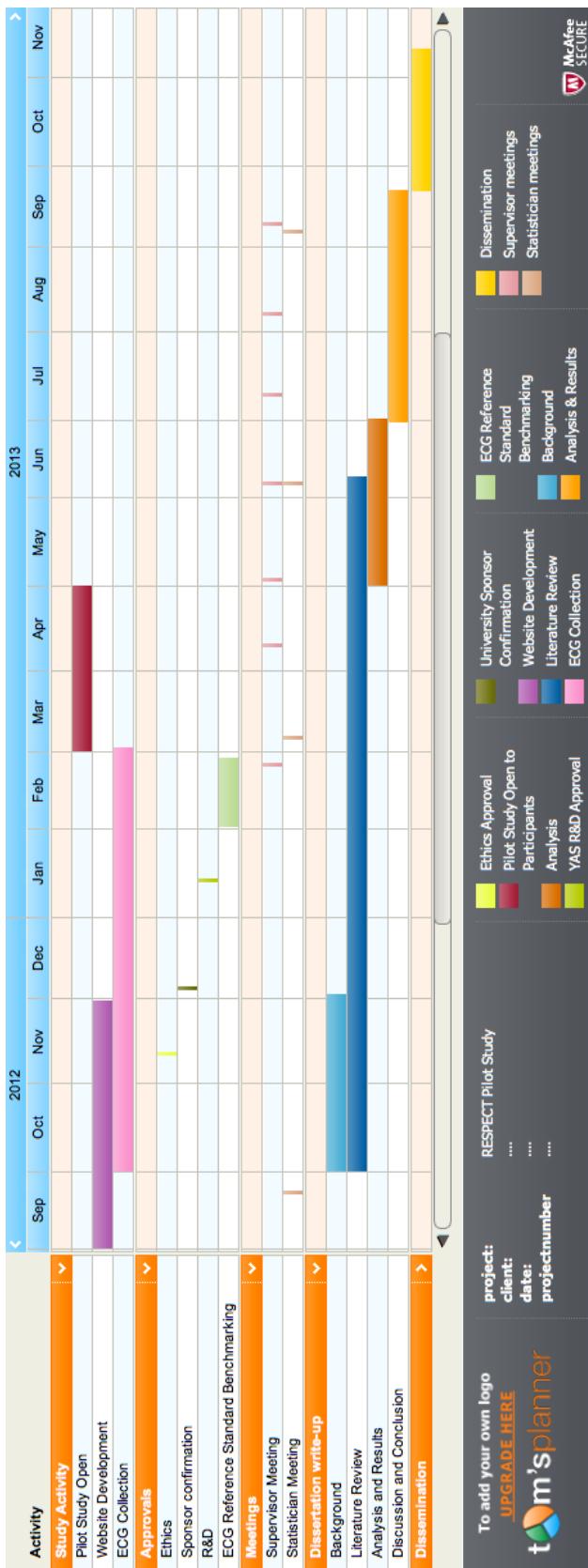


FIGURE 4.5: Gantt chart for RESPECT pilot study

# Chapter 5

## Results

### 5.1 Participants

Figure 5.1 shows the CONSORT diagram for the RESPECT pilot study. In total, 254 participants consented into the study, with 205 completing the first stage and 156 completing the second stage, an attrition rate of 23.9%. Only ECG interpretation attempts from participants who had completed both stages were included in the final analysis. This necessitated the removal of 605 ECG interpretation attempts, leaving 1866 paired ECG attempts for the final analysis.

As part of the consenting process, participants were provided with two, optional, consent statements, allowing:

1. The use of anonymised data from the pilot to be used in subsequent research
2. Permission to contact the participant after the study to take part in a future, qualitative, study on the same topic.

In all, 240/254 (94.5%) of participants agreed to have their data used in subsequent research and 230/254 (90.6%) agreed to be contacted with a view to participating in a future research study.

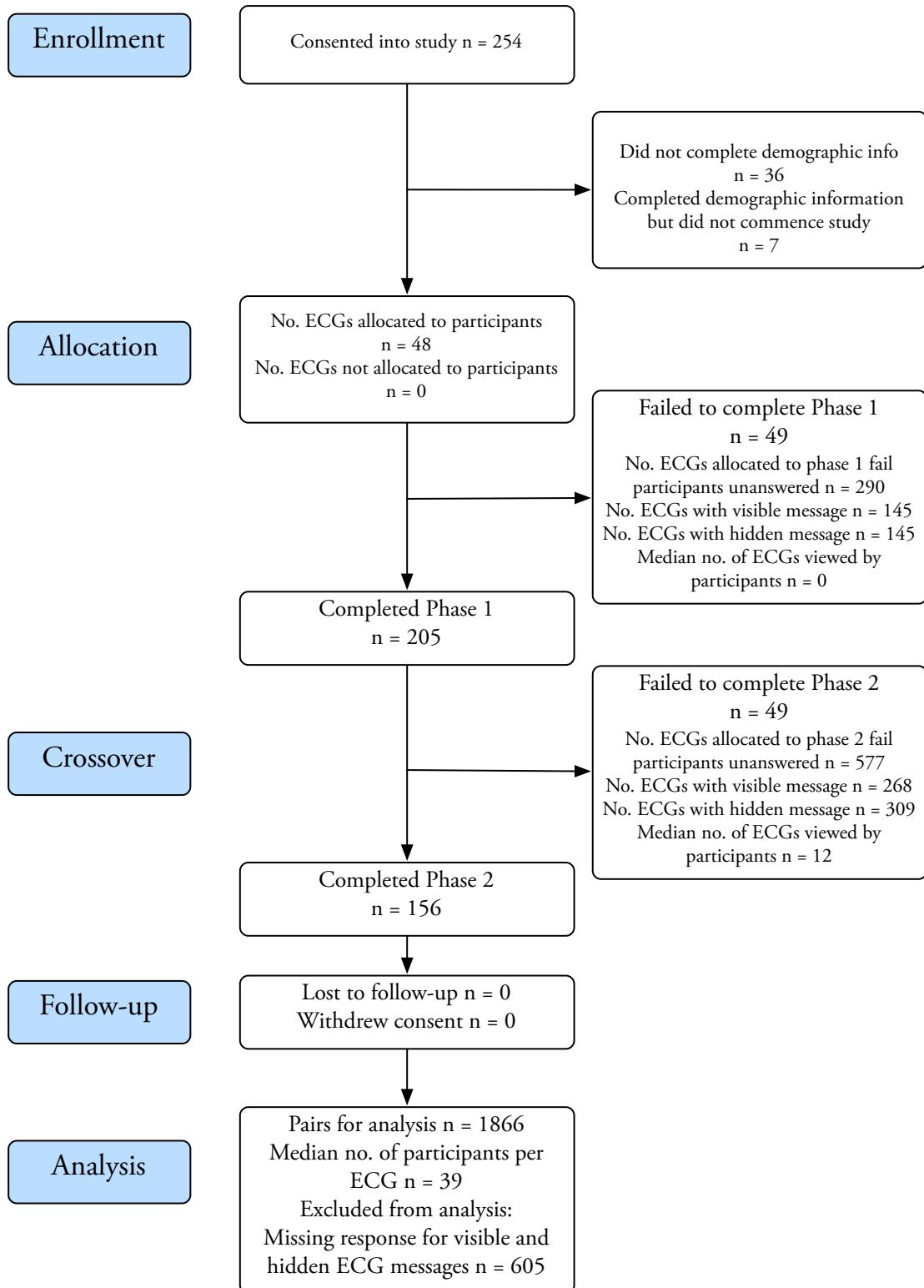


FIGURE 5.1: CONSORT diagram for RESPECT pilot study

Demographic information was provided by 218 participants and this is summarised in [Table 5.1](#). There were 156 participants who completed both phases of the study and were included in the final analysis ([Table 5.2](#)), leaving 62 participants who did not complete the study ([Table 5.3](#)). Aside from a lower median and interquartile range of CPD hours, they appear to have similar demographic characteristics.

TABLE 5.1: Summary of participant characteristics

Characteristic	n	Lowest value	Lower quartile	Median	Upper quartile	Highest value
<b>Training route:</b>						
Traditional	134 (61%)	-	-	-	-	-
University	84 (39%)	-	-	-	-	-
Service (yrs)	-	0	2	5	10	32
CPD (hrs)	-	0	1	4	10	160
pPCI patients	-	0	2	4	6	41

TABLE 5.2: Summary of participant characteristics who completed study

Characteristic	n	Lowest value	Lower quartile	Median	Upper quartile	Highest value
<b>Training route:</b>						
Traditional	96 (62%)	-	-	-	-	-
University	60 (38%)	-	-	-	-	-
Service (yrs)	-	0	2	5	10	32
CPD (hrs)	-	0	2	5	11	160
pPCI patients	-	0	1	3.5	5	41

TABLE 5.3: Summary of participant characteristics who failed to complete study

Characteristic	n	Lowest value	Lower quartile	Median	Upper quartile	Highest value
<b>Training route:</b>						
Traditional	38 (61%)	-	-	-	-	-
University	24 (39%)	-	-	-	-	-
Service (yrs)	-	0	2	5	10	30
CPD (hrs)	-	0	0	2	6	120
pPCI patients	-	0	3	4	6	30

### 5.1.1 Incentives

One of the aims of the pilot study was to examine the effect of incentives on attrition. To achieve this, participants were randomised into receiving one of the following incentive

options:

- A CPD certificate
- A prize draw for a paramedic textbook
- Nothing.

[Table 5.4](#) shows the relation between randomised incentives and completion of the pilot study by participants. The chi-squared test for equality of proportions resulted in a p-value of 0.848, leading to the conclusion that there is no evidence that completion rates were dependent upon the incentive option.

TABLE 5.4: Completion results by incentive offered

<b>Incentive</b>	Completed study		
	<b>Yes</b>	<b>No</b>	<b>Total</b>
Certificate	54 (74%)	19 (26%)	73
Prize draw	51 (71%)	21(29%)	72
None	51 (70%)	22 (30%)	73
<b>Total</b>	156 (72%)	62 (28%)	218

## 5.2 Electrocardiograms

A complete set of summary statistics for each individual ECG, showing participant interpretation attempt and response times, can be found in [Appendix H](#). A concise synopsis of this data is shown in [Table 5.5](#).

The ‘All data’ columns show the median and quartile values for an average ECG in the pilot study, when all ECG interpretation attempts are included. Final data, shows the same values, but only for the ECG interpretation attempts that were included in the final study analysis (i.e. after participants who had not completed both phases of the study were removed). There appears to be no evidence of differential completion rates between the message visibility of ECG interpretation attempts. A median of 39 paired ECG interpretation attempts for each ECG were available for the final analysis.

TABLE 5.5: Summary of participant interaction with ECGs

	All data		Final data	
	Median	Quartiles	Median	Quartiles
ECG interpretation attempts: total	90	87-93	76	74-81
ECG interpretation attempts: message visible	45	44-46	38	37-40
ECG interpretation attempts: message hidden	44	42-46	38	37-41
Paired ECG interpretation attempts	45	44-47	39	37-41

The boxplot figures (Figure 5.2, Figure 5.3, Figure 5.4 and Figure 5.5) show the median ECG interpretation times by participant accuracy and computer interpretation for each ECG, sub-classified by message visibility. They demonstrate a wide range of ECG interpretation attempt completion times, suggesting that the time limit of 60 seconds, was appropriate.

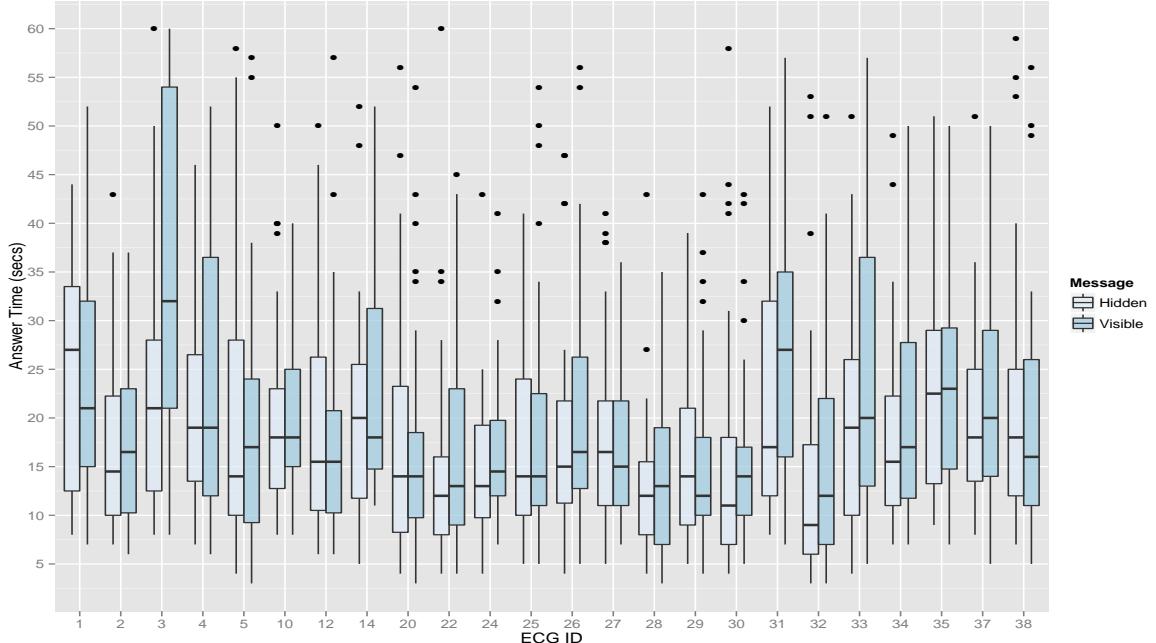


FIGURE 5.2: Median answer time by ECG – correct participant and computer interpretation

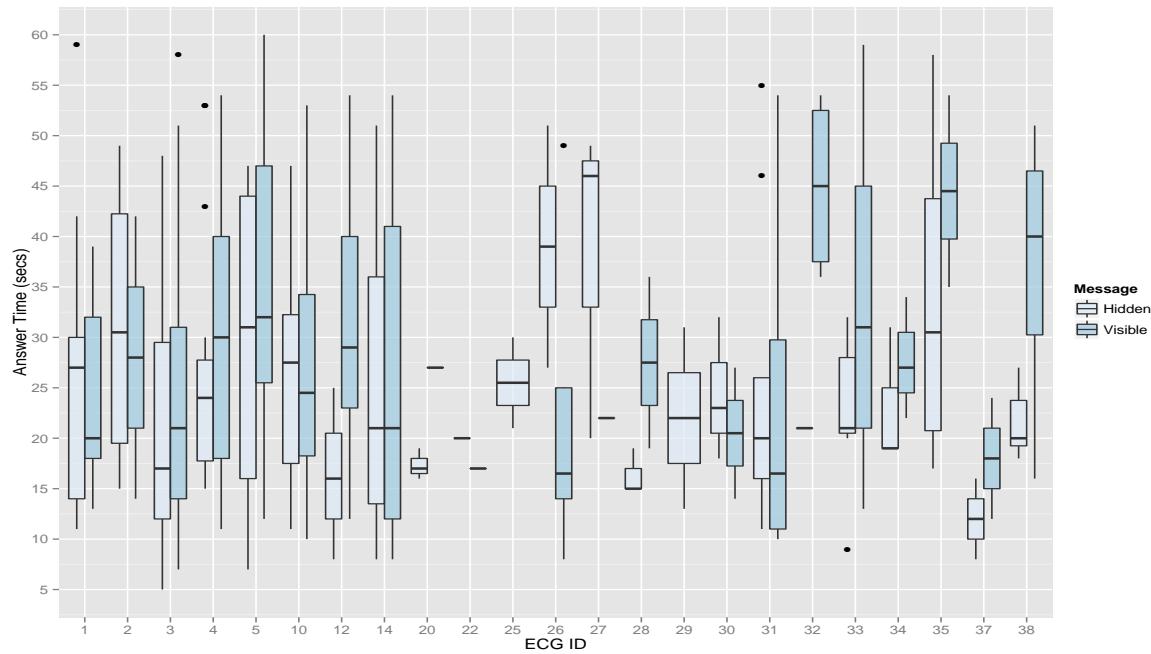


FIGURE 5.3: Median answer time by ECG – incorrect participant, and correct computer, interpretation

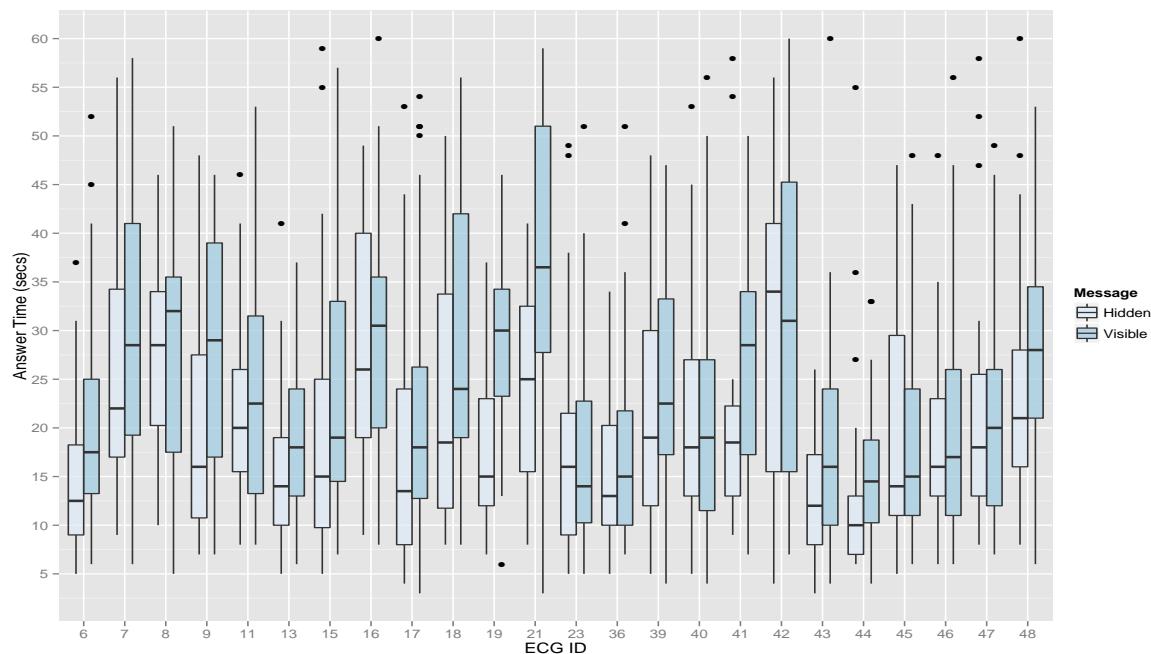


FIGURE 5.4: Median answer time by ECG – correct participant, and incorrect computer, interpretation

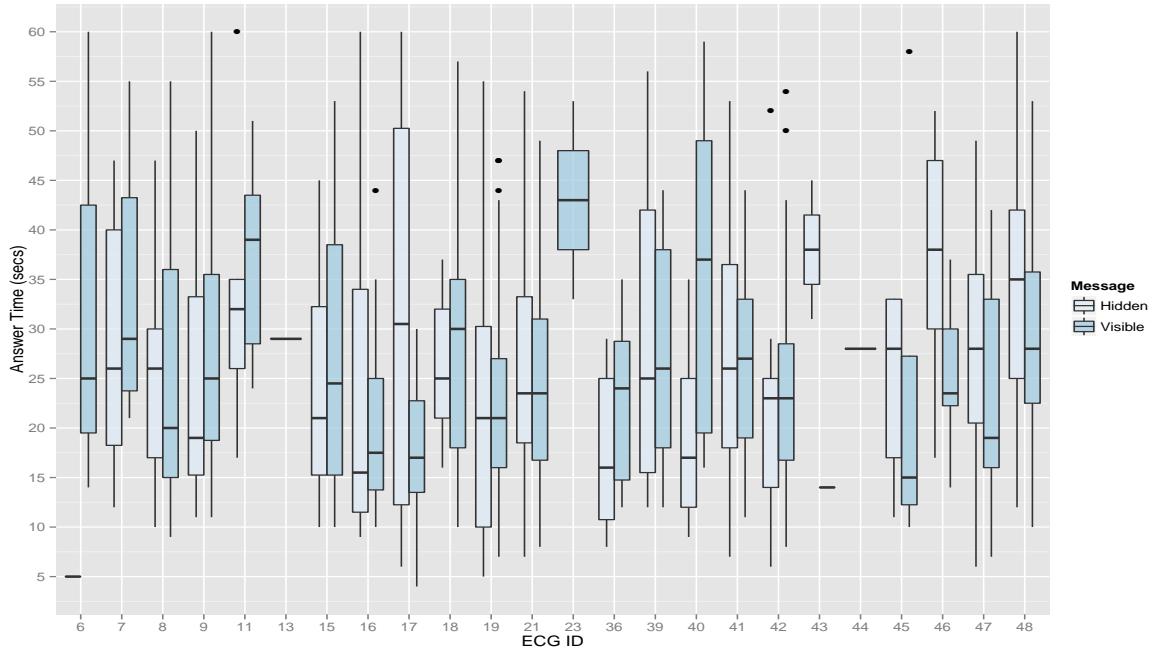


FIGURE 5.5: Median answer time by ECG – incorrect participant and computer interpretation

### 5.3 Accuracy

[Table 5.6](#) shows the sum totals of all responses by message visibility and answer accuracy. Participants in the pilot were correct approximately 80% of the time, irrespective of whether the computer interpretation message was visible.

TABLE 5.6: Two-by-two table for all computer interpretations

Message	Participant interpretation		
	Correct	Incorrect	Total
Visible	1481 (79%)	385 (21%)	1866
Hidden	1500 (80%)	366 (20%)	1866
Total	2981(80%)	751(20%)	3732

When the data are split into correct and incorrect computer interpretations, a different pattern emerges. [Table 5.7](#) shows the results for ECGs with a correct computer interpretation. The results suggest that participants viewing this subset of ECGs, are more likely to make a correct interpretation. In addition, they are even more accurate when the computer interpretation message is visible.

TABLE 5.7: Two-by-two table for all correct computer interpretations

Message	Participant interpretation		
	Correct	Incorrect	Total
Visible	816 (87%)	117 (13%)	933
Hidden	785 (84%)	148 (16%)	933
Total	1601(86%)	265 (14%)	1866

Finally, [Table 5.8](#) shows the results for all ECGs with an incorrect computer interpretation. The results suggest that participants are less accurate in this sub-group, with 77% of answers correct when the computer message is hidden, reducing to 71% when the message is visible.

TABLE 5.8: Two-by-two table for all incorrect computer interpretations

Message	Participant interpretation		
	Correct	Incorrect	Total
Visible	665 (71%)	268 (29%)	933
Hidden	715 (77%)	218 (23%)	933
Total	1380 (74%)	486 (26%)	1866

## 5.4 Sensitivity and specificity

[Table 5.9](#) shows the sensitivities and specificities for the participant responses, depending on computer interpretation accuracy and message visibility. There is little difference in sensitivity and specificity values, when participant ECG interpretation attempts of ECGs with correct and incorrect computer interpretation messages are analysed together.

TABLE 5.9: Summary of sensitivities and specificities of participant responses

Computer interpretation	Message Visible		Message Hidden	
	Sensitivity	Specificity	Sensitivity	Specificity
All	86	75	86	76
Correct	92	85	89	80
Incorrect	80	64	83	72

However, if only the subgroup of participant interpretation attempts when the computer message is correct is considered, participants demonstrate a higher sensitivity and specificity, which increases further when the correct computer message is visible. Conversely,

participant interpretation sensitivity and specificity decrease when only the ECGs which the computer interpreted incorrectly are included.

Overall, paramedics generally balance sensitivity and specificity quite well, with values around the 80% mark, which is useful from a diagnostic perspective, but suggests that there is room for improvement.

## 5.5 Intra-class correlation coefficient

The intra-class correlation coefficient (ICC) is a measure of the degree of similarity between ECG interpretation attempts within a cluster. The ICC for participants is 0.05 and for ECGs, 0.41. The correlation between two randomly selected responses from the same participant, and the same ECG (known as the interaction ICC), was 0.46. These values suggest that taking clustering into account should make a significant difference in the GLM analysis.

## 5.6 Generalised linear modelling results

[Table 5.10](#), [Table 5.11](#) and [Table 5.12](#) shows the results from the GLMs. The unadjusted odds ratios (OR) from the GLM are identical to those calculated from the two-by-two tables ([Table 5.6](#), [Table 5.7](#) and [Table 5.8](#)). Note that  $\sigma_{ecg}^2$  is the between-ECG variance for the random effects model and  $\sigma_{participant}^2$ , the variance between participants.

TABLE 5.10: Odds ratio of correct interpretation

Parameters	OR	z	P> z	95% CI
<i>Unadjusted for clustering</i>				
Constant	4.10	24.20	0.00	3.66 to 4.60
Message	0.94	-0.78	0.44	0.80 to 1.10
<i>Adjusted for clustering</i>				
Constant	6.48	9.42	0.00	4.39 to 9.56
Message	0.92	-0.88	0.38	0.77 to 1.10
$\sigma_{ecg}^2$	1.57			
$\sigma_{participant}^2$	0.21			

[Table 5.11](#) shows the odds ratio of a correct answer when the computer messages are correct. After adjusting for clustering, the odds ratio for the computer message has increased from 1.31 to 1.42. Conversely, in [Table 5.12](#) it can be seen that the opposite result is obtained when the computer message is incorrect, as the odds ratio for the message decreases from 0.76 in the unadjusted model to 0.70 when clustering is taken into account.

TABLE 5.11: Odds ratio of correct interpretation with correct computer message

Parameters	OR	z	P> z	95% CI
<i>Unadjusted for clustering</i>				
Constant	5.30	18.62	0.00	4.46 to 6.35
Message	1.31	2.05	0.04	1.01 to 1.71
<i>Adjusted for clustering</i>				
Constant	9.16	8.32	0.00	5.43 to 15.43
Message	1.42	2.36	0.02	1.06 to 1.89
$\sigma_{ecg}^2$	1.57			
$\sigma_{participant}^2$	0.21			

TABLE 5.12: Odds ratio of correct interpretation with incorrect computer message

Parameters	OR	z	P> z	95% CI
<i>Unadjusted for clustering</i>				
Constant	3.28	15.35	0.00	2.82 to 3.82
Message	0.76	-2.63	0.01	0.61 to 0.93
<i>Adjusted for clustering</i>				
Constant	4.95	5.80	0.00	2.88 to 8.49
Message	0.70	-3.03	0.00	0.56 to 0.88
$\sigma_{ecg}^2$	1.57			
$\sigma_{participant}^2$	0.21			

From the previous section, the ICC values suggested that the odds ratios would be significantly affected when clustering was taken into account. However, the odds ratios and confidence intervals from the GLM results do not appear to show this.

# Chapter 6

## Discussion

### 6.1 Summary of main findings

The RESPECT pilot study has demonstrated that it is possible to conduct a randomised crossover trial to test the accuracy of STEMI recognition by paramedics, using an online assessment tool. The numbers of paramedics who participated in the pilot reflect the advantage of using an online, and access anywhere, method of delivering the assessment tool to maximise recruitment. Conducting this study using physical media would have been difficult to administrate, expensive and time consuming. However, despite the final number of participants being well in excess of the target of 50 for the pilot, almost 24% of participants who completed phase 1, failed to return for phase 2 (the crossover). This is a potential threat to the validity of the study and also could have an impact on the target sample size for the main study. There was no evidence that the incentives offered in the pilot study made any difference to completion rates. However, it is possible that had they been advertised and/or offered together, that they may have been more effective.

Overall, participants were correct approximately 80% of the time, irrespective of whether the computer message was visible (Table 5.6). Participant sensitivity and specificity for all computer interpretations were almost identical, irrespective of whether the message was visible, or not, with a sensitivity of 86% and specificity, 75–76% depending on message visibility (Table 5.9). This suggests that it is worth investigating ways to improve paramedics' recognition of STEMI.

The sub-group analysis does suggest that computer interpretation messages have an effect on participant interpretation, although this must be taken in the context of a non-powered pilot study. In the sub-group of ECGs where the computer interpretation was correct, the proportion of correct answers by participants when the message was hidden was 84%, increasing to 87% when the message was visible. Likewise, sensitivity and specificity increased when participants viewed the correct computer interpretation message. Conversely, in the sub-group of incorrect computer interpretation, the proportion of correct answers fell to 77% with the message hidden, and to 71% when the incorrect computer interpretation message was visible ([Table 5.8](#)). As before, sensitivity and specificity followed suit, with a reduction in both when the incorrect message was displayed. This suggests that both the computer and participant are more likely to correctly, and incorrectly, interpret similar types of ECGs, which is worth investigating in the main study.

Finally, the intra-class correlation coefficients (ICCs) will enable the calculation of the design effect of the main study. This is potentially the most serious threat to the feasibility of the main study, since if the sample size required to ensure the study is adequately powered is too large, then it would not be appropriate to proceed. The ICC for participants, was 0.05, which results in a design effect of 1.55, assuming a cluster size of 12 ECGs per participant. Of greater concern is the ICC for ECGs, which is 0.46. The median number of participants viewing each ECG in the pilot study, was 39, which would lead to a design effect of 18.48. Of course, these design effects are not separate, they both apply together and the calculation for an overall sample size for cross-classified models is non-trivial, may require Bayesian analysis [\[92\]](#) and will require expert statistical assistance.

The logistic regression analysis with random effects modelling appears to have been conducted accurately, having been confirmed in a separate statistics application. The scripts created for the pilot study (an example of which can be seen in [Appendix I](#)), can be utilised for the main study and be modified as required.

Given the ICC values from the pilot study, it is reasonable to assume that larger standard errors and confidence intervals would have been seen when the unadjusted GLM was amended to account for clustering. However, the pilot data does not show this

(Table 5.10, Table 5.11 and Table 5.12) and this requires an explanation prior to commencing the main study. One possibility, is that the paired nature of the data has reduced the effect of the clustering of data. However, this needs to be reviewed by a statistician with an expertise in cluster randomised controlled trials.

## 6.2 Interpretation

Assuming that a satisfactory explanation can be obtained for the smaller than expected standard errors and confidence intervals, the rates of attrition can be addressed, and the required sample size to conduct the main study is not prohibitively large, the results from the pilot study are rather encouraging and support undertaking the main study.

## 6.3 Context

The paramedic studies in the literature review (chapter 2) are difficult to compare directly with the RESPECT pilot since correctly excluded paramedic ECG interpretation attempts, and paramedic ECG interpretation without computer assistance, are not reported. Table 6.1 shows the proportions for the RESPECT pilot where the participants and the computer identified the ECG as a STEMI. This enables some form of comparison with the paramedic studies.

TABLE 6.1: Two-by-two table showing data where computer and participant identified ECG as STEMI

Message	STEMI present		Total
	YES	NO	
Visible	426 (72%)	166 (28%)	592
Hidden	412 (76%)	138 (24%)	550
Total	838 (73%)	304 (27%)	1142

Paramedics appeared to perform slightly better in the Cantor study [43], with paramedics correctly identifying STEMI in 106/134 (79%) of cases (assisted with computer interpretation) compared with 426/592 (72%) in the pilot study, although they would have had the benefit of the patient presentation and history to assist in their decision making. Paramedics in the Selker study [63] did not perform as well, despite having computer

interpretation available, correctly recognising STEMI in 296/437 (68%) of patients. Finally, in the Ting study [46] paramedics performed much better, with 26/30 (87%) of patients correctly identified as STEMI by the paramedic (assisted by computer interpretation), although the sample size is small.

The doctor studies [60–62] are more aligned to the RESPECT pilot methodologically, allowing a more direct comparison of results. The participants in the Tsai study were not as accurate as the pilot participants, but there was similarity in the pattern of the results. In the sub-group of correct computer interpretations, participants in the Tsai study made a correct diagnosis in 255/480 (53%) of ECGs when the message was not visible, which rose to a statistically significant 327/480 (68%,  $p<0.001$ ) when the message was visible. In contrast, when only ECGs with incorrect computer interpretations were considered, 102/180 (57%) were interpreted correctly, reducing to 87/180 (48%) when the incorrect computer interpretation was displayed ( $p=0.131$ ). However, the Tsai study ECGs were not limited to STEMI and STEMI-mimics.

The Massel study showed a more modest change in the decision making of junior doctors when interpreting ECGs: when considering whether to administer thrombolysis, the participants were more likely to undercall a thrombolysis decision when the message was visible. However, further, more in-depth comparison with the pilot study is not possible based on the published results. The Goodacre study, similarly to the pilot study, found that overall the computer message did not significantly effect the junior doctors' decisions, but it was not limited to ECGs with STEMIs and STEMI-mimics, unlike the RESPECT pilot study.

## 6.4 Strengths and limitations

The use of a crossover design is powerful in terms of reducing between-subject variability, making crossover trials more efficient than a similar sized parallel group trial and, in theory, producing more precise estimates of treatment effects with the same sample size. A key drawback with crossover trials is the risk of ‘carry over’, when the wash-out period is insufficient to allow the effects of the first treatment to wear off [93, 94]. In this study the two week wash-out period was considered sufficient to ensure participants could not recall their first phase attempt, and the ECGs they viewed. However, a perceived

poor performance in the first phase, may have prompted the participants to revise their knowledge on ECGs, and so be better prepared for the second phase, or not to return at all. However, the reason for not returning for the second phase was not recorded in the pilot study. Since approximately 24% of participants failed the study, there is a risk of attrition bias, which may have been compounded by the removal of incomplete results for the final analysis.

From the results of the incentive randomisation, it can be seen that there is no statistically significant difference in completion rates between the three incentive options. However, due to an inadvertent usability error, whereby the download link for the certificate did not automatically appear at the end of the study, a number of participants did contact the researcher asking for the certificate. A better advertised incentive at the start of the study, may assist in completion rates.

The website assessment tool performed well, and since the allocation of ECGs and their randomisation was handled automatically, no intervention was required by the researcher, thus minimising the risk of observer bias. In addition, the website handled the wash-out period, not allowing participants to undertake phase two until the allotted time had passed, and inviting them to return by email, as well as sending out periodic reminders. Due to the design, replicating the study is straightforward and can be customised as required (for example, if overseas paramedics take part in a subsequent study).

There was a risk that participants may have utilised textbooks or an expert colleague to assist with their answers, since the study is not supervised by the researcher. However, the time limited nature of the assessment (each ECG is only visible for 60 seconds) and the inability to view the same ECG with a specific message visibility (i.e. visible or hidden) more than once, should have minimised the chance of this happening.

Ultimately, this is an experiment, and a proxy for the interpretation of an ECG in the presence of an acutely ill patient. However, to replicate this study prospectively with genuine patient episodes would be complicated and expensive, and make extracting the role of the computer message alone from the other benefits of an actual patient encounter (such as patient presentation and history) difficult. In addition, this is a pilot with no *a priori* power calculations and the results need to be confirmed by an adequately powered study.

## 6.5 Implications for practice

The results from this pilot study should be interpreted with caution, and an adequately powered study is required before too much emphasis can be placed on the findings. The types of ECGs that the computer algorithms are more likely to misinterpret are known, [36] as are the modifiable factors that lead to error, such as incorrect lead placement [95, 96], incorrect identification of the J-point [97] and even vehicular movement [98]. If it is the case that paramedics' diagnostic accuracy is being adversely affected by computer interpretation, then the education of paramedics in 12-lead ECG acquisition and interpretation would benefit from being reviewed to see whether this could be addressed.

Alternatively, the computer interpretation messages could be turned off. However, there is a risk that if this is undertaken, then correct interpretation by paramedics, based on the pilot study results, would decrease. The accuracy of computer interpretation varies from study to study, but false positive rates are around 22% and false negative, 6–9% [41]. Paramedics' accuracy does appear to improve these rates, with false positive results ranging from 15–18% and false negative, from 1–6% [17, 99, 100]. However, a recent US, multi-EMS system study, used a survey tool on 477 paramedics and found that they were poor at spotting STEMI-mimics, correctly interpreting known STEMI-mimics such as left ventricular hypertrophy (LVH) and left bundle branch block (LBBB) less than 40% of the time [101]. It is difficult to know how generalisable these results are to the UK, since little research has been conducted with UK paramedics in the past 10 years, which can provide an estimate of paramedics' accuracy in the recognition (or exclusion) of STEMI.

## 6.6 Future research

These results need to be confirmed by an adequately powered study, assuming that the required sample size does not make the main study impracticable to conduct. It would also be helpful to conduct a qualitative study to explore how paramedics interpret 12-lead ECGs in the context of STEMI, and try to identify what role the computer interpretation message plays in their decision making. Utilising participants in the RESPECT study, who have consented to be contacted for subsequent research, would make it possible

to identify a purposeful sample of participants for such a study, based on the influence that computer interpretation messages have on their decision about whether a STEMI is present or not.

# **Chapter 7**

## **Conclusion**

The RESPECT pilot study has demonstrated that it is possible to conduct a randomised crossover trial to test the accuracy of STEMI recognition by paramedics, using an online assessment tool. The next step is to calculate the sample size for an adequately powered main study. If this is not prohibitively high, the main study should be conducted to see whether the results suggested from the pilot data can be replicated. The sample size calculation, confirmation of the appropriate model that should be utilised, and an explanation for the smaller than expected standard errors and confidence intervals for the adjusted GLM, will require the services of a statistician with an expertise in cluster randomised controlled trials.

## **Appendix A**

### **Summary of study ECGs**

TABLE A.1: Summary of study ECGs

<b>ECG ID</b>	<b>Classification</b>	<b>Actual interpretation</b>	<b>Computer interpretation</b>
1	True negative	Early repolarisation	Otherwise normal ECG, Sinus bradycardia, Early repolarisation
2	True negative	Normal sinus rhythm, Old inferior MI	Abnormal ECG, Sinus rhythm, Possible inferior infarct - age undetermined
3	True positive	Inferolateral MI	Acute MI suspected, Unusual P axis, Low voltage QRS
4	True negative	Early repolarisation	Normal ECG or non-specific anomalies
5	True negative	Paced rhythm	Abnormal ECG, Demand pacing, LVH with secondary repolarisation abnormality, Widespread ST-T abnormality may be due to hypertrophy and/or ischaemia
6	False positive	Meets voltage criteria for LVH	Abnormal ECG, Meets ST elevation MI criteria, Sinus rhythm, Inferior ST elevation, consider acute
7	False positive	IVCD	Abnormal ECG, Meets ST elevation MI criteria, Sinus rhythm with 1st degree A-V block, Extensive infarct - possibly acute
8	False positive	Pericarditis	Extensive myocardial infarction
9	False positive	Pericarditis	Extensive myocardial infarction
10	True negative	LBBB	Abnormal ECG Unconfirmed, Normal sinus rhythm, Left bundle branch block
11	False positive	Inverted P waves in inferior leads, PR depression	Acute MI suspected, Unusual P axis and short PR, probably junctional rhythm, ST elevation consider inferior injury or acute infarct
12	True negative	Early repolarisation	Otherwise normal ECG, sinus bradycardia

*Continued on next page*

Table A.1 – *Continued from previous page*

ECG ID	Classification	Actual interpretation	Computer interpretation
13	False positive	Atrial flutter	Acute MI suspected, Atrial flutter with 4:1 AV conduction, ST elevation consider inferior injury or acute infarct
14	True negative	NSR, bifascicular block	Abnormal ECG unconfirmed, Normal sinus rhythm, Right bundle branch block, Left anterior fascicular block, Bifascicular block
15	False positive	LBBB	Medium sized myocardial infarction, consider urgent reperfusion therapy
16	False positive	Early repolarisation	Acute MI suspected, Sinus bradycardia with sinus arrhythmia, ST elevation consider anterolateral injury or acute infarct, ST elevation consider inferior injury or acute infarct
17	False positive	Hyperkalaemia	Acute MI suspected, Atrial fibrillation with rapid ventricular response, Indeterminate axis, Low voltage QRS, ST elevation lateral injury or acute infarct
18	False positive	LVH, early repolarisation	Extensive myocardial infarction
19	False positive	Osborne waves	Meets ST elevation criteria, Atrial fibrillation, Prolonged QT interval, Widespread ST elevation, consider acute infarct, Anteroseptal ST depression is probably reciprocal to inferior infarct, ST junctional depression is non-specific
20	True negative	Paced rhythm	Abnormal ECG, Normal sinus rhythm, Ventricular pre-excitation, WPW pattern type B
21	False negative	LAD occlusion, hyperacute T-waves	Abnormal ECG, sinus bradycardia, moderate voltage criteria for LVH, cannot rule out septal infarct, age undetermined

*Continued on next page*

Table A.1 – *Continued from previous page*

<b>ECG ID</b>	<b>Classification</b>	<b>Actual interpretation</b>	<b>Computer interpretation</b>
22	True positive	Anterolateral MI	Meets ST elevation MI criteria, sinus rhythm, anteroseptal infarct - possibly acute, lateral ST elevation, consider acute infarct
23	False negative	Anterolateral MI	ECG override: data quality prohibits interpretation
24	True positive	Anterior MI	Meets ST elevation MI criteria, sinus bradycardia, left axis deviation, anteroseptal ST elevation, consider acute infarct, inferior/lateral ST-T abnormality suggests myocardial injury/ischaemia
25	True positive	Anterolateral MI	Extensive myocardial infarction, consider urgent reperfusion therapy if patient's age <= 80 years
26	True positive	Inferolateral MI	Medium-sized myocardial infarction, consider urgent reperfusion therapy if the patient's age <= 70 years
27	True positive	Inferolateral MI	Extensive myocardial infarction, consider urgent reperfusion therapy if patient's age <= 80 years
28	True positive	Inferior MI	Meets ST elevation MI criteria, sinus rhythm, rightward axis, RVH with secondary repolarisation abnormality, inferior ST elevation consider acute infarct, Ant/septal and lateral ST-T abnormality
29	True positive	Anterolateral MI	Extensive myocardial infarction, consider urgent reperfusion therapy if patient's age <= 80 years
30	True positive	Anterior MI	Meets ST elevation MI criteria, sinus rhythm, Lead(s) unsuitable for analysis: V4, IV conduction defect, septal infarct - possibly acute, inferior T wave abnormality is nonspecific

*Continued on next page*

Table A.1 – *Continued from previous page*

ECG ID	Classification	Actual interpretation	Computer interpretation
31	True negative	LBBB	Abnormal ECG unconfirmed, Atrial fibrillation with PVCs, QRS changes in V2 may be due to LVH but cannot rule out septal infarct, Left ventricular hypertrophy, inferio/lateral ST-T abnormality may be due to hypertrophy and/or ischaemia
32	True positive	Inferolateral MI	Extensive myocardial infarction, consider urgent reperfusion therapy if patient's age <= 80 years
33	True positive	Inferior MI	Extensive myocardial infarction, consider urgent reperfusion therapy if patient's age <= 80 years
34	True negative	Normal variant for age	Normal ECG of non-specific anomalies
35	True positive	Inferolateral MI	Meets ST elevation MI criteria, atrial fibrillation with rapid ventricular response with PVCs or aberrant ventricular conduction, inferior infarct - possibly acute, Lateral ST elevation consider acute infarct, Anteroseptal ST depression is probably
36	False negative	Inferior MI	ECG override: data quality prohibits interpretation
37	True negative	Meets voltage criteria for LVH	Abnormal ECG unconfirmed, sinus tachycardia, Left ventricular hypertrophy, Anterolateral ST-T abnormality is probably due to ventricular hypertrophy
38	True negative	LBBB	Abnormal ECG unconfirmed
39	False negative	Anterior MI	Abnormal ECG unconfirmed, Normal sinus rhythm, Low voltage QRS, Cannot rule out anteroseptal infarct age undetermined
40	False negative	Anterior MI	Abnormal ECG unconfirmed, normal sinus rhythm, septal infarct age undetermined

*Continued on next page*

Table A.1 – *Continued from previous page*

<b>ECG ID</b>	<b>Classification</b>	<b>Actual interpretation</b>	<b>Computer interpretation</b>
41	False negative	Inferolateral MI	Abnormal ECG unconfirmed, sinus bradycardia, ST elevation, consider early repolarisation, pericarditis, or injury, ST abnormality, possible digitalis effect
42	False positive	Early repolarisation	Acute MI suspected, abnormal ECG unconfirmed, sinus bradycardia with sinus arrhythmia, ST elevation consider anterolateral injury or acute infarct, ST elevation consider inferior injury or acute infarct
43	False negative	Inferior MI	ECG override: data quality prohibits interpretation
44	False negative	Inferior MI	ECG override: data quality prohibits interpretation
45	False negative	Anterolateral MI	ECG override: data quality prohibits interpretation
46	False negative	Inferior MI	Abnormal ECG unconfirmed
47	False negative	Inferior MI	Abnormal ECG unconfirmed
48	False negative	Anterolateral MI	Abnormal ECG unconfirmed

## **Appendix B**

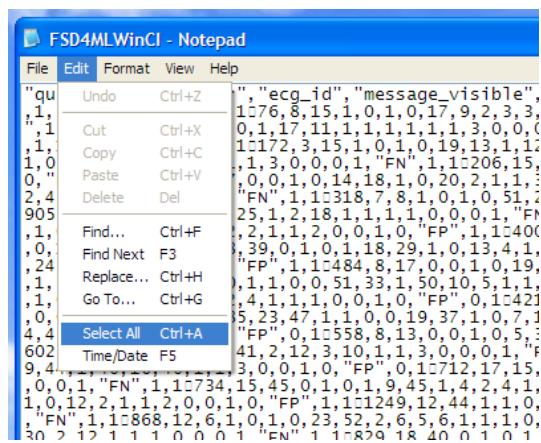
### **MLWin data analysis method**

## MLWin user guide

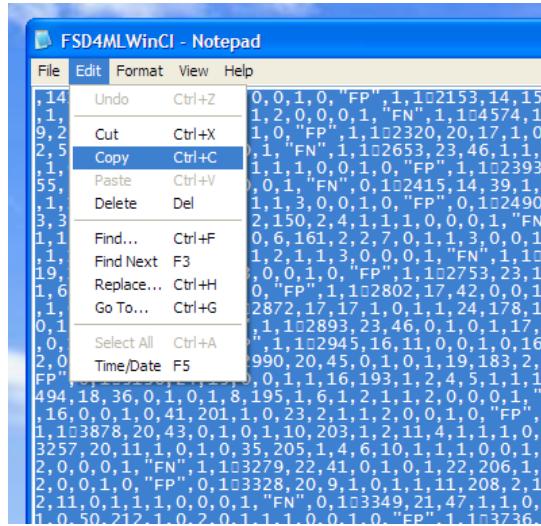
This guide will explain how to take exported CSV files from the R script ProcessRawData.R, import the data into MLWin and run frequentist and Bayesian analysis to compare against the R output.

1. Open FSD4MLWin.csv (or equivalent files for subsets of correct and incorrect computer interpretation) in Notepad

2. Edit > Select All

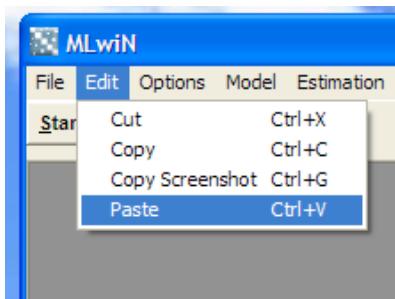


3. Edit > Copy

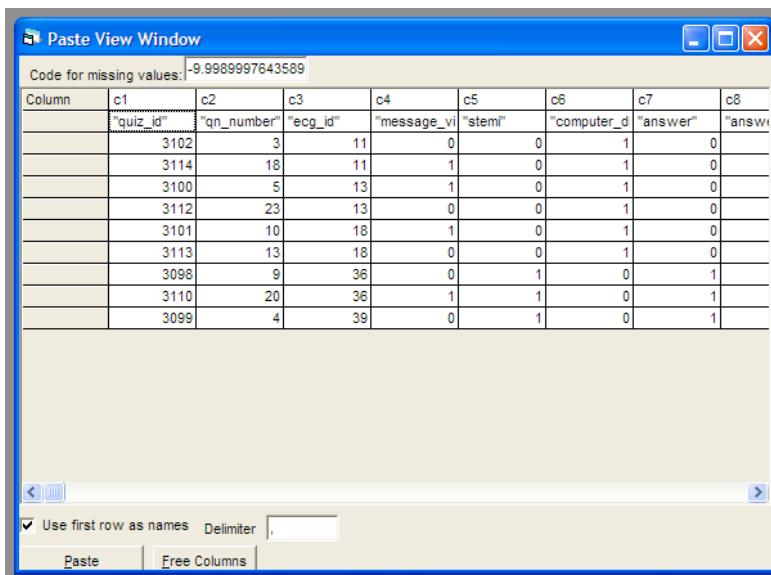


4. Open MLWin and create a new worksheet

## 5. Edit &gt; Paste



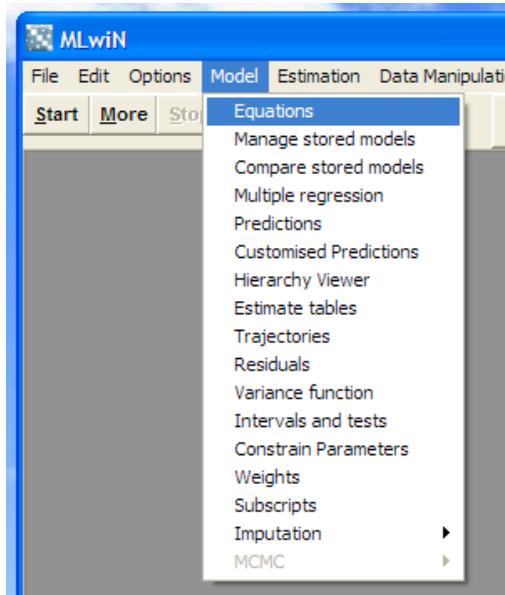
6. The Paste View Window will open. Check that the columns have been filled correctly. Make sure the 'Use first row as names' checkbox is ticked and the click the Paste button



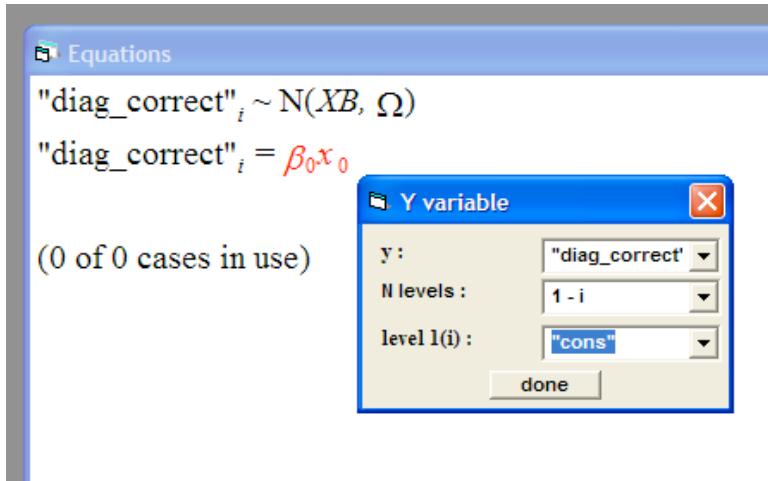
7. The Names window should open showing how the data has been populated into the table. Annoyingly, the double quotes are inserted around the names, which you will have to remember to include in later steps.

Name	Cn	n	missing	min	max	categorical
'quiz_id'	1	1866	0	73	5130	False
"qn_number"	2	1866	0	1	24	False
"ecg_id"	3	1866	0	6	48	False
"message_vি..."	4	1866	0	0	1	False
"stem"	5	1866	0	0	1	False
"computer_d..."	6	1866	0	0	1	False
"answer"	7	1866	0	0	99	False
"answer_time"	8	1866	4	3	60	False
"participant_id"	9	1866	0	2	315	False
"trainroute"	10	1866	0	1	2	False
"cpdhours"	11	1866	0	0	160	False
"servicyears"	12	1866	0	0	32	False
"pcipts"	13	1866	0	0	41	False
"stage1"	14	1866	0	1	1	False
"stage2"	15	1866	0	1	1	False
"incentive"	16	1866	0	1	3	False
"truepos"	17	1866	0	0	0	False
"trueneg"	18	1866	0	0	0	False
"falsepos"	19	1866	0	0	1	False
"falseneg"	20	1866	0	0	1	False

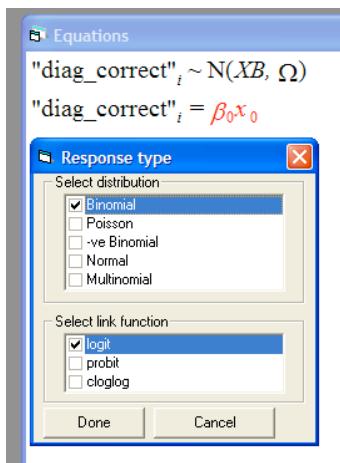
8. Model > Equations This will open the equations window



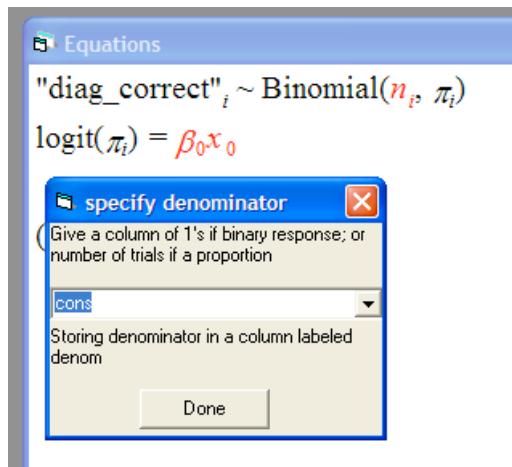
9. Click on the red 'y' in the Equations window and fill out the details as in the image below:



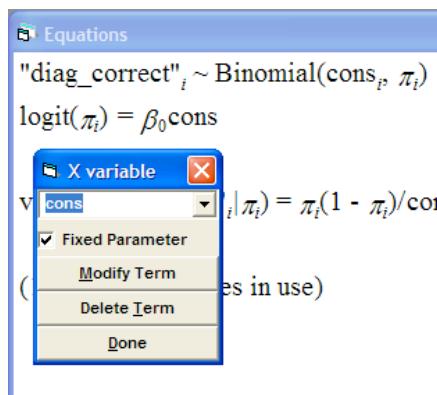
10. Click on N(XB, Omega) and choose the Binomial distribution and logit link function



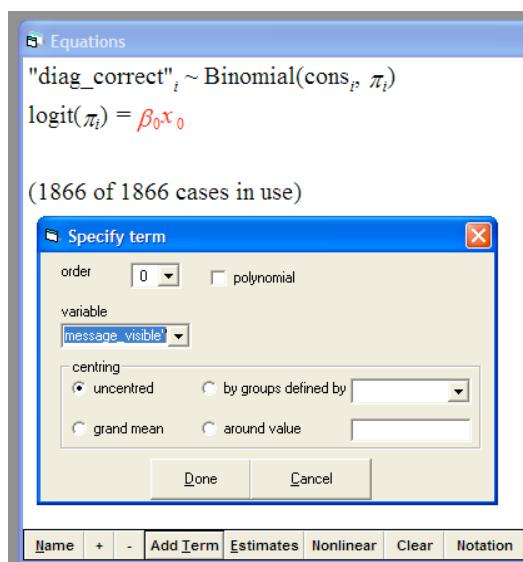
11. Click on the 'ni' just after the word Binomial and select either "cons" or cons as the denominator. They both contain the value of 1 for all rows.



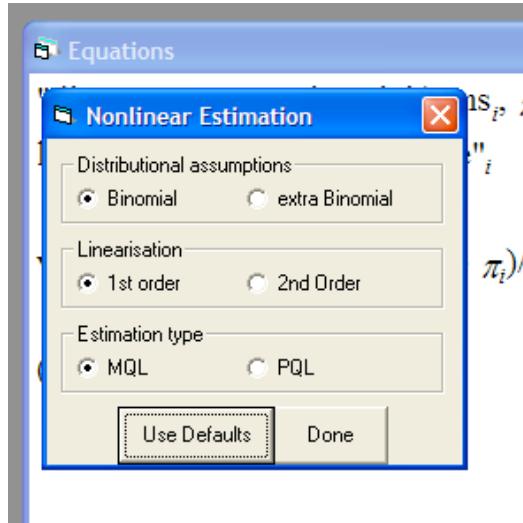
12. Click on the red beta0x0 text. Select 'cons' from the drop-down menu and make sure the 'Fixed Parameter' box is ticked.



13. Click on the 'Add Term' button at the bottom of the Equations window. Select "message\_visible" from the variable drop-down menu and click 'Done'



14. Click on the Nonlinear button and click on the 'Use Defaults' button and then 'Done'



15. Clicking on the 'Estimates' button at the bottom of the Equations menu toggles through a range of views, including the notation and the beta value and its associated standard error.

16. In the main MLWin window, click on the 'Start' button. Click on the 'Estimates' button at the bottom of 'Equations' window until you can see the numerical values. MLWin uses iterative generalised least squares (IGLS) to calculate the values, whereas R used LaPlace approximation, but the results should be similar. Check the results from MLWin with the same R results for GLM no Random Effects.

```

Equations
"diag_correct" ~ Binomial(cons, πi)
logit(πi) = 1.188(0.077)cons + -0.279(0.106)"message_visible"i

var("diag_correct" | πi) = πi(1 - πi)/consi

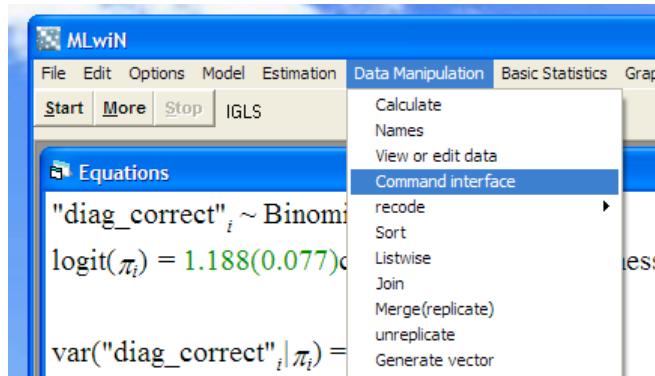
(1866 of 1866 cases in use)

```

TABLE 4.11: Log odds ratio of correct answer and incorrect computer messages

Parameters	Log OR	Standard error	z	P> z	95% CI
<i>GLM no Random Effects</i>					
Constant	1.19	0.08	15.35	0.00	1.04 to 1.34
Message	-0.28	0.11	-2.63	0.01	-0.49 to -0.07

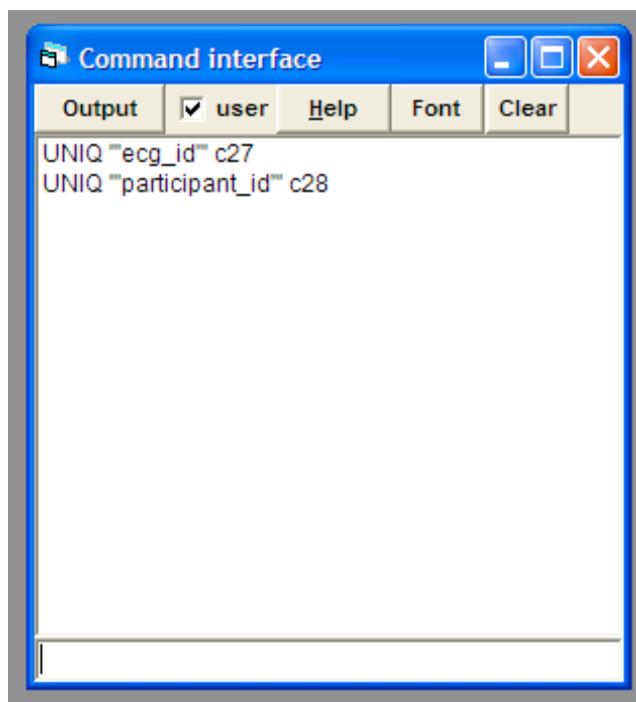
17. In order to conduct the cross-classified random effects analysis, some preparatory work is required in MLWin. Open the command interface, using the menu options: Data Manipulation > Command interface



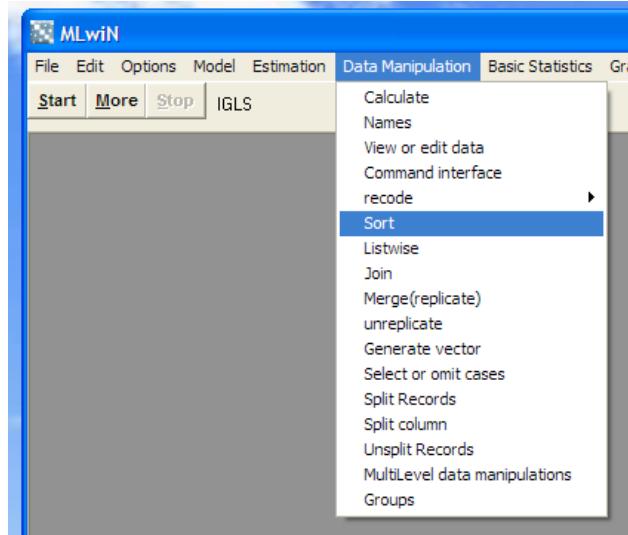
18. Type the following commands in the small data entry window at the bottom of the Command Interface window (Press return after each line):

```
UNIQ "ecg_id" c27  
UNIQ "participant_id" c28
```

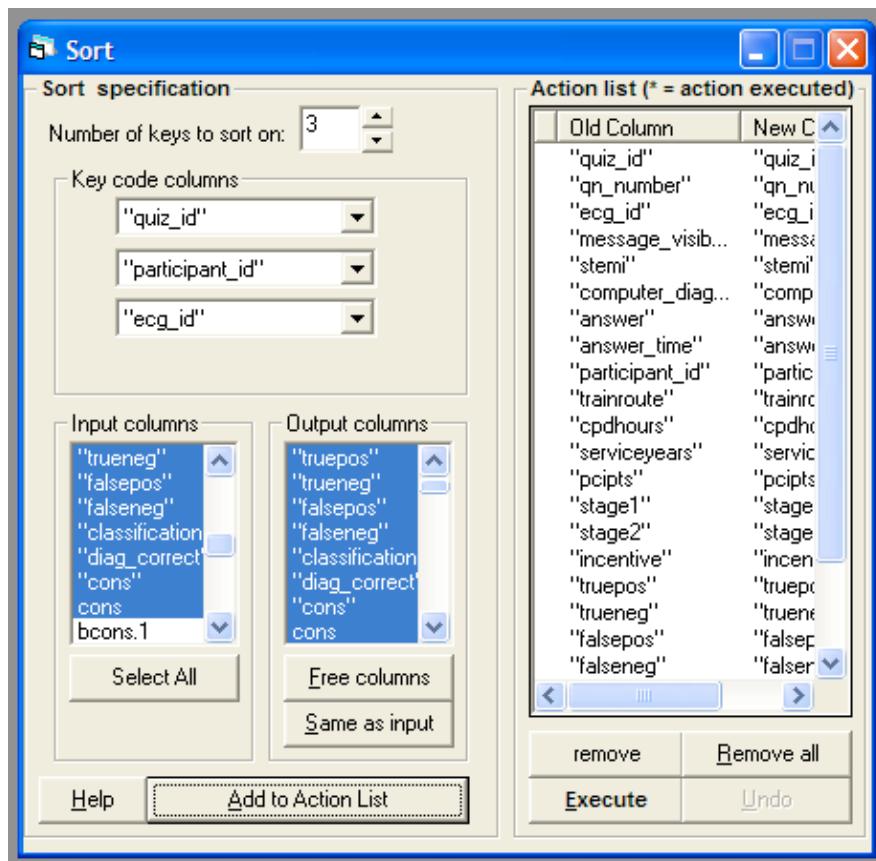
Note that there is a single quote ' and then double quote " required before the variable name and a double quote ", then single ', after.



19. Next, the data needs sorting. Choose the menu option: Data Manipulation > Sort

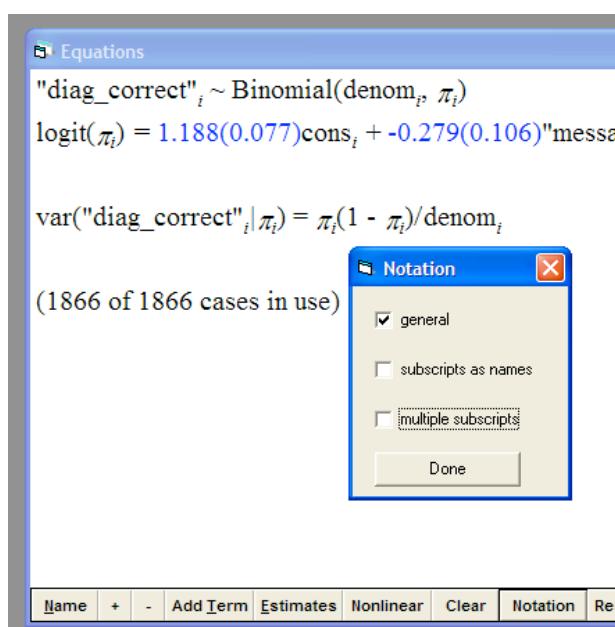


20. Set the number of keys to sort on value to 3 and choose the options from the Key code columns, drop-down menus so that they look like the image below.

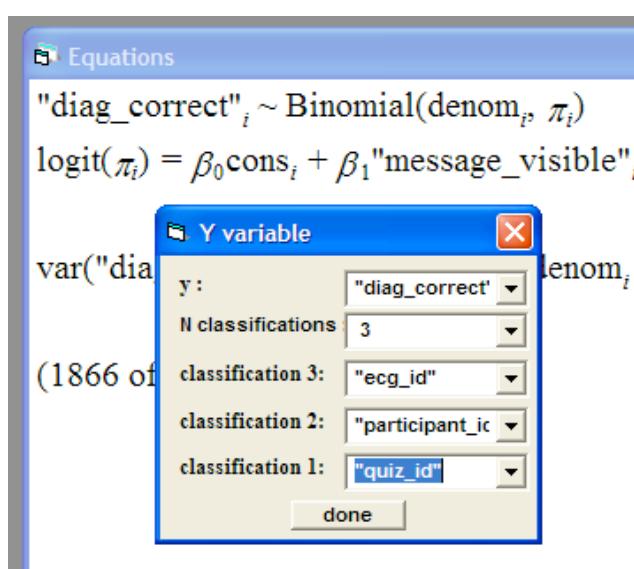


21. In the 'Sort' window, choose the input columns from "quiz\_id" to cons. Under the Output columns, click on the 'Same as input' button and then the large 'Add to Action List' button at the bottom of the 'Sort' window. Finally, click on the 'Execute' button on the bottom right-hand side of the 'Sort' window. Small x's should appear next to the Old Column, column if it succeeds.

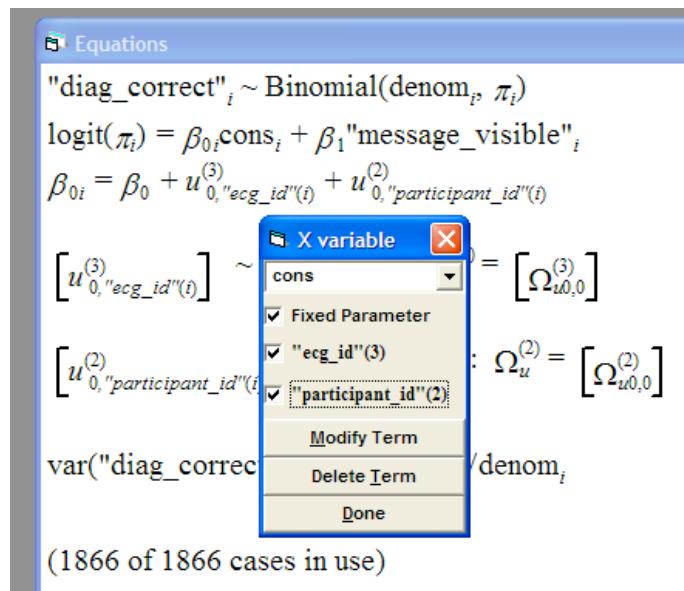
22. Choose the menu option: Model > Equations to bring the Equations window back. Your equation should still be present. Click on the 'Notation' button at the bottom of the Equations window and uncheck the 'multiple subscripts' box.



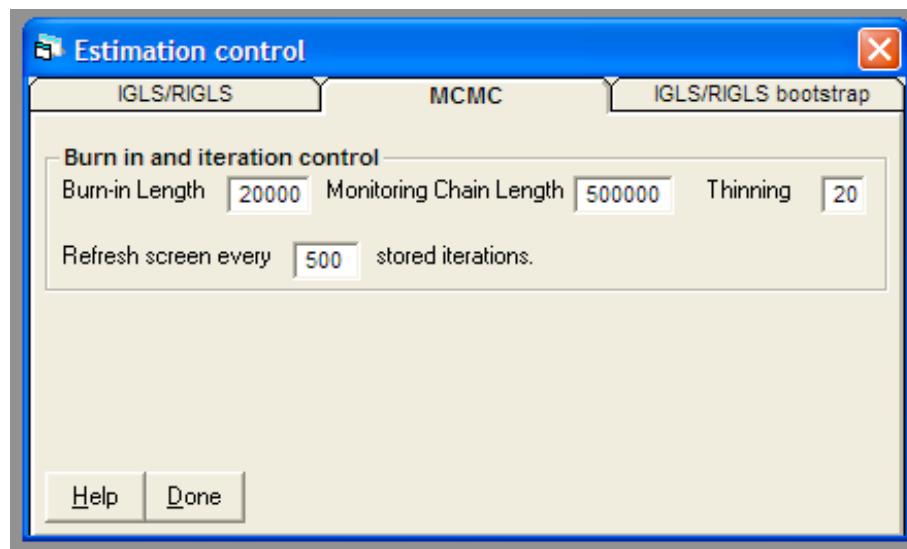
23. In the Equations window, click on the "diag\_correct" $_i$  text and select options from the 'Y variable' window so that it looks the same as below:



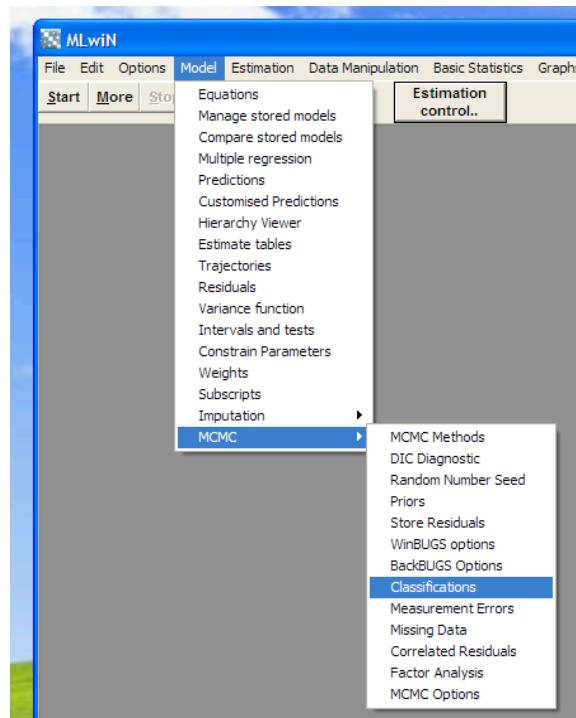
24. In the Equations window, click on the beta0consi text and check all the boxes before clicking on the 'Done' button.



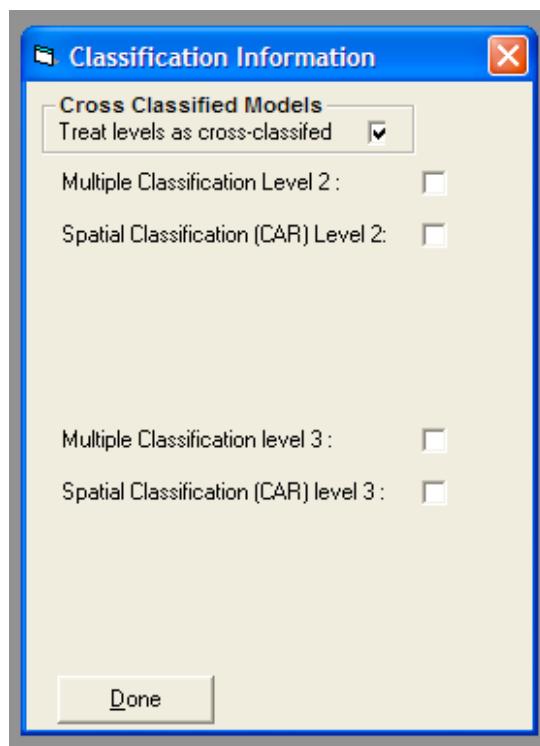
25. In the main MLWin window, click on the 'Start' button to generate some estimates. Once done, click on the 'Estimation control' button and then, in the 'Estimation control' window, click on the MCMC tab. Enter the appropriate numbers into each box, so that it looks the same as the image below and then click 'Done':



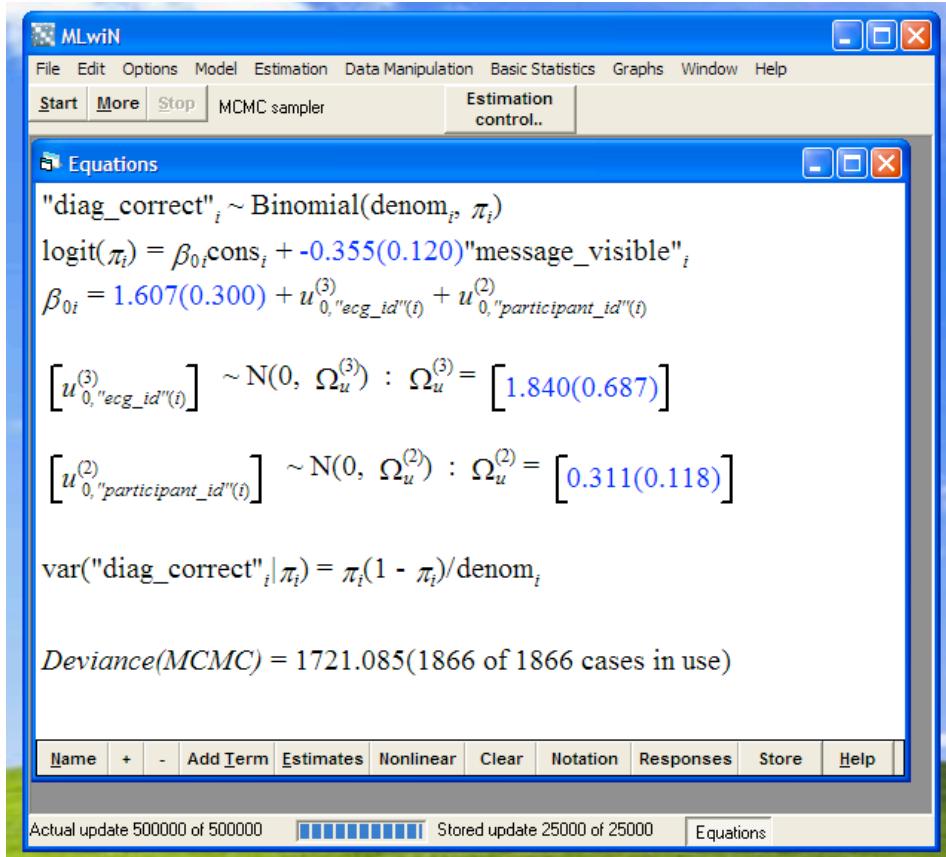
26. From the main MLWin menu, choose the following option: Model > MCMC > Classifications



27. In the 'Classification Information' window, check the box after the 'Treat levels as cross-classified' text.



28. In the main MLWin window, click the 'Start' button, then go and have a cup of tea as 500,000 iterations might take 20-30 minutes to complete, depending on the speed of your computer. Unlike with the IGLS estimation, the variables and standard errors do not turn green, but stay blue. The clue that the iterations have completed are provided by the update figures at the bottom of the MLWin window.



These results can then be compared with the R models, by looking at the GLM with Random Effects rows:

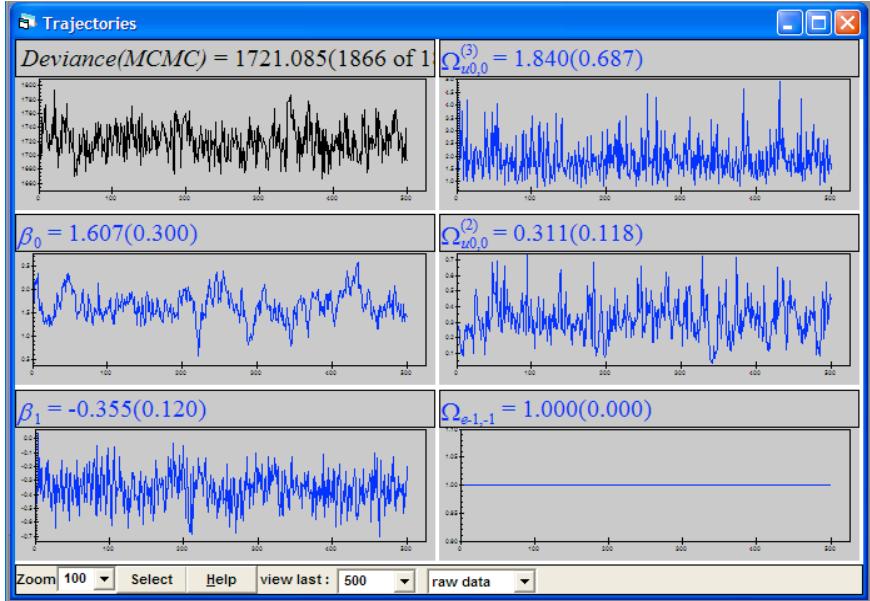
---

### *GLM with Random Effects*

Constant	1.60	0.28
Message	-0.35	0.12
$\sigma_{ecg}^2$	1.57	
$\sigma_{participant}^2$	0.21	

---

29. To check how well the data has been modeled using the Monte-Carlo Markov chain method, click on the following menu option: Model > Trajectories.



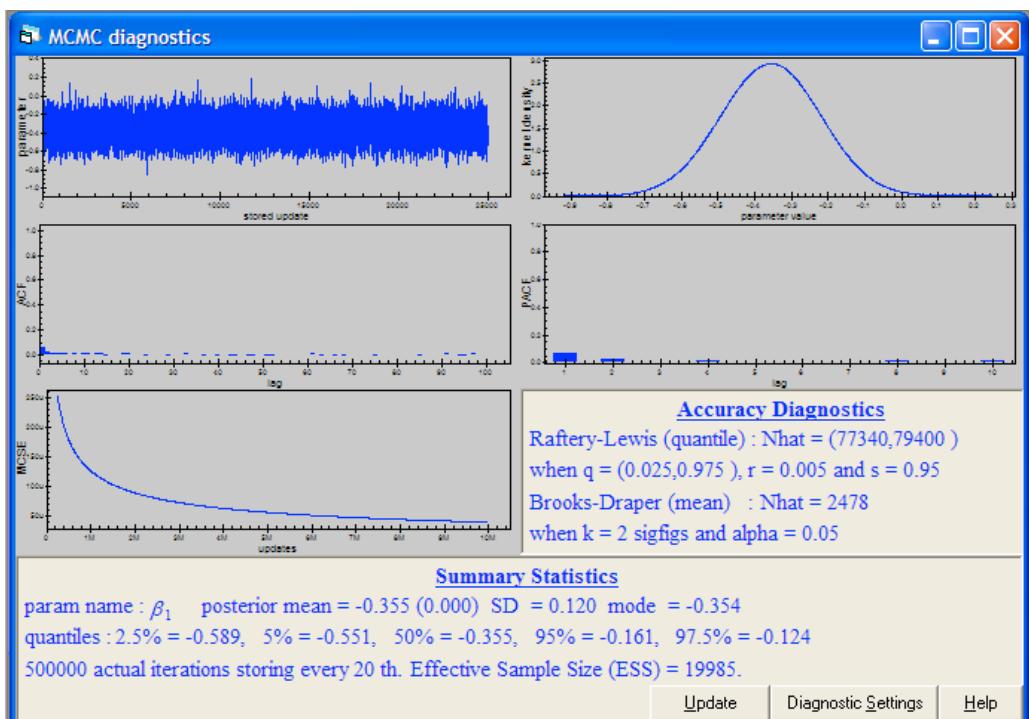
To explore each variable more closely, click on the graph. This will cause a pop-up window to appear asking if you wish to calculate the MCMC diagnostics. Click on the 'Yes' button.

30. Analysis of the convergence diagnostics is rather outside the remit of the dissertation, but the following are useful indicators:

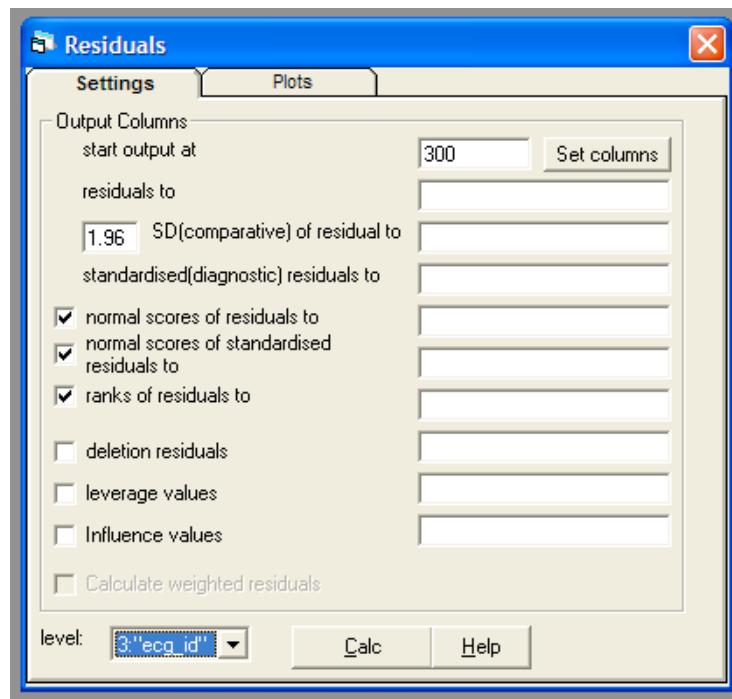
The graph in the top-right hand corner should look like white noise

The top-right hand corner graph should look like a Normal distribution

The number of iterations should be more than both the Raftery-Lewis and Brooks-Draper Nhat values.

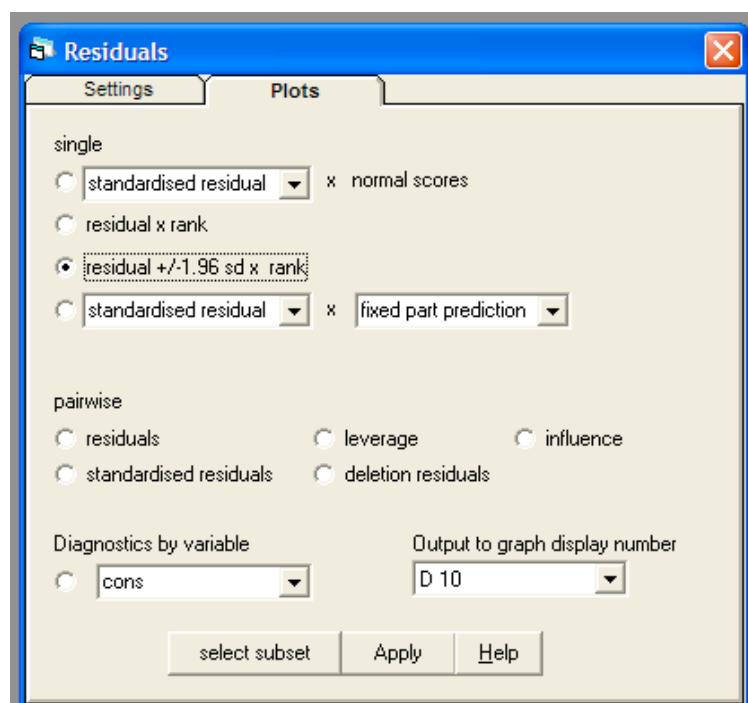


31. Another tool that is quite useful, is the ability to plot the residuals of the model. Select the following menu option: Model > Residuals. To explore the ECGs, change the settings to match the image below:

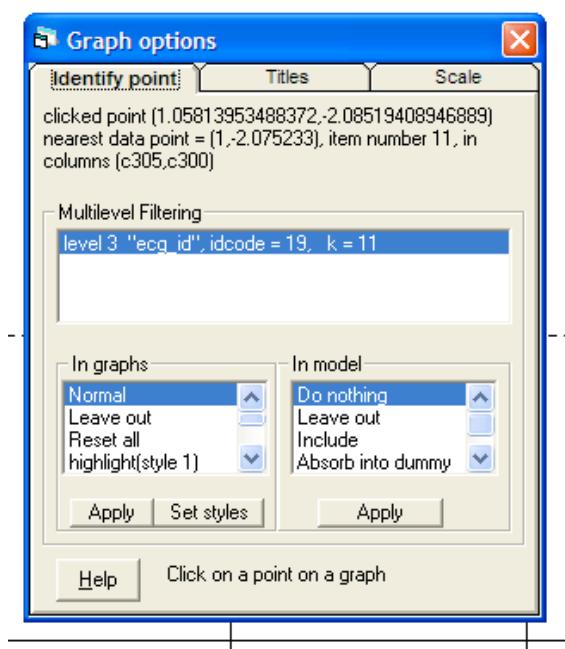
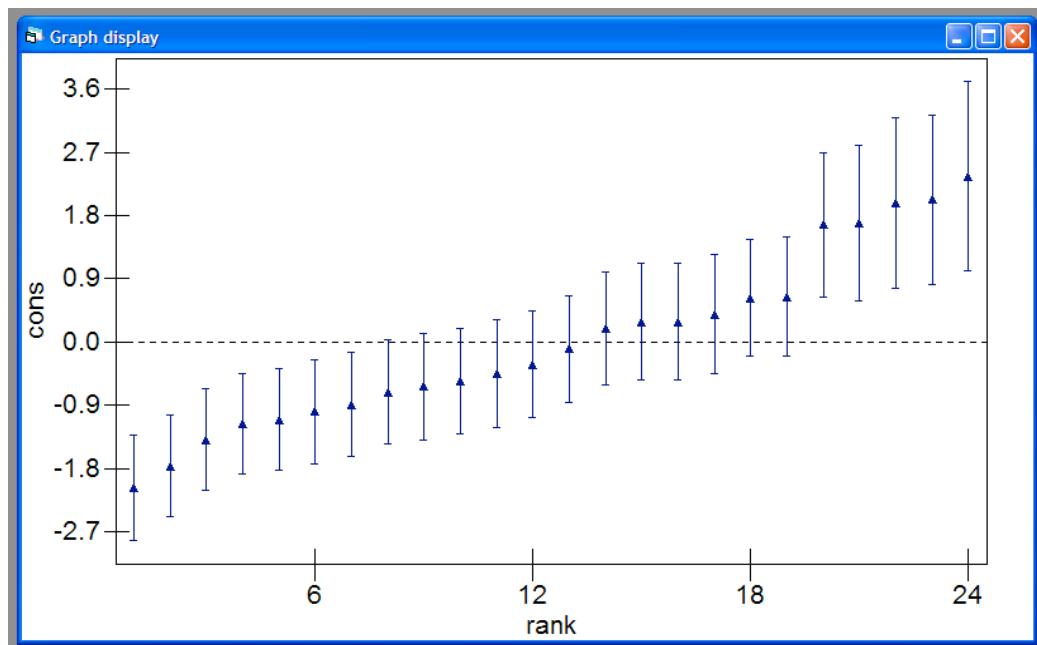


Once you have changed the settings, click on the 'Calc' button at the bottom of the window.

32. Click on the plots tab and check the 'residual +/- 1.96 s.d. x rank' radio button and then click the Apply button at the bottom of the window.



33. This will produce an interactive graph, plotting the magnitudes of the ECG effects and how they differ from the 'average' ECG. This graph is interactive, making it possible to identify the ECG most associated with the least correct answers (ECG ID 19) and the most (ECG ID 44), in the incorrect computer interpretation subset.



## **Appendix C**

# **YAS research and development approval**



Yorkshire Ambulance Service **NHS**  
NHS Trust

Springhill 2  
Brindley Way  
Wakefield 41 Business Park  
Wakefield  
WF2 0XQ

Research & Development

15th January 2013

Tel: 07795 646475  
Email: [jane.shewan@yas.nhs.uk](mailto:jane.shewan@yas.nhs.uk)

Richard Pilbery  
17 Newton Ave  
Stocksbridge  
Sheffield  
S36 1EL

Dear Richard,

**Re: RESPECT study: Do computer diagnoses influence paramedic's interpretation of electrocardiograms? (YASRD54)**

I am happy to confirm that this study has R&D approval from the Yorkshire Ambulance Service. This relates to study documents received in your email of 23<sup>rd</sup> November 2012 and associated documents as approved by University of Sheffield SHREC (their ref 0602/KW) in their letter dated 12<sup>th</sup> November 2012, and includes amendments required by YAS including contacting YAS staff via internal YAS email instead of releasing a list of staff emails to you.

There are some conditions to this approval:

- If the project receives SHREC approval of any amendment, the amendment must be submitted for our review.
- The study must be conducted in compliance with the terms and conditions of this letter, the SHREC approval, and the Research Governance Framework for Health & Social Care (Department of Health, 2005).
- Annual progress reports will be required, and a copy of the final report.

If you agree with these terms, please will you sign and return a copy of this letter to myself.



Yorkshire Ambulance Service **NHS**  
NHS Trust

I would like to take this opportunity to wish you every success with your research.

Yours sincerely

A handwritten signature in black ink, appearing to read "John Smith".

Head of Research & Development

I agree with the terms of approval stipulated by the Yorkshire Ambulance Service.

Signature of Investigator..... Date.....

## **Appendix D**

### **University ethics approval**



Kirsty Woodhead  
Ethics Committee Administrator

Regent Court  
30 Regent Street  
Sheffield S1 4DA  
**Telephone:** +44 (0) 114 2225453  
**Fax:** +44 (0) 114 272 4095 (non confidential)  
**Email:** k.woodhead@sheffield.ac.uk

Our ref: 0602/KW

12 November 2012

Richard Pilberry  
ScHARR

Dear Richard

**Recognition of STEMI by Paramedics and the Effect of Computer Interpretation (RESPECT) Study.**

I am pleased to inform you that your supervisor has reviewed your project and classed it as 'low risk' so you can proceed with your research. The research must be conducted within the requirements of the hosting/employing organisation or the organisation where the research is being undertaken. You are also required to ensure that you meet any research ethics and governance requirements in the country in which you are researching. It is your responsibility to find out what these are.

I have received the necessary electronic copy of your application together with your Supervisor's decision in line with the new streamlined University Ethics procedure, which I will keep on file.

Yours sincerely

A handwritten signature in black ink, appearing to read "K. Woodhead".

**Kirsty Woodhead**  
Ethics Committee Administrator

Cc: Steve Goodacre

## **Appendix E**

# **Research governance sponsorship confirmation**



The  
University  
Of  
Sheffield.

SCHOOL OF  
HEALTH  
AND  
RELATED  
RESEARCH.

Mr Richard Pilbery  
Student  
ScHARR

5 December 2012

Research Ethics Administrator  
Miss Kirsty Woodhead  
  
School of Health and Related Research  
(ScHARR)  
Regent Court  
30 Regent Street  
Sheffield  
S1 4DA  
Telephone: +44 (0) 114 222 5453  
Fax: +44 (0) 114 272 4095  
Email: k.woodhead@sheffield.ac.uk

Project title: Recognition of STEMI by Paramedics and the Effect of Computer Interpretation (RESPECT) study  
6 digit URMS number: 136059

Dear Richard

**LETTER TO CONFIRM THAT THE UNIVERSITY OF SHEFFIELD IS THE PROJECT'S  
RESEARCH GOVERNANCE SPONSOR**

The University has reviewed the following documents:

1. A University approved URMS costing record;
2. Confirmation of independent scientific approval;
3. Confirmation of independent ethics approval.

All the above documents are in place. Therefore, the University now confirms that it is the project's research governance sponsor and, as research governance sponsor, authorises the project to commence any non-NHS research activities. Please note that NHS R&D approval will be required before the commencement of any activities which do involve the NHS.

You are expected to deliver the research project in accordance with the University's policies and procedures, which includes the University's Good Research Practice Standards:  
[http://www.sheffield.ac.uk/polopoly\\_fs/1.92046!/file/research\\_standards.pdf](http://www.sheffield.ac.uk/polopoly_fs/1.92046!/file/research_standards.pdf)  
and Ethics Policy: <http://www.sheffield.ac.uk/ris/other/gov-ethics/ethicspolicy>. If the project has received NHS ethics approval then you are also expected to publish a lay summary of the project on the website of the National Research Ethics Service (NRES), as it appears in the research ethics application.

Your Supervisor, with your support and input, is responsible for monitoring the project on an ongoing basis. Your Head of Department is responsible for independently monitoring the project as appropriate. The project may be audited during or after its lifetime by the University. The monitoring responsibilities are listed in Annex 1.

Yours sincerely

Kirsty Woodhead

## **Appendix F**

### **Risk assessment form**

**University of Sheffield****School of Health and Related Research (ScHARR)****Module HAR679/679****Form HAR1****Risk Assessment Form for Dissertation Projects**

Any Masters of Public Health (MPH) student completing a dissertation must complete this risk assessment form in consultation with their academic supervisor before starting their dissertation. The form should be signed by the student and supervisor. Students are advised to keep an electronic copy (preferably a scanned copy of the signed form) for future reference and to include a copy of the risk assessment form as an appendix in their final dissertation. **The risk assessment should be revisited if any changes are made to the proposed research or any circumstances change.**

Please complete the requested details and/or mark the answer(s) that apply to your particular dissertation project.

**Q1. Overview of Your Research Project**

Your name: Richard Pilbery

Your academic supervisor: Steve Goodacre

Does your project involve any or all of the following?

- primary data collection (e.g. interviewing, surveying or observation in unfamiliar and/or private settings);
- a work-based research placement;
- overseas activities;
- working in an unfamiliar environment in general (i.e. a place that is not known to you, where you have spent little, or no time, previously).

Yes  (If Yes, complete the rest of the form)No  (If No, there is no need to complete the rest of the form, just sign the form - Q5 - and seek your academic supervisor's signature - Q6)

If Yes, please give brief details of your project here (i.e. topic area, details of planned research methods, details of work-based placement, details of any overseas activities, any unfamiliar environments):

Randomised cross-over trial using an online quiz to collect data.

Intended site(s) for the project (e.g. details of organisational setting, town, country if not to be completed in the UK): Various around UK (where computer terminals for participants located)

Over which months will the project will be completed? (approximate start and end dates to the nearest month, e.g. June 2012- August 2012): Data collection 1<sup>st</sup> March, 2013 – 30<sup>th</sup> April, 2013

Will you be working on your own?

All of the time  Some of the time  Never **Q2. Potential security devices**Will you have a personal alarm? Yes  No Will you have a mobile phone? Yes  No

**Q3. Health**

Should we be aware of any medical information concerning your health and fitness, which is relevant to carrying out the project? Please enter 'NONE' if there are no foreseeable health/fitness problems.

NONE

**Q4. Potential hazards inherent in project site(s) and/or research methods to be used**

Are there any hazards associated with the sites at which you will be conducting your project and/or the research methods you will use? For example, will you be working on your own in private spaces (e.g. people's homes), travelling through potentially unsafe areas to reach your project site, or conducting interviews in politically volatile or potentially hazardous environments (e.g. around dirty water, at night, busy urban markets)?

If so, what are these hazards and what arrangements will you make to manage and reduce these?

**Please use the space/table below to record identified risks, who might be affected and how you will manage the risks.**

**The risk assessment should be revisited if any changes are made to the proposed research or any circumstances change.**

No

**Q5. Student's declaration**

I have reviewed safety considerations for my project with my supervisor. I have read and understood the **Dissertation Research Safety Guidelines** in the **Dissertation Module Handbook** and I agree to abide by the recommendations made therein.

I understand that I am responsible for my own safety during this project and will take any necessary steps to minimise the risks the project poses to me and/or other people. I will not undertake the project if circumstances increase the risk of accident or injury (e.g. the presence of suspicious individuals).

**Student's signature**



**Date 1<sup>st</sup> March 2013**

**Q6. Supervisor's approval**

I have read this risk assessment and discussed it with him/her. I think it identifies all readily foreseeable risks in the project as planned at this date. If the appropriate precautions are taken by the student the project should be permitted.

**Supervisor's signature**



**Date 1<sup>st</sup> March 2013**

## **Appendix G**

### **Participant information sheet**

## The Recognition of STEMI by Paramedics and the Effect of Computer Interpretation (RESPECT) pilot study

Before you decide to take part in this pilot study, it is important for you to understand why the research is being done and what it will involve. Please take time to read the following information carefully and discuss it with others if you wish. Ask us if there is anything that is not clear or if you would like more information. Take time to decide whether or not you wish to take part. Thank you for reading this.

### **What is the purpose of the study?**

Approximately 124,000 people a year suffer a heart attack (myocardial infarction) in the United Kingdom, which can result in serious ill-health and death. This situation can be improved by timely pre-hospital diagnosis and early reperfusion of the blocked coronary arteries. Central to this, is accurate interpretation of the electrocardiogram (ECG) by paramedics, in particular a specific pattern known as ST-segment elevation myocardial infarction (STEMI). Studies have shown that paramedics can recognise STEMI, but they can mis-interpret the ECG in 20–30% of cases. The ECG machines commonly used by paramedics have some diagnostic capability in the form of printed computer interpretation messages that appear on the ECGs, but it is not clear how helpful or influential these are for paramedics. This study intends to find out what effect these computer messages have on paramedics recognition of STEMI.

### **Why have I been chosen?**

You have been contacted to take part in this study as you are a paramedic member of the College of Paramedics, or a paramedic registered on the continuous professional development portfolio builder (<http://www.resuscitate.me.uk>).

### **Do I have to take part?**

No. It is up to you to decide whether or not to take part. If you do decide to take part you can still withdraw at any time and you do not have to give a reason. Please note that research and development approval has been obtained from Yorkshire Ambulance Service NHS Trust, but no other ambulance service, at present. If you undertake the study, it should be done in your own time as an independent practitioner, rather than as an employee of a particular ambulance service.

### **What will happen to me if I take part?**

Once you click the Sign up button on the invitation email, you will be taken to the consent page on the study website. Once consent has been obtained, you will be asked four simple questions:

1. How long have you been a paramedic (in years)?
2. Which educational route did you take to become a paramedic (e.g. IHCD, University)
3. How much time have you spent on 12 lead ECG training / continuous professional development in the past 12 months (in hours)?
4. How patients have you taken for primary percutaneous coronary intervention or thrombolysed in the past 12 months?

After this, you will be shown 12 randomly chosen ECGs, one at a time. They will consist of a mixture of STEMI and STEMI-mimic patterns and may or may not show the computer interpretation message. You will be asked whether the ECG shows as STEMI pattern or not (YES/NO response). There will be a maximum time limit of 60 seconds per ECG. This means that the first stage of the study is likely to take a little over 12 minutes to complete.

You will then have a two week break before being asked to return to the website (via email, or optionally, if you prefer, by text message), where you will see the same 12 ECGs, but with the computer message visibility reversed. So, if you saw ECG 1 with the message in the first part of the study, it will be hidden for the second, and vice-versa. Again, there will be a

time-limit of 60 seconds per ECG, meaning that this stage will take a maximum of 12 minutes to complete.

**What are the possible disadvantages and risks of taking part?**

It is not anticipated that you will experience any disadvantage for taking part in the study, although you will need to give up some of your time. This will amount to about 20 minutes in total.

**What are the possible benefits of taking part?**

This study will provide you with a chance to practice your ECG interpretation. It is hoped that the results from the study and subsequent related studies will help determine whether computer interpretation messages are helpful for paramedics in making decisions about STEMI as well as identify any areas for future education of paramedics on ECG interpretation.

**What if something goes wrong?**

Should you wish to make a complaint about this study, you should not contact the researcher directly. Instead, please email the study supervisor, Professor Steve Goodacre ([s.goodacre@sheffield.ac.uk](mailto:s.goodacre@sheffield.ac.uk)). In the unlikely even that this does not resolve the complaint to your satisfaction, you can contact the University of Sheffield's Registrar and Secretary ([registrar@sheffield.ac.uk](mailto:registrar@sheffield.ac.uk)).

**Will my taking part in this project be kept confidential?**

Yes, all the information that we collect about you during the course of the research will be kept strictly confidential. Your email address will be encrypted prior to saving on the research database and you will not be able to be identified in any reports or publications.

**What will happen to the results of the research project?**

The results of this study will be published as widely as possible in peer-reviewed journals, pre-hospital and emergency conferences and via plain-English summaries in free publications that are delivered to ambulance stations.

**Who is organising and funding the research?**

This research is being conducted by a student as part of the MSc in Clinical Research run by the University of Sheffield, which is funded by the National Institute of Healthcare Research. There is no specific funding for this research project.

**Who has ethically reviewed the project?**

Yes, the University of Sheffield's School of Health and Related Research ethics committee has reviewed this project and given it a favourable opinion.

**Contact for further information**

For further information, please contact the researcher:

Richard Pilbery  
Middlewood Ambulance Station  
Yorkshire Ambulance Service  
Middlewood Road, Sheffield S6 1TP  
Contact Number: 07557 395 280

**This information sheet and consent form are available to download on the study website (<http://respect.ambulanceresearch.co.uk>)**

**Thank you for taking part in this study**

## **Appendix H**

# **Summary tables of participant responses to individual ECGs**

Key:

V message visible

H message hidden

T All messages

Data pairs - Paired responses with an answer for message visible and hidden for a single ECG and single participant

Excl. Orphaned data (ie missing one of message visible or hidden for a single ECG and single participant). This response will be deleted from the data set.

TABLE H.1: Summary of participant interaction with ECGs

ECG ID	Attempts with answer			Data pairs	Not attempted			Unviewed			Excl.
	V	H	T		V	H	T	V	H	T	
1	45	46	91	46	0	0	0	9	8	17	11
2	49	44	93	44	1	0	1	4	10	14	12
3	44	44	88	45	1	1	2	10	10	20	12
4	45	48	93	48	0	0	0	10	7	17	7
5	45	43	88	45	1	2	3	8	9	17	9
6	48	48	96	48	1	0	1	5	6	11	7
7	45	44	89	44	0	0	0	9	10	19	13
8	49	45	94	46	1	1	2	4	8	12	10
9	48	42	90	44	0	2	2	6	10	16	14
10	44	44	88	45	1	1	2	10	10	20	14
11	42	44	86	44	0	0	0	13	11	24	14
12	42	45	87	47	0	2	2	13	8	21	15
13	44	41	85	41	1	0	1	9	13	22	16
14	44	45	89	45	3	0	3	8	10	18	14
15	44	42	86	45	1	3	4	10	10	20	16
16	45	48	93	48	1	0	1	8	6	14	10
17	43	43	86	44	2	1	3	10	11	21	11
18	46	42	88	42	0	0	0	9	13	22	12
19	48	40	88	40	1	0	1	6	15	21	15
20	43	48	91	48	0	0	0	11	6	17	15
21	42	49	91	49	1	0	1	12	6	18	12
22	48	48	96	49	1	1	2	5	5	10	8
23	46	46	92	46	1	0	1	7	8	15	13
24	47	41	88	41	0	0	0	7	13	20	16
25	45	41	86	42	0	1	1	9	13	22	16
26	47	48	95	48	1	0	1	7	7	14	8
27	45	48	93	48	0	0	0	9	6	15	11
28	44	45	89	47	0	1	1	11	8	19	13
29	46	42	88	42	0	0	0	8	12	20	10
30	45	46	91	46	0	0	0	9	8	17	11
31	46	47	93	47	1	0	1	8	8	16	10
32	46	47	93	47	1	0	1	7	7	14	12
33	42	40	82	42	0	2	2	13	13	26	18
34	45	46	91	47	0	1	1	9	7	16	12
35	45	45	90	45	0	0	0	10	10	20	14
36	43	44	87	44	2	0	2	10	11	21	15
37	46	44	90	44	0	0	0	9	11	20	16
38	39	41	80	41	1	0	1	14	13	27	17
39	46	48	94	48	1	0	1	8	7	15	11
40	39	43	82	43	1	0	1	14	11	25	15
41	43	37	80	39	1	2	3	10	15	25	13
42	50	45	95	45	0	0	0	5	10	15	13
43	43	44	87	45	1	1	2	10	9	19	13
44	46	49	95	49	0	0	0	8	5	13	11
45	49	43	92	44	0	1	1	6	11	17	11
46	49	46	95	46	1	0	1	5	9	14	10
47	44	43	87	46	0	3	3	10	8	18	16
48	48	40	88	42	1	2	3	6	13	19	13

TABLE H.2: Summary of individual ECG answer times

ECG ID	Median correct answer time (secs)			Median incorrect answer time (secs)			No. Correct answers			No. Incorrect answers		
	V	H	T	V	H	T	V	H	T	V	H	T
	1	24	27	26	20	27	27	38	26	64	7	20
2	17	14	16	42	27	33	45	38	83	5	6	11
3	32	23	29	22	17	18	17	14	31	28	31	59
4	20	19	19	30	24	24	32	29	61	13	19	32
5	18	14	17	32	45	39	35	39	74	11	6	17
6	18	12	16	25	5	20	46	47	93	3	1	4
7	28	22	23	25	27	26	30	29	59	15	15	30
8	32	28	30	20	26	26	25	27	52	25	19	44
9	26	20	22	25	21	24	31	33	64	17	11	28
10	20	18	18	28	28	28	40	34	74	5	11	16
11	22	19	20	39	32	35	36	39	75	6	5	11
12	16	16	16	28	25	26	34	42	76	8	5	13
13	18	14	15	29	29	29	42	41	83	3	0	3
14	18	20	20	20	24	20	31	33	64	16	12	28
15	20	15	17	25	25	25	24	25	49	21	20	41
16	30	26	27	18	16	17	22	28	50	24	20	44
17	18	14	17	17	30	17	39	38	77	6	6	12
18	27	18	23	30	24	28	28	30	58	18	12	30
19	32	18	24	20	20	20	19	15	34	30	25	55
20	13	14	14	19	16	16	41	44	85	2	4	6
21	38	28	32	22	23	23	17	20	37	26	29	55
22	14	12	13	17	20	18	48	48	96	1	1	2
23	14	16	14	51	38	51	44	44	88	3	2	5
24	15	12	13				47	41	88	0	0	0
25	14	14	14		26	26	45	40	85	1	2	3
26	18	15	16	17	42	25	43	45	88	5	3	8
27	16	17	17	22	34	28	44	43	87	1	5	6
28	14	12	12	28	17	19	42	42	84	2	5	7
29	14	14	14		22	22	46	40	86	0	2	2
30	14	12	14	27	28	27	42	42	84	3	4	7
31	26	17	19	16	20	20	37	33	70	10	14	24
32	12	10	10	52	21	45	42	46	88	5	1	6
33	20	16	19	38	21	24	36	34	70	6	8	14
34	18	16	18	27	25	27	40	43	83	5	4	9
35	24	20	23	35	30	35	42	41	83	3	4	7
36	15	13	15	24	16	24	37	37	74	8	7	15
37	20	17	18	24	12	16	43	42	85	3	2	5
38	16	18	18	26	20	20	34	34	68	6	7	13
39	21	19	20	26	25	25	34	37	71	13	11	24
40	19	18	19	37	24	25	27	30	57	13	13	26
41	25	19	22	26	25	26	29	27	56	15	12	27
42	36	31	33	24	16	22	21	25	46	29	20	49
43	16	12	12	25	38	34	42	43	85	2	2	4
44	14	11	12		40	40	46	47	93	0	2	2
45	15	15	15	15	28	20	43	38	81	6	6	12
46	16	16	16	22	38	24	42	39	81	8	7	15
47	20	18	19	21	28	28	34	35	69	10	11	21
48	28	21	26	27	38	30	33	32	65	16	10	26

## **Appendix I**

### **R statistics analysis script**

## Analysis.R

This document shows the scripts written to undertake the statistic analysis in R for the RESPECT pilot study.

```
# OddsRatio and GLM
# This script produces odds ratio calculations, a simple GLM and then GLM with random effects

# Load in data
load("FSD4knitr99.Rdata")

# Create data frame (saves having to amend everything)
# FinalStudy99 marks all non-answers (timed out) as incorrect

FinalStudyData99$classification <- factor(FinalStudyData99$classification)

# FSD99CC - Return subset of data where computer was correct
FSD99CC <- subset(FinalStudyData99,FinalStudyData99$truepos==1|FinalStudyData99$trueneg==1)
# FSD99CI <- Return subset of data where computer was incorrect
FSD99CI <- subset(FinalStudyData99,FinalStudyData99>falsepos==1|FinalStudyData99$falseneg==1)

cat("Preparing Odds Ratio table...\n\n")

Preparing Odds Ratio table...

# Load in epitools package
require('epitools')

Loading required package: epitools

require('xtable')

Loading required package: xtable

----- ODDS RATIO TABLE -----
cat("Odds ratio table and statistics\n")

Odds ratio table and statistics

# Function to create basic OR tables with percentages

makeBasicORTable <- function(ORtableName='') {
  # NULL is FinalStudyData99 i.e. all data pairs
  # FSD99CC - only includes data with correct computer interpretation
  # FSD99CI - only includes data with incorrect computer interpretation
  if(ORtableName=='FSD99CC') FSD = FSD99CC
  else if(ORtableName=='FSD99CI') FSD = FSD99CI
  else FSD = FinalStudyData99
  ORT <- epitools::oddsratio(FSD$diag_correct,FSD$message_visible,verbose=T)
  print(ORT)
}

# OR table for both computer correct and incorrect
ORTable <- makeBasicORTable()
```

```
$x
      Outcome
Predictor 0   1
  0 366 385
  1 1500 1481

$data
      Outcome
Predictor 0   1 Total
  0     366 385 751
  1    1500 1481 2981
  Total 1866 1866 3732

$p.exposed
      Outcome
Predictor 0   1 Total
  0     0.1961 0.2063 0.2012
  1     0.8039 0.7937 0.7988
  Total 1.0000 1.0000 1.0000

$p.outcome
      Outcome
Predictor 0   1 Total
  0     0.4874 0.5126 1
  1     0.5032 0.4968 1
  Total 0.5000 0.5000 1

$measure
odds ratio with 95% C.I.
Predictor estimate lower upper
  0     1.0000    NA    NA
  1     0.9386 0.7996 1.102

$conf.level
[1] 0.95

$p.value
two-sided
Predictor midp.exact fisher.exact chi.square
  0       NA       NA       NA
  1     0.4383     0.4624     0.4379

$correction
[1] FALSE

attr(,"method")
[1] "median-unbiased estimate & mid-p exact CI"
```

```
# OR table for both computer correct results
ORtableCC <- makeBasicORTable("FSD99CC")
```

```
$x
      Outcome
Predictor 0   1
          0 148 117
          1 785 816

$data
      Outcome
Predictor 0   1 Total
          0   148 117 265
          1   785 816 1601
      Total 933 933 1866

$p.exposed
      Outcome
Predictor 0       1 Total
          0   0.1586 0.1254 0.142
          1   0.8414 0.8746 0.858
      Total 1.0000 1.0000 1.000

$p.outcome
      Outcome
Predictor 0       1 Total
          0   0.5585 0.4415 1
          1   0.4903 0.5097 1
      Total 0.5000 0.5000 1

$measure
      odds ratio with 95% C.I.
Predictor estimate lower upper
          0   1.000   NA   NA
          1   1.314 1.012 1.71

$conf.level
[1] 0.95

$p.value
      two-sided
Predictor midp.exact fisher.exact chi.square
          0       NA       NA       NA
          1   0.04008   0.04649   0.03979

$correction
[1] FALSE

attr(,"method")
[1] "median-unbiased estimate & mid-p exact CI"

# OR table for both computer incorrect results
ORtableCI <- makeBasicORTable("FSD99CI")
```

```
$x
      Outcome
Predictor 0   1
          0 218 268
          1 715 665

$data
      Outcome
Predictor 0   1 Total
          0 218 268 486
          1 715 665 1380
      Total 933 933 1866

$p.exposed
      Outcome
Predictor 0   1 Total
          0 0.2337 0.2872 0.2605
          1 0.7663 0.7128 0.7395
      Total 1.0000 1.0000 1.0000

$p.outcome
      Outcome
Predictor 0   1 Total
          0 0.4486 0.5514 1
          1 0.5181 0.4819 1
      Total 0.5000 0.5000 1

$measure
      odds ratio with 95% C.I.
Predictor estimate lower upper
          0 1.0000    NA    NA
          1 0.7567 0.6145 0.9311

$conf.level
[1] 0.95

$p.value
      two-sided
Predictor midp.exact fisher.exact chi.square
          0     NA        NA        NA
          1 0.008408 0.009708 0.008356

$correction
[1] FALSE

attr(),"method")
[1] "median-unbiased estimate & mid-p exact CI"
```

```
#----- GLM WITHOUT RANDOM EFFECTS -----
cat("Unadjusted GLM without random effects - message visibility\n")
```

```
Unadjusted GLM without random effects - message visibility
```

```
# GLM model all computer messages
fit <- glm(diag_correct~message_visible,data=FinalStudyData99,family=binomial("logit"))
summary(fit)
```

```

Call:
glm(formula = diag_correct ~ message_visible, family = binomial("logit"),
     data = FinalStudyData99)

Deviance Residuals:
    Min      1Q  Median      3Q      Max
-1.805   0.661   0.661   0.680   0.680

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) 1.4106    0.0583 24.20 <2e-16 ***
message_visible -0.0634    0.0817 -0.78    0.44
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 3747.7 on 3731 degrees of freedom
Residual deviance: 3747.1 on 3730 degrees of freedom
AIC: 3751

Number of Fisher Scoring iterations: 4

```

```
#GLM model with only computer correct messages
fitcc <- glm(diag_correct~message_visible,data=FSD99CC,family=binomial("Logit"))
summary(fitcc)
```

```

Call:
glm(formula = diag_correct ~ message_visible, family = binomial("logit"),
     data = FSD99CC)

Deviance Residuals:
    Min      1Q  Median      3Q      Max
-2.038   0.518   0.518   0.588   0.588

Coefficients:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) 1.6685    0.0896 18.62 <2e-16 ***
message_visible 0.2738    0.1334  2.05    0.04 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 1524.9 on 1865 degrees of freedom
Residual deviance: 1520.7 on 1864 degrees of freedom
AIC: 1525

Number of Fisher Scoring iterations: 4

```

```
#GLM model with only computer INCORRECT messages
fitci <- glm(diag_correct~message_visible,data=FSD99CI,family=binomial("Logit"))
summary(fitcc)
```

```

Call:
glm(formula = diag_correct ~ message_visible, family = binomial("logit"),
     data = FSD99CC)

Deviance Residuals:
    Min      1Q  Median      3Q     Max 
-2.038   0.518   0.518   0.588   0.588 

Coefficients:
            Estimate Std. Error z value Pr(>|z|)    
(Intercept) 1.6685    0.0896 18.62   <2e-16 ***
message_visible 0.2738    0.1334  2.05     0.04 *  
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

(Dispersion parameter for binomial family taken to be 1)

Null deviance: 1524.9 on 1865 degrees of freedom
Residual deviance: 1520.7 on 1864 degrees of freedom
AIC: 1525

Number of Fisher scoring iterations: 4

```

```

#----- FUNCTIONS FOR GLM WITH RANDOM EFFECTS -----
suppressPackageStartupMessages(require(lme4))

```

```
Warning: package 'Matrix' was built under R version 2.15.3
```

```
Warning: package 'lattice' was built under R version 2.15.3
```

```

makeTablesGLMERexp <- function(tableX,namex) {
  #tableOUT <- data.frame((coef(summary(tableX))[,c("Estimate","Std. Error","z
  value","Pr(>|z|)")]),check.names=F)
  tableOUT <- as.data.frame(coef(summary(tableX)))
  lower <- tableOUT[,1] + qnorm(.025)*tableOUT[,2]
  upper <- tableOUT[,1] + qnorm(.975)*tableOUT[,2]
  tableOUT[,1] <- exp(tableOUT[,1])
  tableOUTCIfinal <- paste(round(exp(lower),3),round(exp(upper),3),sep=' to ')
  tableOUT <- cbind(round(tableOUT,3), tableOUTCIfinal)
  tableOUT[,2] <- NULL
  parameters<- c("Constant",namex)
  tableOUT <- cbind(parameters, tableOUT)
  colnames(tableOUT) <- c("Parameters","OR","z","P>|z|","95% CI")
  return(tableOUT)
}

#----- GLMS WITH RANDOM EFFECTS -----
#cat("GLM model with random effects - message visibility and classification\n")
# fitGLMAll <- glmer(diag_correct~1+message_visible+falseneg+falsepos+trueneg+(1|ecg_id)+
# (1|participant_id),data=FinalStudyData99,family=binomial("logit"))
#summary(fitGLMAll)

# cat("GLM mode with only random effects, no fixed effects\n")
#fitGLMOne <- glmer(diag_correct~1+(1|ecg_id)+
#(1|participant_id),REML=F,data=FinalStudyData99,family=binomial("logit"))
#summary(fitGLMOne)

cat("GLM model with random effects - message visibility\n")

```

```
GLM model with random effects - message visibility
```

```
# GLM model with random effects - all computer messages
fitGLM <- glmer(diag_correct~1+message_visible+(1|ecg_id)+  
(1|participant_id),data=FinalStudyData99,family=binomial("logit"))
summary(fitGLM)
```

```
Generalized linear mixed model fit by the Laplace approximation
Formula: diag_correct ~ 1 + message_visible + (1 | ecg_id) + (1 | participant_id)
Data: FinalStudyData99
AIC BIC logLik deviance
3210 3235 -1601 3202
Random effects:
 Groups Name Variance Std.Dev.
 participant_id (Intercept) 0.208 0.456
 ecg_id (Intercept) 1.571 1.253
Number of obs: 3732, groups: participant_id, 156; ecg_id, 48
Fixed effects:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) 1.8688    0.1984   9.42 <2e-16 ***
message_visible -0.0798   0.0903  -0.88    0.38
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Correlation of Fixed Effects:
          (Intr)
messag_vsbl -0.233
```

```
# GLM model with random effects - all correct computer messages
fitGLMcc <- glmer(diag_correct~1+message_visible+(1|ecg_id)+  
(1|participant_id),data=FSD99CC,family=binomial("logit"))
summary(fitGLMcc)
```

```
Generalized linear mixed model fit by the Laplace approximation
Formula: diag_correct ~ 1 + message_visible + (1 | ecg_id) + (1 | participant_id)
Data: FSD99CC
AIC BIC logLik deviance
1322 1344 -657 1314
Random effects:
 Groups Name Variance Std.Dev.
 participant_id (Intercept) 0.559 0.748
 ecg_id (Intercept) 1.320 1.149
Number of obs: 1866, groups: participant_id, 156; ecg_id, 24
Fixed effects:
            Estimate Std. Error z value Pr(>|z|)
(Intercept) 2.214     0.266   8.32 <2e-16 ***
message_visible 0.347     0.147   2.36   0.018 *
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1
Correlation of Fixed Effects:
          (Intr)
messag_vsbl -0.243
```

```
# GLM model with random effects - all incorrect computer messages
fitGLMci <- glmer(diag_correct~1+message_visible+(1|ecg_id)+  
(1|participant_id),data=FSD99CI,family=binomial("logit"))
summary(fitGLMci)
```

```

Generalized linear mixed model fit by the Laplace approximation
Formula: diag_correct ~ 1 + message_visible + (1 | ecg_id) + (1 | participant_id)
Data: FSD99CI
      AIC BIC logLik deviance
1863 1885   -927    1855
Random effects:
Groups        Name        Variance Std.Dev.
participant_id (Intercept) 0.291    0.539
ecg_id         (Intercept) 1.561    1.250
Number of obs: 1866, groups: participant_id, 156; ecg_id, 24

Fixed effects:
            Estimate Std. Error z value Pr(>|z|)
(Intercept)  1.599     0.275   5.80  6.5e-09 ***
messageVisible -0.354     0.117  -3.03  0.0025 **
---
Signif. codes:  0 '***' 0.001 '**' 0.01 '*' 0.05 '.' 0.1 ' ' 1

Correlation of Fixed Effects:
              (Intr)
messag_vsbl -0.229

```

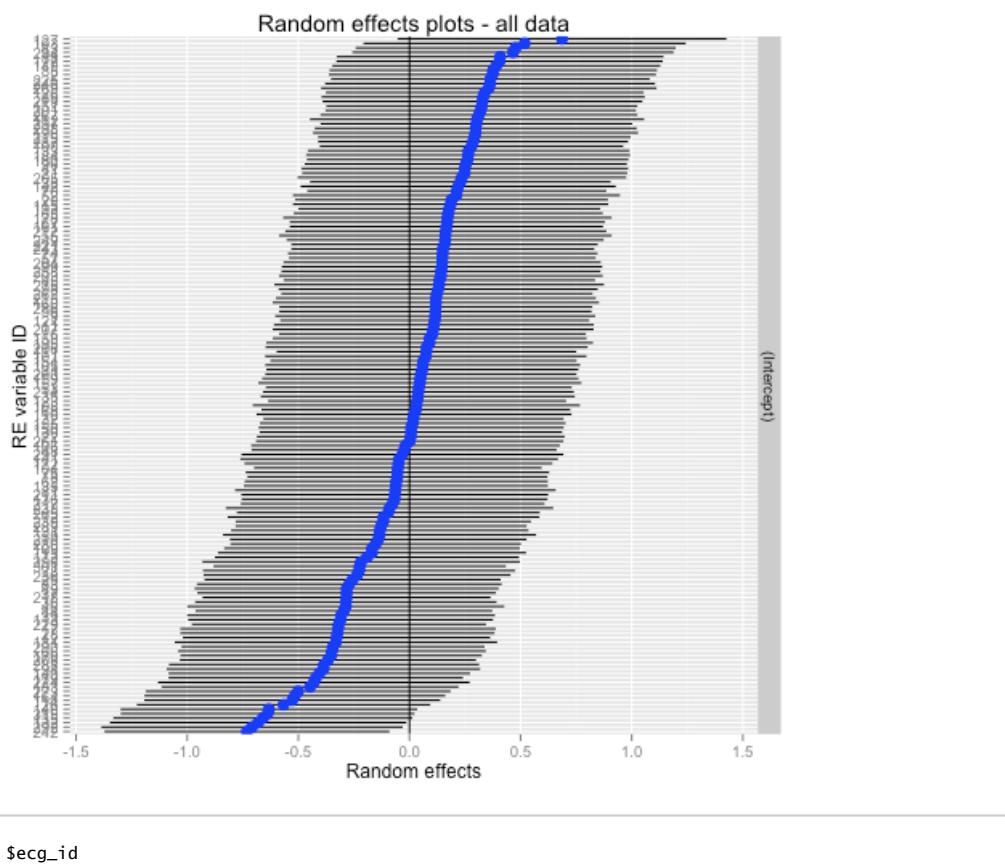
```

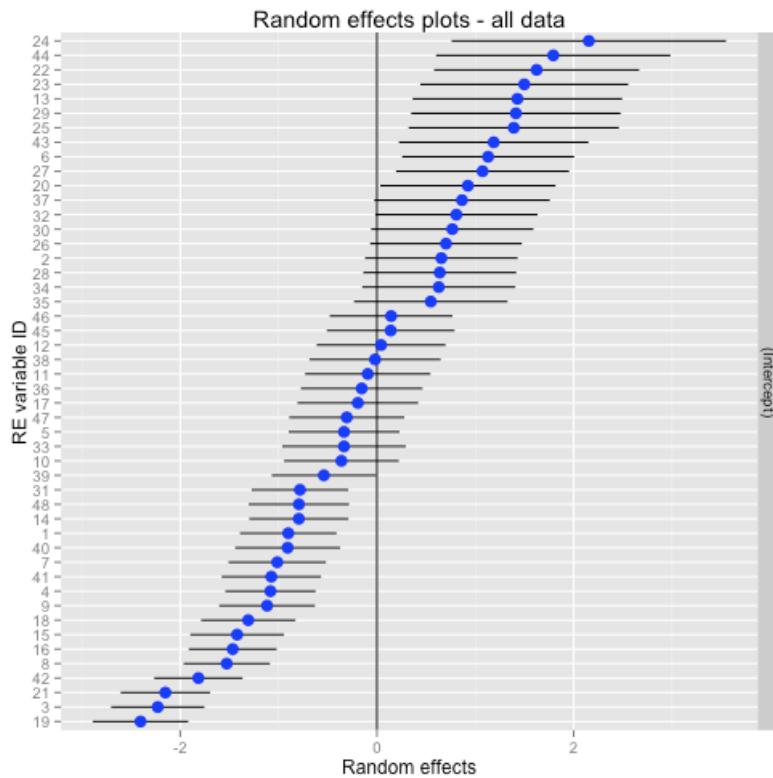
#----- QQPlots -----
# http://stackoverflow.com/questions/13847936/in-r-plotting-random-effects-from-lmer-
lme4-package-using-qqmath-or-dotplot
ggCaterpillar <- function(re, QQ=TRUE, likeDotplot=TRUE, thetitle="ggCaterpillar") {
  require(ggplot2)
  f <- function(x) {
    pv <- attr(x, "postVar")
    cols <- 1:(dim(pv)[1])
    se <- unlist(lapply(cols, function(i) sqrt(pv[i, i, ])))
    ord <- unlist(lapply(x, order)) + rep(0:(ncol(x) - 1)) * nrow(x), each=nrow(x))
    pdf <- data.frame(y=unlist(x)[ord],
                       ci=1.96*se[ord],
                       nQQ=rep(qnorm(ppoints(nrow(x))), ncol(x)),
                       ID=factor(rep(rownames(x), ncol(x))[ord], levels=rownames(x)[ord]),
                       ind=gl(ncol(x), nrow(x), labels=names(x)))
    if(QQ) { ## normal QQ-plot
      p <- ggplot(pdf, aes(nQQ, y))
      p <- p + facet_wrap(~ ind, scales="free")
      p <- p + xlab("Standard normal quantiles") + ylab("Random effect quantiles")
    } else { ## caterpillar dotplot
      p <- ggplot(pdf, aes(ID, y)) + coord_flip()
      if(likeDotplot) { ## imitate dotplot() -> same scales for random effects
        p <- p + facet_wrap(~ ind)
      } else { ## different scales for random effects
        p <- p + facet_grid(ind ~ ., scales="free_y")
      }
      # Custom xlabel just for this study
      p <- p + xlab("RE variable ID") + ylab("Random effects")
    }
    p <- p + theme(legend.position="none")
    p <- p + geom_hline(yintercept=0)
    p <- p + geom_errorbar(aes(ymin=y-ci, ymax=y+ci), width=0, colour="black")
    p <- p + geom_point(aes(size=1.2), colour="blue")
    p <- p + ggtitle(thetitle)
    return(p)
  }
  lapply(re, f)
}

# Print plots for RE variance
print(ggCaterpillar(ranef(fitGLM, postVar=TRUE), QQ=FALSE, likeDotplot=FALSE, "Random effects
plots - all data"))

```

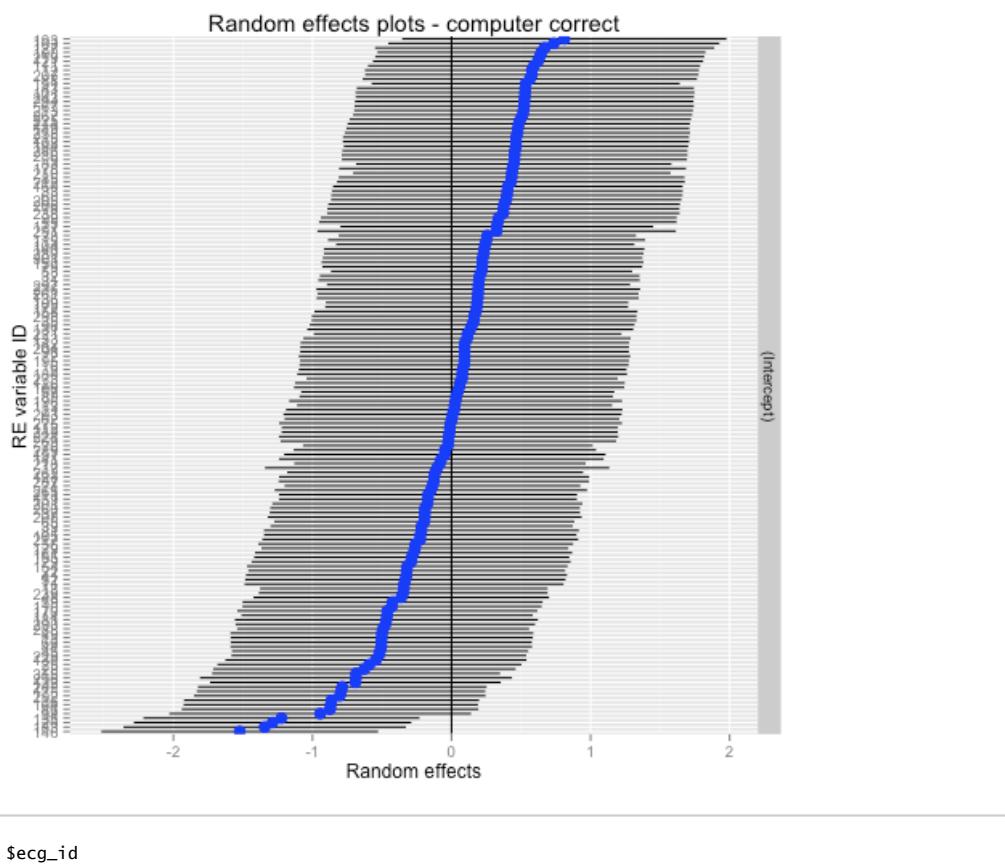
```
$participant_id
```

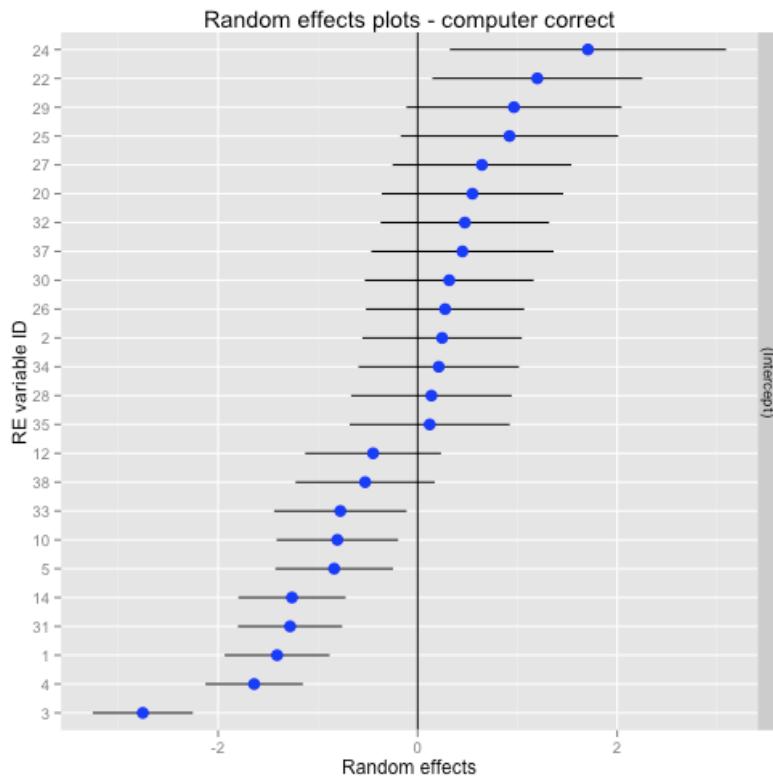




```
# Just correct computer interpretations
print(ggCaterpillar(ranef(fitGLMcc, postVar=TRUE), QQ=FALSE, likeDotplot=FALSE, "Random effects
plots - computer correct"))
```

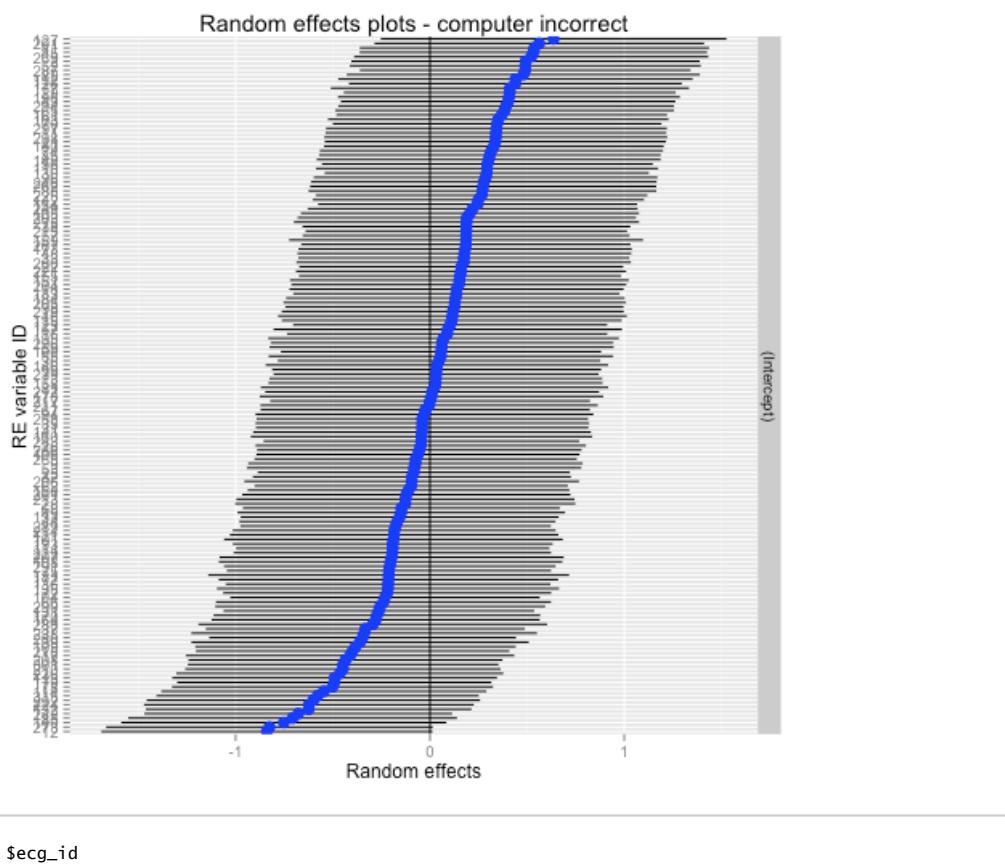
```
$participant_id
```

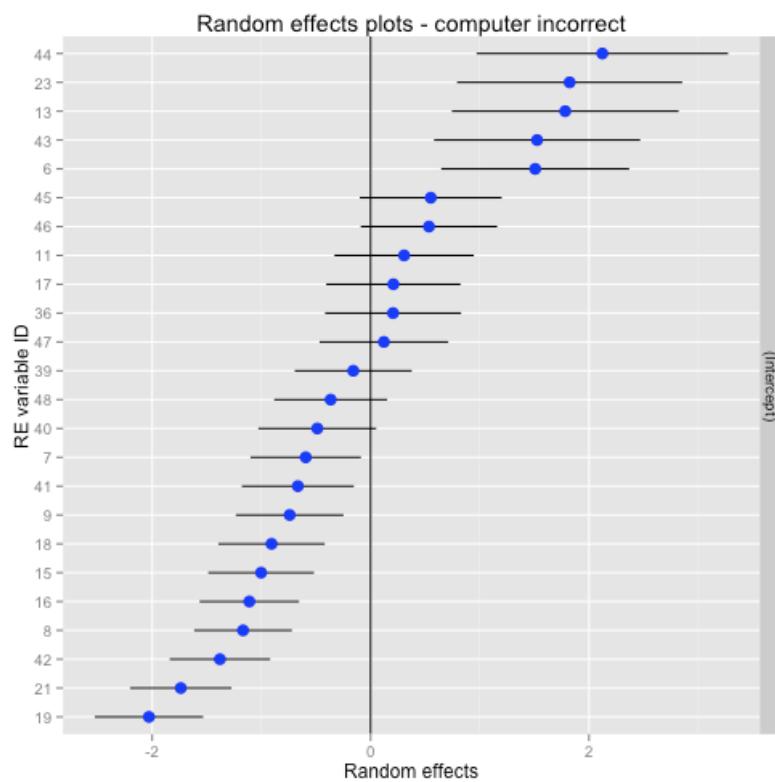




```
# Just incorrect computer interpretations
print(ggCaterpillar(ranef(fitGLMci, postVar=TRUE), QQ=FALSE, likeDotplot=FALSE, "Random effects
plots - computer incorrect"))
```

```
$participant_id
```





```

#----- COMBINED logOR TABLES -----
combiTable <- function(glm,glmre,caption1,label1,filename) {
  tableOUT <- data.frame((coef(summary(glm))[,c("Estimate","Std. Error","z
value","Pr(>|z|)"])),check.names=F)
  tableOUTCI <- confint(glm)
  tableOUTCIfinal <- paste(sprintf("%.2f",
(tableOUTCI[,1])),sprintf("%.2f",tableOUTCI[,2]),sep=' to ')
  tableOUT[,1] <- sprintf("%.2f",tableOUT[,1])
  tableOUT[,2] <- sprintf("%.2f",tableOUT[,2])
  tableOUT[,3] <- sprintf("%.2f",tableOUT[,3])
  tableOUT[,4] <- sprintf("%.2f",tableOUT[,4])
  tableOUT <- cbind(tableOUT, tableOUTCIfinal)
  parameters<- c("Constant","Message")
  tableOUT <- cbind(parameters, tableOUT)
  colnames(tableOUT) <- c("Parameters","Log OR","Standard error","z","P>|z|","95% CI")
  tableOUT$Parameters <- as.character(tableOUT$Parameters)
  #Prepare GLM RE model
  tableOUT1 <- as.data.frame(coef(summary(glmre)))
  lower <- (tableOUT1[,1]+qnorm(.025)*tableOUT1[,2])
  upper <- (tableOUT1[,1]+qnorm(.975)*tableOUT1[,2])
  tableOUTCIfinal <- paste(sprintf("%.2f",lower),sprintf("%.2f",upper),sep=' to ')
  tableOUT1 <- cbind(round(tableOUT1,3), tableOUTCIfinal)
  parameters<- c("Constant","Message")
  tableOUT1[,1] <- sprintf("%.2f",tableOUT1[,1])
  tableOUT1[,2] <- sprintf("%.2f",tableOUT1[,2])
  tableOUT1[,3] <- sprintf("%.2f",tableOUT1[,3])
  tableOUT1[,4] <- sprintf("%.2f",tableOUT1[,4])
  tableOUT1 <- cbind(parameters, tableOUT1)
  colnames(tableOUT1) <- c("Parameters","Log OR","Standard error","z","P>|z|","95% CI")
  tableOUT <- rbind(c("GLM",NA,NA,NA,NA),tableOUT)
  tableOUT <- rbind(tableOUT,c("RE",NA,NA,NA,NA))
  tableOUT <- rbind(tableOUT,tableOUT1)
  tableOUT <- rbind(tableOUT,c("sigzma",NA,NA,NA,NA))
  tableOUT <-
  rbind(tableOUT,c("$\\sigma^2_{ecg}$",round(VarCorr(fitGLM)$ecg_id[1],2),NA,NA,NA,NA))
  tableOUT <-
  rbind(tableOUT,c("$\\sigma^2_{participant}$",round(VarCorr(fitGLM)$participant[1],2),NA,NA,NA,NA))
  colnames(tableOUT) <- c("Parameters","Log OR","Standard error","z","P>|z|","95% CI")
  table1 <- xtable(tableOUT,caption=caption1,label=label1,align=c("l","l","c","c","c","c"))
  finalTable <-
  print(table1,append=F,table.placement="htbp",caption.placement="top",include.rownames=FALSE,booktabs=TRUE)
  # cat(finalTable)
  finalTable <- sub("GLM & & & & & \\\\" ,\"\\textit{GLM no Random Effects} & & & & & \\
\\\" ,finalTable,fixed=T)
  finalTable <- sub("RE & & & & & \\\\" ,\"\\midrule
\\textit{GLM with Random Effects} & & & & & \\\\" ,finalTable,fixed=T)
  finalTable <- sub("sigzma & & & & & \\\\" ,\"\\midrule ",finalTable,fixed=T)
  finalTable <- sub("\\begin{tabular}{lccccc}",
"\\newcolumntype{V}{>{\\centering\\arraybackslash}p{0.1\\textwidth}}
\\newcolumntype{W}{>{\\arraybackslash}p{0.31\\textwidth}}
\\newcolumntype{X}{>{\\centering\\arraybackslash}p{0.15\\textwidth}}
\\begin{tabular}{wvuvux}",finalTable,fixed=T)
  print(finalTable)
  cat(finalTable)
  cat(finalTable,file=paste("Tables/",filename,sep=''))
}

combiTable(fit,fitGLM,"Log odds ratio of correct answer with all
messages","lormesgall","logORTablesmesg.tex")

```

Waiting for profiling to be done...

```
% latex table generated in R 2.15.2 by xtable 1.7-1 package
% Mon Jul 15 17:49:25 2013
\begin{table}[htbp]
\centering
\caption{Log odds ratio of correct answer with all messages}
\label{lormesgal1}
\begin{tabular}{lccccc}
\toprule
Parameters & Log OR & Standard error & z & P$>$$|z|\$ & 95\% CI \\
\midrule
GLM & & & & & \\
Constant & 1.41 & 0.06 & 24.20 & 0.00 & 1.30 to 1.53 \\
Message & -0.06 & 0.08 & -0.78 & 0.44 & -0.22 to 0.10 \\
RE & & & & & \\
Constant & 1.87 & 0.20 & 9.42 & 0.00 & 1.48 to 2.26 \\
Message & -0.08 & 0.09 & -0.88 & 0.38 & -0.26 to 0.10 \\
\sigma_{\text{ecg}} & 1.57 & & & & \\
\sigma_{\text{participant}} & 0.21 & & & & \\
\bottomrule
\end{tabular}
\end{table}
[1] "% latex table generated in R 2.15.2 by xtable 1.7-1 package\n% Mon Jul 15 17:49:25 2013\n\\begin{table}[htbp]\\n\\centering\\n\\caption{Log odds ratio of correct answer with all\\nmessages} \\n\\label{lormesgal1}\\n\\newcolumntype{U}\\{\\centering\\arraybackslash\\p{0.08\\textwidth}\\}\\n\\newcolumntype{V}\\{\\centering\\arraybackslash\\p{0.1\\textwidth}\\}\\n\\newcolumntype{W}\\{\\arraybackslash\\p{0.31\\textwidth}\\}\\n\\newcolumntype{X}\\{\\centering\\arraybackslash\\p{0.15\\textwidth}\\}\\n\\begin{tabular}{wvuxx}\\n \\toprule\\nParameters & Log\\nOR & Standard\\nerror & z & P$>$$|z|\$ & 95\%\\nCI \\\\n\\midrule\\n\\textit{GLM no Random\\nEffects} & & & & & \\\\nConstant & 1.41 & 0.06 & 24.20 & 0.00 & 1.30 to 1.53 \\\\nMessage & -0.06 & 0.08 & -0.78 & 0.44 & -0.22 to 0.10 \\\\n\\midrule\\n\\textit{GLM with\\nRandom Effects} & & & & & \\\\nConstant & 1.87 & 0.20 & 9.42 & 0.00 & 1.48 to 2.26 \\\\nMessage & -0.08 & 0.09 & -0.88 & 0.38 & -0.26 to 0.10 \\\\n\\midrule\\n\\sigma_{\\text{ecg}} & 1.57 & & & & \\\\n\\sigma_{\\text{participant}} & 0.21 & & & & \\\\n\\bottomrule\\n\\end{tabular}\\n\\end{table}\\n"
% latex table generated in R 2.15.2 by xtable 1.7-1 package
% Mon Jul 15 17:49:25 2013
\begin{table}[htbp]
\centering
\caption{Log odds ratio of correct answer with all messages}
\label{lormesgal1}
\newcolumntype{U}\\{\\centering\\arraybackslash\\p{0.08\\textwidth}\\}
\newcolumntype{V}\\{\\centering\\arraybackslash\\p{0.1\\textwidth}\\}
\newcolumntype{W}\\{\\arraybackslash\\p{0.31\\textwidth}\\}
\newcolumntype{X}\\{\\centering\\arraybackslash\\p{0.15\\textwidth}\\}
\begin{tabular}{wvuxx}
\toprule
Parameters & Log OR & Standard error & z & P$>$$|z|\$ & 95\% CI \\
\midrule
\textit{GLM no Random Effects} & & & & & \\
Constant & 1.41 & 0.06 & 24.20 & 0.00 & 1.30 to 1.53 \\
Message & -0.06 & 0.08 & -0.78 & 0.44 & -0.22 to 0.10 \\
\midrule
\textit{GLM with Random Effects} & & & & & \\
Constant & 1.87 & 0.20 & 9.42 & 0.00 & 1.48 to 2.26 \\
Message & -0.08 & 0.09 & -0.88 & 0.38 & -0.26 to 0.10 \\
\midrule
\sigma_{\text{ecg}} & 1.57 & & & & \\
\sigma_{\text{participant}} & 0.21 & & & & \\
\bottomrule
\end{tabular}
\end{table}

```

combiTable(fitcc,fitGLMCC,"Log odds ratio of correct answer and correct computer messages","lormesgcc","logORTablesmesgcc.tex")

Waiting for profiling to be done...

```
% latex table generated in R 2.15.2 by xtable 1.7-1 package
% Mon Jul 15 17:49:26 2013
\begin{table}[htbp]
\centering
\caption{Log odds ratio of correct answer and correct computer messages}
\label{lormesgcc}
\begin{tabular}{lccccc}
\toprule
Parameters & Log OR & Standard error & z & P$>$$|z|\$ & 95\% CI \\
\midrule
GLM & & & & & \\
Constant & 1.67 & 0.09 & 18.62 & 0.00 & 1.50 to 1.85 \\
Message & 0.27 & 0.13 & 2.05 & 0.04 & 0.01 to 0.54 \\
RE & & & & \\
Constant & 2.21 & 0.27 & 8.32 & 0.00 & 1.69 to 2.74 \\
Message & 0.35 & 0.15 & 2.36 & 0.02 & 0.06 to 0.64 \\
\sigma_{\text{fecg}} & 1.57 & & & & \\
\sigma_{\text{participant}} & 0.21 & & & & \\
\bottomrule
\end{tabular}
\end{table}
[1] "% latex table generated in R 2.15.2 by xtable 1.7-1 package\n% Mon Jul 15 17:49:26 2013\n
\\begin{table}[htbp]\n\\centering\n\\caption{Log odds ratio of correct answer and correct\ncomputer messages}\n\\label{lormesgcc}\n\\newcolumntype{U}{>{\\centering\\arraybackslash}p{0.08\\textwidth}}\n\\newcolumntype{V}{>{\\centering\\arraybackslash}p{0.1\\textwidth}}\n\\newcolumntype{W}{>{\\arraybackslash}p{0.31\\textwidth}}\n\\newcolumntype{X}{>{\\centering\\arraybackslash}p{0.15\\textwidth}}\n\\begin{tabular}{wvuxx}\n\\toprule
Parameters & Log\nOR & Standard\nerror & z & P$>$$|z|\$ & 95\% CI \\
\midrule
\\textit{GLM no Random Effects} & & & & & \\
Constant & 1.67 & 0.09 & 18.62 & 0.00 & 1.50 to 1.85 \\
Message & 0.27 & 0.13 & 2.05 & 0.04 & 0.01 to 0.54 \\
\\textit{GLM with Random Effects} & & & & & \\
Constant & 2.21 & 0.27 & 8.32 & 0.00 & 1.69 to 2.74 \\
Message & 0.35 & 0.15 & 2.36 & 0.02 & 0.06 to 0.64 \\
\sigma_{\text{fecg}} & 1.57 & & & & \\
\sigma_{\text{participant}} & 0.21 & & & & \\
\bottomrule
\\end{tabular}\n\\end{table}\n"
% latex table generated in R 2.15.2 by xtable 1.7-1 package
% Mon Jul 15 17:49:26 2013
\begin{table}[htbp]
\centering
\caption{Log odds ratio of correct answer and correct computer messages}
\label{lormesgcc}
\newcolumntype{U}{>{\\centering\\arraybackslash}p{0.08\\textwidth}}
\newcolumntype{V}{>{\\centering\\arraybackslash}p{0.1\\textwidth}}
\newcolumntype{W}{>{\\arraybackslash}p{0.31\\textwidth}}
\newcolumntype{X}{>{\\centering\\arraybackslash}p{0.15\\textwidth}}
\begin{tabular}{wvuxx}
\toprule
Parameters & Log OR & Standard error & z & P$>$$|z|\$ & 95\% CI \\
\midrule
\textit{GLM no Random Effects} & & & & & \\
Constant & 1.67 & 0.09 & 18.62 & 0.00 & 1.50 to 1.85 \\
Message & 0.27 & 0.13 & 2.05 & 0.04 & 0.01 to 0.54 \\
\midrule
\textit{GLM with Random Effects} & & & & & \\
Constant & 2.21 & 0.27 & 8.32 & 0.00 & 1.69 to 2.74 \\
Message & 0.35 & 0.15 & 2.36 & 0.02 & 0.06 to 0.64 \\
\midrule
\sigma_{\text{fecg}} & 1.57 & & & & \\
\sigma_{\text{participant}} & 0.21 & & & & \\
\bottomrule
\end{tabular}
\end{table}

```

combiTable(fitci, fitGLMci, "Log odds ratio of correct answer and incorrect computer messages", "lormesgcc", "logORTablesmesgcc.tex")

Waiting for profiling to be done...

```
% latex table generated in R 2.15.2 by xtable 1.7-1 package
% Mon Jul 15 17:49:26 2013
\begin{table}[htbp]
\centering
\caption{Log odds ratio of correct answer and incorrect computer messages}
\label{lormesgci}
\begin{tabular}{lccccc}
\toprule
Parameters & Log OR & Standard error & z & P$>$$|z|\$ & 95\% CI \\
\midrule
GLM & & & & & \\
Constant & 1.19 & 0.08 & 15.35 & 0.00 & 1.04 to 1.34 \\
Message & -0.28 & 0.11 & -2.63 & 0.01 & -0.49 to -0.07 \\
RE & & & & & \\
Constant & 1.60 & 0.28 & 5.80 & 0.00 & 1.06 to 2.14 \\
Message & -0.35 & 0.12 & -3.03 & 0.00 & -0.58 to -0.12 \\
\sigma_{\text{ecg}} & 1.57 & & & & \\
\sigma_{\text{participant}} & 0.21 & & & & \\
\bottomrule
\end{tabular}
\end{table}
[1] "% latex table generated in R 2.15.2 by xtable 1.7-1 package\n% Mon Jul 15 17:49:26 2013\n
\\begin{table}[htbp]\\n\\centering\\n\\caption{Log odds ratio of correct answer and incorrect computer messages} \\n\\label{lormesgci}\\n\\newcolumntype{U}\\{>{\\centering\\arraybackslash}p{0.08\\textwidth}\\}\\n\\newcolumntype{V}\\{>{\\centering\\arraybackslash}p{0.1\\textwidth}\\}\\n\\newcolumntype{W}\\{>{\\arraybackslash}p{0.31\\textwidth}\\}\\n\\newcolumntype{X}\\{>{\\centering\\arraybackslash}p{0.15\\textwidth}\\}\\n\\begin{tabular}{wvuxx}\\n \\toprule\\nParameters & Log OR & Standard error & z & P$>$$|z|\$ & 95\% CI \\n \\midrule\\n\\textit{GLM no Random Effects} & & & & & \\
Constant & 1.19 & 0.08 & 15.35 & 0.00 & 1.04 to 1.34 \\
Message & -0.28 & 0.11 & -2.63 & 0.01 & -0.49 to -0.07 \\
\\textit{GLM with Random Effects} & & & & & \\
Constant & 1.60 & 0.28 & 5.80 & 0.00 & 1.06 to 2.14 \\
Message & -0.35 & 0.12 & -3.03 & 0.00 & -0.58 to -0.12 \\
\\bottomrule\\n\\end{tabular}\\n\\end{table}\\n"
% latex table generated in R 2.15.2 by xtable 1.7-1 package
% Mon Jul 15 17:49:26 2013
\begin{table}[htbp]
\centering
\caption{Log odds ratio of correct answer and incorrect computer messages}
\label{lormesgci}
\begin{tabular}{lccccc}
\toprule
Parameters & Log OR & Standard error & z & P$>$$|z|\$ & 95\% CI \\
\midrule
\textit{GLM no Random Effects} & & & & & \\
Constant & 1.19 & 0.08 & 15.35 & 0.00 & 1.04 to 1.34 \\
Message & -0.28 & 0.11 & -2.63 & 0.01 & -0.49 to -0.07 \\
\midrule
\textit{GLM with Random Effects} & & & & & \\
Constant & 1.60 & 0.28 & 5.80 & 0.00 & 1.06 to 2.14 \\
Message & -0.35 & 0.12 & -3.03 & 0.00 & -0.58 to -0.12 \\
\midrule
\sigma_{\text{ecg}} & 1.57 & & & & \\
\sigma_{\text{participant}} & 0.21 & & & & \\
\bottomrule
\end{tabular}
\end{table}
```

```

#----- COMBINED OR TABLES WITH RANDOM EFFECTS -----
combiTableEXP <- function(glm,glmre,caption1,label1,filename) {
  tableOUT <- data.frame((coef(summary(glm))[,c("Estimate","z
value","Pr(>|z|)"))],check.names=F)
  tableOUT[,1] <- exp(tableOUT[,1])
  tableOUTCI <- exp(confint(glm))
  tableOUTCIfinal <- paste(sprintf("%.2f",tableOUTCI[,1]),sprintf("%.2f",tableOUTCI[,2]),sep='
to ')
  tableOUT[,1] <- sprintf("%.2f",tableOUT[,1])
  tableOUT[,2] <- sprintf("%.2f",tableOUT[,2])
  tableOUT[,3] <- sprintf("%.2f",tableOUT[,3])
  tableOUT <- cbind(tableOUT, tableOUTCIfinal)
  parameters<- c("Constant","Message")
  tableOUT <- cbind(parameters, tableOUT)
  colnames(tableOUT) <- c("Parameters","OR","z","P>|z|","95% CI")
  tableOUT$Parameters <- as.character(tableOUT$Parameters)
  #print(tableOUT)
  #Prepare GLM RE model
  tableOUT1 <- as.data.frame(coef(summary(glmre)))
  #str(tableOUT1)
  #print(tableOUT1)
  lower <- (tableOUT1[,1]+qnorm(.025)*tableOUT1[,2])
  upper <- (tableOUT1[,1]+qnorm(.975)*tableOUT1[,2])
  tableOUT1CIfinal <- paste(sprintf("%.2f",exp(lower)),sprintf("%.2f",exp(upper)),sep=' to ')
  #tableOUT1 <- cbind(tableOUT1, tableOUT1CIfinal)
  parameters<- c("Constant","Message")
  tableOUT1[,1] <- sprintf("%.2f",exp(tableOUT1[,1]))
  tableOUT1[,2] <- sprintf("%.2f",tableOUT1[,3])
  tableOUT1[,3] <- sprintf("%.2f",tableOUT1[,4])
  tableOUT1[,4] <- tableOUT1CIfinal
  tableOUT1 <- cbind(parameters, tableOUT1)
  colnames(tableOUT1) <- c("Parameters","OR","z","P>|z|","95% CI")
  # print(tableOUT1)
  tableOUT <- rbind(c("GLM",NA,NA,NA,NA),tableOUT)
  tableOUT <- rbind(tableOUT,c("RE",NA,NA,NA,NA))
  tableOUT <- rbind(tableOUT,tableOUT1)
  tableOUT <- rbind(tableOUT,c("sigzma",NA,NA,NA,NA))
  tableOUT <-
  rbind(tableOUT,c("$\\sigma^2_{\{ecg\}}$",round(VarCorr(fitGLM)$ecg_id[1],2),NA,NA,NA))
  tableOUT <-
  rbind(tableOUT,c("$\\sigma^2_{\{participant\}}$",round(VarCorr(fitGLM)$participant[1],2),NA,NA,NA))
  colnames(tableOUT) <- c("Parameters","OR","z","P$>|z|$","95\\% CI")
  # print(tableOUT)
  table1 <- xtable(tableOUT,caption=caption1,label=label1,align=c("l","l","c","c","c","c"))
  finalTable <-
  print(table1,append=F,table.placement="htbp",caption.placement="top",include.rownames=FALSE,booktabs
= function(x) x)
  # cat(finalTable)
  finalTable <- sub("GLM & & & & \\\\"","\\textit{GLM no Random Effects} & & & &
\\\"",finalTable,fixed=T)
  finalTable <- sub("RE & & & & \\\\"","\\midrule
\\textit{GLM with Random Effects} & & & & \\\\",finalTable,fixed=T)
  finalTable <- sub("sigzma & & & & \\\\"","\\midrule ",finalTable,fixed=T)
  cat(finalTable,file=paste("Tables/",filename,sep=''))
}

combiTableEXP(fit,fitGLM,"Odds ratio of correct answer with all
messages","ormesgall","ORtablesmsg.tex")

```

waiting for profiling to be done...

```
% latex table generated in R 2.15.2 by xtable 1.7-1 package
% Mon Jul 15 17:49:26 2013
\begin{table}[htbp]
\centering
\caption{Odds ratio of correct answer with all messages}
\label{ormesall}
\begin{tabular}{lcccc}
\toprule
Parameters & OR & z & P>$$|z|\$ & 95\% CI \\
\midrule
GLM & & & & \\
Constant & 4.10 & 24.20 & 0.00 & 3.66 to 4.60 \\
Message & 0.94 & -0.78 & 0.44 & 0.80 to 1.10 \\
RE & & & \\
Constant & 6.48 & 9.42 & 0.00 & 4.39 to 9.56 \\
Message & 0.92 & -0.88 & 0.38 & 0.77 to 1.10 \\
sigzma & & & \\
$\sigma^2_{\text{ecg}}$ & 1.57 & & \\
$\sigma^2_{\text{participant}}$ & 0.21 & & \\
\bottomrule
\end{tabular}
\end{table}
```

```
combiTableEXP(fitcc,fitGLMcc,"Odds ratio of correct answer and correct computer
messages","ormesgcc","ORtablesmesgcc.tex")
```

Waiting for profiling to be done...

```
% latex table generated in R 2.15.2 by xtable 1.7-1 package
% Mon Jul 15 17:49:27 2013
\begin{table}[htbp]
\centering
\caption{Odds ratio of correct answer and correct computer messages}
\label{ormesgcc}
\begin{tabular}{lcccc}
\toprule
Parameters & OR & z & P>$$|z|\$ & 95\% CI \\
\midrule
GLM & & & & \\
Constant & 5.30 & 18.62 & 0.00 & 4.46 to 6.35 \\
Message & 1.31 & 2.05 & 0.04 & 1.01 to 1.71 \\
RE & & & \\
Constant & 9.16 & 8.32 & 0.00 & 5.43 to 15.43 \\
Message & 1.42 & 2.36 & 0.02 & 1.06 to 1.89 \\
sigzma & & & \\
$\sigma^2_{\text{ecg}}$ & 1.57 & & \\
$\sigma^2_{\text{participant}}$ & 0.21 & & \\
\bottomrule
\end{tabular}
\end{table}
```

```
combiTableEXP(fitci,fitGLMci,"Odds ratio of correct answer and incorrect computer
messages","ormesgci","ORtablesmesgci.tex")
```

Waiting for profiling to be done...

```
% latex table generated in R 2.15.2 by xtable 1.7-1 package
% Mon Jul 15 17:49:27 2013
\begin{table}[htbp]
\centering
\caption{Odds ratio of correct answer and incorrect computer messages}
\label{ormesgci}
\begin{tabular}{lcccc}
\toprule
Parameters & OR & z & P>$$|z| & 95\% CI \\
\midrule
GLM & & & & \\
Constant & 3.28 & 15.35 & 0.00 & 2.82 to 3.82 \\
Message & 0.76 & -2.63 & 0.01 & 0.61 to 0.93 \\
RE & & & & \\
Constant & 4.95 & 5.80 & 0.00 & 2.88 to 8.49 \\
Message & 0.70 & -3.03 & 0.00 & 0.56 to 0.88 \\
sigma & & & & \\
$\sigma^2_{\text{ecg}}$ & 1.57 & & & \\
$\sigma^2_{\text{participant}}$ & 0.21 & & & \\
\bottomrule
\end{tabular}
\end{table}
```

```
#----- ICC CALCULATIONS -----
# Create functions to calculate ICC
xVars <- function(model) {
  exvars = lme4::VarCorr(model)
  vars = c(exvars$ecg_id[1,1], exvars$participant_id[1,1])
  names(vars) <- c('ecg var', 'participant var')
  vars
}

# helper function for ICC(k) variations
icck <- function(variances, var='both') {
  # Binomial distribution (logit), residual variance fixed at pi^2/3
  # Need to discuss whether this is important - 1 is also sometimes used

  resVar <- (pi^2/3)
  if(var=='ecg') icc = variances[1] / (variances[1] + variances[2] + resVar)
  else if(var=='participant') icc = variances[2] / (variances[1] + variances[2] + resVar)
  else icc = (variances[1] + variances[2]) / (variances[1] + variances[2] + resVar)
}

fitGLMOnly <- glmer(diag_correct~(1|ecg_id)+ (1|participant_id), data=FinalStudyData99, family=binomial("logit"))

cat("calculate ICC values\n")
```

Calculate ICC values

```
# ICC calculation for participant and ECG
print(icck(xVars(fitGLMOnly)))
```

```
ecg var
0.4591
```

```
# CC calculation for ECG only
print(icck(xVars(fitGLMOnly),'ecg'))
```

```
ecg var
0.4055
```

```
# ICC calculation for participant only  
print(icck(xVars(fitGLMOnly),'participant'))
```

```
participant var  
0.05362
```

# References

- [1] Smith GC, Pell JP. Parachute use to prevent death and major trauma related to gravitational challenge: systematic review of randomised controlled trials. *British Medical Journal*. 2003;327(7429):1459. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC300808/>.
- [2] Steg G, James SK, Atar D, Badano LP, Lundqvist CB, Borger MA, et al. ESC Guidelines for the management of acute myocardial infarction in patients presenting with ST-segment elevation The Task Force on the management of ST-segment elevation acute myocardial infarction of the European Society of Cardiology (ESC). *European Heart Journal*. 2012 Oct;33(20):2569–2619. Available from: <http://eurheartj.oxfordjournals.org/content/33/20/2569>.
- [3] Widimsky P, Wijns W, Fajadet J, de Belder M, Knot J, Aaberge L, et al. Reperfusion therapy for ST elevation acute myocardial infarction in Europe: description of the current situation in 30 countries. *European Heart Journal*. 2009 Nov;31(8):943–957. Available from: <http://eurheartj.oxfordjournals.org/cgi/doi/10.1093/eurheartj/ehp492>.
- [4] Bilgi M, Gülpalp B, Erol T, Güllü H, Karagün Ö, Altay H, et al. Interpretation of Electrocardiogram Images Sent Through the Mobile Phone Multimedia Messaging Service. *Telemedicine and e-Health*. 2012;18(2):126—131. Available from: <http://online.liebertpub.com/doi/abs/10.1089/tmj.2011.0108>.
- [5] British Heart Foundation Health Promotion Research Group, University of Oxford. Coronary heart disease statistics 2012 edition. Department of Public Health, University of Oxford; 2012. Available from: <http://www.bhf.org.uk/publications/view-publication.aspx?ps=1001546>.

- [6] Falk E, Thuesen L. Pathology of coronary microembolisation and no reflow. *Heart.* 2003 Sep;89(9):983–985. PMID: 12923001 PMCID: PMC1767861. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC1767861/>.
- [7] Sakakura K, Nakano M, Otsuka F, Ladich E, Kolodgie FD, Virmani R. Pathophysiology of Atherosclerosis Plaque Progression. *Heart, Lung and Circulation.* 2013 Jun;22(6):399–411. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S1443950613000711>.
- [8] Windecker S, Bax JJ, Myat A, Stone GW, Marber MS. Future treatment strategies in ST-segment elevation myocardial infarction. *The Lancet.* 2013;382(9892):644–657. Available from: <http://www.sciencedirect.com/science/article/pii/S014067361361452X>.
- [9] Mittleman MA, Mostofsky E. Physical, psychological and chemical triggers of acute cardiovascular events: preventive strategies. *Circulation.* 2011 Jul;124(3):346–354. PMID: 21768552.
- [10] Curzen N, Gurbel PA, Myat A, Bhatt DL, Redwood SR. What is the optimum adjunctive reperfusion strategy for primary percutaneous coronary intervention? *The Lancet.* 2013;382(9892):633–643. Available from: <http://www.sciencedirect.com/science/article/pii/S0140673613614531>.
- [11] Thygesen K, Alpert JS, Jaffe AS, Simoons ML, Chaitman BR, White HD, et al. Third universal definition of myocardial infarction. *European Heart Journal.* 2012 Aug;33(20):2551–2567. Available from: <http://eurheartj.oxfordjournals.org/cgi/doi/10.1093/eurheartj/ehs184>.
- [12] Department of Health. Treatment of heart attack national guidance: final report of the National Infarct Angioplasty Project (NIAP); 2008. Available from: <http://www.bcis.org.uk/resources/documents/NIAP%20Final%20Report.pdf>.
- [13] Kligfield P, Gettes LS, Bailey JJ, Childers R, Deal BJ, Hancock EW, et al. Recommendations for the Standardization and Interpretation of the Electrocardiogram. Part I: The Electrocardiogram and Its Technology. A Scientific Statement From the American Heart Association Electrocardiography and Arrhythmias Committee, Council on Clinical Cardiology; the American College of Cardiology Foundation; and the Heart Rhythm Society. Endorsed by the International Society

- for Computerized Electrocardiology. *Circulation*. 2007 Feb; Available from: <http://circ.ahajournals.org/cgi/doi/10.1161/CIRCULATIONAHA.106.180200>.
- [14] Thomas Garcia. 12-lead ECG: The Art of Interpretation. Sudbury, MA: Jones and Bartlett Publishers; 2000.
- [15] Association of Ambulance Chief Executives. UK Ambulance Services Clinical Practice Guidelines 2013. Bridgwater: Class Professional Publishing; 2013.
- [16] Swor R, Hegerberg S, McHugh-McNally A, Goldstein M, McEachin C. Prehospital 12-lead ECG: efficacy or effectiveness? *Prehospital Emergency Care*. 2006 Sep;10(3):374–377.
- [17] Feldman JA, Brinsfield K, Bernard S, White D, Maciejko T. Real-time paramedic compared with blinded physician identification of ST-segment elevation myocardial infarction: results of an observational study. *The American Journal Of Emergency Medicine*. 2005 Jul;23(4):443–448.
- [18] Woppard M, Pitt K, Hayward AJ, Taylor NC. Limited benefits of ambulance telemetry in delivering early thrombolysis: a randomised controlled trial. *Emergency Medicine Journal*. 2005 Mar;22(3):209 –215. Available from: <http://emj.bmjjournals.com/content/22/3/209.abstract>.
- [19] Keeling P. Safety and feasibility of prehospital thrombolysis carried out by paramedics. *British Medical Journal*. 2003 Jul;327(7405):27–28. Available from: <http://www.bmjjournals.com/content/327/7405/27>.
- [20] Johnston S, Brightwell R, Ziman M. Paramedics and pre-hospital management of acute myocardial infarction: diagnosis and reperfusion. *Emergency Medicine Journal*. 2006 May;23(5):331–334.
- [21] Ludman P. National Audit fo Percutaneous Coronary Interventional Procedures Public Report; 2013. Available from: <http://www.ucl.ac.uk/nicor/audits/adultcardiacintervention/publicreports/documents/pcireport2012>.
- [22] Waller AD. A demonstration on man of electromotive changes accompanying the heart's beat. *The Journal of Physiology*. 1887;8(5):229—234. Available from: <http://jp.physoc.org/content/8/5/229.full.pdf>.

- [23] Herring N, Paterson DJ. ECG diagnosis of acute ischaemia and infarction: past, present and future. Quarterly Journal of Medicine. 2006 Apr;99(4):219–230. Available from: <http://qjmed.oxfordjournals.org/content/99/4/219>.
- [24] Willems JL. Computer analysis of the electrocardiogram. Endeavour. 1981;5(1):37—43. Available from: <http://www.sciencedirect.com/science/article/pii/0160932781900776>.
- [25] Willems JL, Arnaud P, van Bemmel JH, Degani R, MacFarlane PW, Zywietz C. Comparison of diagnostic results of ECG computer programs and cardiologists. In: Computers in Cardiology 1991, Proceedings.; 1991. p. 93–96. Available from: [http://ieeexplore.ieee.org/xpls/abs\\_all.jsp?arnumber=169053](http://ieeexplore.ieee.org/xpls/abs_all.jsp?arnumber=169053).
- [26] Willems JL, Abreu-Lima C, Arnaud P, van Bemmel JH, Brohet C, Degani R, et al. The Diagnostic Performance of Computer Programs for the Interpretation of Electrocardiograms. New England Journal of Medicine. 1991;325(25):1767–1773. Available from: <http://www.nejm.org/doi/full/10.1056/NEJM199112193252503>.
- [27] International Electrotechnical Commission. Medical electrical equipment – Part 2-25: Particular requirements for the basic safety and essential performance of electrocardiographs. 2nd ed. Geneva: International Electrotechnical Commission; 2011.
- [28] Rautaharju P, Ariet M, Pryor T, Arzbaecher RC, Bailey JJ, Bonner R, et al. Task force III: Computers in diagnostic electrocardiography. The American Journal of Cardiology. 1978 Jan;41(1):158–170. Available from: <http://linkinghub.elsevier.com/retrieve/pii/0002914978901509?showall=true>.
- [29] GE Healthcare. Marquette 12SL ECG Analysis Program: Physician's Guide. Revision a ed. Milwaukee: GE Healthcare; 2010.
- [30] Selker HP, Beshansky JR, Griffith JL, Aufderheide TP, Ballin DS, Bernard SA, et al. Use of the acute cardiac ischemia time-insensitive predictive instrument (ACI-TIPI) to assist with triage of patients with chest pain or other symptoms suggestive of acute cardiac ischemia. A multicenter, controlled clinical trial. Annals of Internal Medicine. 1998 Dec;129(11):845–855. PMID: 9867725.
- [31] Eggers KM, Ellenius J, Dellborg M, Groth T, Oldgren J, Swahn E, et al. Artificial neural network algorithms for early diagnosis of acute myocardial infarction and

- prediction of infarct size in chest pain patients. International Journal of Cardiology. 2007 Jan;114(3):366–374. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S016752730600252X>.
- [32] Physio Control. Glasgow 12-lead ECG Analysis Program: Physician's Guide. Redmond: Physio Control; 2009.
- [33] GE Healthcare. Marquette 12SL ECG Analysis Program: Statement of Validation and Accuracy. Revision c ed. Milwaukee: GE Healthcare; 2008.
- [34] GE Healthcare. Marquette 12SL ECG Analysis Program: Statement of Validation and Accuracy. Revision b ed. Milwaukee: GE Healthcare; 2007.
- [35] Deakin CD. Does telephone triage of emergency (999) calls using advanced medical priority dispatch (AMPDS) with Department of Health (DH) call prioritisation effectively identify patients with an acute coronary syndrome? An audit of 42 657 emergency calls to Hampshire Ambulance Service NHS Trust. Emergency Medicine Journal. 2006 Mar;23(3):232–235. Available from: <http://emj.bmjjournals.org/cgi/doi/10.1136/emj.2004.022962>.
- [36] Ting HH, Krumholz HM, Bradley EH, Cone DC, Curtis JP, Drew BJ, et al. Implementation and integration of prehospital ECGs into systems of care for acute coronary syndrome A scientific statement from the American Heart Association Interdisciplinary Council on quality of care and outcomes research, emergency cardiovascular care committee, council on cardiovascular nursing, and council on clinical cardiology. Circulation. 2008;118(10):1066—1079. Available from: <http://circ.ahajournals.org/content/118/10/1066.short>.
- [37] Ducas RA, Wassef AW, Jassal DS, Weldon E, Schmidt C, Grierson R, et al. To Transmit or Not to Transmit: How Good Are Emergency Medical Personnel in Detecting STEMI in Patients With Chest Pain? Canadian Journal of Cardiology. 2012 Jul;28(4):432–437. Available from: <http://www.sciencedirect.com/science/article/pii/S0828282X12001948>.
- [38] The Joint Royal Colleges Ambulance Liaison Committee, The Ambulance Services Association. Pre-Hospital Thrombolysis. JRCALC; 2001. Available from: [http://www.jrcalc.org.uk/events/annex02\\_0302.pdf](http://www.jrcalc.org.uk/events/annex02_0302.pdf).

- [39] Watts N. Thrombolysis Up Front; 2013. Personal communication.
- [40] Bhalla MC, Mencl F, Gist MA, Wilber S, Zalewski J. Prehospital Electrocardiographic Computer Identification of ST-segment Elevation Myocardial Infarction. *Prehospital Emergency Care*. 2013 Apr;17(2):211–216. Available from: <http://informahealthcare.com/doi/abs/10.3109/10903127.2012.722176>.
- [41] 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. *The American Journal of Cardiology*. 2010 Dec;106(12):1696–1702. Available from: <http://www.sciencedirect.com/science/article/pii/S0002914910016188>.
- [42] Youngquist ST, Shah AP, Niemann JT, Kaji AH, French WJ. A Comparison of Doortoballoon Times and Falsepositive Activations between Emergency Department and Outofhospital Activation of the Coronary Catheterization Team. *Academic Emergency Medicine*. 2008 Aug;15(8):784–787. Available from: <http://onlinelibrary.wiley.com/doi/10.1111/j.1553-2712.2008.00186.x/abstract>.
- [43] Cantor WJ, Hoogeveen P, Robert A, Elliott K, Goldman LE, Sanderson E, et al. Prehospital diagnosis and triage of ST-elevation myocardial infarction by paramedics without advanced care training. *American Heart Journal*. 2012 Aug;164(2):201–206. Available from: <http://www.sciencedirect.com/science/article/pii/S0002870312003651>.
- [44] Ioannidis JP, Salem D, Chew PW, Lau J. Accuracy and clinical effect of out-of-hospital electrocardiography in the diagnosis of acute cardiac ischemia: A meta-analysis. *Annals of Emergency Medicine*. 2001 May;37(5):461–470. Available from: <http://www.sciencedirect.com/science/article/pii/S0196064401458422>.
- [45] Mixon TA, Suhr E, Caldwell G, Greenberg RD, Colato F, Blackwell J, et al. Retrospective description and analysis of consecutive catheterization laboratory ST-segment elevation myocardial infarction activations with proposal, rationale, and use of a new classification scheme. *Circulation: Cardiovascular Quality and Outcomes*. 2012;5(1):62–69. Available from: <http://circoutcomes.ahajournals.org/content/5/1/62.short>.

- [46] Ting H, Myers L, Bjerke C, Lennon R, Schultz J, Nestler D, et al. Abstract 1586: Accuracy of Prehospital Electrocardiograms Interpreted by Paramedics in Olmsted County: The Mayo Clinic Prehospital Electrocardiogram Program. *Circulation*. 2009;S523(120).
- [47] Young DR, Murinson M, Wilson C, Hammond B, Welch M, Block V, et al. Paramedics as decision makers on the activation of the catheterization laboratory in the presence of acute ST-elevation myocardial infarction. *Journal Of Electrocardiology*. 2011 Feb;44(1):18–22.
- [48] Davis DP, Graydon C, Stein R, Wilson S, Buesch B, Berthiaume S, et al. The positive predictive value of paramedic versus emergency physician interpretation of the prehospital 12-lead electrocardiogram. *Prehospital Emergency Care: Official Journal Of The National Association Of EMS Physicians And The National Association Of State EMS Directors*. 2007 Dec;11(4):399–402.
- [49] Rokos IC, French WJ, Mattu A, Nichol G, Farkouh ME, Reiffel J, et al. Appropriate Cardiac Cath Lab activation: Optimizing electrocardiogram interpretation and clinical decision-making for acute ST-elevation myocardial infarction. *American Heart Journal*. 2010 Dec;160(6):995–1003.e8. Available from: [http://www.ahjonline.com/article/S0002-8703\(10\)00758-1/abstract](http://www.ahjonline.com/article/S0002-8703(10)00758-1/abstract).
- [50] Swan PY, Nighswonger B, Boswell GL, Stratton SJ. Factors Associated With False-Positive Emergency Medical Services Triage for Percutaneous Coronary Intervention. *Western Journal of Emergency Medicine*. 2009 Nov;10(4):208–212. PMID: 20046233 PMCID: 2791717.
- [51] Smith SW. ST-elevation Acute Myocardial Infarction; A Critical but Difficult Electrocardiographic Diagnosis. *Academic Emergency Medicine*. 2001;8(4):382—385. Available from: <http://onlinelibrary.wiley.com/doi/10.1111/j.1553-2712.2001.tb02117.x/abstract>.
- [52] Nicholl J, West J, Goodacre S, Turner J. The relationship between distance to hospital and patient mortality in emergencies: an observational study. *Emergency Medicine Journal*. 2007;24(9):665 –668. Available from: <http://emj.bmjjournals.org/content/24/9/665.abstract>.

- [53] Khan SN, Murray P, McCormick L, Sharples LS, Salahshouri P, Scott J, et al. Paramedic-led prehospital thrombolysis is safe and effective: the East Anglian experience. *Emergency Medicine Journal*. 2009 Jun;26(6):452–455. Available from: <http://emj.bmjj.com/content/26/6/452>.
- [54] Pitt K. Prehospital selection of patients for thrombolysis by paramedics. *Emergency Medicine Journal*. 2002 May;19(3):260 –263. Available from: <http://emj.bmjj.com/content/19/3/260.abstract>.
- [55] Smith AM, Hardy PJ, Sandler DA, Cooke J. Paramedic decision making: prehospital thrombolysis and beyond. *Emergency Medicine Journal*. 2010;28(8):700–702.
- [56] Sayers A. Tips and tricks in performing a systematic review. *The British Journal of General Practice*. 2008 Feb;58(547):136. PMID: 18307870 PMCID: PMC2233974. Available from: <http://www.ncbi.nlm.nih.gov/pmc/articles/PMC2233974/>.
- [57] Critical Appraisal Skills Programme. Appraising the Evidence; 2013. Available from: <http://www.casp-uk.net/find-appraise-act/appraising-the-evidence/>.
- [58] Jensen JL, Cheung KW, Tallon JM, Travers AH. Comparison of tracheal intubation and alternative airway techniques performed in the prehospital setting by paramedics: a systematic review. *CJEM*. 2010;12(2):135—140. Available from: <http://www.cjem-online.ca/v12/n2/p135>.
- [59] The Cochrane Collaboration. Cochrane Handbook for Systematic Reviews of Interventions; 2011. Available from: <http://www.cochrane.org/training/cochrane-handbook>.
- [60] Goodacre S, Webster A, Morris F. Do computer generated ECG reports improve interpretation by accident and emergency senior house officers? *Postgraduate Medical Journal*. 2001 Jul;77(909):455 –457. Available from: <http://pmj.bmjj.com/content/77/909/455.abstract>.
- [61] Massel D. Observer variability in ECG interpretation for thrombolysis eligibility: experience and context matter. *Journal of Thrombosis and Thrombolysis*. 2003;15(3):131–40.

- [62] Tsai TL, Fridsma DB, Gatti G. Computer Decision Support as a Source of Interpretation Error: The Case of Electrocardiograms. *Journal of the American Medical Informatics Association*. 2003 Sep;10(5):478–483. Available from: <http://jamia.bmjjournals.org/content/10/5/478>.
- [63] Selker HP, Beshansky JR, Ruthazer R, Sheehan PR, Sayah AJ, Atkins JM, et al. Emergency medical service predictive instrument-aided diagnosis and treatment of acute coronary syndromes and ST-segment elevation myocardial infarction in the IMMEDIATE trial. *Prehospital Emergency Care*. 2011;15(2):139—148. Available from: <http://informahealthcare.com/doi/abs/10.3109/10903127.2010.545478>.
- [64] Nestler DM, White RD, Rihal CS, Myers LA, Bjerke CM, Lennon RJ, et al. Impact of Prehospital Electrocardiogram Protocol and Immediate Catheterization Team Activation for Patients With ST-Elevation–Myocardial Infarction. *Circulation: Cardiovascular Quality and Outcomes*. 2011;4(6):640—646. Available from: <http://circoutcomes.ahajournals.org/content/4/6/640.short>.
- [65] Selker HP, Beshansky JR, Griffith JL. Use of the electrocardiograph-based thrombolytic predictive instrument to assist thrombolytic and reperfusion therapy for acute myocardial infarction. A multicenter, randomized, controlled, clinical effectiveness trial. *Annals of Internal Medicine*. 2002 Jul;137(2):87–95. PMID: 12118963.
- [66] Selker HP, Beshansky JR, Sheehan PR, Massaro JM, Griffith JL, D'Agostino RB, et al. Out-of-hospital administration of intravenous glucose-insulin-potassium in patients with suspected acute coronary syndromes: the IMMEDIATE randomized controlled trial. *Journal of the American Medical Association*. 2012 May;307(18):1925–1933. PMID: 22452807.
- [67] Schulz KF, Altman DG, Moher D, Group C. CONSORT 2010 Statement: updated guidelines for reporting parallel group randomised trials. *BMC Medicine*. 2010;8(1):18. Available from: <http://www.biomedcentral.com/1741-7015/8/18>.

- [68] Lijmer JG. Empirical Evidence of Design-Related Bias in Studies of Diagnostic Tests. *Journal of the American Medical Association*. 1999 Sep;282(11):1061. Available from: <http://jama.jamanetwork.com/article.aspx?doi=10.1001/jama.282.11.1061>.
- [69] Whiting P, Rutjes AW, Reitsma JB, Glas AS, Bossuyt PM, Kleijnen J. Sources of Variation and Bias in Studies of Diagnostic AccuracyA Systematic Review. *Annals of Internal Medicine*. 2004;140(3):189—202. Available from: <http://annals.org/article.aspx?articleid=717161>.
- [70] Bland JM, Kerry SM. Statistics notes. Trials randomised in clusters. *British Medical Journal*. 1997;315(7108):600.
- [71] Arain M, Campbell MJ, Cooper CL, Lancaster GA. What is a pilot or feasibility study? A review of current practice and editorial policy. *BMC Medical Research Methodology*. 2010;10(1):67. Available from: <http://www.biomedcentral.com/1471-2288/10/67>.
- [72] Health and Care Professions Council. Standards of conduct, performance and ethics; 2008. Available from: <http://www.hpc-uk.org/aboutregistration/standards/standardsofconductperformanceandethics/>.
- [73] NHS Research Ethics Service. Does my project require review by a Research Ethics Committee?; 2012. Available from: <http://www.nres.nhs.uk/EasySiteWeb/GatewayLink.aspx?alId=134016>.
- [74] Fielding NG, Lee RM, Blank G. *The Handbook of Online Research Methods*. London: Sage Publications Ltd; 2008.
- [75] Sedgwick P. Block randomisation. *BMJ*. 2011 Nov;343(nov09 2):d7139–d7139. Available from: <http://www.bmjjournals.com/content/343/bmj.d7139>.
- [76] Torgerson DJ. Designing randomised trials in health, education and the social sciences: an introduction. Basingstoke [England]; New York: Palgrave Macmillan; 2008.
- [77] Ho WK, Matthews JN, Henderson R, Farewell D, Rodgers LR. Dropouts in the AB/BA crossover design. *Statistics in Medicine*. 2012 Jul;31(16):1675–1687. Available from: <http://doi.wiley.com/10.1002/sim.4497>.

- [78] Baraldi AN, Enders CK. An introduction to modern missing data analyses. *Journal of School Psychology*. 2010 Feb;48(1):5–37. Available from: <http://linkinghub.elsevier.com/retrieve/pii/S0022440509000661>.
- [79] Campbell MK, Piaggio G, Elbourne DR, Altman DG, for the CONSORT Group. Consort 2010 statement: extension to cluster randomised trials. *BMJ*. 2012 Sep;345(sep04 1):e5661–e5661. Available from: <http://www.bmjjournals.org/cgi/doi/10.1136/bmj.e5661>.
- [80] Petrie A, Sabin C. *Medical Statistics at a Glance*. Oxford: Wiley-Blackwell; 2000.
- [81] Kirkwood BR. *Essential medical statistics*. 2nd ed. Malden, Mass: Blackwell Science; 2003.
- [82] Campbell MJ, Machin D, Walters SJ. *Medical Statistics: A Textbook for the Health Sciences*. 4th ed. Chichester: Wiley-Blackwell; 2007.
- [83] Goldstein H, Browne W, Rasbash J. Multilevel modelling of medical data. *Statistics in Medicine*. 2002;21(21):3291—3315. Available from: <http://onlinelibrary.wiley.com/doi/10.1002/sim.1264/full>.
- [84] Clements MA, Bolt D, Hoyt W, Kratochwill TR. Using multilevel modeling to examine the effects of multitiered interventions. *Psychology in the Schools*. 2007 May;44(5):503–513. Available from: <http://doi.wiley.com/10.1002/pits.20242>.
- [85] Leckie G. Cross-Classified Multilevel Models. Centre for Multilevel Modelling; 2013. Available from: <http://www.bristol.ac.uk/cmm/learning/course.html>.
- [86] Browne WJ, Goldstein H, Rasbash J. Multiple membership multiple classification (MMMC) models. *Statistical Modelling*. 2001;1(2):103—124. Available from: <http://smj.sagepub.com/content/1/2/103.short>.
- [87] Eldridge SM, Ukoumunne OC, Carlin JB. The Intra-Cluster Correlation Coefficient in Cluster Randomized Trials: A Review of Definitions. *International Statistical Review*. 2009 Dec;77(3):378–394. Available from: <http://doi.wiley.com/10.1111/j.1751-5823.2009.00092.x>.
- [88] Yelland LN, Salter AB, Ryan P, Laurence CO. Adjusted intraclass correlation coefficients for binary data: methods and estimates from a cluster-randomized

- trial in primary care. *Clinical Trials*. 2011 Feb;8(1):48–58. Available from: <http://ctj.sagepub.com/cgi/doi/10.1177/1740774510392256>.
- [89] Watson JM, Torgerson DJ. Increasing recruitment to randomised trials: a review of randomised controlled trials. *BMC Medical Research Methodology*. 2006 Jul;6(1):34. Available from: <http://www.biomedcentral.com/1471-2288/6/34>.
- [90] Ross JS, Lehman R, Gross CP. The Importance of Clinical Trial Data Sharing Toward More Open Science. *Circulation: Cardiovascular Quality and Outcomes*. 2012 Mar;5(2):238–240. PMID: 22438465. Available from: <http://circoutcomes.ahajournals.org/content/5/2/238>.
- [91] Lord SJ, Gebski VJ, Keech AC. Multiple analyses in clinical trials: sound science or data dredging? *Medical Journal of Australia*. 2004;181:452—454. Available from: [https://www.mja.com.au/system/files/issues/181\\_08\\_181004/lor10602\\_fm.pdf](https://www.mja.com.au/system/files/issues/181_08_181004/lor10602_fm.pdf).
- [92] Browne WJ, Draper D. A comparison of Bayesian and likelihood-based methods for fitting multilevel models. *Bayesian Analysis*. 2006;1(3):473—514. Available from: <http://projecteuclid.org/euclid.ba/1340371047>.
- [93] Mills E, Chan AW, Wu P, Vail A, Guyatt G, Altman D. Design, analysis, and presentation of crossover trials. *Trials*. 2009 Apr;10(1):27. Available from: <http://www.trialsjournal.com/content/10/1/27/abstract>.
- [94] Sibbald B, Roberts C. Understanding controlled trials: Crossover trials. *British Medical Journal*. 1998 Jun;316(7146):1719–1720. Available from: <http://www.bmjjournals.org/content/316/7146/1719>.
- [95] McCann K, Holdgate A, Mahammad R, Waddington A. Accuracy of ECG electrode placement by emergency department clinicians. *Emergency Medicine Australasia*. 2007;19(5):442—448. Available from: <http://onlinelibrary.wiley.com/doi/10.1111/j.1742-6723.2007.01004.x/abstract>.
- [96] Rajaganeshan R, Ludlam CL, Francis DP, Parasramka SV, Sutton R. Accuracy in ECG lead placement among technicians, nurses, general physicians and cardiologists. *International Journal of Clinical Practice*. 2008;62(1):65—70. Available from: <http://onlinelibrary.wiley.com/doi/10.1111/j.1742-1241.2007.01390..x/full>.

- [97] Williams B, Boyle M, Lord B. Paramedic identification of electrocardiograph J-point and ST-segments. *Prehospital and Disaster Medicine: The Official Journal of the National Association of EMS Physicians and the World Association for Emergency and Disaster Medicine in Association with the Acute Care Foundation.* 2008 Dec;23(6):526–529. PMID: 19557969. Available from: <http://www.ncbi.nlm.nih.gov/pubmed/19557969>.
- [98] Hebel GA, Hutton K, Kanowitz A, Neuman T, Martinson L, Rosen P. The accuracy of ST segment deviation in prehospital cardiac monitoring. *The Journal of Emergency Medicine.* 1994 Mar;12(2):207–211. Available from: <http://www.sciencedirect.com/science/article/pii/0736467994907005>.
- [99] Trivedi K, Schuur J, Cone D. Can paramedics read ST-segment elevation myocardial infarction on prehospital 12-lead electrocardiograms? *Prehospital Emergency Care.* 2009 Jun;13(2):207–214.
- [100] Le May MR, So DY, Dionne R, Glover CA, Froeschl MPV, Wells GA, et al. A citywide protocol for primary PCI in ST-segment elevation myocardial infarction. *New England Journal of Medicine.* 2008;358(3):231—240. Available from: <http://www.nejm.org/doi/full/10.1056/NEJMoa073102>.
- [101] Mencl F, Wilber S, Frey J, Zalewski J, Maiers JF, Bhalla MC. Paramedic Ability to Recognize ST-segment Elevation Myocardial Infarction on Prehospital Electrocardiograms. *Prehospital Emergency Care.* 2013 Feb;p. 130212134656006. Available from: <http://informahealthcare.com/doi/abs/10.3109/10903127.2012.755585>.