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A benchmark study of the frequency and variability of haemolysis reporting across pathology laboratories

THE IMPLICATIONS FOR QUALITY USE OF PATHOLOGY AND SAFE AND EFFECTIVE PATIENT CARE

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CHSSR Overview

The Centre for Health Systems and Safety Research (CHSSR) conducts innovative research aimed at understanding and improving the way in which health care delivery and patient outcomes are enhanced through the effective use and exchange of information. It is one of three research centres that form the Australian Institute of Health Innovation (AIHI) at Macquarie University.

Mission

The Centre's mission is to lead in the design and execution of innovative health systems research focused on patient safety and the evaluation of information and communication technologies in the health sector, to produce a world-class evidence base which informs policy and practice.

Aims

The Centre's research is underpinned by a systems perspective, exploiting highly innovative and wide-ranging research methods. Its research team is characterised by its talent and enthusiasm for working within and across discipline areas and sectors. The Centre has a focus on translational research, aimed at turning research evidence into policy and practice, while also making fundamental contributions to international knowledge.

The Centre's research program has four central aims:

- Produce research evidence of the impact of information and communication technologies (ICT) on the efficiency and effectiveness of health care delivery, on health professionals' work and on patient outcomes
- Develop and test rigorous and innovative tools and approaches for health informatics evaluation
- Design and apply innovative approaches to understand the complex nature of health care delivery systems and make assessments of health care safety
- Disseminate evidence to inform policy, system design, practice change and the integration and safe and effective use of ICT in healthcare

Preamble

This report is the product of the Centre of Health Systems and Safety Research (CHSSR) funded by the Royal College of Pathologists Australasia Quality Assurance Program (RCPAQAP).

The contract was signed when CHSSR was part of the Faculty of Medicine at UNSW Australia (The University of New South Wales) and much of the work reported herein was conducted by CHSSR within UNSW Australia.

CHSSR was affiliated with the Faculty of Medicine and Health Sciences at Macquarie University starting on 3rd November 2014 and the report content was finalised by CHSSR within Macquarie University.

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Table of Contents

CHSSR Overview i
Preamble ii
EXECUTIVE SUMMARY 1
Project aim 1
Project setting 1
Literature Review 2
Key findings 2
GLOSSARY 4
CONTEXT AND INTRODUCTION 6
Project aim 6
EVIDENCE SCAN ON THE RATES OF HAEMOLYSIS IN LABORATORY TESTING 8
Aim 8
Search Strategy 8
Results 9
Recommendations 29
METHODS 31
Study Setting 31
Ethics approval 31
Data Sources 31
Data Analysis and Statistical Methods 32
Outcome Measures 32
STAGE 1: HAEMOLYSIS RATES ACROSS AUSTRALIAN LABORATORIES (KIMMS PROJECT) 33
Introduction 33
Methods 33
SECTION 1.1: CHARACTERISTICS OF KIMMS PROJECT PARTICIPANTS 35
Laboratory practice characteristics 35
Haemolysis detection location and methods 36
Reporting practices 36
SECTION 1.2: PREVALENCE AND VARIATION OF SPECIMENS REJECTED DUE TO HAEMOLYSIS IN KIMMS PARTICIPANT LABORATORIES 38
STAGE 2: DETAILED ANALYSIS OF HAEMOLYSIS RATES AT FIVE METROPOLITAN HOSPITALS IN SYDNEY 40
Introduction 40
Methods 40
Definitions 43
Data Extraction 44
Data Linkage 44
SECTION 2.1: IMPACT OF CHANGING THE DENOMINATOR IN REPORTED HAEMOLYSIS RATES 45
Introduction 45
Methods 45

Results 45
SECTION 2.2: ASSESSING OVERALL HAEMOLYSIS RATES 47
Introduction 47
Methods 47
Results 47
SECTION 2.3: ASSESSING HAEMOLYSIS FOR HOSPITAL INPATIENTS 53
Introduction 53
Methods 53
Results 53
SECTION 2.4: ASSESSING HAEMOLYSIS FOR ED PATIENTS 56
Introduction 56
Methods 56
Results 56
SECTION 2.5: HOLISTIC EXAMINATION OF HAEMOLYSIS AT EDs AND IN HOSPITALS 59
Aims 59
Study population and haemolysis 59
SECTION 2.6: IMPACT OF HAEMOLYSIS ON REPEAT TEST ORDERS 67
Definitions 67
Potassium tests 67
Troponin tests 71
SECTION 2.7: IMPACT OF HAEMOLYSIS ON EMERGENCY DEPARTMENT LENGTH OF STAY 76
ED LOS 76
Modelling 79
SECTION 2.8: RISK FACTORS ASSOCIATED WITH HAEMOLYSIS IN HOSPITALS 80
Baseline characteristics 80
Modelling 81
STAGE 3: HAEMOLYSIS: DETECTION AND REPORTING PRACTICES ACROSS THE PATHOLOGY SERVICE 83
Introduction 83
Methods 83
Results 84
DISCUSSION AND IMPLICATIONS 87
Limitations 88
Conclusion 89
APPENDIX A: STRUCTURED INTERVIEW FOR HAEMOLYSIS PRACTICES 91
REFERENCES 94

EXECUTIVE SUMMARY

Haemolysis refers to the breakdown of Red Blood Cells (RBCs; also referred to as erythrocytes) and the release of haemoglobin into the surrounding fluid. Haemolysis is one of the most common causes of preanalytical errors which can affect the integrity of the specimen and the reliability of results, and hence has a major bearing on the quality and efficiency of the laboratory process.

Haemolysed specimens occur frequently in laboratory practice and prevalence can be up to 12.5% of all routine specimens and up to 70% of all specimens deemed to be unsuitable. Existing evidence suggests that the incidence of haemolysis is increasing. This increase is related to multiple factors including blood collection and transportation practices associated with specific clinical settings, e.g. the Emergency Departments (EDs).

Benchmark data about the prevalence and variation of haemolysis across laboratories can make a valuable contribution to the development of safe practices to reduce haemolysis and potential errors in laboratory results. This can aid the effectiveness of laboratory services and their contribution to safe and quality patient care.

PROJECT AIM

This study aims to:

- Compare the reported frequency and prevalence, risk and detection variability for haemolysed specimens using Key Incident Monitoring & Management Systems (KIMMS) data sources from contributing biochemistry laboratory data sources (nationally); and the data from a single pathology provider servicing hospitals in metropolitan Sydney and regional NSW.
- Measure the levels of haemolysed specimens involving Troponin from EDs and the number of tests not reported using linkage of hospital data sources and pathology service data, and to examine the impact on test request repeats, and consequent variables affecting patient care (e.g. test rates per patient ED encounter and ED length of stay).
- Investigate the measures employed by the pathology service laboratories to identify variation and their impact on the quality and effectiveness of laboratory processes.

PROJECT SETTING

Stage 1 of the project was undertaken using data extracted from a Key Incident Monitoring & Management Systems (KIMMS) database that described the haemolysis rejection incidence rate at 68 participant groups of laboratories across Australia. Stage 2 of the project was undertaken in five hospitals belonging to a single Local Health District (LHD) in metropolitan Sydney. The five hospitals were serviced by a single pathology provider which provides comprehensive biomedical laboratory services including the following laboratory

specialties: Anatomical Pathology, Blood Bank, Chemical Pathology, Microbiology, Haematology, Molecular Genetics and Immunology. In addition to the LHD encompassing the five study hospitals, the pathology laboratory service also serviced four other LHDs and, in 2012, employed over 1000 staff. Stage 3 of the project was undertaken at the same five study hospitals as Stage 2, and at a selection of regional NSW laboratories belonging to the same pathology service.

LITERATURE REVIEW

An evidence scan was conducted across PUBMED, Embase, Medline and CINAHL databases to review previous audits and studies which have reported the frequency or proportion of specimens affected by in vitro haemolysis and how this rate differs between different clinical contexts (e.g. inpatient wards compared to Emergency Departments). The database searches and hand-searching of relevant articles resulted in a total of 56 articles meeting the inclusion criteria. The articles included in the evidence scan were published between 1965 and 2014. The majority of studies reported haemolysis rates between 1% and 20% of specimens. Many studies reported that haemolysis accounted for the largest proportion of preanalytical errors; up to 91% of all preanalytical errors. Six studies (out of 15) which reported the haemolysis rate as a proportion of preanalytical errors noted that haemolysed specimen errors accounted for more than 50% of the preanalytical errors recorded. Forty-four studies compared the rates of haemolysis between different clinical contexts.

KEY FINDINGS

- The analysis of Australia-wide KIMMS data describing the rate of haemolysis rejections revealed that there was variation in how laboratories assigned accessions and counted haemolysis rejections. The group of laboratories accounting for the majority of participants and accessions (laboratories which assigned accessions by episode, and counted haemolysis rejections by specimen) reported a mean haemolysis rejection rate of 0.18% of accessions. The second largest group of participants (accessions assigned by episode, haemolysis rejections counted by episode) reported a mean haemolysis rejection rate of 0.25% of accessions.
- In the analysis of detailed pathology data from five study hospitals in Sydney, the overall haemolysis rate was 1.70% of accessions when considering all accessions (in the Biochemistry and Haematology laboratories only). The overall rate was 2.47% when considering only biochemistry specimens that had been assessed for haemolysis, and the rate was 6.37% when considering only biochemistry specimens that had been assessed for haemolysis and that had had a Potassium test ordered and that had been received from the ED.
- When using the scope of all biochemistry specimens that had been assessed for haemolysis, the overall rate of haemolysed specimens was approximately three times higher for clinical staff (2.33%) than it was

for laboratory phlebotomists (0.79%).

- Patients who were triaged in the most urgent triage category (Triage 1) had the highest rate of haemolysed specimens at a rate of 8.28% across all EDs. There was little difference between the overall rate of haemolysed specimens for the other triage categories which ranged between 5.78% for Triage 5 to 6.27% for Triage 4 presentations.
- In the EDs, 2,962 repeat Potassium tests (39.7%) occurred after the preceding Potassium test was haemolysed, and in these cases there was a median interval of 2.2 hours between the previous test and the repeat Potassium test. This was a significantly shorter time than when the previous Potassium test was not haemolysed (median interval of 6.3 hours).
- In the EDs, 1,296 repeat Troponin tests (10.8%) occurred after the preceding Troponin test was haemolysed, and in these cases there was a median interval of 2.5 hours between the previous test and the repeat Troponin test. This was a significantly shorter time than when the previous Troponin test was not haemolysed (median interval of 5.1 hours).
- After adjusting for all the baseline characteristics, we estimated the ED LOS for patients was, on average, 18 minutes longer for patients who experienced one or more haemolysed specimens, than for those who did not.
- The outcome of this project was to produce a detailed analysis of the prevalence and variation of haemolysis at an international level by performing an evidence scan and reporting the incidence rates found in the existing literature, then conducting analyses of the haemolysis rejection rates at a broad national scale using the KIMMS dataset, and finally, at a more specific level, assessing the rate of haemolysis according to clinical and patient characteristics, within five study hospitals, and the impact that haemolysis had on patient outcomes such as ED LOS.

GLOSSARY

Glossary of general terms	
95% CIs	95% Confidence Intervals
Abbott Architect	Biochemistry analyser by Abbott Diagnostics
AMI	Acute Myocardial Infarction
AMS Omnilab	Analyzer Management System middleware system
AS ISO 15189-2013	Australian Standard International Organization for Standardization: Medical laboratories - Requirements for quality and competence
AUSLAB	A Laboratory Information System by PJA Solutions
Cat	Catastrophic
CC	Complication or Comorbidity
Collector: Clinical Staff	Doctor, nurse or other ward staff that conducts the blood draw
Collector: Laboratory phlebotomist	A laboratory service employee that conducts the blood draw
CSV	Comma-separated Values file
DRG	Diagnosis-Related Groups
ED	Emergency Department
Emergency Patient	Patient presenting at and triaged within an Emergency Department
Hemolysis	U.S. English spelling of haemolysis
HI index	Haemolysis Index
Inpatient	Patients admitted as a hospital inpatient
In vitro haemolysis	Haemolysis that occurs outside the body as a consequence methods used for drawing, storing, and transporting the blood specimen
In vivo haemolysis	Haemolysis that occurs inside the body as a consequence of illness or disease (also known as intravascular haemolysis)
IQR	Interquartile Range
IV	Intravenous
KIMMS	Key Incident Monitoring & Management Systems
LIS	Laboratory Information System
Other Patient	Outpatient, referred patients, and other non-admitted patients
PAS	Patient Administration System
Proc(s)	Procedure(s)
RCPA	Royal College of Pathologists Australasia
RCPAQAP	Royal College of Pathologists Australasia Quality Assurance Program
Previous test	The test of the same type immediately preceding the repeat test for the same patient during the same hospital admission or ED presentation
Repeat test	A test ordered that is the same as a previous test for the same patient during the same hospital admission or ED presentation
SEM	Standard Error of the Mean
Sev	Severe
W/	With
W/O	Without

Glossary of pathology tests	
AST	Aspartate Aminotransferase
BMP	Basic Metabolic Panel
CMP	Comprehensive Metabolic Panel
Electrolytes	Electrolytes panel to identify electrolytes or acid-base imbalance
Troponin	Cardiac Troponin

Glossary of draw method, equipment, and site terms	
Antecubital fossa	A small triangular indented area of the forearm, just below the elbow, enabling access to several veins and commonly used for drawing blood.
Aspiration	The generation of suction to draw blood out of vein or artery
Basilic vein	Vein which extends down the length of the inner arm. Referred to as the 'median basilic vein' at the elbow area
BD Vacutainer™	A sealed collection tube evacuated to create a vacuum inside, to enable easier blood collection (a type of evacuated tube system)
BD Venflon™	An IV catheter device with an inbuilt safety shield
Butterfly needle	A short needle attached to a tube, with two 'wings' on either side for ease of use and handling
BD Interlink® device	Device with two cannulas, a cap and a shield. It simplifies the process of syringe filling and serum access
Cephalic vein	Vein which extends down the length of the outer arm, and forms one side of the antecubital fossa. Referred to as the 'median cephalic vein' at the elbow area
Evacuated tube system	A sealed collection tube evacuated to create a vacuum inside, to enable easier blood collection (e.g. BD Vacutainer™ and Greiner Bio-One Vacuette™)
Greiner Bio-One Vacuette™	A sealed collection tube evacuated to create a vacuum inside, to enable easier blood collection (a type of evacuated tube system)
Intravenous access	The puncturing of a vein for a blood draw
IV catheter	A tube placed intravenously to administer medication or fluids or take a blood specimen
Metacarpal plexus	The veins of the back of the hand
Phlebotomy	Blood draw
Resistance	Used here to mean difficulty establishing blood flow during phlebotomy
Venepuncture	The puncture of a vein to conduct a blood draw (also written as venipuncture or venopuncture)

CONTEXT AND INTRODUCTION

Haemolysis refers to the breakdown of Red Blood Cells (RBCs also known as erythrocytes) and the release of haemoglobin into the surrounding fluid.[1] Haemolysis is one of the most common causes of preanalytical errors which can affect the integrity of the specimen and the reliability of laboratory results,[2,3] and hence has a major bearing on the quality and efficiency of the laboratory process.[4] The issue of haemolysis involves important factors related to compliance with standards and best-practice protocols. The presence of haemolysed specimens has major implications for the quality and safety of patient care[5,6] and constitutes an area of major importance for pathology laboratories in Australia and internationally.[2]

Haemolysed specimens occur frequently in the laboratory practice and prevalence can be up to 12.5% of all routine specimens and up to 70% of all unsuitable specimens.[2] Existing evidence suggests that the incidence of haemolysis is increasing. This increase is related to multiple factors including blood collection and transportation practices associated with specific clinical settings, e.g. the ED.

The adoption of suitable responses to deal with the issue is complicated by lack of harmonisation in the reporting and measurement of haemolysis.[2] There is also a wide variation (across different pathology laboratories, governance areas, and countries) about the reporting of haemolysis. In the past, the identification of haemolysed specimens relied on visual inspection often on an arbitrary basis.[7] This practice is strongly discouraged today because of the unreliability and variability in results,[3,7,8] instead using the HI index from the analyser is now considered best practice.[7,9,10]

In 2012, Lippi and colleagues produced a book "In Vitro and In Vivo Hemolysis - An Unresolved Dispute in Laboratory Medicine" which provided a detailed description and analysis of various clinical and contextual factors associated with haemolysis, its underlying causal mechanisms, and recommendations to improve harmonisation in laboratory practices.[10]

Benchmark data about the prevalence and variation of haemolysis across laboratories can make a valuable contribution to the development of harmonised, safe and quality practices to reduce haemolysis and potential errors in laboratory results. This can contribute to an enhancement in the effectiveness of laboratory services and their contribution to safe and quality patient care.[2]

PROJECT AIM

This study aims to:

- Compare the reported frequency and prevalence, risk and detection variability for haemolysed specimens using Key Incident Monitoring & Management Systems (KIMMS) data sources from contributing chemical chemistry data sources (nationally); and the data from a single pathology provider servicing hospitals in metropolitan Sydney and regional NSW.

- Measure the levels of haemolysed specimens involving Troponin from EDs and the number of tests not reported using linkage of hospital data sources for Pathology Service data, and to examine the impact on test request repeats, and consequent variables affecting patient care (e.g. test rates per patient ED encounter and ED length of stay).
- Investigate the measures employed by pathology service laboratories to identify variation and their impact on the quality and effectiveness of laboratory processes.

EVIDENCE SCAN ON THE RATES OF HAEMOLYSIS IN LABORATORY TESTING

AIM

The aim of this section is to report on an evidence scan of previous audits and studies which have investigated the frequency or proportion of specimens affected by in vitro haemolysis and existing comparisons of the rate of haemolysed specimens in different clinical contexts (e.g. inpatient wards compared to EDs).

SEARCH STRATEGY

Our search criteria imposed no age limit on articles, allowing us to gather all relevant papers to understand the temporal variation in the interest in haemolysis rates. Likewise, we did not limit our search to certain countries, but we did require that, at a minimum, the study abstract was available in English. We required the texts to report on primary data, and specify an overall rate of haemolysis (or the information needed to calculate such a rate). We considered articles that focused on preanalytical errors, rejected specimens or in vitro haemolysis, and which examined blood drawing or testing or laboratory practices. The search criteria are summarised in Table 1.

Search terms included different combinations of "haemolysis / hemolysis," "pre-analytical / preanalytical error/s," "rate / frequency/ prevalence," "error/s," "retrospective analysis / audit," "rejection rate," "haemolysed / haemolyzed / hemolysed / hemolyzed," "blood specimen collection," and "blood sample collection."

Literature searches of PUBMED, Embase, Medline and CINAHL databases were conducted. Potentially relevant texts were identified by their titles. The abstracts of the collected texts were then scrutinised and non-relevant titles were excluded. Bibliographies of the selected papers were also hand-searched for relevant articles. Finally, a review of the full text of each article was conducted and each study was described according to the following factors: the year the study was conducted; country and continent of the study; overall rate of haemolysis as a proportion of accessions, and rate of haemolysis as a proportion of preanalytical errors; comparison rates of haemolysis (e.g. between different patient groups such as inpatients and ED patients); any recommendations made by authors for strategies to reduce the incidence of haemolysis.

Table 1. Inclusion criteria for the evidence scan.
Inclusion Criteria
English language abstract available
Specified an overall rate of haemolysis, or the information required to calculate a rate
Reported primary data
Focused on in vitro haemolysis, preanalytical errors or rejected specimens
Focused on blood drawing or testing or laboratory practices

RESULTS

The database searches and hand-searching of relevant articles resulted in a total of 56 articles meeting the inclusion criteria. The articles included in the evidence scan were published between 1965 and 2014. While the majority of these studies have been published since 2006, 13 were published prior to 2006[5,11-22] (six were 2000 and prior) [12,16,18-21]. There were almost as many studies published in 2014 as there were during the previous four years combined (2010-2013), possibly reflecting a growing interest in haemolysis research and its relevance to harmonising and improving pathology services. Table 2 shows the articles categorised by publication year.

Table 2: Studies in the evidence scan classified by year published.

Year	No. of Studies	Study Authors		
Pre-2006	13	Bonini *et al.*[5] Burns and Yoshikawa[11] Carraro *et al.*[12] Cox *et al.*[13] Dugan *et al.*[14]	Fernandes *et al.*[15] Fernandes *et al.*[21] Glick *et al.*[16] Grant[17] Jones *et al.*[18]	Kennedy *et al.*[19] Michaëlsson and Sjölin[20] Tanabe et al.[22]
2006- 2009	16	Alsina *et al.*[23] Dwyer *et al.*[24] Ellis[25] Fang *et al.*[26] Lippi, Bassi *et al.*[27] Lowe *et al.*[28]	Ong *et al.*[29] Ong *et al.*[30] Pretlow *et al.*[31] Romero *et al.*[32] Salvagno *et al.*[33] Saleem *et al.*[34]	Shah *et al.*[35] Söderberg *et al.*[36] Sodi *et al.*[37] Stark *et al.*[38]
2010-2013	14	Ashakiran *et al.*[39] Berg *et al.*[40] Berger-Achituv et al.[41] Bhat *et al.*[42] Brunel *et al.*[43]	Carraro *et al.*[44] Chawla *et al.*[45] Dietrich[8] Goswami *et al.*[46] Munnix et al.[47]	Stauss *et al.*[48] Straszewski et al.[49] Upreti *et al.*[50] Wollowitz *et al.*[51]
2014	13	Ahmad *et al.*[52] Atay *et al.*[53] Bölenius *et al.*[54] Davidson[55] Fernandez *et al.*[56]	Giménez-Marin *et al.*[57] Grecu *et al.*[58] Kara *et al.*[59] Lippi, Bonelli, *et al.*[60] Lippi, Avanzini *et al.*[61]	Ortells-Abuye *et al.*[62] Sinici Lay *et al.*[63] Tóth *et al.*[64]

The majority of the research originated in Europe: seven studies from Italy,[5,12,27,33,44,60,61] five from Spain,[23,32,56,57,62] five from the UK,[25,34,37,40,55] three from Sweden,[20,36,54] and one study each from France,[43] Hungary,[64] Romania[58] and the Netherlands.[47] Eighteen studies were conducted in North America: sixteen in the USA[8,11,13,14,16-19,22,28,31,35,38,48,49,51] and two in Canada.[15,21] Thirteen studies occurred in Asia: six in India,[39,42,45,46,50,52] three in Turkey,[53,59,63] two in Singapore,[29,30] one in Israel[41] and one in Taiwan.[26] One study was conducted in Australia.[24] Table 3 shows the included articles, arranged by the continent and country of origin.

Table 3: Studies in the evidence scan classified by continent and country.

Continent (No. of Studies)	Country (No. of Studies)	Study Authors		
Asia (13)	India (6)	Ahmad *et al.*[52] Ashakiran *et al.*[39]	Bhat *et al.*[42] Chawla *et al.*[45]	Goswami *et al.*[46] Upreti *et al.*[50]
	Israel (1)	Berger-Achituv *et al.*[41]		
	Taiwan (1)	Fang *et al.*[26]		
	Turkey (3)	Atay *et al.*[53]	Kara *et al.*[59]	Sinici Lay *et al.*[63]
	Singapore (2)	Ong *et al.*[29]	Ong *et al.*[30]	
Australia (1)	Australia (1)	Dwyer *et al.*[24]		
North America (18)	Canada (2)	Fernandes *et al.*[15]	Fernandes, Walker *et al.*[21]	
	USA (16)	Burns *et al.*[11] Cox *et al.*[13] Dietrich[8] Dugan *et al.*[14] Glick *et al.*[16] Grant[17]	Jones *et al.*[18] Kennedy *et al.*[19] Lowe *et al.*[28] Pretlow *et al.*[31] Shah *et al.*[35] Stark *et al.*[38]	Stauss *et al.*[48] Straszewski *et al.*[49] Tanabe *et al.*[22] Wollowitz *et al.*[51]
Europe (24)	France (1)	Brunel *et al.*[43]		
	Hungary (1)	Tóth *et al.*[64]		
	Italy (7)	Bonini *et al.*[5] Carraro *et al.*[12] Carraro *et al.*[44]	Lippi, Bassi *et al.*[27] Lippi, Bonelli, *et al.*[60] Lippi, Avanzini, *et al.*[61]	Salvagno *et al.*[33]
	Romania (1)	Grecu *et al.*[58]		
	Spain (5)	Alsina *et al.*[23] Giménez-Marin *et al.*[57]	Fernandez *et al.*[56] Ortells-Abuye *et al.*[62]	Romero *et al.*[32]
	Sweden (3)	Bölenius *et al.*[54]	Söderberg *et al.*[36]	Michaëlsson and Sjölin[20]
	Netherlands (1)	Munnix *et al.*[47]		
	UK (5)	Berg *et al.*[40] Davidson[55]	Ellis[25] Saleem *et al.*[34]	Sodi *et al.*[37]

During the data extraction phase, we noticed similarities between the haemolysis rates reported in two studies (Ahmad *et al.*[52] and Söderberg *et al.*[36]). These two studies were conducted in different years and

countries, with different sized sample groups, yet they reported identical numbers for the overall haemolysis rate and for their comparisons of the haemolysis rates for male and female patients and older and younger patients.

OVERALL RATE OF HAEMOLYSIS

Table 4 shows all of the relevant articles found during the evidence scan, including the year and country that the study occurred in, the overall rate of haemolysis both as a proportion of accessions and as a proportion of preanalytical errors (when available), and concluding remarks or comments made about factors that may have led to higher rates of haemolysis or potential strategies for reducing haemolysis rates.

Thirty-three papers reported a rate between 1% and 20%.[5,11-16,19,21,22,24-26,28-34,36,37,40,43,47,49,51,52,54-57,61] A further sixteen studies reported a haemolysed specimen rate below 1%.[5,8,18,23,27,38,39,42,44-46,50,53,58,63,64] One study found no haemolysis among a population of 40 specimens.[41] Six studies reported haemolysis rates above 20%. The oldest paper, from 1965 reported a very high rate of haemolysed specimens (85.5%) coming from neonatal patients.[20] Kara *et al.* observed a rate of 59% of specimens being haemolysed;[59] Shah *et al.*,[35] Ortells-Abuye *et al.*,[62] Stauss *et al.*,[48] Lippi *et al.*[61] and Grant[17] found similar rates of 25.5%, 27.2%, 30.3%, 30%, and 32%, respectively.

RATE OF HAEMOLYSIS AS PROPORTION OF PREANALYTICAL ERRORS

An alternative method for assessing the incidence of haemolysis and its impact on the laboratory is to consider the proportion of preanalytical errors accounted for by haemolysed specimens. Seventeen studies reported a rate of haemolysis as a proportion of preanalytical errors.[5,18,23,27,32,33,38,39,42,44-46,50,53,58,63,64] Tóth *et al.* reported the highest rate, finding that 91% of rejected specimens were due to haemolysis.[64] On the other hand, Sinici Lay *et al.*[63] reported that haemolysed specimens accounted for only 1.3% of all rejected specimens (the lowest proportion of any study).

Table 4. Descriptions (including the authors, year of publication, title, country where the study took place, rate of haemolysed specimens and as a proportion of preanalytical errors, and concluding remarks) of the final selection of articles that met all the inclusion criteria.

Study Authors	Year	Title	Country	Rate of haemolysis as proportion of accessions	Rate of haemolysis as proportion of preanalytical errors	Concluding remarks or comments
Ahmad, Ramesh, Kumar[52]	2014	Preanalytical quality in clinical chemistry laboratory	India	11.38% (401/3,521)		Preanalytical conditions, collection and handling procedures and difficulty gaining venous access in the elderly were likely responsible for higher rates of haemolysis.
Atay, Demir, Cuhadar, Saglam, Unal, Aksun, Arslan, Ozkan, Sutcu[53]	2014	Clinical biochemistry laboratory rejection rates due to various types of preanalytical errors	Turkey	0.05% (542/1,035,743)	8% (542/6,775)	Phlebotomy specific education, continued education and training, evacuated tubes and prompt transport were recommended.
Davidson[55]	2014	A survey of some preanalytical errors identified from the Biochemistry Department of a Scottish hospital	UK	3.2% (24,585/763,577)		Recommended the use of trained phlebotomists, or training other staff to that level.
Fernandez, Llopis, Perich, Alsina, Alvarez, Biosca, Busquets, Domenech, Gómez, Llovet, Minchinela, Pastor, Luiz, Tarrés, Ibarz, Simón, Montesinos[56]	2014	Harmonization in hemolysis detection and prevention. A working group of the Catalonian Health Institute (ICS) experience	Spain	2.42% (1573/64,747)		Factors producing lower hemolysis rates are: centrifugation in the centre where the blood collection was carried out; transport time under 15 min; transport at room temp and lower tube volume. Therefore, a beneficial balance should be sought, between distance-time-cooling in the specimen transport for most tests.
Giménez-Marin, Rivas-Ruiz, del Mar Pérez-Hidalgo, Molina-Mendoza[57]	2014	Preanalytical errors management in the clinical laboratory: a five-year study	Spain	8.76% (65,827/751,441)		Recommended standardised procedures, including the use of plasma, not serum, and appropriate staff training.
Grecu, Vlad, Dumitrascu[58]	2014	Quality Indicators in the Preanalytical Phase of Testing in a Stat Laboratory	Romania	0.40% (676/168,728)	46.39% (676/1,457)	

Study Authors	Year	Title	Country	Rate of haemolysis as proportion of accessions	Rate of haemolysis as proportion of preanalytical errors	Concluding remarks or comments
Kara, Bayir, Ak, Degirmenci, Akinci, Agacayak, Marcil, Azap[59]	2014	Haemolysis associated with pneumatic tube system transport for blood samples	Turkey	59.8% (61/102)		Specimens transported by the pneumatic tube system had a markedly greater frequency of haemolysis than specimens transported manually.
Lippi, Avanzini, Aloe, Cervellin[61]	2014	Blood Collection From Intravenous Lines: Is One Drawing Site Better Than Others?	Italy	29.85% (20/67)		Blood specimens drawn from catheters placed distally from the median vein carried a higher risk of haemolysis.
Lippi, Bonelli, Graiani, Caleffi, Cervellin[60]	2014	Low volume tubes are not effective to reduce the rate of haemolysed specimens from the emergency department	Italy	4.35% (1,385/31,786)		These authors recommend that labs test specific effects, before changing local practices based on published literature.
Ortells-Abuye, Busquets-Puigdevall, Díaz-Bergara, Paguina-Marcos, Sánchez-Pérez[62]	2014	A cross-sectional study to compare two blood collection methods: direct venous puncture and peripheral venous catheters	Spain	27.2% (10/272)		Blood drawing methods using direct venous puncture and peripheral venous catheter or cannula can be used interchangeably for most routine lab tests.
Sinici Lay, Pınar, Akbıyık[63]	2014	Classification of reasons for rejection of biological specimens based on pre-preanalytical processes to identify quality indicators at a university hospital clinical laboratory in Turkey	Turkey	0.03% (325/971,780)	1.24% (325/26,070)	Concluded that the low rate of specimen haemolysis indicated the successful use of evacuated collection tubes.
Tóth, Lenkey, Oláh, Köteles, Kissné Sziráki, Kerényi, Kappelmayer[64]	2014	Pneumatic tube system for transport of laboratory samples: preanalytical aspects	Hungary	0.51% (1,365/267,857)	91% (1,365/1,500)	
Bölenius, Söderberg, Hultdin, Lindkvist, Bnrulin, Grankvist [54]	2013	Minor improvement of venous blood specimen collection ractices in primary health care after a large-scale educational intervention.	Sweden	11.12% (1420.73/12773)		Educational interventions may be effective in wards demonstrating large deviations from guidelines.

Study Authors	Year	Title	Country	Rate of haemolysis as proportion of accessions	Rate of haemolysis as proportion of preanalytical errors	Concluding remarks or comments
Dietrich[8]	2013	One Poke or Two: Can Intravenous Catheters Provide an Acceptable Blood Sample? A Data Set Presentation, Review of Previous Data Sets, and Discussion	USA	0.64% (58/8,944)		Haemolysis rates were below the 2% benchmark for both IV catheter and venepuncture draws. The authors made no recommendations.
Upreti, Upreti, Bansal, Jeelani, Bharat[50]	2013	Types and Frequency of Preanalytical Errors in Haematology Lab	India	0.09% (134/135,808)	10.00% (134/1,339)	Specimens not centrifuged in haematology labs may lead to falsely lower rates of haemolysed specimens. Phlebotomy practices may also influence haemolysis rates.
Wollowitz, Bijur, Esses, Gallagher[51]	2013	Use of Butterfly Needles to Draw Blood Is Independently Associated With Marked Reduction in Haemolysis Compared to Intravenous Catheter	USA	12.49% (564/4,513)		Higher haemolysis rates were reported for specimens drawn using IV catheters, than those obtained using butterfly needles.
Bhat, Tiwari, Chavan, Kelkar[42]	2012	Analysis of laboratory sample rejections in the preanalytical stage at an oncology centre	India	0.05% (19/32,548)	11.44% (19/166)	Directed interventions and training sessions could help reduce the number of specimen rejections.
Brunel, Larson, Peschanski, Cauliez[43]	2012	Evaluation of haemolysis in emergency department samples requesting high sensitivity troponin T measurement	France	10.92% (~273/~2,500)		Recommended that the Haemolysis Index (HI) be incorporated into troponin T (TnT) measurement procedures and that high-sensitivity TnT (hsTnT) results should be validated if the HI is above 220 (i.e. haemoglobin 0.25 g/L).
Carraro, Zago, Plebani[44]	2012	Exploring the Initial Steps of the Testing Process: Frequency and Nature of Pre-Preanalytical Errors	Italy	0.89% (143/15,917)	45.54% (143/314)	There is a need for agreed upon Standard Operating Procedures for all stages of the testing process and appropriate training for staff.

Study Authors	Year	Title	Country	Rate of haemolysis as proportion of accessions	Rate of haemolysis as proportion of preanalytical errors	Concluding remarks or comments
Stauss, Sherman, Pugh, Parone, Looby-Rodriguez, Bell, Reed[48]	2012	Haemolysis of Coagulation Specimens: A Comparative Study of Intravenous Draw Methods	USA	30.83% (37/120)		Observed higher haemolysis rates in blood specimens obtained from IV catheters without extension tubing. The authors recommend venepuncture. It is best not to rely on visual methods to detect haemolysis.
Ashakiran, Sumati, Murthy[39]	2011	A study of preanalytical variables in clinical biochemistry laboratory	India	0.28% (34/11,883)	19.20% (34/177)	General mechanisms to reduce preanalytical errors include appropriate staffing.
Berg, Ahee, Berg[40]	2011	Variation in phlebotomy techniques in emergency medicine and the incidence of haemolysed samples	UK	5.98% (94/1,570)		Deviation from standard practice, and the use of small diameter pink cannulas (20G) were associated with higher haemolysis rates.
Straszewski, Sanchez, McGillicuddy, Boyd, DuFresne, Joyce, Wolfe, Lee, Fisher, Mottley[49]	2011	Use of separate venipuncture for IV access and laboratory studies decreases hemolysis rates	USA	8.37% (241/2,879)		Separate venepuncture from a butterfly needle to obtain lab specimens decreases the rate of haemolysis and may assist in decreasing the overall ED LOS.
Berger-Achituv, Budde-Schwartzman, Ellis, Shenkman, Erez [41]	2010	Blood sampling through peripheral venous catheters is reliable for selected basic analytes in children	Israel	0% (0/40)		Drawing blood through a peripheral venous catheter is reliable, except for glucose measurements, and causes less discomfort.
Chawla, Goswami, Tayal, Mallika[45]	2010	Identification of the types of preanalytical errors in the clinical chemistry laboratory: 1-Year study at G.B. Pant Hospital	India	0.73% (712/96,328)	70.41% (607/862)	Recommended the implementation of a standardized protocol for blood collection in inpatient wards, as well as appropriate staff training.

Study Authors	Year	Title	Country	Rate of haemolysis as proportion of accessions	Rate of haemolysis as proportion of preanalytical errors	Concluding remarks or comments
Goswami, Singha, Chawla, Mallika[46]	2010	Evaluation of errors in a clinical laboratory: a one-year experience	India	0.75% (508/67,438)	69.02% (508/736)	Concluded that incorrect phlebotomy procedure, inappropriate specimen volume, collection in the wrong container, lack of knowledge, incorrect transport and centrifugation before clotting contributed to higher rates of haemolysed specimens.
Munnix, Schellart, Gorissen, Kleinveld[47]	2010	Factors reducing hemolysis rates at the emergency department	The Netherlands	16% (96/600)		Drawing blood through IV catheters was found to produce higher rates of haemolysed specimens.
Ellis[25]	2009	An episode of increased hemolysis due to a defective pneumatic air tube delivery system	UK	9.08% (2,032/22,363)		There was some benefit to bubble wrapping specimens before transporting them in the tube system. Labs should be vigilant to the possibility that tube systems can become defective after satisfactory installation and testing; the issue may not be picked up until it becomes a serious issue.
Ong, Chan, Lim[30]	2009	Reducing Blood Sample Hemolysis at a Tertiary Hospital Emergency Department	Singapore	12.76% (55/431)		These authors demonstrated the success of an education program for staff, and that syringes could reduce haemolysis of specimens.
Romero, Cobos, López-León, Ortega, Muñoz[32]	2009	Preanalytical mistakes in samples from primary care patients	Spain	2.67% (1,408/52,669)	36.24% (1,408/3,885)	Recommended education and training programs, involving all staff in efforts to reduce mistakes and continuous improvement, and the adoption of a safety focused culture to reduce the number of rejected specimens.
Saleem, Mani, Chadwick, Creanor, Ayling[34]	2009	A prospective study of causes of haemolysis during venepuncture: tourniquet time should be kept to a minimum	UK	6.51% (23/353)		Observed that tourniquet time of over a minute significantly increased the rate of haemolysis and recommended continuing education on this issue to reduce the risk.

Study Authors	Year	Title	Country	Rate of haemolysis as proportion of accessions	Rate of haemolysis as proportion of preanalytical errors	Concluding remarks or comments
Shah, Idrovo, Nicastro, McMullen, Molmenti, Coppa[35]	2009	A retrospective analysis of the incidence of haemolysis in type and screen specimens from trauma patients	USA	25.20% (155/615)		Suggested that improved blood collection practice for staff, improved handling and transportation procedures, and the assistance by more experienced staff in blood collection, could reduce haemolysis rates.
Söderberg, Brulin, Grankvist, Wallin[36]	2009	Haemolysis Index - an estimate of preanalytical quality in primary health care	Sweden	11.40% (1,084/9,504)		Concluded that higher haemolysis rates were likely due to varying preanalytical, collection and handling procedures, and use of the IV catheter to collect blood in the ED.
Alsina, Alvarez,Barba, Bullich, Cortés, Escoda, Martínez-Brú[23]	2008	Preanalytical quality control program - an overview of results (2001-2005 summary)	Spain	0.20% (9,563/4,715,132)	28.99% (9,563/32,977)	
Fang, Fang, Chung, Chien[26]	2008	Collecting factors related to the haemolysis of blood specimens	Taiwan	19.70% (54/274)		Suggested that standard protocols for blood collection, including drawing from antecubital sites, using syringes and delivery by laboratory staff, should be developed.
Lowe, Stike, Pollack, Bosley, O'Brien, Hake, Landis, Billings, Gordon, Manzella, Stover[28]	2008	Nursing Blood Specimen Collection Techniques and Haemolysis Rates in an Emergency Department: Analysis of Venipuncture Versus Intravenous Catheter Collection Techniques	USA	3.39% (29/853)		Blood specimens collected via venepuncture produced less haemolysis that blood specimens drawn from an IV catheter.
Ong, Chan, Lim[29]	2008	Observational Study to determine factors associated with blood sample haemolysis in the Emergency Department	Singapore	19.82% (45/227)		The authors recommend an educational program for staff and using a syringe, rather than evacuated tube systems.

Study Authors	Year	Title	Country	Rate of haemolysis as proportion of accessions	Rate of haemolysis as proportion of preanalytical errors	Concluding remarks or comments
Pretlow, Gandy, Leibach, Russell, Kraj[31]	2008	A Quality Improvement Cycle: Hemolyzed Specimens in the Emergency Department	USA	2.55% (264/10,324)		Concluded that blood collection techniques employed in the ED may be the cause of the higher rates of haemolysed specimens seen in this department.
Salvagno, Lippi, Bassi, Poli, Guidi[33]	2008	Prevalence and type of preanalytical problems for inpatients samples in coagulation laboratory	Italy	1.08% (706/65,283)	19.51% (706/3,617)	Recommended the implementation of a 'total quality system' incorporating a systematic error-tracking component, to gather information on local laboratory issues which require further attention.
Stark, Jones, Chapman, Well, Krajenta, Meier, Zarbo[38]	2007	Clinical laboratory specimen rejection – association with the site of patient care and patients' characteristics: findings from a single health care organization	USA	0.61% (8,414/1,364,117)	83.35% (8,414/10,094)	Concluded that a variety of factors, including blood collection procedures, multiple draws and higher complexity examinations were the cause of an increased number of specimen rejections.
Dwyer, Fry, Somerville, Holdgate[24]	2006	Randomized, single blinded control trial comparing haemolysis rate between two cannula aspiration techniques	Australia	6.83% (95/1,390)		Results indicated that draw difficulty may affect specimen haemolysis.
Lippi, Bassi, Brocco, Montagnana, Salvagno, Guidi[27]	2006	Pre-analytic Error Tracking in a Laboratory Medicine Department: Results of a 1-Year Experience	Italy	0.51% (2,166/423,075)		Recommended the introduction of systematic error tracking, enabling the identification of local issues and the development of appropriate interventions.
Sodi, Darn, Davison, Stott, Shenkin[37]	2006	Mechanism of interference by haemolysis in the cardiac troponin T immunoassay	UK	6.35% (781/12,287) (TnT specimens only)		Haemolysis, haemoglobin *per se*, and possibly proteolysis, play a role in the negative interference in cTnT assays. Measures to reduce this interference must be implemented.

Study Authors	Year	Title	Country	Rate of haemolysis as proportion of accessions	Rate of haemolysis as proportion of preanalytical errors	Concluding remarks or comments
Dugan, Leech, Speroni, Corriher[14]	2005	Factors Affecting Haemolysis Rates in Blood Samples Drawn From Newly Placed IV Sites in the Emergency Department	USA	12.82% (49/382)		Recommended that the use of 22G or smaller IV catheter be discontinued (straight needle stick is preferred), and that appropriate training and education be provided for staff, and regular competency testing be considered.
Cox, Dages, Jarjoura, Hazelett[13]	2004	Blood samples drawn from IV catheters have less hemolysis when 5-ml (vs 10-ml) collection tubes are used	USA	1.60% (296/18,439)		The authors recommend the use of 5-ml tubes rather than 10-ml tubes
Fernandes, Worster, Hill, McCallum, Eva[15]	2004	Root cause analysis of laboratory turnaround times for patients in the emergency department	Canada	4.76% (7/147)		The volume of tests, instrument time, queues and processing times caused the laboratory delays.
Grant[17]	2003	The Effect of Blood Drawing Techniques and Equipment on the Hemolysis of ED Laboratory Blood Samples	USA	31.71% (144/454)		Phlebotomists are encouraged to draw blood with a syringe through an IV catheter instead of evacuated tube systems and then transfer the blood to a tube via the special needleless connector.
Tanabe, Kyriacou, Garland[22]	2003	Factors affecting the risk of blood bank specimen hemolysis	USA	7.27%		Specimens drawn from Vialon IV angio-catheters (esp. 20G, 22G) and from veins outside the antecubital fossa are at an increased risk of haemolysing.
Bonini, Plebani, Ceriotti, Rubboli[5]	2002	Errors in Laboratory Medicine	Italy	0.18% (8,750/4,615,983)	53.69% (8,750/16,295)	Recommended more vigorous error detection and appropriate use of new technologies.
Burns, Yoshikawa[11]	2002	Haemolysis in Serum Samples Drawn by Emergency Department Personnel versus Laboratory Phlebotomists	USA	9.64% (388/4,021)		Recommended the implementation of a standardised protocol for blood collection and the use of newer spectrophotometers to replace visual detection of haemolysis.

Study Authors	Year	Title	Country	Rate of haemolysis as proportion of accessions	Rate of haemolysis as proportion of preanalytical errors	Concluding remarks or comments
Carraro, Servidio, Plebani[12]	2000	Hemolyzed Specimens: A Reason for Rejection or a Clinical Challenge?	Italy	1.83% (505/27,540)		These authors recommend a well-designed set of guidelines agreed upon by laboratory and ward staff; the use of evacuated tubes rather than syringes and immediate transmission of results.
Fernandes, Walker, Price, Marsden, Haley[21]	1997	Root cause analysis of laboratory delays to an emergency department	Canada	10.6% (20/188)		While nurses are quicker at drawing specimens, there is a higher rate of haemolysis among their specimens, compared with specimens drawn by lab assistants.
Jones, Calam, Howanitz[18]	1997	Chemistry specimen acceptability	USA	0.21% (22,531/10,709,701)	59.55% (22,531/37,833)	Suggested replacing visual inspection with spectrophotometry to detect haemolysis, and adopting educational efforts focused on collection techniques.
Kennedy, Angermuller, King, Noviello, Walker, Warden, Vang[19]	1996	A comparison of haemolysis rates using intravenous catheters versus venipuncture tubes for obtaining blood samples	USA	9.09% (15/165)		Haemolysis was more likely when specimens were obtained using an IV catheter, than when obtained using an evacuated tube system.
Glick, Ryder, Glick, Woods[16]	1989	Unreliable Visual Estimation of the Incidence and amount of Turbidity, Hemolysis and Icterus in Serum from Hospitalised Patients	USA	9.38% (244/2,599)		This study concluded that even when provided with a visual reference specimen, visual determination of haemolysis was inaccurate.
Michaëlsson, Sjölin[20]	1965	Haemolysis in Blood Samples from Newborn Infants	Sweden	85.51% (313/366)		The authors recommend that infant blood specimens be taken via venepuncture rather than skin-pricks, with heparinised glass tubes rather than test tubes, and that a silicone ointment be applied to the heel before the skin-prick is done.

COMPARISONS

Forty-four of the articles compared the rates of haemolysis between different groups. By making these comparisons the authors were able to isolate factors that may contribute to haemolysis rates. These comparisons included blood specimens drawn in different parts of the hospital or by different staff, from patients with different characteristics, different phlebotomy methods, or using different equipment. We divided these comparisons into four different groups, as shown in Figure 1:

Hospital / Laboratory department characteristics (H) describe the location within the hospital, such as hospital inpatients, outpatients, and the ED; whether the phlebotomy was conducted by laboratory staff or clinical staff; and the time of day or day of the week that the phlebotomy occurred.

Patient characteristics (Pa) describe patient demographics such as age and gender or the illness/discharge diagnosis the patient was classified with for that encounter.

Phlebotomy / draw method characteristics (Ph) describe the methods used for the phlebotomy including the draw site, any site preparation (e.g. tourniquet time), the degree to which the specimen tube was filled, whether any difficulty or complication was encountered during the phlebotomy, and how the specimen was transported.

Equipment characteristics (E) describe the draw equipment used for intravenous access (e.g. IV catheter compared to needle venepuncture) and aspiration (e.g. evacuated tube system compared to a syringe), the thickness of the needle or catheter, the size and type of the specimen tube and whether any extension tubing was used during the specimen collection.

However, many of these studies confounded different variables together, making it difficult to disentangle the relationships. One such example of this is the study by Dietrich, in which all blood draws with a new IV catheter were conducted by a member of the ED staff, all draws using existing IV catheter were conducted by critical care, medical or surgical nurses and all needle-and-syringe draws were conducted by laboratory technicians and phlebotomists.[8] It is impossible, therefore, to determine whether the differences in haemolysis rates were due to the staff member conducting the blood draw or the equipment used.

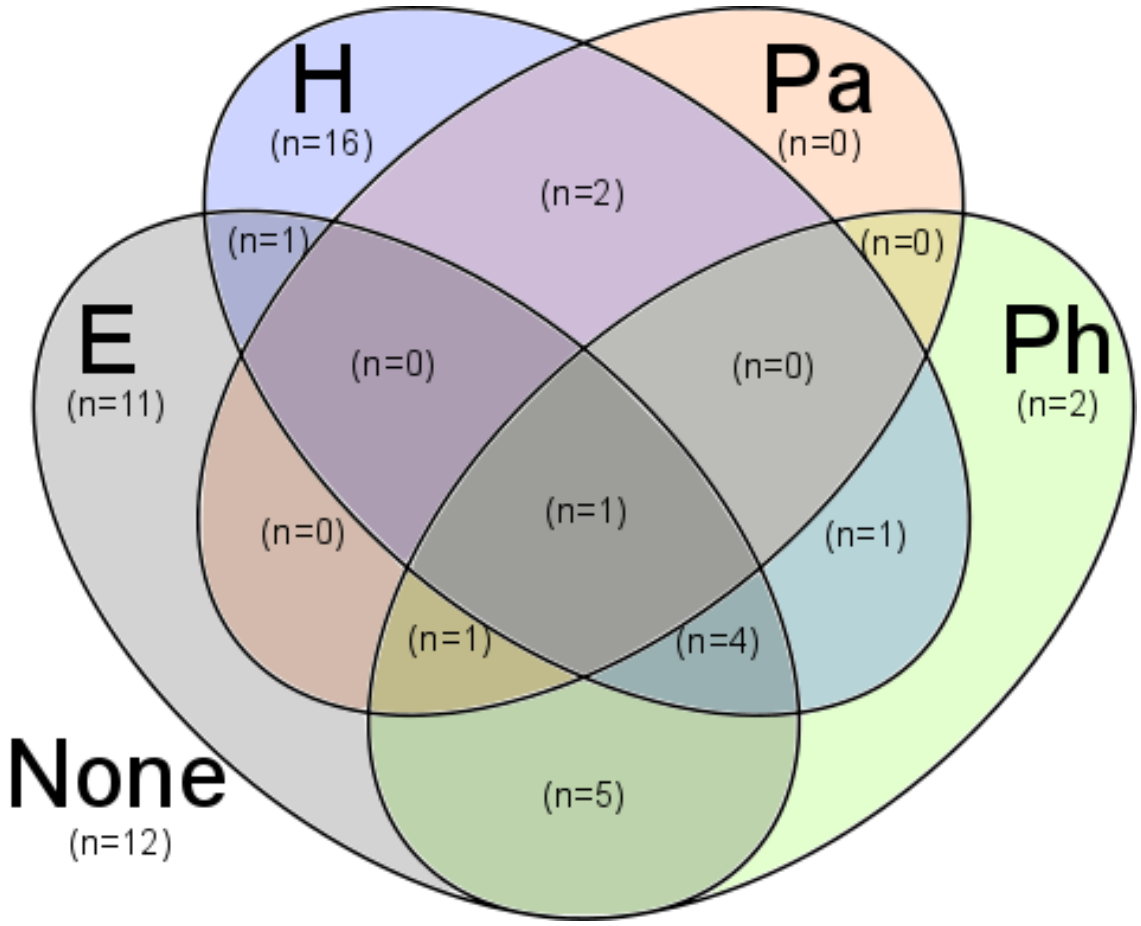

Figure 1. Venn chart showing the classification of all the "Articles included" according to the nature of the haemolysis rate comparisons that they reported (N=56). H = Hospital / Laboratory department characteristics, Pa = Patient characteristics, Ph = Phlebotomy / draw method characteristics, E = Equipment characteristics.

HOSPITAL / LABORATORY DEPARTMENT CHARACTERISTICS

LOCATION

Twelve studies considered haemolysis rates according to the patient's location, comparing the rates among inpatients, outpatients and ED patients.[5,11,12,25,27,31,33,36,38,40,45,50] One study also considered haemolysis rates in a local primary healthcare centre and nursing home.[36] The majority of studies observed the highest haemolysis among specimens from EDs.[11,31,33,38,40] Stark *et al.*[38] detected the lowest ED rate, of 1.8% and Söderberg *et al.*[36] found the highest ED rate, of 31.3%. In-patient rates were all below 3%; Upreti *et al.*[50] observed the lowest in-patient rate, of 0.1%, and Carraro *et al.*[12] detected a rate of 2.9%. Haemolysis rates among out-patients were the lowest of all, with all studies reporting rates of below 1%. Bonini *et al.*[5] identified an out-patient rate of 0.1% and Lippi, Bassi *et al.*[27] found a rate of 0.37%.

Among the studies that directly compared the haemolysis rates between inpatients and the ED, one observed haemolysis rates of 2.9% and 10.7%, respectively, with a 24% haemolysis rate in the 'Majors' section of their ED.[40] A second study compared the 'medical floor' with the ED and observed haemolysis rates of 1.6% and 12.4% respectively.[11] Another compared "other departments" with the ED and found rates of 0.7% and 18.1%,

respectively.[31]

Two studies made comparisons between multiple health care locations. One study compared the haemolysis rate at an ED (31.1%) with a nursing home (12.5%) and a local primary healthcare centre (10.4%).[36] And the other study compared the haemolysis rate in their ED (3.9%) with several hospital departments: the clinical department (0.14%), the ICU (0.85%), the surgical department (0.70%) and paediatric department (0.82%).[33]

COLLECTOR STAFF TYPE

Seven studies compared the haemolysis rates of different collector staff types.[14,18,29,30,34,52,55] Two of these studies simultaneously compared the staff type and the location within the hospital.[52,55] The first of these studies observed the following haemolysis rates: inpatient department sections staffed by emergency physicians (31.1%); inpatient department sections staffed by primary healthcare physicians (11.3%) and outpatient departments staffed by trained laboratory phlebotomists (10.4%).[52] The second study compared rates between EDs and outpatient departments at two hospitals. The haemolysis rates at the EDs (blood draws by clinical staff) were 11.2% and 9.4%, respectively, while both the outpatient departments (blood draws by laboratory phlebotomists) had a haemolysis rate of 1.6%.[55]

Two papers by Ong and colleagues both reported on the same study, in which they compared haemolysis rates from junior attending doctors/registrars (11.1%), residents/medical officers (16.1%), senior attending doctors/consultants (22.2%) and students/nurses (31.5%).[29,30]

Fernandes *et al.* observed a significant difference between haemolysis rates among specimens drawn by nurses and lab assistants. The rate among nurse drawn specimens was 20%, while for lab assistants the rate was 1%.[21] Saleem *et al.* also observed the highest haemolysis rates among specimens drawn by nurses, with their findings as follows: Allied health professionals including laboratory phlebotomists (3.6%), medical staff (9.8%) and nurses (14.1%).[34] Patient care technicians had higher rates of haemolysis (14.1%) than did registered nurses (11.7%).[14] One other study reported rates below 1% for all staff types: 0.1% for laboratory personnel, 0.4% for in-hospital non-laboratory phlebotomy personnel, and 0.6% for other in-hospital non-laboratory personnel (e.g. nurses) and the lowest haemolysis rate for out-of-hospital non-laboratory personnel (0.06%).[18]

DAY OF WEEK AND TIME OF DAY

Two research groups assessed the haemolysis rates on different days of the week or at different times of day. Higher rates of haemolysed specimens were found on weekends (7.3%) compared with weekdays (2.9%);[55] during the evening and night (12.4% and 19%, respectively) compared to the morning and afternoon (8.3% and 11.6%, respectively).[14]

PATIENT CHARACTERISTICS

PATIENT GENDER

All three of the papers that considered the gender of the patient observed higher haemolysis rates for specimens drawn from males than those drawn from females.[26,36,52] Ahmad *et al.* and Söderberg *et al.*'s comparisons of haemolysis rates according to gender reported identical rates (as previously mentioned), 13.1% for males and 10.1% for females.[36,52] The other study found a 21.2% rate for males and a 16.7% rate among females.[26]

PATIENT AGE

Two studies compared the haemolysis rates among patients belonging to different age groups and found that older patients exhibited higher rates of haemolysed specimens than younger patients.[36,52] However, these studies compared haemolysis rates for patient age using the median to split the population into two groups: younger than and older than 63 years,[36] and younger than and older than 69.5 years.[52]

Both studies reported that specimens from the older patient group haemolysed 1.2 times more often (95% Confidence Intervals [CIs] 1.1-1.4) than specimens from the younger group,[36,52] and both reported haemolysis rates of 12.4% for specimens from the older group of patients, and 10.5% for specimens from the younger group.[36,52]

A different study reported that blood specimens taken from neonates using a skin-prick method were found to have much more severe haemolysis than when the same skin-prick method was used to conduct a blood draw on an adult.[20]

PATIENT DISCHARGE DIAGNOSIS

One study considered the patient discharge diagnosis and observed the highest haemolysis rates in patients with a respiratory system illness (52.9% of specimens), reproductive system illness (31.0% of specimens) and cardiovascular system illness (16.7%).[14]

PHLEBOTOMY / DRAW METHOD CHARACTERISTICS

DRAW SITE

Eight articles reported the haemolysis rate according to the draw site.[11,14,22,26,29,30,47,61] Two articles describing a single study compared the haemolysis rate for arterial (14.3%) and venous (20.1%) draw sites.[29,30] The remaining six studies all compared the haemolysis rates for antecubital blood draws with blood draws from other sites and found specimens taken from the antecubital region had consistently lower rates of haemolysis.[11,14,22,26,47,61] One study found the haemolysis rate was lower in antecubital blood draws (4.2%) than for distal arm draws (18.0%),[11] another study found that the haemolysis rate for antecubital blood draws was 12.6% compared to 33.7% for non-antecubital blood draws.[26] Tanabe *et al.* observed a 4.9% haemolysis

rate for specimens drawn from the antecubital fossa; the haemolysis rate for specimens drawn from the hand was 15.5%, a 5.9% rate from the wrist, a 10.7% rate from the forearm, a 0% rate from the feet and a 2.3% rate from other sites.[22] Investigations with more fine-grained analyses of draw sites compared several sites and concluded that specimens drawn from the right hand and forearm exhibited higher rates of haemolysis (40.9% and 30.3% of specimens, respectively) than other sites (e.g. right antecubital: 5.5% of specimens; left forearm: 5.3% of specimens).[14] Similarly, another study found the highest haemolysis rates for blood specimens drawn from the veins of the metacarpal plexus in the back of the hand (75.0%), compared to blood specimens drawn from the basilic (33.3%) and the cephalic veins (28.6%).[61] They reported the lowest haemolysis rates for blood specimens drawn from the median cephalic and basilic veins located near the antecubital fossa (17.4%).[61] Munnix *et al.* observed haemolysis rates of 13% and 4% for the left and right antecubital fossa, respectively, 20% and 12% for the left and right forearm, respectively, and the highest rates for the back of the hand, with 67% and 60% for the left and right hands, respectively.[47]

TRANSPORT METHOD

Four research teams compared the methods by which specimens were transported. One compared transport by laboratory staff with transport by ward assistant and observed higher rates among specimens transported by ward assistants (51.9%) compared to laboratory staff (12.2%).[26] This may be because ward assistants were less skilled and careful to ensure specimens did not get shaken during transport. The other three studies compared transport by hand with transport by pneumatic tube system, and all three observed higher haemolysis rates among the pneumatic tube group (7.4%, 10.9% and 100% of specimens, respectively) compared to the specimens transported by hand (0%, 3.3%, 16% of specimens, respectively).[25,34,59] One of these studies found a slight reduction in the haemolysis rate for ED specimens transported by pneumatic tube when the specimen was packaged in bubble wrap for transportation (7.12% compared to 10.9%).[25] They also reported that a temporary fault in the pneumatic tube delivery system, that introduced a rapid deceleration at one section, was associated with a large increase in the haemolysis rate (an increase to 54% of specimens) until it was repaired.[25]

TUBE FULLNESS

Two studies compared haemolysis rates among specimens where the tube was filled less than, or more than, halfway. They both observed higher rates when the tubes were filled less than halfway (18.6%, and 23.0% of specimens, respectively) than when the tube was filled over halfway (6.2%, and 10.8% of specimens, respectively).[11,51]

TOURNIQUET TIME

Two studies considered the tourniquet time before the blood draw. Both authors reported higher haemolysis rates when the tourniquet time exceeded one minute (17.5% and 20.2%, respectively) compared to when the tourniquet time was less than one minute (1.3% and 10.7%, respectively).[34,51]

DRAW DIFFICULTY AND RESISTANCE

Seven studies looked at blood draws where difficulty was encountered in either gaining intravenous access or drawing blood, or multiple attempts were required for the blood draw.[14,24,29,30,34,47,51] The majority of these studies concluded that rates of haemolysis were higher for difficult draws (range: 17%-44%), compared with easier draws (2.7%-15.4%). However, two papers reporting on the same study, found the highest haemolysis rate for draws rated as 'moderately' difficult, followed by the 'easy' draws, and the lowest haemolysis rate for 'hard' draws.[30] Another study considered difficulty in terms of resistance encountered while attempting to draw blood. They reported higher haemolysis rates when resistance was encountered while aspirating blood into the syringe (20.0%) compared to when no resistance was encountered (15.4%).[14]

EQUIPMENT CHARACTERISTICS

DRAW EQUIPMENT

Eighteen studies investigated haemolysis rates according to draw equipment,[8,11,14,17,19,22,24,26,28-30,34,41,48,49,51,56,62] with thirteen studies comparing different methods for intravenous access (newly placed IV catheter, existing IV catheter, and venepuncture) and six articles comparing blood aspiration methods (syringes and evacuated tube systems such as BD Vacutainer™ and Greiner Bio-One Vacuette™).

Concerning the intravenous access method, two articles describing a single study reported haemolysis rates of 24.4% for draws through IV catheters and a haemolysis rate of 6.8% for draws through venepunctures.[29,30] Grant reported a haemolysis rate of 49.4% for newly placed IV catheters, compared with 24.4% for existing IV catheters and 3.4% for straight needle venepuncture.[17] Fang *et al.* reported the findings of a study conducted in both inpatient and ED settings and found a haemolysis rate of 18.5% for blood specimens taken through an IV catheter, and 4.5% for those taken through a steel needle venepuncture.[26] Another equipment comparison reported a lower haemolysis rate for specimens drawn using butterfly needles (a category of straight needle), with 2.7% specimens found to be haemolysed, compared with a 14.6% rate for specimens drawn from IV catheters, when they were both aspirated using an evacuated tube system.[51] Another study made similar findings, when they compared a period of use of butterfly needles (6.6%), with a period of using butterfly needles and IV catheters (23.0%).[49] Ortells-Abuye *et al.* observed a 3.7% haemolysis rate for blood specimens drawn using a peripheral venous catheter or cannula and no haemolysed specimens among specimens drawn using venepuncture.[62] One study reported a higher rate of haemolysis for blood specimens taken through an IV catheter (13.7%) than those taken through a fresh venepuncture using an evacuated tube system (3.8%).[19] Similarly, Lowe *et al.* reported a haemolysis rate for blood specimens taken through an IV catheter of 5.6%, and a rate of only 0.3% for specimens taken through a venepuncture.[28] Berger-Achituv *et al.* looked at 40 specimens drawn from syringes and catheters, and found that one venepuncture specimen (2.5%) and none of the catheter specimens were haemolysed.[41] Tanabe *et al.* compared steel needle

venepuncture (1.5%) with catheters (10%).[22] Dietrich reported that haemolysis rates were greater with a new IV catheter (1.1%) than for an existing IV catheter (0.8%) while the lowest haemolysis rates were for blood specimens taken through a venepuncture (0.1%).[8] However, that study confounded the intravenous access method with the staff type conducting the blood draw: all blood draws using a new IV catheter were done by ED staff, all blood draws using an existing IV catheter were done by critical care, surgical, or medical nurses, and all steel needle venepunctures were done by a laboratory phlebotomist.[8] Another study compared the haemolysis rates for different intravenous access and aspiration methods but did not explicitly specify how they were combined.[34] They reported a haemolysis rate for syringes (3.2%), butterfly needles (4.3%), evacuated tube system (4.7%) and BD Venflon™ IV catheter devices (16.7%).[34]

It is worth noting that the vast majority of these studies occurred in, or at least partially in, EDs, which may have some bearing on the conditions under which specimens are drawn. The study by Tanabe *et al.* took place in an ED and a Labour/Delivery ward. Their multivariate analysis found that intravenous access via catheters was a factor associated with greater rates of haemolysis, even when the collection ward was controlled for statistically.[22]

There were six articles that compared the haemolysis rates for different blood aspiration methods. Two articles reported the findings of a single study and found a much lower haemolysis rate when syringes were used (11.0%), compared with evacuated tube systems (35.8%)[29,30] Two studies found the reverse, but observed only small differences between the methods; one found a 13.5% haemolysis rate for syringes, compared to 12.6% for evacuated tube systems.[14] The other observed a 5.29% rate for syringes and a 2.41% rate for vacuum systems.[56] Grant also reported that blood specimens aspirated with an evacuated tube system had a higher rate of haemolysis than a syringe aspiration when the blood specimen was taken through a new IV catheter (77.4% compared to 28.3%); but the opposite pattern was evident, with lower haemolysis rates for the evacuated tube system (2.9% compared to 9.1%), when the intravenous access was through a straight needle.[17] Dwyer *et al.* reported that there was no significant difference in haemolysis rates between blood specimens drawn using a syringe directly through the IV cannula hub (6.5%) and those drawn using a syringe through a BD Interlink™ device connected to the IV cannula cap (7.2%).[24]

Higher haemolysis rates were also encountered when an extension tube was not used (12% vs 9.1%),[48] and when the IV cannula was plastic rather than metal (13.5% vs 0%).[11]

NEEDLE / CATHETER GAUGE SIZES

Seven studies made some comparison of the various sizes of needle or catheter gauges used to draw blood.[11,17,19,22,29,30,47] Four studies considered the effect of IV gauge sizes [11,17,19,47] and three studies considered both IV and needle gauge sizes.[22,29,30] Smaller gauge sizes refer to larger diameters, for example a 7G needle has the largest available diameter, while a 33G needle is among the smallest.

The results of many of these comparisons should be considered with extreme caution, due to very small sample sizes in the analyses. For example, Kennedy *et al.*[19] compared the haemolysis rate for different diameter IV catheters, and found a 100% haemolysis rate for the largest (24G) IV catheter and a 0% haemolysis rate for the 14G IV catheter, but only a single specimen was collected with catheters of these two sizes.

Of the studies with larger sample sizes, Tanabe *et al.*[22] found a 3.9% haemolysis rate for 16G IV catheters, with rates tending to rise as the IV gauge increased (i.e. as the needle got finer). For 18G IV catheters, Kennedy *et al.*,[19] Tanabe *et al.*[22] and Munnix *et al.*[47] observed rates of between 10% and 15%. The findings of Grant[17] were slightly above the other studies, with a 40% haemolysis rate for 18G IV catheters and a 51% rate for 20G IV catheters. The other findings for 20G IV catheters, from Burns *et al.*, [11] Kennedy *et al.*, [19] Munnix *et al.*[47] and Tanabe *et al.*[22] ranged from between 10.4% to 20.5%. Considering 22G IV catheters, Kennedy *et al.*[19] and Tanabe *et al.*[22] both used sample sizes of only four, and reported haemolysis rates of 25% and 50% respectively. Burns *et al.*[11] used a sample of 33 and reported a rate of 30.3%.

When considering needle gauge sizes, Tanabe *et al.*[22] observed a 0% (0/1) rate for 18G needles, 6.2% (1/16) for 19G, 1.1% (1/88) for 21G and 3% (1/33) for 23G needles. The two other papers, both by Ong and colleagues, reported the findings from the same study. They combined needle and IV catheter sizes into two groups, reporting gauge sizes as greater than or less than 21G. Of specimens drawn using IV catheters or needles with a gauge size equal to or larger than 21G, 17.4% were haemolysed, while the specimens drawn with needles finer than 21G needle had a 21.3% haemolysis rate.

SPECIMEN TUBE SIZE

The four studies[13,14,56,61] which compared specimen tube sizes reached differing conclusions. The first two reported the highest haemolysis rates when larger tubes were used.[13,14] One of these reported the lowest rate of haemolysis for 3.0ml tubes (9.3%) and higher haemolysis rates when larger tubes were used, with the highest rate of haemolysis (26.3%) when the tubes were 6.0ml.[14] The second study reported finding a significantly lower haemolysis rate among smaller 5ml tubes, compared with 10ml tubes, although they did not report the exact rate.[13] The third study found low rates across all tube sizes, with a 5.2% rate for 3.5ml tubes and 3.5% rate for 5ml tubes.[61] Fernandez *et al.* found little difference between 3.5-4mL tubes (2.28%) and 8-9mL tubes (2.87%).[56]

TUBE TYPE

There are several types of blood collection tubes and five studies investigated their effect on haemolysis rates. One study compared haemolysis rates by tube type, and observed the highest haemolysis rate among blue sodium citrate tubes used for coagulation testing (17.4%).[14] Another two studies also compared tube types, with one concluding that the highest haemolysis rates were found in serum tubes, compared to non-serum

tubes (23.8% and 16.7%, respectively)[26] and the other finding the highest rates in gel tubes, compared to non-gel tubes or syringes (62.5% and 53.7%, respectively).[18] One study dating back to 1965, using a relatively rigorous experimental design, found lower mean severity of haemolysis if the neonate's heel was coated in silicone ointment before a skin-prick blood draw and when the blood was drawn into heparinised glass tubes open at both ends rather than test tubes.[20]

RECOMMENDATIONS

Many of the studies made recommendations for methods, strategies and policies that might facilitate reducing the frequency of haemolysed specimens. Like the comparisons, the recommendations fell into categories: those relating to education and training, those relating to blood drawing practices, equipment related recommendations, and other recommendations.

Education and training related recommendations included: the development of guidelines or protocols for phlebotomy;[12,44] adherence to standard operating procedures;[11,14,40] further, improved or more haemolysis-prevention specific staff training;[14,26,29-31,40,44] more frequent training;[14,31,50] and some form of proficiency training or competency testing for staff performing phlebotomies.[14,31,50]

Ten studies discussed the relationship of blood draw practices to haemolysed specimens. Three studies recommended the antecubital fossa as the first choice for blood collection site.[11,14,26] This recommendation is compatible with another recommendation that sites distal to the median basilic vein (the vein running down the inner arm) and the cephalic vein (the vein running down the outer arm and outlining one side of the antecubital fossa) should be avoided, along with the metacarpal plexus (the back of the hand).[61] It is also best if the specimen tube is completely filled rather than only half-filled,[11] that the tourniquet time be kept to under one minute (which may require placing the tourniquet more than once during the blood collection process)[34,65] and, if the blood draw encounters difficulties, a second specimen should be taken because the risk of haemolysis is higher.[24] Munnix *et al.* observed that when four blood specimens were drawn from the same IV catheter, it was the first specimen that was most often haemolysed, while the subsequent three specimens were usually not haemolysed.[47] When clinical conditions allow, the effective rate of haemolysis can be reduced considerably by drawing more than one blood specimen.

Regarding the method used for intravenous access, from the perspective of minimising the possibility of a blood specimen being haemolysed, it is recommended that a venepuncture (using either a straight needle or a butterfly needle) be performed rather than through an IV catheter.[17,26,29,30] Concerning the equipment used to aspirate the blood, it is recommended that syringes be used rather than the evacuated tube system.[29,30,34,66] However, using the evacuated tube system is recommended when used in conjunction with a venepuncture rather than an IV catheter for intravenous access.[17]

One reason for not using needle-and-syringe for phlebotomies is that they are associated with greater risk of

needle-stick injury and phlebotomist exposure to blood-borne pathogens.[29] Therefore, the current NSW Health policy directive is to minimise the use of needle-and-syringe as a blood draw method; safety-engineered blood collection needles (e.g. evacuated tube systems such as BD Vacutainer™ and Greiner Bio-One Vacuette™) are recommended instead.[67]

Further equipment related recommendations are the avoidance of 22G or finer needles or IV catheters,[14] and that 5ml tubes be employed.[13] It is also recommended that the needle be removed from the syringe before the blood is transferred to the test tube.[20]

Specimen transportation factors were also discussed by three studies: one recommended that specimens be placed into a basket container and kept steady during transport.[26] The other recommended the monitoring of haemolysis rates among specimens transported via the pneumatic tube system and that speed, pressure and changes of direction be monitored during the design and installation of new pneumatic tube systems in healthcare institutions.[59] Defects with pneumatic tube delivery systems can cause large increases in the rate of haemolysed specimens so pneumatic tube systems should be monitored and maintained adequately. Packaging blood specimens in bubble wrap for transport in the pneumatic tube may also reduce the chance of haemolysis.[25]

Some of the other recommendations included using the HI from the analyser for the detection of haemolysis[8] because using visual checks to detect haemolysis has been shown to be unreliable[3,7,20] (even with the colour chart for comparison);[16] the HI can also be valuable as an indicator of laboratory quality;[36] and a standardised approach to haemolysed specimen rejection criteria.[8,9] One study recommended laboratories and hospitals consider the actual costs associated with higher rates of repeat blood draws caused by the higher rates of haemolysis from specimens taken through an existing IV catheter, compared to the costs of doing a new venepuncture for all patients including those that already have an existing IV access.[8] That study also recommended the issue of haemolysis be made a hospital-wide issue, with all departments receiving education and training and being involved in improvement efforts.[8] However, each hospital or laboratory should analyse their own circumstances and issues, and devise their own targeted solutions, rather than blindly implementing measures which have been effective elsewhere.[61] Finally, one study recommended that it may be appropriate to deploy small groups of dedicated laboratory phlebotomist staff in EDs where high rates of haemolysed specimens are often seen.[40]

METHODS

STUDY SETTING

Each stage of this project was undertaken in a different study setting so each is described in further detail in the relevant section of the report.

ETHICS APPROVAL

Stage 1 of the project (using the KIMMS dataset) received ethical approval from the UNSW Australia Human Research Ethics Advisory Panel I (9_13_037). Stage 2 of the project (using the pathology service and hospital datasets) received ethical approval from the relevant Local Health District Human Research Ethics Committee (RESP/14/16). Stage 3 of the project (Detection and Reporting Practices) was part of an internal feedback exercise at the pathology service and for the KIMMS project so did not require ethical approval.

DATA SOURCES

Table 5 shows the different datasets used in this project, the source of the data, the type of data contained, the organisations described, time period covered, and the size of the dataset. Stage 1 of the project used the KIMMS dataset and Stage 2 used a single dataset created by linking the LabNo, Requests, and Haemolysis datasets (from the Laboratory Information System [LIS]), and the Patient Administration System [56] and ED datasets (described later in further detail). Stage 3 used data from structured interviews as part of an internal feedback exercise so did not utilise any datasets.

Table 5. A summary of the different datasets and, for each dataset, the source, the type of data contained, the organisations described, the period of time described, and the number of rows (prior to data cleaning).

Dataset name	Dataset source	Data content	Organisation Described	Period covered	No. of rows
KIMMS	RCPAQAP	Aggregate data on preanalytical laboratory errors	68 KIMMS participant laboratories	Jan 2011 – Dec 2013	760
LabNo	Pathology Service LIS	Laboratory Accessions	5x study hospitals + EDs	01/10/2009 – 30/09/2013	3,744,097
Requests	Pathology Service LIS	Test Request codes		01/10/2009 – 30/09/2013	14,515,614
Haemolysis	Pathology Service LIS	Degree of haemolysis	5x study hospitals + EDs	01/10/2009 – 30/09/2013	1,628,992
PAS	Health Information Exchange	Hospital Inpatient Admissions	5x study hospitals	01/10/2009 – 30/09/2013	491,544
ED	Health Information Exchange	ED presentation information	5x study EDs	01/10/2009 – 30/09/2013	684,897

DATA ANALYSIS AND STATISTICAL METHODS

Data analyses were conducted using IBM SPSS Statistics 22.0.0, SAS Institute Statistical Analysis System (SAS) 9.3 and Microsoft Excel 2013. Further details of the data analysis methods are provided in the relevant sections of the report.

OUTCOME MEASURES

The outcome measures used in this study are the following:

- The frequency of haemolysis rejections in laboratories across Australia submitting incidence data to the KIMMS database.
- The proportion of all accessions rejected due to haemolysis in laboratories across Australia submitting incidence data to the KIMMS database.
- The proportion of all rejections due to preanalytical errors accounted for by haemolysis in laboratories across Australia submitting incidence data to the KIMMS database.
- The frequency and proportions of specimens found to be haemolysed in five laboratories connected with five public hospitals in metropolitan Sydney.
- Haemolysis rates in different clinical and patient contexts and across time.
- The impact of haemolysis on the timing for repeat Potassium and Troponin testing in inpatient wards and in EDs.
- The impact of haemolysis on ED Length of Stay (ED LOS).
- Patient and collection characteristics associated with higher rates of haemolysis.
- An evaluation of the practices used by five Sydney laboratories, and a selection of regional laboratories belonging to the same pathology service, in identifying and measuring haemolysis, including whether haemolysis is detected visually or by using the HI from the analyser; whether the haemolysis parameters in the analyser were based on manufacturer parameters or an internal or external study; what policy the laboratory follows with regards to reporting; adding a comment, suppressing, or estimating the results when a specimen in haemolysed; and the haemoglobin concentration limits for adding a comment or suppressing the results for five different analytes (Troponin, Potassium, Direct Bilirubin, Lactate Dehydrogenase, Aspartate Aminotransferase).

STAGE 1: HAEMOLYSIS RATES ACROSS AUSTRALIAN LABORATORIES (KIMMS PROJECT)

INTRODUCTION

The KIMMS project was developed by the Royal College of Pathologists of Australasia Quality Assurance Program (RCPAQAP) and funded by the Australian Department of Health via a Quality Use of Pathology Program (QUPP) grant. The aim of the KIMMS project is to monitor the preanalytical and postanalytical phase of the laboratory quality systems.[68]

Pathology laboratories from across all Australian states and territories submitted data on a quarterly basis to a centralised repository that would enable the creation of benchmark incidence and monitoring data for a variety of different types of preanalytical errors (e.g. patient mis-identification, incorrect specimen labelling, haemolysed specimens, and other specimen problems) and post-analytical errors (e.g. results going to the incorrect place, and amendment or retraction of pathology results already issued).

The aim of this stage of the project was to use the KIMMS project database to evaluate the prevalence of haemolysis rejections in pathology laboratories across Australia by reporting the proportion of accessions that are rejected because of haemolysis; how much variation there is between laboratories; the impact of the definition of haemolysis rejections (the numerator) and accessions (the denominator) on reported haemolysis rates; and whether there have been changes in the incidence of haemolysis rejections across time.

METHODS

PARTICIPANTS

In the KIMMS database, the term “participants” can refer to either a single laboratory or a group of affiliated laboratories submitting a single set of responses to the KIMMS database. While each participant reported how many accessions they processed during each data collection period, they did not report how many laboratories contributed to the data they were submitting.

Structured telephone interviews with participants were conducted to understand the source of the majority of specimens arriving at participant laboratories, whether most specimens were collected by laboratory phlebotomists or clinical staff, participant practices for assigning accessions, and whether haemolysis rejections were identified in the Central Specimen Reception (CSR) or in each department, how they were identified, recorded in the LIS, and defined for the numerical counts submitted to KIMMS.

Table 6 shows that there were 68 participants. Most were in Western Australia (WA; 31 participants, 45.59%), New South Wales (NSW; 17, 25%) and Victoria (VIC; 10, 14.71%). However, when considering the number of accessions processed, NSW accounted for more accessions than any other state or territory (42.99% of all accessions), WA and VIC accounted for 19.60% and 16.75% of accessions, respectively.

Table 6. Number of laboratory participants in each state/territory sorted by proportion of accessions accounted for.

State	No. of participants	% of participants	No. of accessions	% of accessions
NSW	17	25.00%	35,044,006	42.99%
WA	31	45.59%	15,977,910	19.60%
VIC	10	14.71%	13,654,755	16.75%
SA	2	2.94%	9,390,530	11.52%
QLD	4	5.88%	3,319,959	4.07%
TAS	2	2.94%	1,873,409	2.30%
ACT	1	1.47%	1,685,188	2.07%
NT	1	1.47%	575,690	0.71%
Total	68		81,521,447	

DEFINITIONS

HAEMOLYSIS REJECTION

Haemolysis rejection errors were recorded in the KIMMS database when a specimen was *rejected* due to haemolysis; not all haemolysed specimens were necessarily rejected. Individual laboratories could take many factors into consideration when deciding whether to reject a specimen, including the types of tests that were requested on a specimen, each requested test's sensitivity to haemolysis, and other operational factors.

ACCESSION

A laboratory identification number assigned by the pathology laboratory to allow identification, tracking, and reporting of results in the LIS for one or more tests. Accessions can be assigned by episode, by laboratory department, by specimen, or by test.

EPISODE

A collection of one or more tests, to be conducted on one or more specimens, that constitute a single request for a single patient.

SPECIMEN

A single test tube of blood or serum for which one or more tests have been requested.

TEST

An individual pathology test assay request to be processed by the laboratory.

DATA EXTRACTION AND ANALYSIS

Data were extracted from the KIMMS database containing 12 three-month long data collection periods covering a total period of three calendar years (2011 to 2013). The extracted data were in Microsoft Excel format. Data analyses were conducted using Excel's built-in mathematical and charting functions.

SECTION 1.1: CHARACTERISTICS OF KIMMS PROJECT PARTICIPANTS

The next section reports the findings from the structured interviews of operating characteristics and practices at participant laboratories.

LABORATORY PRACTICE CHARACTERISTICS

Table 7 shows that the majority of participants (n=50, 73.53%) responded that they received most of their specimens from public hospitals; this group accounted for around one quarter of all accessions and three participants who received accessions from both public and private hospitals. A prominent group of participants (n=13, 19.12%) reported that most of their accessions came from other sources (outpatient, referred patient etc.), accounted for over half of all accession in the KIMMS database.

Table 7. Where did the accessions come from?

Specimen Origin	No. of participants	% of participants	No. of accessions	% of accessions
Hospital - public	50	73.53%	22,202,769	27.24%
Hospital - private	1	1.47%	768,159	0.94%
Hospital - public & private	3	4.41%	4,727,430	56.01%
Other (outpatient, referred patient etc.)	13	19.12%	45,656,515	5.80%
(Missing/unknown)	1	1.47%	8,166,574	10.02%
Total	68		81,521,447	

Table 8 shows that the majority of participants (n=47), accounting for about 70% of all accessions, responded that laboratory phlebotomists did most of the specimen collections. Only 14 participants, accounting for about 15% of accessions, reported that clinical staff were responsible for either an equal amount (7.49% of accessions) or the majority of collections (7.52% of accessions).

Table 8. Who collected accessions?

Specimen Collectors	No. of participants	% of participants	No. of accessions	% of accessions
Mostly Laboratory Phlebotomist	47	69.12%	57,661,244	70.73%
Mostly Clinical Staff	11	16.18%	6,130,045	7.52%
Approximately equal proportions	3	4.41%	6,103,049	7.49%
(Missing/unknown)	7	10.29%	11,627,109	14.26%
Total	68		81,521,447	

HAEMOLYSIS DETECTION LOCATION AND METHODS

Table 9 shows that most participants (89.39%) reported that the haemolysis detection process occurred when the specimen arrived in the destination laboratory department and that they used the HI from the analyser to detect and assess the degree of haemolysis in a specimen.

A minority of participants (n=4; 6.06%) reported that the haemolysis detection process occurred in either CSR or the destination laboratory departments, and four participants (6.06%) used a visual check to detect haemolysed specimens

Two participants reported incomplete data and are excluded from this analysis.

Table 9. Distribution of participants according to whether they used HI index to determine haemolysis and whether the decision to reject an accession occurs in the CSR or in each individual laboratory.

	Who decided rejections		
Using HI index	Laboratory Department		Total
No	3	1	4
Yes	59	3	62
Total	62	4	66 [a]

[a] Two participants provided incomplete data and are excluded.

REPORTING PRACTICES

Haemolysis only affects blood specimens but laboratories contributing data to the KIMMS database report their activity by the number of accessions for all types of specimens (including tissue specimens, urine, faeces, etc.) where haemolysis is not necessarily relevant. Since the denominator in haemolysis rate calculations reported here is the total number of accessions processed by the laboratory (regardless of specimen type), the haemolysis rate reported by a laboratory will also be influenced by the amount of testing activity on blood specimens as a proportion of all accessions.

There are a variety of methods that pathology laboratories can use for accessioning and for counting haemolysis rejections. Each method can influence the rate of haemolysis rejections that a laboratory records and reports.

Laboratories can assign accessions by episode, where one or more tests to be conducted on one or more specimens will all be assigned a single accession number, or by specimen, where each specimen will be assigned its own accession number (even if it belongs to the same episode). The latter method will result in a laboratory reporting a greater number of accessions, and therefore lower rates of haemolysis rejections, for any given level of activity than the former.

Similarly, laboratories can choose to count haemolysis rejections according to the number of episodes

affected by haemolysis, according to the specimens affected by haemolysis, or according to the number of tests affected by haemolysis. Counting haemolysis rejections according to episode would result in only a single haemolysis rejection being recorded even if multiple specimens, or multiple tests, within the episode were affected by haemolysis. Counting haemolysis rejections according to the specimen would result in only a single haemolysis rejection being recorded even if multiple tests on that specimen were affected by haemolysis. Lastly, counting haemolysis rejections according to the tests would result in a haemolysis rejection being recorded for each test affected by haemolysis, even when they were all ordered for a single specimen, or single episode.

The results presented reveal considerable differences between participants with respect to where the majority of specimens came from; who did the actual blood collections; where haemolysis detection occurred in the laboratory process, and what method of detection was used; and how rejections for haemolysis were counted for submission to the KIMMS database. Broadly speaking, the prototypical KIMMS participant received most of the specimens from public hospitals, received a majority of specimens that had been collected by laboratory phlebotomists, identified haemolysed specimens within each laboratory department using the HI index result from the analyser, assigned accessions according to the episode and counted haemolysis rejections per specimen.

Of greatest relevance to the planned analysis of the rates of haemolysis rejections was the finding that participants varied both in how they assigned accessions (whether it was according to the specimen or the episode) and how they counted haemolysis rejections for submission to the KIMMS database (by episode, by specimen, or by test). Episodes can contain multiple specimens upon each of which multiple tests might be requested. Since the haemolysis rejection rate would be calculated by dividing the number of haemolysis rejections by the number of accessions processed by the participant for a given time period, differences in how these are defined will systematically alter the resultant rate: a participant who counts haemolysis rejections per test and assigns accessions per episode will appear to have a lower rate of haemolysis rejections than if they had counted haemolysis rejections per episode and assigned accessions per specimen. Unfortunately, the relationship between episodes, specimens, and tests naturally has great variability so it is not possible to mathematically correct for participants having used different definitions. Therefore, due to these differences in definitions, it is best for comparisons to be done between groups of participants who used the same definitions. We chose the participants who used the most common definition (by number of participants, number of submissions to the KIMMS database, and number of accessions accounted for): accessions assigned per episode, and haemolysis rejections counted by specimen; and compared the haemolysis rejection rate for that subset of participants. Thirty-eight participants (55.88%), accounting for 430 (57.72%) submissions to the KIMMS database, and 29.5 million (36.1%) accessions operated in this way and are included in the following analyses.

SECTION 1.2: PREVALENCE AND VARIATION OF SPECIMENS REJECTED DUE TO HAEMOLYSIS IN KIMMS PARTICIPANT LABORATORIES

Table 10 shows the overall haemolysis rejection rate for participants using five different combinations of accessioning practices and methods for counting haemolysis. It is not appropriate to calculate an overall haemolysis rejection rate for the entire KIMMS dataset because participants assigned accessions and counted haemolysis rejections using a variety of definitions. The group of participants accounting for the most participants and the most accessions (accessions assigned by episode, haemolysis rejections counted by specimen) reported a mean haemolysis rejection rate of 0.18% of accessions. The second largest group of participants (accessions assigned by episode, haemolysis rejections counted by episode) reported a mean haemolysis rejection rate of 0.25% of accessions.

Table 10. Haemolysis rates by reporting groups

Accession assigned by	Haemolysis rejections counted by	No. of haemolysis rejections	No. of Accessions	Rate
Per specimen	Per specimen	9,365	10,929,625	0.09%
	Per episode	68,304	4,026,037	1.70%
Per episode	Per test	1,802	16,232,322	0.01%
	Per specimen	51,594	29,456,294	0.18%
	Per episode	52,062	20,877,169	0.25%
Total		183,127	81,521,447	

Figure 2 shows the mean haemolysis rejection rate as a proportion of accessions, for only the KIMMS participants who assigned accessions per episode and counted haemolysis rejections per specimen, for each year and quarter of the data collection period. The haemolysis rejection rate in 2011 and 2012 fluctuated between 0.12% and 0.20% of all accessions. The haemolysis rate dropped in 2013 and remained between 0.10% and 0.12% of all accessions for the entire year. However, the variation between laboratories was also greatest in 2013 as indicated by the widest SEM intervals for the first three quarters of the year.

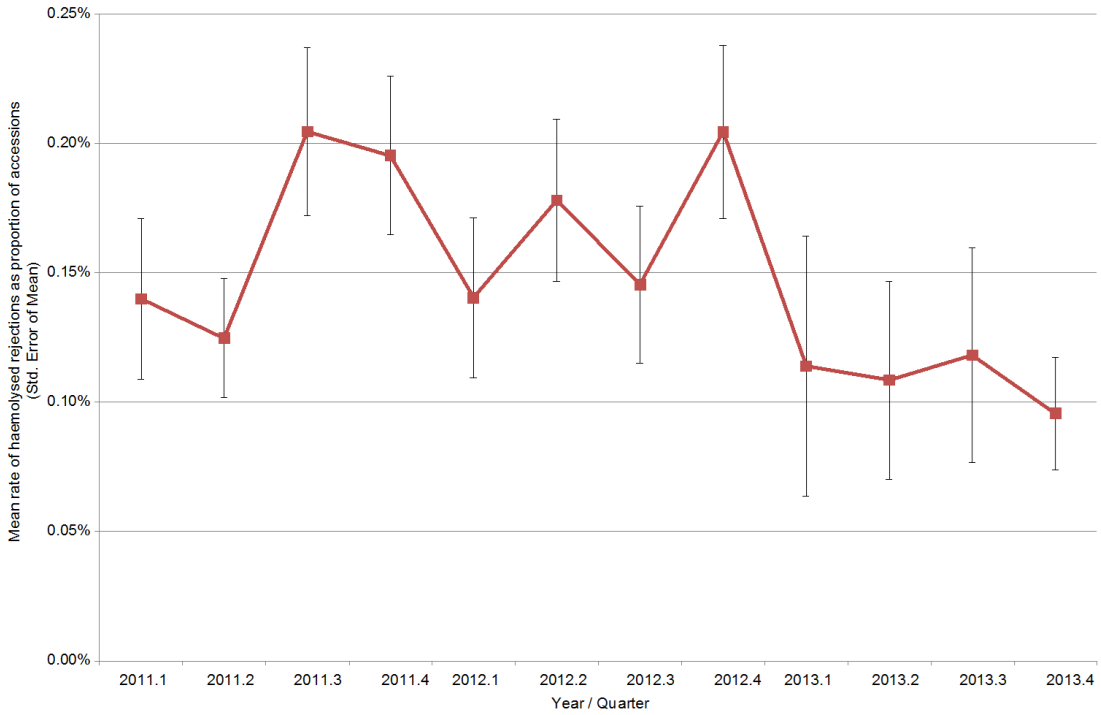

Figure 2. Mean rate (and SEM) of haemolysis rejections as a proportion of accessions, for KIMMS participants who assigned accessions per episode and counted haemolysis rejections per specimen, for each quarter in the data collection period.

STAGE 2: DETAILED ANALYSIS OF HAEMOLYSIS RATES AT FIVE METROPOLITAN HOSPITALS IN SYDNEY

INTRODUCTION

The goal of this stage of the project was to undertake an extensive data linkage exercise of data coming from both pathology service computer systems and key hospital data sources, to assess the incidence rate of haemolysed specimens in the five study hospitals and describe differences in haemolysis rates in different clinical contexts including: comparisons of the haemolysis rates between the five hospitals; between patients in the ED, the inpatient setting, and other sources; whether the blood collection was performed by a laboratory phlebotomist or a clinical staff member; and how the haemolysis rate changed over a four year study period. We also aimed to examine the impact of haemolysis on repeat Potassium and Troponin testing in both the hospital inpatient and ED context, and to use multilevel modelling to estimate the impact of haemolysed specimens on the duration of a patient's length of stay in the ED. Lastly, we aimed to use multilevel modelling methods to estimate the increased risk of haemolysed specimens occurring according to various patient and collection characteristics

METHODS

STUDY SETTING

The project was undertaken in five hospitals belonging to a single Local Health District (LHD) in metropolitan Sydney. The five hospitals were serviced by a single pathology provider which provides comprehensive biomedical laboratory services including the following laboratory specialties: Anatomical Pathology, Blood Bank, Chemical Pathology, Microbiology, Haematology, Molecular Genetics and Immunology. In addition to the LHD encompassing the five study hospitals, the pathology provider also serviced four other LHDs and, in 2012, employed over 1000 staff.

Table 11 shows the biochemistry analyser, LIS, and middleware in operation at each of the five study hospitals, when they were installed and what system they replaced. At the time this report was written all the laboratories used Abbott Architect biochemistry analysers (that were all installed during the study period), AUSLAB LIS systems, and AMS Omnilab middleware.

Table 11. Details of the biochemistry analyser, LIS, and middleware in operation at the five study hospitals and the date that they were installed.

Hospital	Biochemistry Analyser		LIS		Middleware	
	Manufacturer/Model	Installed	Name	Installed	Name	Installed
A	Abbott Architect ci8200 (replaced Siemens Dimension RxL and Roche e411)	Jan 2013	AUSLAB	1998	AMS Omnilab	Sep 2013
B	Abbott Architect ci4100 (replaced Siemens Dimension Xpand and Roche e411)	Dec 2012	AUSLAB	1998	AMS Omnilab	Sep 2013
C	Abbott Architect ci4100 (replaced Siemens Dimension Xpand and Roche e411)	Feb 2013	AUSLAB	1998	AMS Omnilab	Sep 2013
D	Abbott Architect 2x ci16000 & 1x ci8000 (replaced Roche Modular system)	Oct 2012	AUSLAB	1998	AMS Omnilab	Apr 2013
E	Abbott Architect ci4100 (replaced Siemens Dimension Xpand and Roche e411)	Feb 2013	AUSLAB	1997	AMS Omnilab 2.4F	Sep 2013

Table 12 provides descriptive details related to the operations of the five study hospitals for the month of September 2013. Hospital D was by far the largest hospital by number of available beds and the number of inpatient and ED separations and also accounted for the bulk of pathology testing. Hospital A was the next largest hospital by bed numbers and pathology testing activity. Hospitals B, C, and E were the smallest hospitals by bed numbers and testing activity and had broadly similar size and similar amount of pathology testing activity.

Table 12. The number of beds, inpatient admissions, ED presentations, patients who had at least one pathology test, and the total number of pathology tests at each of the five study hospitals for the month of September 2013.

Hospital	Available Beds	Inpatient Separations	ED Presentations	No. Patients who had Tests [a]	No. of Tests [a]
A	275	1,496	2,860	2,038	39,304
B	169	1,114	1,924	1,264	22,279
C	176	1,515	2,652	1,360	28,066
D	687	5,209	5,653	6,639	201,591
E	155	914	2,137	1,191	23,886
Total	1,462	10,248	15,226	12,534	318,560

[a] Includes outpatients, referred patients, and other non-admitted patients

Figure 3 shows the proportion of blood specimens received from each hospital according to whether the patient was an ED patient, an inpatient, or other type of patient (outpatient, referred patient etc.). Overall,

nearly two-thirds of specimens came from inpatients (63.4%, ranging from 61.7% to 64.2%), 21.4% came from ED patients (14.9% to 34.3%), and the smallest proportion (15.3%, ranging from 4.0% to 20.9%) come from other types of patients. As noted, there was little variation between hospitals in the proportion of specimens coming from inpatient wards. The hospitals can be grouped into three broad profile groups according the number of specimens coming from ED patients in proportion to other patients: compared to the other hospitals, Hospitals C and E had the largest proportion of specimens coming from ED patients (34.3% and 32.6%, respectively) and the smallest proportion coming from other patients (4.0% and 4.4%); Hospital D inverted these two groups where, relative to other hospitals, the smallest proportion came from ED patients (14.9%) and the largest proportion came other patients (20.9%); Hospitals A and B occupied the middle ground.

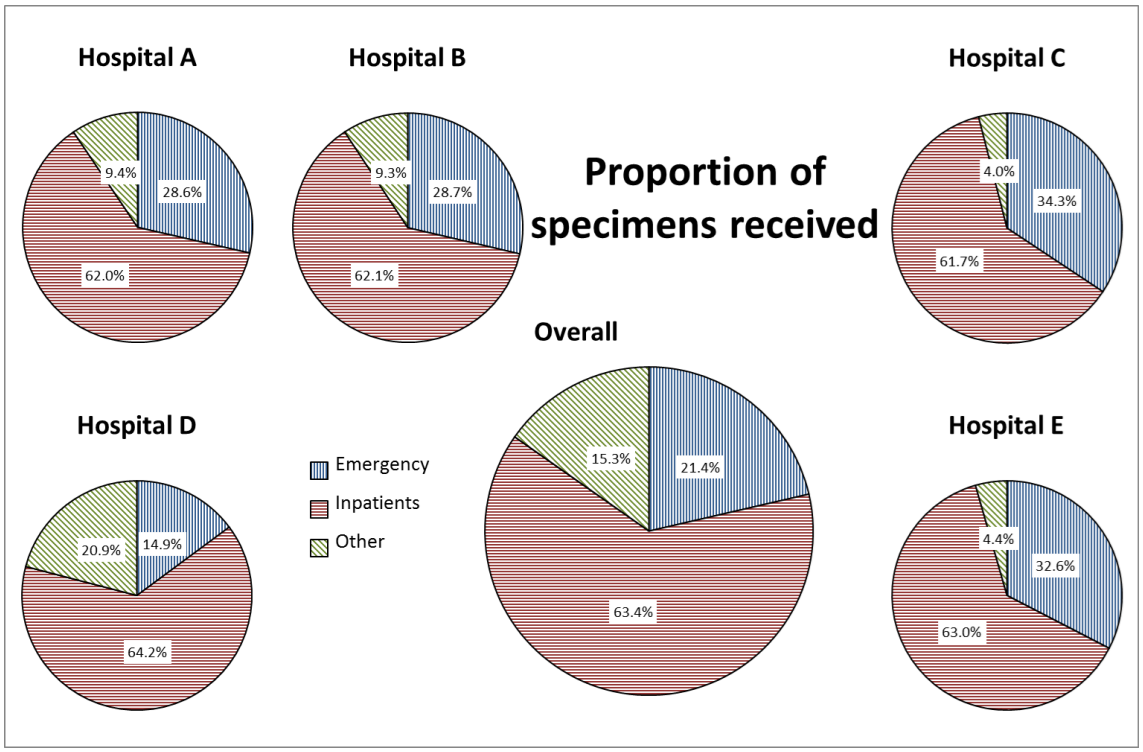

Figure 3. Distribution of specimens received from Emergency Department patients, inpatients, and other patients, at each of the five study hospitals for the study period (October 2009-September 2013).

Figure 4 shows the proportion of blood specimens received from each hospital according to the age groups of the patients. Overall, 58.2% of specimens came from patients older than 60 years of age; babies younger than one year of age provided 2.7% of specimens. The distribution of age groups for the specimens allows the hospitals to be grouped into the same three broad profile groups as for the patient types: compared to the other hospitals, Hospitals C and E had the largest proportion of specimens coming from patients older than 80 years of age (43.2% and 44.6%%, respectively) and the smallest proportion coming from babies (1.3% and 0.1%); Hospital D had the smallest proportion of specimens coming from patients older than 80 years of age (17.5%) and the largest proportion coming from the 18-60 and 60-80 years of age groups (42.0% and 35.4%, respectively); while Hospitals A and B once again occupied the middle ground for the proportion of

specimens from patients over 80 years of age (34.7% and 32.4%, respectively) and the 18-60 year old group (31.7% and 35.0%, respectively). Hospitals A and B had a similar proportion of specimens from patients 60-80 years of age (26.5% and 28.4%, respectively) as Hospitals C and E, and a similar proportion of specimens from babies younger than 1 year of age (3.4% and 3.1%, respectively) as Hospital D.

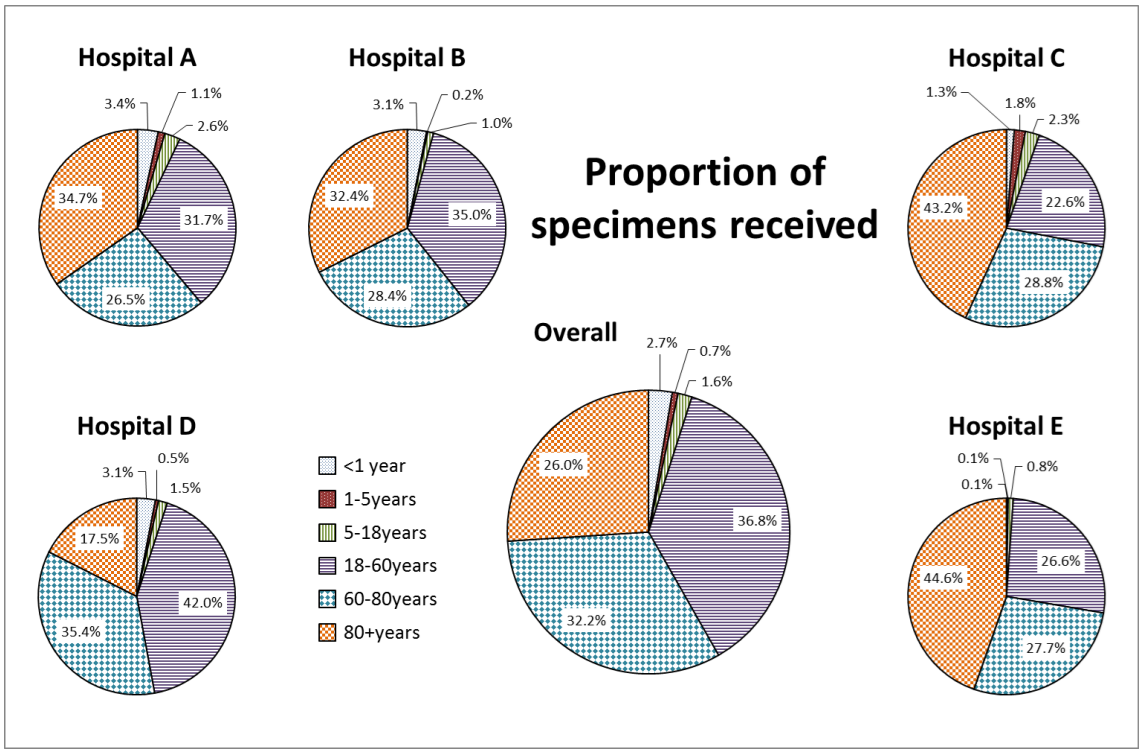

Figure 4. Distribution of specimens received from six different patient age groups (babies, toddlers, children/adolescents, working-age adults, older adults, and the elderly) at each of the five study hospitals for the study period (October 2009-September 2013).

DEFINITIONS

HAEMOLYSIS

All specimens that were analysed on a biochemistry analyser in the five laboratories were assessed for haemolysis within the biochemistry analyser itself. The "Haemolysis" dataset recorded a HI value between 1 and 6 for specimens in which haemolysis was detected, where a HI value of 1 was the least severe and a HI value of 6 was the most severe. In addition, a binary value was also recorded to reflect whether *any* haemolysis was detected in the specimen (i.e. any HI value between 1 and 6). The analyses reported here counted haemolysis according to this binary value: whether a specimen was haemolysed to any degree, or not.

Haemolysis was counted on a "per specimen" basis and did not take into account how many of the requested tests were actually affected by the haemolysis that had occurred (i.e. whether any of the results were suppressed, or whether a comment was added to the result to indicate the specimen was haemolysed).

DATA EXTRACTION

All data integrity and validity checks, and linkage were performed in IBM SPSS Statistics 22.0.0. The datasets extracted from the PAS and ED information systems were comma-separated values (CSV) format; the in-built SPSS data opening functions were used to import the data.

DATA LINKAGE

This dataset covered five study hospitals for the four year study period between Oct 2009 and Sep 2013. The linkage began with the "Requests" dataset extracted from the pathology service, the "LabNo" dataset, also extracted from the LIS, was merged to the "Requests" dataset using the accession number as the linkage field. Next the "Haemolysis" dataset, also extracted from the LIS, was merged to the existing merged dataset using the accession number as the linkage field. Now that the different LIS datasets were merged, the patient admission dataset from the PAS and the ED presentation dataset from the ED information system were merged with the already-merged "Requests/LabNo/Haemolysis" dataset, using the de-identified patient Medical Record Number (MRN) as the linkage field, and the entire merged dataset was sorted by patient MRN, inpatient admission or ED presentation dates and times, and specimen collection dates and times. Test orders where the specimen was collected after the patient admission, or presentation at ED, and before the patient discharge could be confidently attributed to those patient encounters. Data linkage between the three datasets allowed a single test order in the "Requests/LabNo/Haemolysis" to be linked with either the PAS or ED information system dataset, or both datasets simultaneously. The SPSS "LAG" function was used to compare the patient, inpatient admission or ED presentation dates/times, and specimen collection dates/times of the sorted merged datasets and to associate, where valid and appropriate data were found, inpatient admission or ED presentation, discharge, and demographic information with the relevant test order data. In cases where specimen collection for a test order occurred either before patient admission or ED presentation, after patient discharge, or where no patient encounter data could be found, no linkage was performed. Therefore, these test orders were excluded from all analyses where linked data were necessary (e.g., comparisons of haemolysis rates for different DRGs in inpatient wards or presenting problems in EDs). Once the linkable patient presentation and admission data from the ED information system and PAS datasets were merged, the merged dataset was cleaned to remove orphan patient admission or ED presentation information (presentations and admissions for which no associated pathology tests were found).

SECTION 2.1: IMPACT OF CHANGING THE DENOMINATOR IN REPORTED HAEMOLYSIS RATES

INTRODUCTION

In addition to being able to count haemolysis rejections according to three different units of measurement (per episode, per specimen, and per test) and laboratories being able to choose between assigning accessions per episode or per specimen, pathology services can also alter the scope of any analysis of haemolysis rates in their laboratories. The scope that a pathology service chooses when assessing their haemolysis rate can influence the magnitude of the haemolysis rate.

The aim of this section is to compare the apparent haemolysis rate for five different potential scopes for a haemolysis rate analysis. The five scopes compared here are by no means exhaustive, but they were chosen to illustrate the potential for variation from a broad scope (All Accessions) to a narrow scope (Accessions from Biochemistry laboratory that were assessed for haemolysis on the analyser that had a Potassium test ordered and that came from an ED).

METHODS

Each haemolysis rate was generated by restricting the dataset to the appropriate scope and then counting the number of haemolysed accessions and the number of total accessions for each hospital. The entire study period (October 2009 to September 2013) was utilised.

RESULTS

Table 13 shows the overall haemolysis rate for all hospitals, and for each of the study hospitals, for five different potential scopes. The overall haemolysis rate was 1.7% of accessions when considering all accessions (in the Biochemistry and Haematology laboratories only) and the apparent haemolysis rate increased as a narrower scope was chosen. The overall rate was 2.47% when considering only biochemistry specimens that had been assessed for haemolysis, and the rate was 6.37% when considering only biochemistry specimens that had been assessed for haemolysis and that had had a Potassium test ordered and which had been received from the ED.

Table 13. Comparison of the haemolysis rate generated according to the scope selected for calculating the haemolysis rate at each of the five study hospitals for the study period (October 2009-September 2013).

	Rate of Haemolysed Accessions (No. of Haemolysed Accessions / No. of Total Accessions)				
Hospital	**All Accessions (Biochemistry and Haematology Only)**	**Biochemistry Only**	**Biochemistry Assessed for Haemolysis Only**	**Biochemistry Assessed for Haemolysis with Potassium ordered Only**	**Biochemistry Assessed for Haemolysis with Potassium ordered in ED only**
A	1.81% (5,163/285,090)	1.87% (5,163/276,450)	2.44% (5,163/211,482)	2.65% (5,039/190,351)	5.40% (3,437/63,683)
B	2.94% (5,451/185,118)	3.13% (5,451/17,4046)	4.17% (5,451/130,787)	4.42% (5,263/119,018)	7.47% (3,133/41,928)
C	3.11% (5,858/188,252)	3.31% (5,858/177,042)	4.07% (5,858/144,027)	4.27% (5,723/134,001)	8.42% (3,947/46,874)
D	1.21% (14,587/1,200,612)	1.26% (14,587/1,160,049)	1.92% (14,587/760,245)	2.05% (13,868/674,906)	6.08% (7,930/130,439)
E	2.02% (3,612/178,489)	2.05% (3,612/176,051)	2.33% (3,612/154,865)	2.50% (3,489/139,370)	5.45% (2,535/46,525)
Total	1.70% (34,671/2,037,561)	1.77% (34,671/1,963,638)	2.47% (34,671/1,401,406)	2.65% (33,382/1,257,646)	6.37% (20,982/329,449)

SECTION 2.2: ASSESSING OVERALL HAEMOLYSIS RATES

INTRODUCTION

The existing literature described in the Evidence Scan supports the belief that a number of factors play a role in the likelihood that a blood draw will result in a haemolysed specimen. These factors include: (a) the hospital characteristics, such as whether the blood draw is occurring in the ED or in an inpatient ward,[5,11,12,25,27,31,33,36,38,40,45,50] and whether the collector is a laboratory phlebotomist or hospital clinical staff;[14,18,29,30,34,52,55] (b) patient characteristics such as age and sex can lead to patients having smaller, weaker, or less accessible veins which alters the blood draw equipment and technique used.[26,36,52]

The aim of this section was to (a) report the overall rate of haemolysis for all hospitals and the rate for individual hospitals; (b) explore the impact on haemolysis rate, of hospital and patient characteristics such as their location in the hospital and patient age; and (c) to show the degree of change that has occurred in the haemolysis rate over a 4 year period (October 2009 to September 2013).

METHODS

The rates of haemolysed specimens were calculated by counting the number of specimens that were found to have any level of haemolysis (as indicated by the biochemistry analyser) and dividing that number by the number of specimens processed.

As was demonstrated in Table 13, the choice of scope of analysing haemolysis rates can influence the magnitude of the reported rate. For the following analyses, the scope was set to "Biochemistry Assessed for Haemolysis Only"; that is specimens that were not processed in the biochemistry department, or were not assessed for haemolysis, were excluded.

RESULTS

Table 14 shows the overall rates of haemolysis at each of the five study hospitals for the entire study period (October 2009 to September 2013). The overall rate of haemolysed specimens was 2.47%. The haemolysis rate was highest at Hospitals B and C (which also happened to be the smallest laboratories as measured by the total number of specimens processed), with rates of 4.17% and 4.07%, respectively. The haemolysis rate was lowest at the largest hospital (accounting for 54.26% of all specimens processed), Hospital D, with a rate of 1.92%.

Table 14. The number of haemolysed specimens, total number of specimens processed (excluding those not assessed for haemolysis), and the overall rate of haemolysis at each of the five study hospitals for the study period (October 2009-September 2013).

Hospital	No. of Haemolysed Specimens	Total Specimens Assessed for Haemolysis	Rate of Haemolysed Specimens
A	5,163	211,482	2.44%
B	5,451	130,790	4.17%
C	5,858	144,027	4.07%
D	14,587	760,449	1.92%
E	3,612	154,866	2.33%
Total	34,671	1,401,614	2.47%

Figure 5 compares the proportion of specimens that were found to be haemolysed between patients in the ED, patients in inpatient wards, and other patients (including outpatients, referred patients etc.) at each of the five hospitals. The overall rate of haemolysed specimens for inpatients was 1.33%, while the rate in the ED was more than four times higher at 6.12%, the rate of haemolysed specimens was lowest for other patients at 1.01%. The rate of haemolysis in EDs exceeded the rate for inpatients by a large margin in all five study hospitals. The difference in rates was smallest in Hospital B, where the rate was 3.3 times higher in EDs than for inpatients, while the difference was greatest in Hospital E where the ratio was 5.5 times. The haemolysis rate was lowest for other patients at Hospitals A and D (the two largest hospitals), but the rate for other patients was higher than for inpatients in Hospitals B, C, and E. In the case of Hospital B, the haemolysis rate for other patients was almost 2.5 times higher than for inpatients.

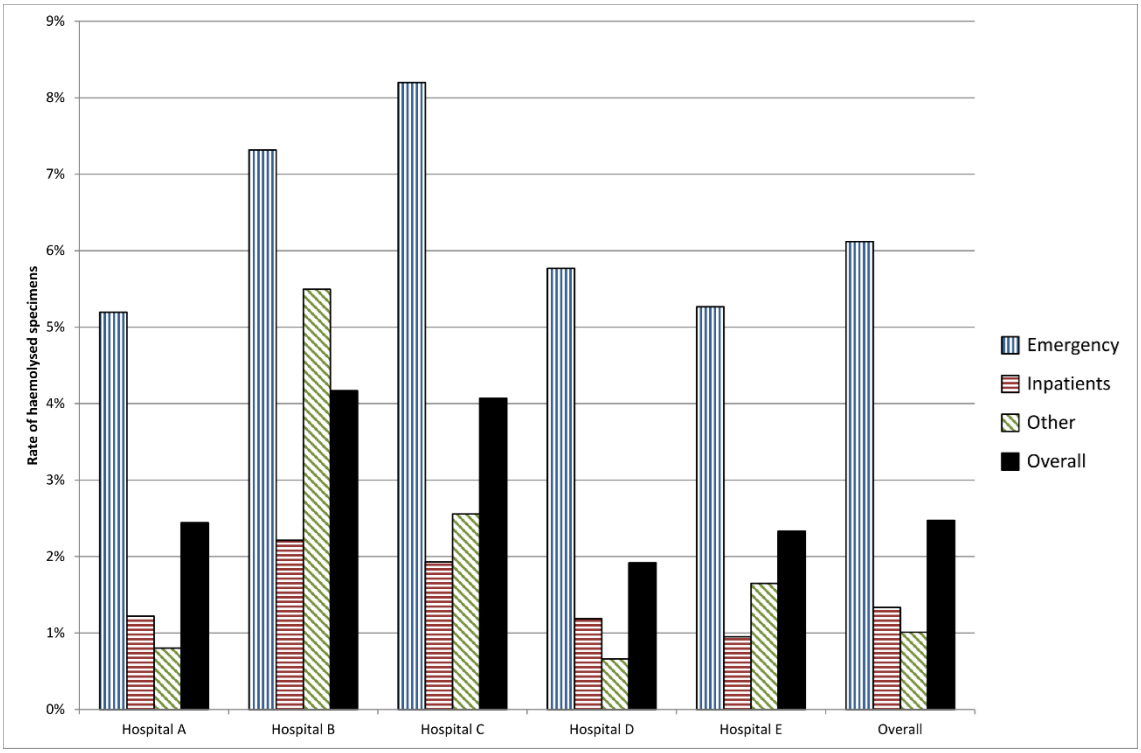

Figure 5. Comparison of haemolysis rate between Emergency Department patients, inpatients, and outpatient/ referred patients, at each of the five study hospitals for the study period (October 2009-September 2013).

Figure 6 compares the rate of haemolysis according to the age group of the patient. Overall, the rate of haemolysed specimens was highest for babies younger than 1 year of age (4.60%), and lower for each successive age group until the older adult group (60-80 years of age) who had a haemolysis rate of 2.18%. The rate of haemolysis for the elderly (over 80 years of age) was higher at 2.52%. Generally, when looking at individual hospitals, babies (younger than 1 year) and toddlers (1-5 years) had higher rates of haemolysis than older patients. In all hospitals, except for Hospital A, the rate of haemolysis was higher for babies than toddlers; Hospital E had the greatest disparity between the haemolysis rate for babies and toddlers: the rate for babies was 2.9 times higher than it was for toddlers. Hospital D, followed by Hospital A (which were the two largest hospitals in this analysis) had the smallest differences between the haemolysis rates for patients belonging to different age groups.

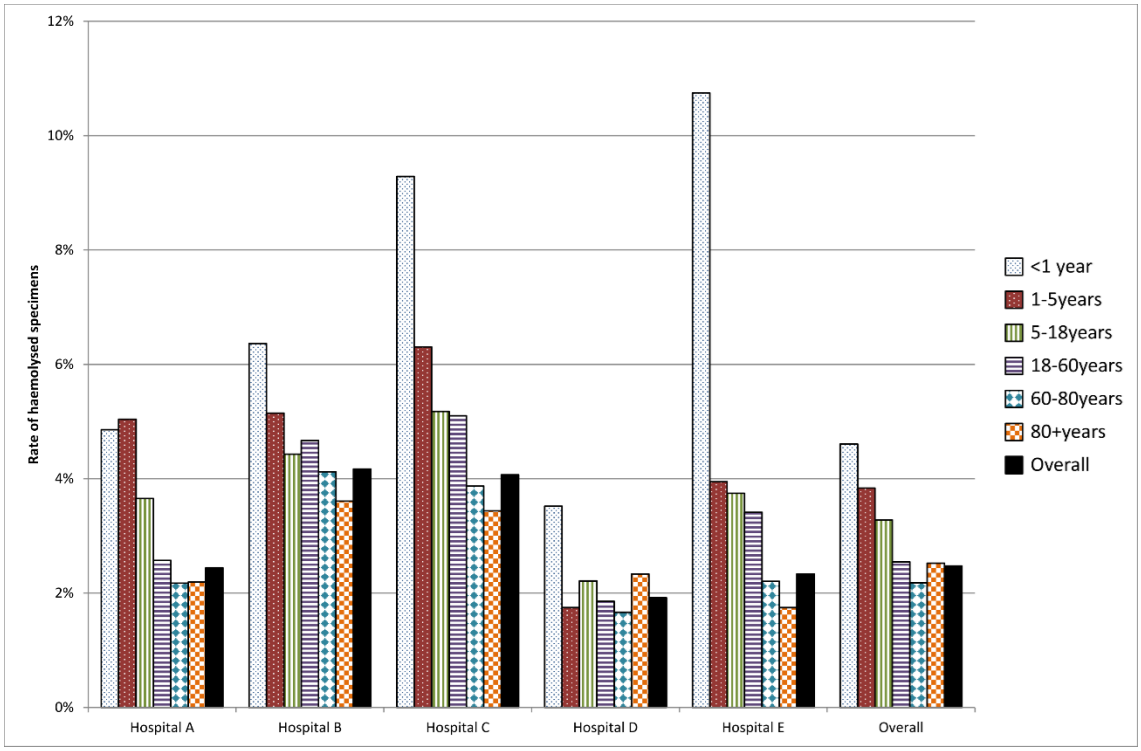

Figure 6. Comparison of haemolysis rate between patients belonging to each of six different age groups (babies, toddlers, children/adolescents, working-age adults, older adults, and the elderly) at each of the five study hospitals for the study period (October 2009-September 2013).

Figure 7 shows how the overall proportion of specimens found to be haemolysed varied across time (black solid line) as well as the variation across time of the haemolysis rate at each hospital. For the first two years of the study period (October 2009 to September 2011) the overall haemolysis rate remained fairly stable between 1.4% and 1.9% of specimens. The following year-long period (October 2011 to October 2012) saw a jump in the overall haemolysis rate, where it fluctuated between 2.0% and 2.7% of specimens. This period coincided with a period of time that the haemolysis detection parameters, in the Siemens Dimension analysers at Hospitals A, B, C, and E, were altered in response to the results of an internal study which resulted in increased sensitivity to haemolysis. No change was made to the parameters for the Roche Modular analysers operating at Hospital D. The Abbott Architect analysers were installed in the five study hospitals between October 2012 and February 2013 and the haemolysis detection parameters were modified according to the manufacturer instructions. This coincided with a drop in both the overall haemolysis rate and the haemolysis rate at each study hospital. For the majority of 2013 the haemolysis rate was lower than 1% of specimens. As was shown in Table 14, Hospitals B and C had a higher rate of haemolysis compared to the other hospitals. This difference was most pronounced between October 2011 and October 2012 where the haemolysis rate for both hospitals exceeded 4% in most months and peaked at a rate above 6% of specimens. The rate of haemolysis at Hospitals A and E increased by a much smaller degree during the same time, rising up to a rate between 2% and 4%. In comparison, Hospital D did not show any increase in the haemolysis rate during the same period and the rate of haemolysis remained around 1.5% of specimens.

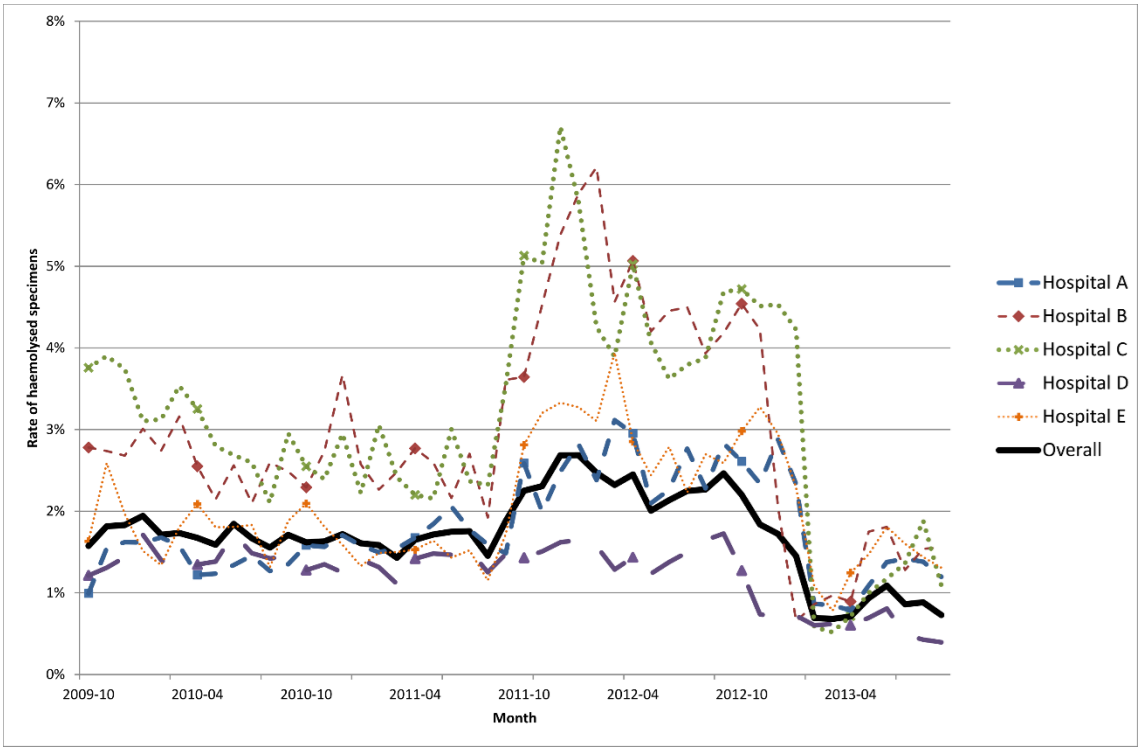

Figure 7. Variation in the rate of haemolysed specimens at each of the five study hospitals over time for the four-year study period (October 2009-September 2013).

Table 15 compares the proportion of specimens that had a Troponin test ordered that were found to be haemolysed between patients in the ED, patients in inpatient wards, and other patients (including outpatients, referred patients etc.) at each of the five hospitals. The overall haemolysis rate for specimens undergoing Troponin testing was 4.43%. For inpatients the rate was 2.09% while the rate in the ED was nearly three times higher at 5.63%. There was relatively little Troponin testing conducted for other patients. The rate of haemolysis in EDs exceeded the rate for inpatients by a large margin in all five study hospitals. The difference in rates was smallest in Hospital C, where the rate was 1.96 times higher in EDs than for inpatients, while the difference was greatest in Hospital A where the ratio was 3.19 times.

Table 15. The overall rate of haemolysis for specimens that had a Troponin test ordered at each of the five study hospitals for the study period (October 2009-September 2013).

	Rate of Haemolysed Troponin Specimens (No. of Haemolysed Troponin Specimens / Total Troponin Specimens Assessed for Haemolysis)			
Hospital	**Emergency**	**Inpatient**	**Other**	**Overall**
A	4.60% (977/21,233)	1.44% (160/11,091)	2.77% (11/397)	3.51% (1,148/32,721)
B	6.56% (778/11,851)	2.26% (86/3,803)	4.93% (11/223)	5.51% (875/15,877)
C	5.17% (621/12,005)	2.64% (101/3,832)	5.26% (11/209)	4.57% (733/16,046)
D	6.30% (2,816/44,671)	2.23% (668/29,944)	4.47% (76/1,700)	4.66% (3,560/76,315)
E	4.62% (636/13,780)	2.09% (87/4,160)	4.29% (7/163)	4.03% (730/18,103)
Total	5.63% (5,828/103,540)	2.09% (1102/52,830)	4.31% (116/2,692)	4.43% (7,046/159,062)

SECTION 2.3: ASSESSING HAEMOLYSIS FOR HOSPITAL INPATIENTS

INTRODUCTION

In this section we focused on hospital inpatients to compare the proportion of specimens found to be haemolysed when they were collected by a laboratory phlebotomist with the proportion that were found to be haemolysed when they were collected by clinical staff in the hospital. We also investigated which types of patient admissions, as indicated by the Diagnosis-Related Group (DRG) code, were associated with the most haemolysed specimens.

METHODS

The same method was used to calculate the rate of haemolysed specimens as for the previous section. Specimens that were not assessed for haemolysis were excluded.

The Top-10 DRGs with the highest frequency of haemolysis were reported and ranked according to the raw frequency of haemolysed specimens.

RESULTS

Figure 8 compares the rate of haemolysed specimens for clinical staff (vertical blue stripes) and laboratory phlebotomists (horizontal red stripes) at each hospital and overall across all study hospitals for the entire four year study period. The overall rate of haemolysed specimens was approximately three times higher for clinical staff (2.33%) than it was for laboratory phlebotomists (0.79%). This pattern was evident at all study hospitals. The difference was greatest at Hospital E, where the haemolysis rate was 3.54 times larger for clinical staff than for laboratory phlebotomists (2.37% compared to 0.67%), and smallest at Hospital C where the it was 2.47 times larger (3.60% compared to 1.46%).

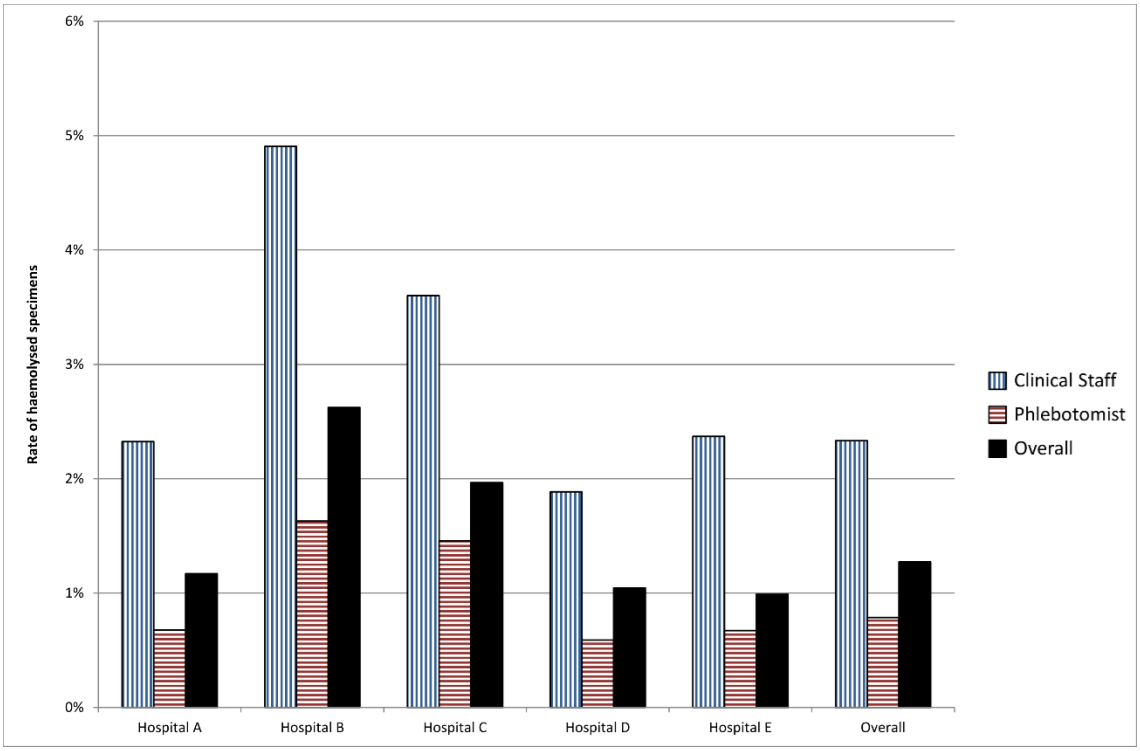

Figure 8. Comparison of haemolysis rate between specimens that were collected by a Laboratory Phlebotomist and Clinical Staff in the Hospital, excluding patients within the ED (where all specimens were collected by Clinical Staff) at each of the five study hospitals for the study period (October 2009-September 2013).

Table 16 shows a list of the Top-10 DRGs that had the highest frequency of haemolysed specimens along with the number and proportion of specimens that were found to be haemolysed at each of the five study hospitals. Patients registered with the "Chest Pain, <2 days" DRG had 546 haemolysed specimens representing 3.18% of biochemistry specimens for that DRG, and 2.21% of all haemolysed specimens. Out of the Top-10 DRGs, "Oesophagitis and Gastroenteritis W/O Cat or Sev CC" had the highest rate of haemolysed specimens at a rate of 3.44% across all hospitals.

Table 16. The Top-10 DRGs with the highest frequency of haemolysed specimens for inpatients at the five study hospitals for the study period (October 2009-September 2013).

	Rate of Haemolysed Specimens (No. of Haemolysed Specimens / Total Specimens Assessed for Haemolysis)					
DRG	**Hospital A**	**Hospital B**	**Hospital C**	**Hospital D**	**Hospital E**	**Overall**
1. Chest Pain, <2 Days	2.17% (39/1,800)	4.02% (95/2,365)	4.11% (115/2,801)	2.98% (175/5,863)	2.82% (122/4,332)	3.18% (546/17,161)
2. Respiratory Infections/Inflammations W/ Cat CC	1.71% (93/5,438)	2.32% (82/3,532)	2.60% (102/3,924)	1.79% (119/6,649)	1.68% (109/6,479)	1.94% (505/26,022)
3. Rehabilitation	0.66% (105/15,825)	2.17% (26/1,200)	1.29% (143/11,079)	0.83% (98/11,867)	0.46% (20/4,347)	0.88% (392/44,318)
4. Oesophagitis and Gastroenteritis W/O Cat or Sev CC	4.51% (70/1,553)	4.00% (52/1,299)	4.73% (79/1,669)	2.54% (117/4,615)	3.20% (48/1,500)	3.44% (366/10,636)
5. Kidney and Urinary Tract Infections W/O Cat or Sev CC	2.68% (44/1,641)	3.59% (55/1,534)	3.44% (68/1,977)	2.75% (127/4,611)	2.15% (45/2,092)	2.86% (339/11,855)
6. Chronic Obstructive Airways Disease W/O Cat CC	1.63% (33/2,019)	2.69% (68/2,524)	2.30% (60/2,612)	1.88% (96/5,103)	1.36% (58/4,253)	1.91% (315/16,511)
7. Respiratory Infections / Inflammations W/ Sev or Mod CC	1.92% (40/2,078)	2.80% (61/2,177)	3.10% (86/2,777)	1.81% (81/4,464)	1.58% (47/2,980)	2.18% (315/14,476)
8. Other Digestive System Disorders W/O Cat or Sev CC	2.04% (33/1,614)	5.43% (69/1,270)	4.25% (62/1,458)	2.43% (103/4,233)	2.47% (43/1,739)	3.01% (310/10,314)
9. Heart Failure and Shock W/ Cat CC	1.42% (62/4,363)	2.80% (70/2,503)	2.55% (58/2,274)	1.63% (78/4,789)	1.33% (40/3,017)	1.82% (308/16,946)
10. Kidney and Urinary Tract Infections W/ Cat or Sev CC	2.06% (61/2,959)	2.59% (43/1,660)	2.98% (68/2,284)	2.05% (91/4,438)	1.25% (40/3,208)	2.08% (303/14,549)
Total (All DRGs)	1.52% (3,352/220,477)	2.58% (3,891/150,958)	2.65% (4,198/158,558)	1.20% (10,693/890,852)	1.70% (2,524/148,261)	1.57% (24,658/1,569,106)

W/: With
W/O: Without
Mod: Moderate
Sev: Severe
Cat: Catastrophic
CC: Complications and Comorbidities

SECTION 2.4: ASSESSING HAEMOLYSIS FOR ED PATIENTS

INTRODUCTION

In this section we focused on ED patients to assess which illnesses, as indicated by the ED presenting problem, were associated with the most haemolysed specimens, and to evaluate whether the urgency associated with the ED presentation, as indicated by the Triage category, affected the rate of haemolysis.

METHODS

The same method was used to calculate the rate of haemolysed specimens as for the previous section. Similarly, specimens that were not assessed for haemolysis were excluded.

The Top-10 ED presenting problems with the highest frequency of haemolysis were selected and ranked according to the raw frequency of haemolysed specimens. The ED information system recorded presenting problem as a free text field so, prior to this analysis, the Top-5 most frequently recorded presenting problems were selected and relevant keyword search terms were used to merge related presenting problems into these five categories.

RESULTS

Table 17 shows a list of the Top-10 ED presenting problems with the highest frequency of haemolysed specimens and, for each of the five study EDs. Patients who presented with “Pain, chest” had 2,214 haemolysed specimens which represented 5.14% of biochemistry specimens for that presenting problem, and 10.5% of all haemolysed specimens. Out of the Top-10 presenting problems, “Pain, other” had the highest rate of haemolysed specimens at a rate of 8.73% across all EDs.

Table 18 shows the number and proportion of specimens that were found to be haemolysed for each triage category at each of the five EDs. Patients who were triaged in the most urgent triage category (Triage 1; “Immediately life threatening”) had the highest rate of haemolysed specimens at a rate of 8.28% across all EDs. There was little difference between the overall rate of haemolysed specimens for the other triage categories which ranged between 5.78% for Triage 5 to 6.27% for Triage 4 presentations.

Table 17. The Top-10 Presenting Problems with the highest frequency of haemolysed specimens for ED patients at the five study hospitals for the study period (October 2009-September 2013).

	Rate of Haemolysed Specimens (No. of Haemolysed Specimens / Total Specimens Assessed for Haemolysis)					
Presenting Problem	**Hospital A**	**Hospital B**	**Hospital C**	**Hospital D**	**Hospital E**	**Overall**
1. Pain, chest*	4.43% (292/6,589)	7.13% (312/4,376)	7.92% (422/5,327)	5.38% (910/16,920)	5.17% (278/5,373)	5.74% (2,214/38,585)
2. Pain, abdominal*	5.01% (328/6,553)	7.00% (304/4,345)	8.57% (405/4,724)	5.79% (828/14,304)	5.84% (276/4,725)	6.18% (2,141/34,651)
3. Vomiting*	5.51% (198/3,592)	8.29% (172/2,074)	8.71% (230/2,641)	5.78% (320/5,533)	6.15% (156/2,536)	6.57% (1,076/16,376)
4. Falls*	6.40% (151/2,358)	9.18% (166/1,808)	9.49% (232/2,445)	7.02% (357/5,086)	5.22% (161/3,087)	7.22% (1,067/14,784)
5. Respiratory: shortness of breath*	5.84% (136/2,328)	8.49% (127/1,496)	9.18% (195/2,124)	6.36% (308/4,839)	5.81% (120/2,066)	6.89% (886/12,853)
6. Unwell	4.67% (26/557)	8.11% (24/296)	11.45% (53/463)	5.63% (85/1,510)	5.90% (37/627)	6.52% (225/3,453)
7. Dizziness	4.83% (26/538)	7.86% (32/407)	7.85% (31/395)	6.56% (100/1,525)	6.47% (24/371)	6.58% (213/3,236)
8. Headache	5.15% (28/544)	6.48% (25/386)	8.26% (30/363)	5.72% (115/2,012)	5.33% (13/244)	5.95% (211/3,549)
9. Cellulitis suspected	8.53% (44/516)	8.67% (39/450)	9.27% (51/550)	6.14% (40/651)	11.31% (32/283)	8.41% (206/2,450)
10. Pain, other	7.83% (18/230)	11.07% (28/253)	15.28% (35/229)	7.48% (101/1,350)	7.61% (14/184)	8.73% (196/2,246)
Total (All Presenting Problems)	5.19% (3,441/66,249)	7.36% (3,126/42,449)	8.42% (3,907/46,392)	5.82% (8,031/138,047)	5.29% (2,534/47,946)	6.17% (21,039/341,083)

* These Presenting Problem groups were generated from the sum of multiple relevant Presenting Problem descriptions.

Table 18. The rate of haemolysis for ED patients triaged to each of the five triage categories at the five study hospitals for the study period (October 2009-September 2013).

	Rate of Haemolysed Specimens (No. of Haemolysed Specimens / Total Specimens Assessed for Haemolysis)					
Triage Category	**Hospital A**	**Hospital B**	**Hospital C**	**Hospital D**	**Hospital E**	**Overall**
Immediately life threatening (1)	7.74% (27/349)	9.15% (27/295)	11.13% (52/467)	7.70% (211/2,739)	8.63% (39/452)	8.28% (356/4,302)
Imminently life threatening (2)	5.04% (518/10,274)	7.41% (617/8,324)	8.45% (644/7,617)	5.44% (2,090/38,393)	5.60% (408/7,280)	5.95% (4,277/71,888)
Potentially life threatening (3)	4.91% (1,075/21,896)	7.39% (1,647/22,301)	8.33% (1,718/20,629)	5.84% (3,163/54,185)	5.16% (1,291/25,019)	6.18% (8,894/144,030)
Potentially serious (4)	5.41% (1,656/30,621)	7.31% (810/11,085)	8.50% (1,419/16,697)	6.06% (2,417/39,879)	5.32% (802/15,084)	6.27% (7,104/113,366)
Less Urgent (5)	5.38% (194/3,606)	6.30% (43/683)	8.78% (115/1,310)	5.27% (206/3,911)	3.95% (19/481)	5.78% (577/9,991)
Total (All Triage)	5.20% (3,470/66,746)	7.37% (3,144/42,688)	8.45% (3,948/46,720)	5.81% (8,087/139,107)	5.30% (2,559/48,316)	6.17% (21,208/343,577)

SECTION 2.5: HOLISTIC EXAMINATION OF HAEMOLYSIS AT EDs AND IN HOSPITALS

AIMS

In the following sections, we aimed to:

- Measure the rate of haemolysed specimens across EDs and hospitals over the study period (October 2009 to September 2013)
- Examine the impact of haemolysis on:
- Repeat testing for hospital inpatients and in the EDs.
- ED Length Of Stay (ED LOS)
- Identify the risk factors associated with haemolysis for hospital inpatients

STUDY POPULATION AND HAEMOLYSIS

We included all blood specimens collected during the study period. Approximately 12% of blood specimens were not subjected to testing on the main biochemistry analyser and thus were not assessed for haemolysis. In practice, apart from cases of visually detectable gross haemolysis, these specimens and their test results were treated as though the specimens were not haemolysed. For the following analyses, the scope was set to "Biochemistry Only" (see Table 13); that is, all biochemistry specimens were included even if they were not assessed for haemolysis.

AT EDS

ED PRESENTATIONS

In total, between 1st October 2009 and 30th September 2013, there were 220,390 blood specimens collected for 158,934 ED presentations (93,161 ED patients) at the five study EDs. All these specimens were sent to biochemistry analysers.

Some patients had multiple ED presentations.

- On average each patient had 1.7 presentations at one of the study EDs (SD=1.6, max=75)
- There were 44 patients who presented at study EDs more than 20 times during the four year study period.

HAEMOLYSIS RATES

Of 220,390 specimens collected from study EDs, 11,108 (5.04%; 95% CIs: 4.95% 5.13%) were haemolysed. The haemolysis rates and their 95% CIs varied across EDs over the years (Figure 10, Figure 11, and Figure 12; the actual rates across EDs/years are presented in Table 19). A year was defined from October of the previous year to September of the specified year. For example, the year 2010 was from 1st October 2009 to 30th September 2010. The haemolysis rate for 2012 was much higher than for other years, which was also true for all individual EDs except for ED D.

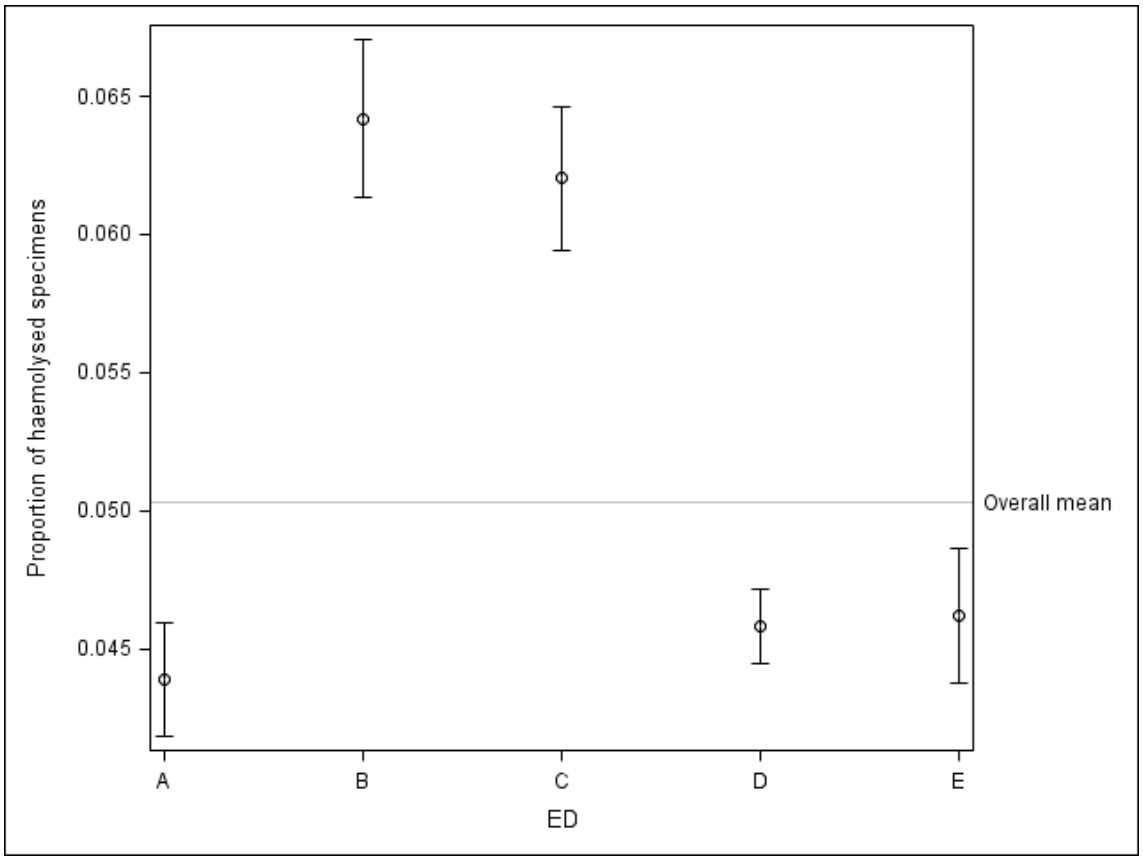

Figure 9. Comparison of haemolysis rates between the five study EDs, collapsed across study years. Error bars represent 95% CIs.

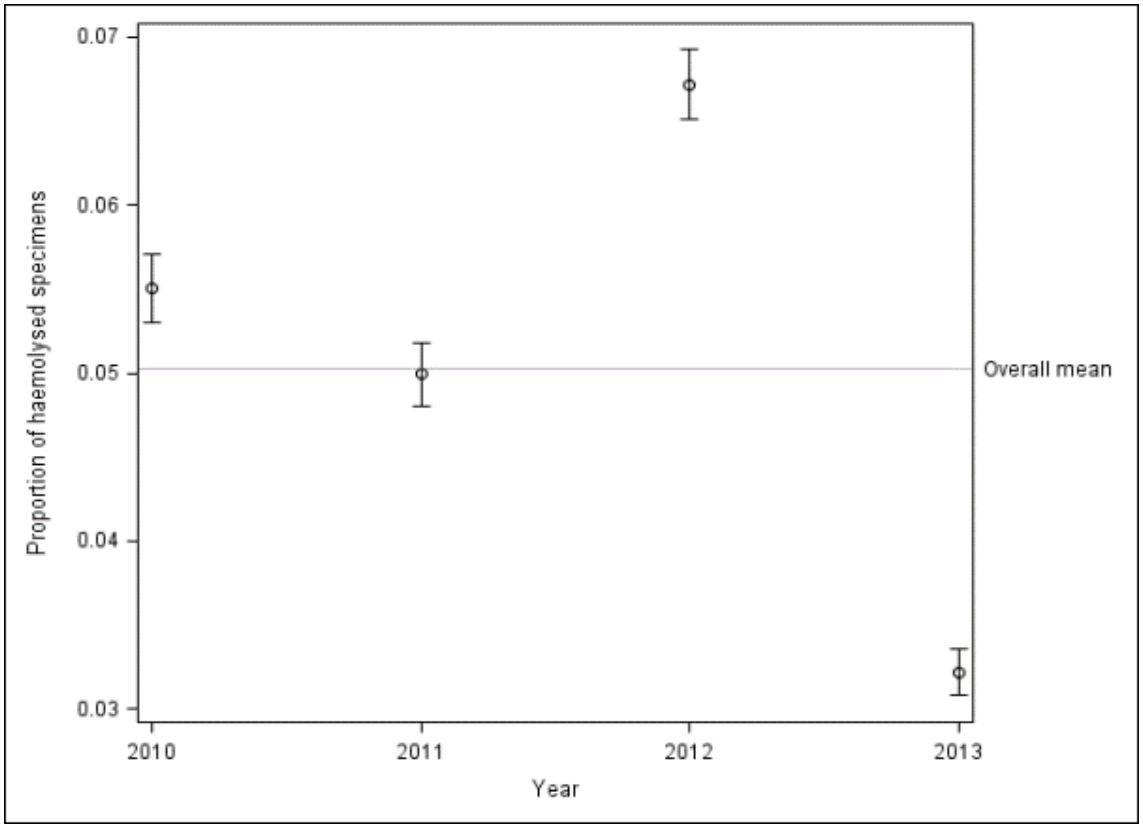

Figure 10. Comparison of haemolysis rates for each of the four study years, collapsed across EDs. Error bars represent 95% CIs.

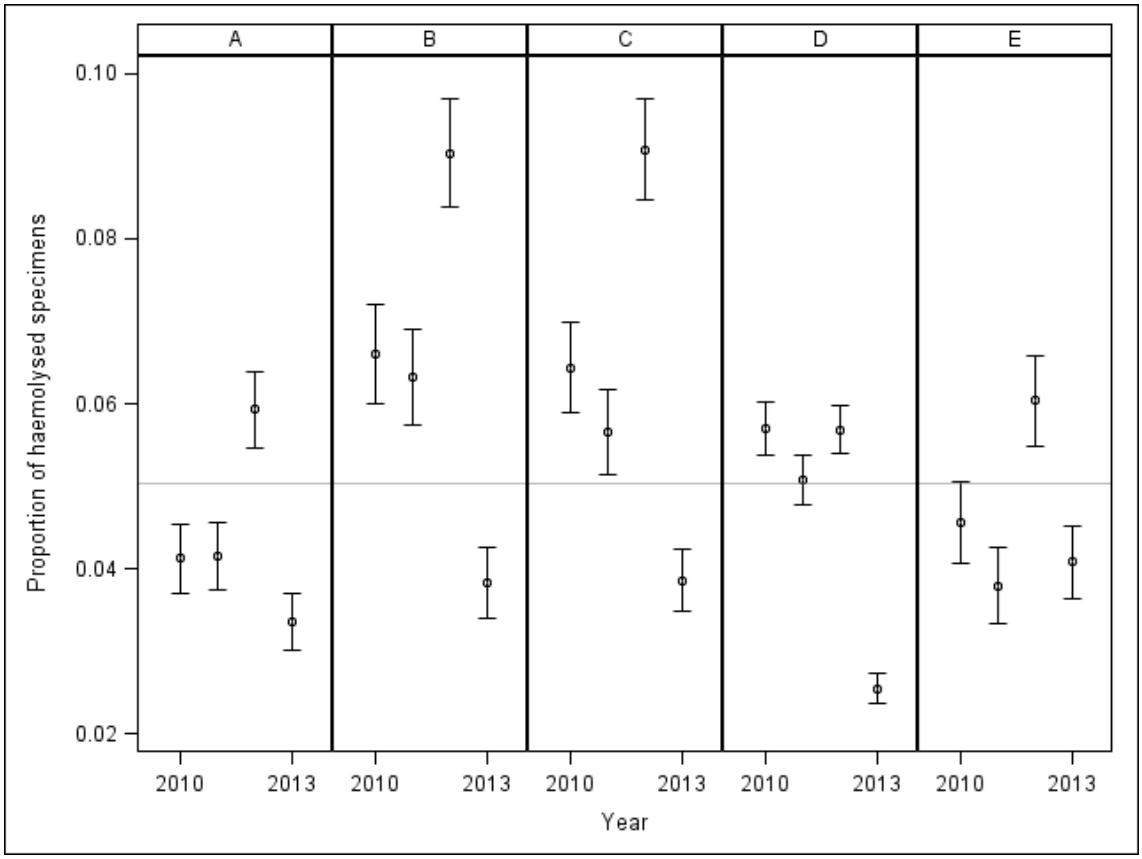

Figure 11. Comparison of haemolysis rates at each of the five study EDs for each of the four study years. Error bars represent 95% CIs.

Table 19. Haemolysis rates at each of the five study EDs for each of the four study years.

ED	Year*	No. of specimens	% of haemolysed specimens (95% CIs)
A	2010	8,254	4.10% (3.70%-4.50%)
	2011	9,187	4.10% (3.70%-4.60%)
	2012	10,086	5.90% (5.50%-6.40%)
	2013	10,750	3.40% (3.00%-3.70%)
B	2010	6,593	6.60% (6.00%-7.20%)
	2011	6,714	6.30% (5.70%-6.90%)
	2012	7,327	9.00% (8.40%-9.70%)
	2013	7,592	3.80% (3.40%-4.30%)
C	2010	7,535	6.40% (5.90%-7.00%)
	2011	7,753	5.70% (5.10%-6.20%)
	2012	8,662	9.10% (8.50%-9.70%)
	2013	9,636	3.90% (3.50%-4.20%)
D	2010	19,251	5.70% (5.40%-6.00%)
	2011	20,843	5.10% (4.80%-5.40%)
	2012	23,750	5.70% (5.40%-6.00%)
	2013	28,258	2.50% (2.40%-2.70%)
E	2010	6,709	4.60% (4.10%-5.10%)
	2011	6,623	3.80% (3.30%-4.20%)
	2012	7,125	6.00% (5.50%-6.60%)
	2013	7,742	4.10% (3.60%-4.50%)

* From October of the previous year to September of the specified year.

HOSPITAL INPATIENTS

The laboratories at the five study hospitals also processed some specimens coming from an additional five hospitals in the surrounding areas. In total, between 1st October 2009 and 30th September 2013, there were 974,963 blood specimens collected for 158,745 hospital inpatients (222,982 patient admissions) at the ten hospitals (five study hospitals hosting the laboratories, and five additional hospitals). All these specimens were sent to biochemistry analysers. Each patient admission had an average of 4.4 blood specimens (SD=12.7). Each patient was admitted, during the study period, an average of 1.4 times to any one of the ten hospitals (SD=1.9).

HAEMOLYSIS RATES

Of 974,963 specimens, 8,190 (0.84%; 95% CIs: 0.82%-0.85%) were haemolysed. The haemolysis rate for each hospital in each of the study years are shown in Figure 12, Figure 13 and Figure 14 (the actual rates across hospitals/years are presented in Table 20). The rate for 2012 was higher than for the other years; this pattern was evident at four of the study hospitals (A, B, C, and E) but not at study Hospital D or any of the surrounding hospitals that utilised the study laboratories.

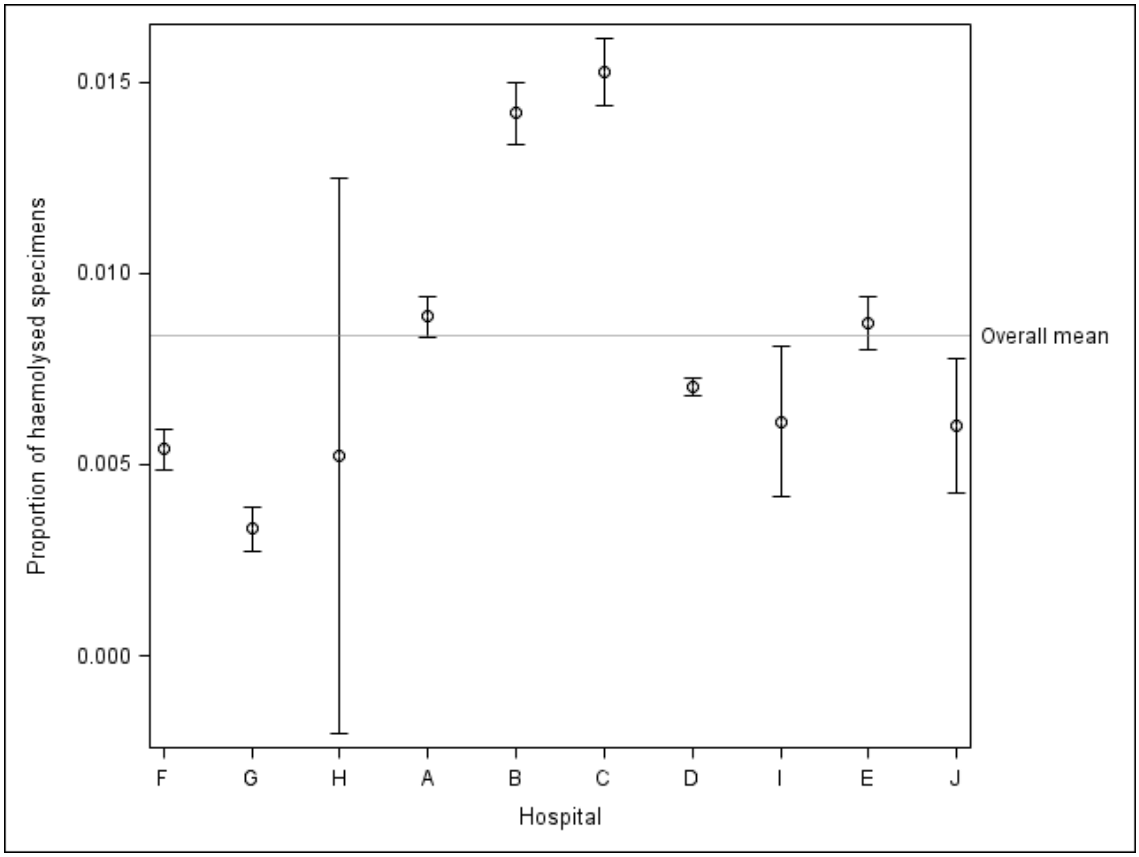

Figure 12: Comparison of haemolysis rates between the five study hospitals (A, B, C, D, and E), and five additional surrounding hospitals (F, G, H, I, J), collapsed across study years. Error bars represent 95% CIs.

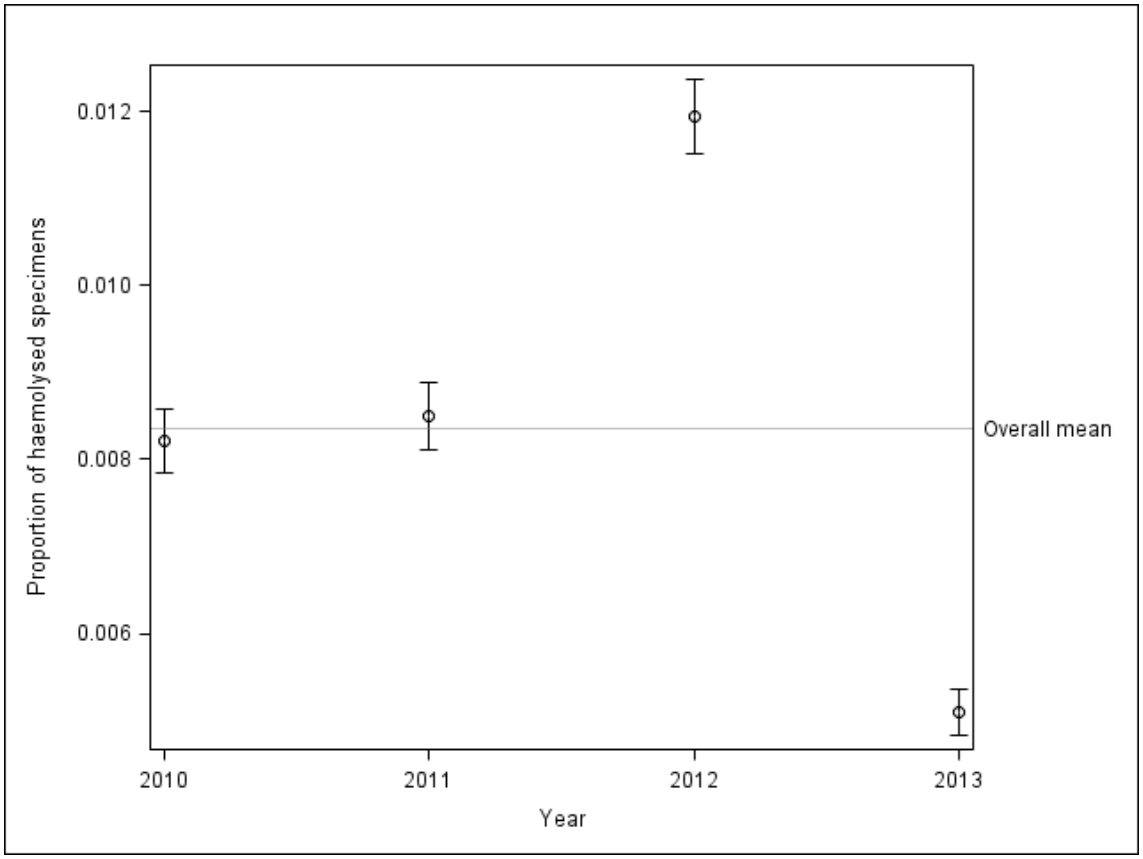

Figure 13. Comparison of haemolysis rates for each of the four study years, collapsed across the five study hospitals, and five additional surrounding hospitals. Error bars represent 95% CIs.

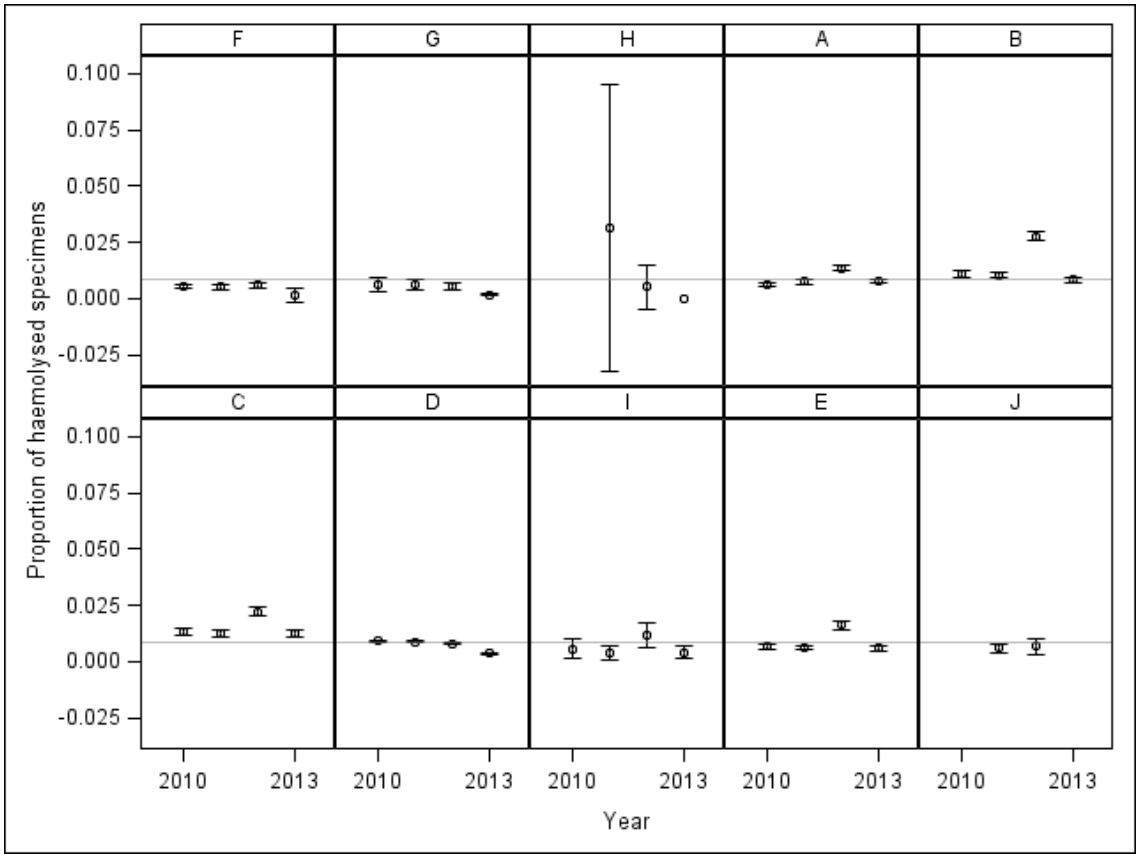

Figure 14. Comparison of haemolysis rates at each of the five study hospitals (A, B, C, D, and E), and five additional surrounding hospitals (F, G, H, I, J), for each of the four study years. Error bars represent 95% CIs.

Table 20. Haemolysis rates at each of the five study hospitals (A, B, C, D, and E), and five additional surrounding hospitals (F, G, H, I, J), for each of the four study years.

Hospital	Year*	No. of specimens	% of haemolysed specimens (95% CIs)
F	2010	43,611	0.53% (0.46%-0.60%)
	2011	11,982	0.50% (0.37%-0.63%)
	2012	15,521	0.61% (0.48%-0.73%)
	2013	604	0.17% (0.00%-0.49%)
G	2010	2,495	0.64% (0.33%-0.95%)
	2011	4,971	0.62% (0.40%-0.84%)
	2012	6,846	0.54% (0.37%-0.71%)
	2013	21,616	0.16% (0.11%-0.22%)
H	2011	32	3.13% (0.00%-9.50%)
	2012	198	0.51% (0.00%-1.50%)
	2013	152	<0.01% (n/a)
A	2010	26,735	0.59% (0.50%-0.68%)
	2011	27,699	0.74% (0.64%-0.84%)
	2012	33,999	1.36% (1.24%-1.49%)
	2013	31,959	0.76% (0.67%-0.86%)

Hospital	Year*	No. of specimens	% of haemolysed specimens (95% CIs)
B	2010	19,260	1.10% (0.95%-1.25%)
	2011	21,055	1.04% (0.90%-1.17%)
	2012	19,425	2.78% (2.55%-3.01%)
	2013	20,717	0.83% (0.70%-0.95%)
C	2010	17,298	1.32% (1.15%-1.49%)
	2011	17,837	1.26% (1.10%-1.43%)
	2012	20,359	2.23% (2.03%-2.43%)
	2013	21,250	1.25% (1.10%-1.40%)
D	2010	108,330	0.90% (0.84%-0.95%)
	2011	114,899	0.88% (0.83%-0.94%)
	2012	126,531	0.80% (0.75%-0.85%)
	2013	153,502	0.35% (0.32%-0.38%)
I	2010	1,247	0.56% (0.15%-0.98%)
	2011	1,491	0.40% (0.08%-0.72%)
	2012	1,483	1.15% (0.60%-1.69%)
	2013	1,978	0.40% (0.12%-0.68%)
E	2010	17,473	0.67% (0.55%-0.79%)
	2011	19,148	0.62% (0.51%-0.73%)
	2012	17,720	1.60% (1.42%-1.79%)
	2013	18,064	0.61% (0.50%-0.72%)
J	2011	5,358	0.58% (0.38%-0.78%)
	2012	2,118	0.66% (0.32%-1.01%)

* From October of the previous year to September of the labelled year.

SECTION 2.6: IMPACT OF HAEMOLYSIS ON REPEAT TEST ORDERS

The free haemoglobin in a haemolysed specimen can interfere with the results of some analytes.[69] When a pathology laboratory detects a haemolysed specimen, it is common for the laboratory to request another specimen be collected before they can proceed with processing a test. Haemolysed specimens can, therefore, result in repeat tests being ordered that would not have been ordered in normal circumstances. It is likely that repeat tests ordered within a short time after the previous test where the specimen was haemolysed were necessary because of haemolysis. When the specimen is not haemolysed, the time interval between the previous test and the repeat test indicates the temporal repeat testing profile in normal clinical practice. The impact of haemolysis on repeat testing can be assessed by comparing the temporal repeat testing profile when a haemolysed specimen is detected to the temporal repeat testing profile of normal clinical practice when the specimen is not haemolysed. In this section, we examine the impact of haemolysis on repeat testing of Potassium and cardiac Troponin tests in EDs and in hospital inpatient wards.

DEFINITIONS

REPEAT TEST

A test is considered as a repeat test if an identical test has already been ordered for (1) the same patient and (2) the same ED presentation or hospital inpatient admission.

PREVIOUS TEST

When a repeat test is ordered for a patient, the previous test refers to the preceding test of the same type that was ordered for that patient.

POTASSIUM TESTS

Potassium tests are very sensitive to the free haemoglobin in haemolysed specimens and the result can be affected with as little as 0.5 g/L free haemoglobin concentration.[70] In the study pathology service, a comment indicating that the specimen was haemolysed is added to Potassium test results when the haemoglobin level exceeds 0.5 g/L, and the result is suppressed (i.e. it results in a rejection) when the haemoglobin level exceeds 1.0 g/L.

Potassium tests are infrequently ordered on their own and are usually ordered as part of a panel. Common panels that include Potassium tests are Electrolytes, Urea, and Creatinine (EUC), the Basic Metabolic Panel (BMP), and Comprehensive Metabolic Panel (CMP).[71] The LIS contained a binary field that indicated whether a Potassium test had been ordered on a specimen. This binary field was used to assess the number of Potassium tests that had been processed.

ED PATIENTS

There were 165,397 specimens collected for Potassium testing for 155,411 ED presentations at the five study EDs. The majority of these presentations (94.1%) had only one Potassium test ordered. The maximum number of Potassium tests in a single ED presentation was 14 tests. In total, 10,941 specimens collected for a Potassium test (6.6%) were found to be haemolysed. There were 9,963 repeat Potassium tests.

Figure 15 compares the mean and median and variability in the time interval between the previous Potassium test and the repeat Potassium test when the previous test specimen was not found to be haemolysed (upper bar) and for when the previous test specimen was found to be haemolysed (lower bar).

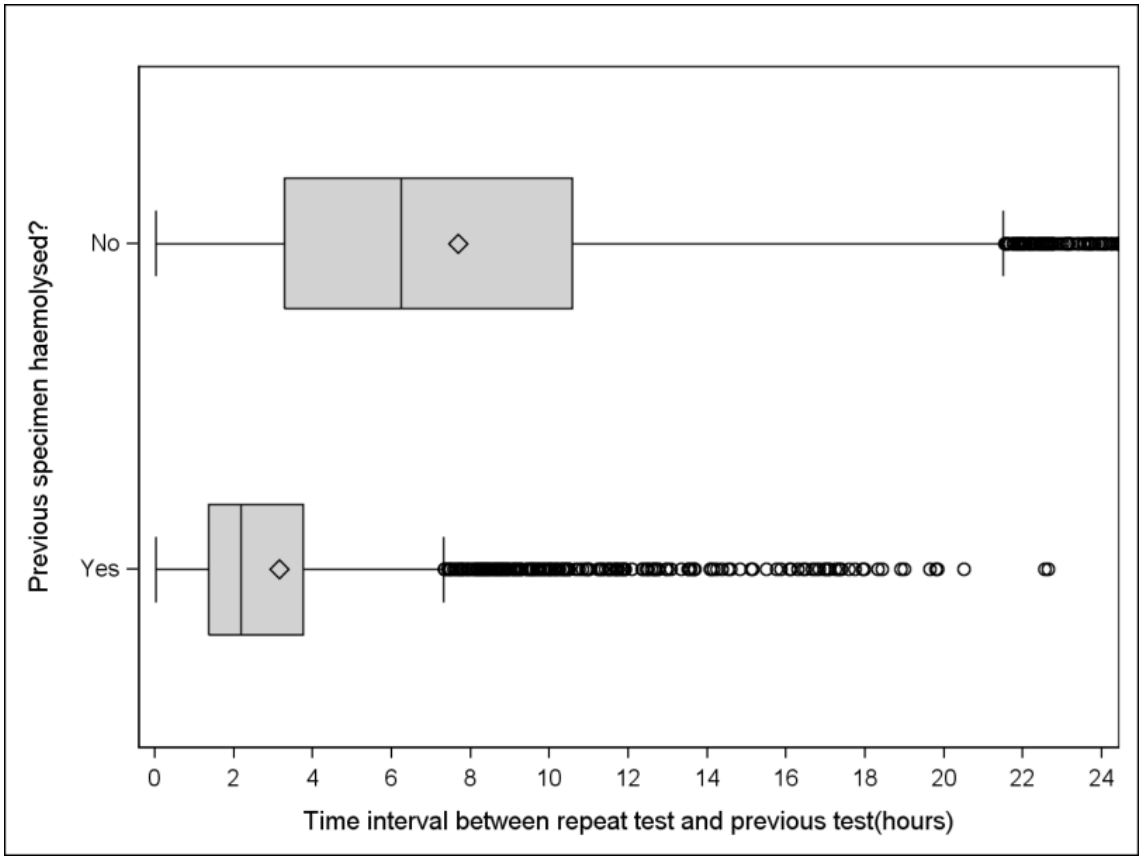

Figure 15. Time intervals between the previous Potassium test and the repeat Potassium test (hours) in the ED.

Table 21 shows that 2,962 repeat Potassium tests (39.7%) occurred after the preceding Potassium test was haemolysed, and in these cases there was a median interval of 2.2 hours between the previous test and the repeat Potassium test. In comparison, when the preceding Potassium test was not haemolysed, there was a median interval of 6.3 hours between it and the repeat Potassium test. This was a significant difference ($p<0.0001$ from the Wilcoxon Rank Sum test).

Table 21. Time intervals between the previous Potassium test and the repeat Potassium test (hours) in the ED.

Previous specimen haemolysed?	N (%)	Mean time interval in hours (95% CIs)	Median time interval in hours (IQR)	Maximum time interval in hours
No	7,001 (70.3%)	7.7 (7.5-7.8)	6.3 (3.3-10.6)	193.4
Yes	2,962 (39.7%)	3.1 (3.0-3.3)	2.2 (1.4-3.8)	28.3

Figure 16 shows the cumulative proportion of repeat Potassium tests, out of all Potassium tests, that occurred up to 30 hours after the previous Potassium test in the ED, when the specimen for the previous test was haemolysed (blue solid line) and when the previous specimen was not haemolysed (red dashed line). The function was much steeper when the previous Potassium test was haemolysed, indicating that haemolysed specimens for Potassium tests did in fact result in a repeat Potassium test within a much shorter interval than if the previous specimen had not been haemolysed.

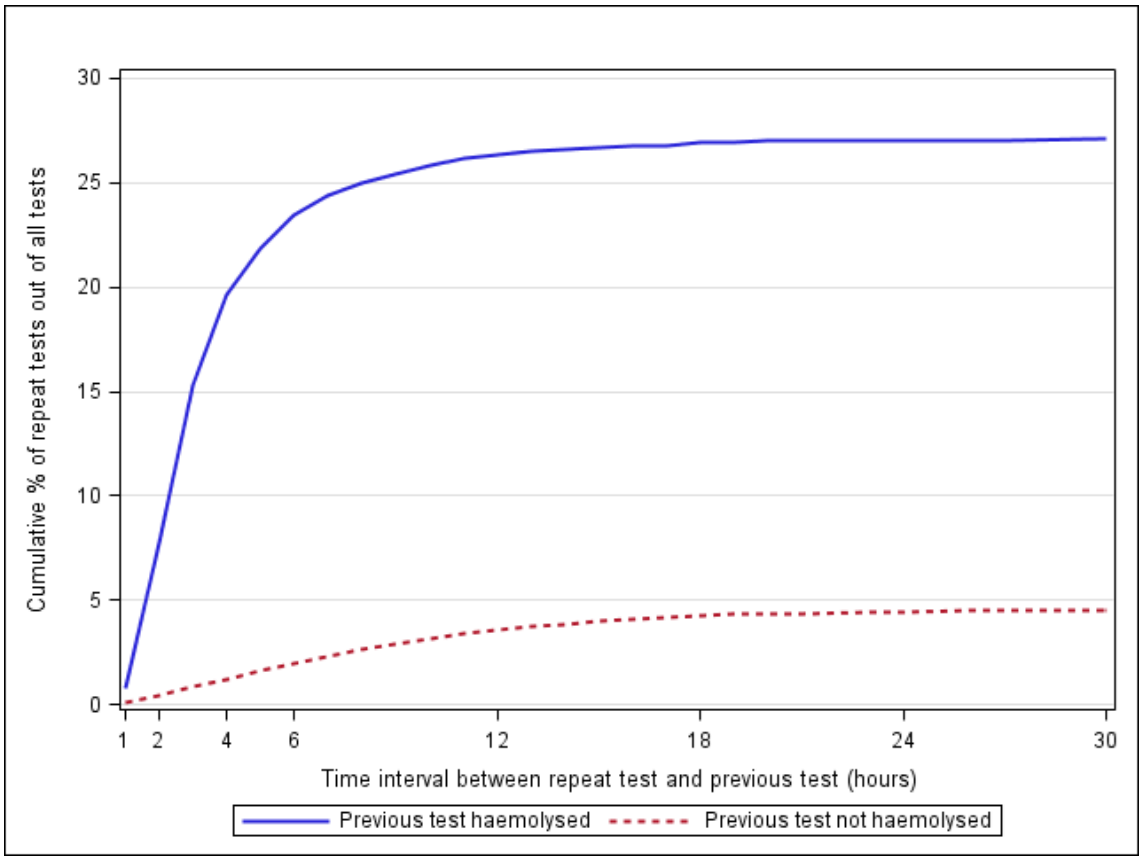

Figure 16. Cumulative percentage of repeat Potassium tests over time, in the ED.

HOSPITAL INPATIENTS

There were 573,272 specimens collected for Potassium testing for 150,664 hospital inpatients at the five study hospitals. About half of these admissions (48.6%) had only one Potassium test ordered. The maximum number of Potassium tests in a single hospital inpatient admission was 208 tests. In total, 7,564 of the specimens collected for a Potassium test (1.3%) were found to be haemolysed. There were 422,608 repeat

Potassium tests.

Figure 17 compares the mean and median and variability in the time interval between the previous Potassium test and the repeat Potassium test when the previous test specimen was not found to be haemolysed (upper bar) and for when the previous test specimen was found to be haemolysed (lower bar).

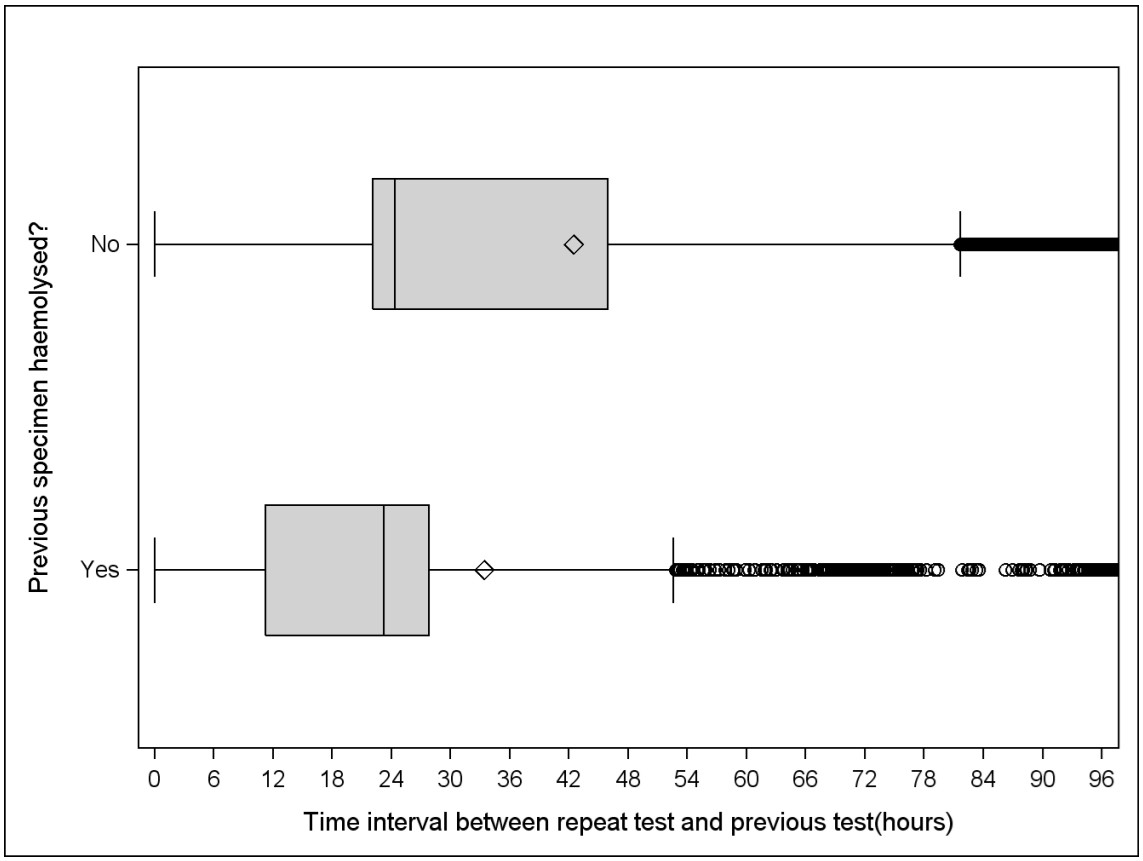

Figure 17. Time intervals between the previous Potassium test and the repeat Potassium test (hours), for hospital inpatients.

Table 22 shows that 5,889 repeat Potassium tests (1.4%) occurred after the preceding Potassium test was haemolysed, and in these cases there was a median interval of 23.3 hours between the previous test and the repeat Potassium test. In comparison, when the previous Potassium test was not haemolysed (98.6%), there was a median interval of 24.3 hours between it and the repeat Potassium test. Although the difference between medians was less dramatic than it was in the ED, this difference was significant ($p<0.0001$ from the Wilcoxon Rank Sum test).

Table 22. Time intervals between the previous Potassium test and the repeat Potassium test (hours), for hospital inpatients.

Previous specimen haemolysed?	N (%)	Mean time interval in hours (95% CIs)	Median time interval in hours (IQR)	Maximum time interval in hours
No	416,719 (98.6%)	42.5 (42.2-42.8)	24.3 (22.1-45.9)	12195.1
Yes	5,889 (1.4%)	33.4 (31.7-35.2)	23.3 (11.3-27.8)	1846.9

Figure 18 shows the cumulative proportion of repeat Potassium tests, out of all Potassium tests, that occurred up to 36 hours after the previous Potassium test in hospital inpatient wards, when the specimen for the previous test was haemolysed (blue solid line) and when the previous specimen was not haemolysed (red dashed line). At all time points indicated on the graph, a larger proportion of Potassium tests was accounted for by repeat tests when the specimen for the previous Potassium test was haemolysed than if the previous specimen had not been haemolysed.

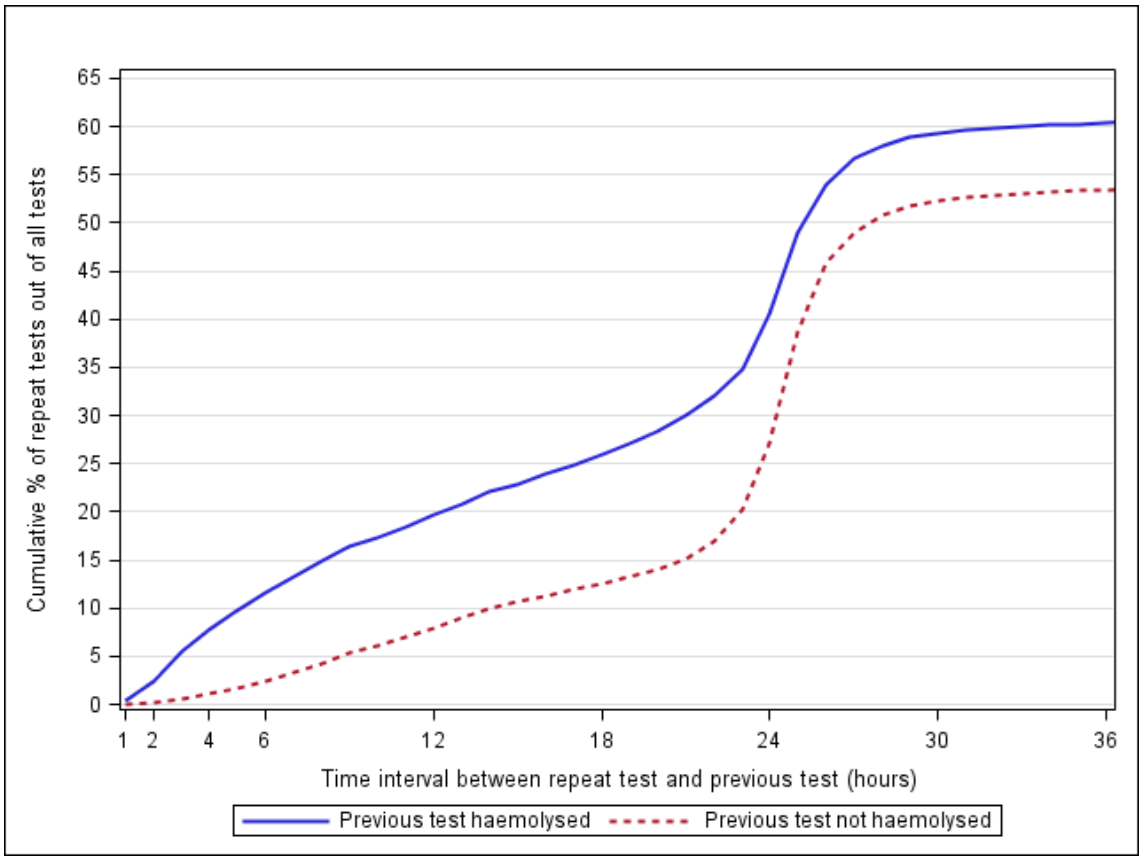

Figure 18. Cumulative percentage of repeat Potassium tests over time, for hospital inpatients.

TROPONIN TESTS

Cardiac troponin tests are currently the recommended cardiac biomarker to be used for the detection of Acute Myocardial Infarction (AMI).[72] They are also one of the most frequently requested tests in EDs [73] and we have already shown (Table 15) that an average of 5.63% of specimens for Troponin tests in the study hospitals were found to be haemolysed. Another study found that 3.9% of Troponin tests were rejected because the specimen was found to be haemolysed.[74]

ED PATIENTS

There were 60,832 specimens collected for Troponin testing for 48,849 ED presentations at the five study EDs. The majority of these presentations (77.1%) had only one Troponin test ordered. The maximum number of Troponin tests in a single ED presentation was 4 tests. In total, 3,235 specimens collected for a Troponin test (5.3%) were found to be haemolysed. There were 11,983 repeat Troponin tests.

Figure 19 compares the mean and median and variability in the time interval between the previous Troponin test and the repeat Troponin test for when the previous test specimen was not found to be haemolysed (upper bar) and for when the previous test specimen was found to be haemolysed (lower bar).

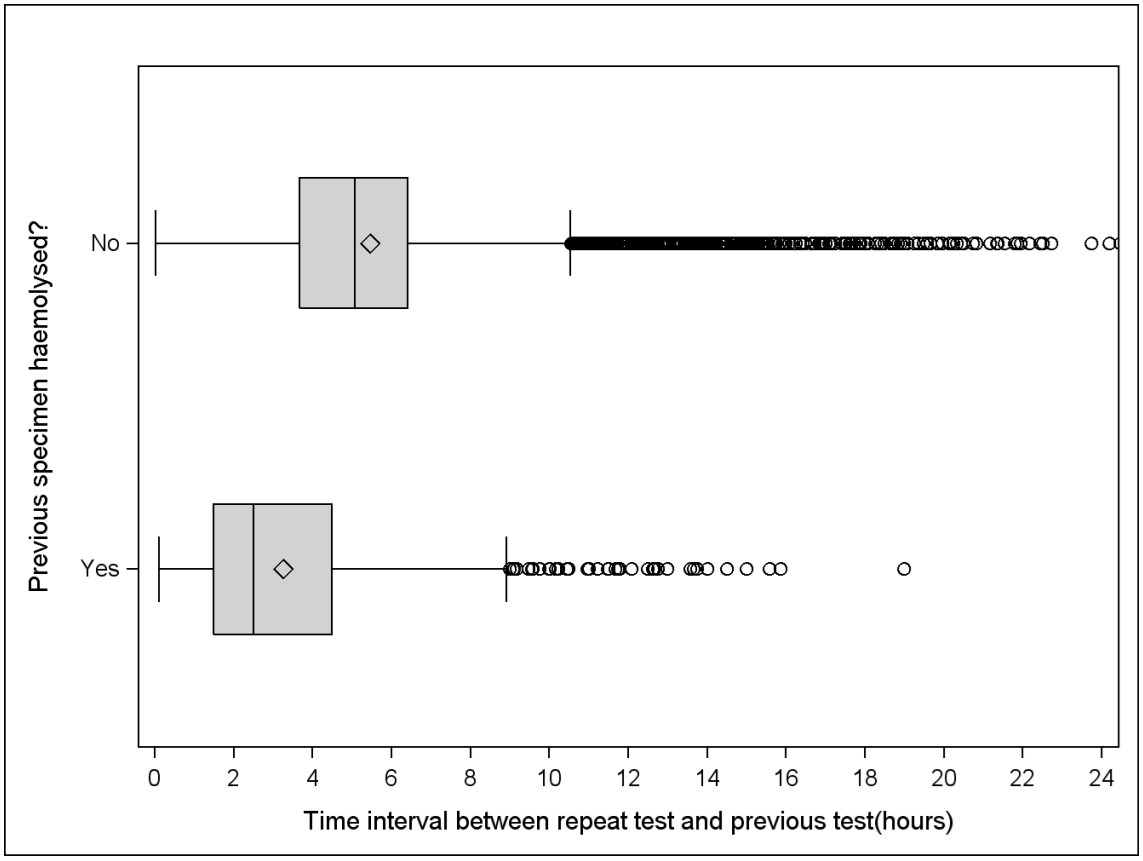

Figure 19. Time intervals between the previous Troponin test and the repeat Troponin test (hours), in the ED.

Table 23 shows that 1,296 repeat Troponin tests (10.8%) occurred after the preceding Troponin test was haemolysed, and in these cases there was a median interval of 2.5 hours between the previous test and the repeat Troponin test. In comparison, when the previous Troponin test was not haemolysed, there was a median interval of 5.1 hours between it and the repeat Troponin test. This was a significant difference ($p<0.0001$ from the Wilcoxon Rank Sum test).

Table 23. Time intervals between the previous Troponin test and the repeat Troponin test (hours), in the ED.

Previous specimen haemolysed?	N (%)	Mean time interval in hours (95% CIs)	Median time interval in hours (IQR)	Maximum time interval in hours
No	10,687 (89.2%)	5.5 (5.4-5.5)	5.1 (3.7-6.4)	69.1
Yes	1,296 (10.8%)	3.3 (3.1-3.4)	2.5 (1.5-4.5)	19

Figure 20 shows the cumulative proportion of repeat Troponin tests, out of all Troponin tests, that occurred up to 20 hours after the previous Troponin test in the ED, when the specimen for the previous test was haemolysed (blue solid line) and when the previous specimen was not haemolysed (red dashed line). As was

the case for repeat Potassium tests, the function was much steeper when the preceding Troponin test was haemolysed, indicating that haemolysed specimens for Troponin tests did in fact result in a repeat Troponin test within a much shorter interval than if the specimen for the preceding Troponin test had not been haemolysed.

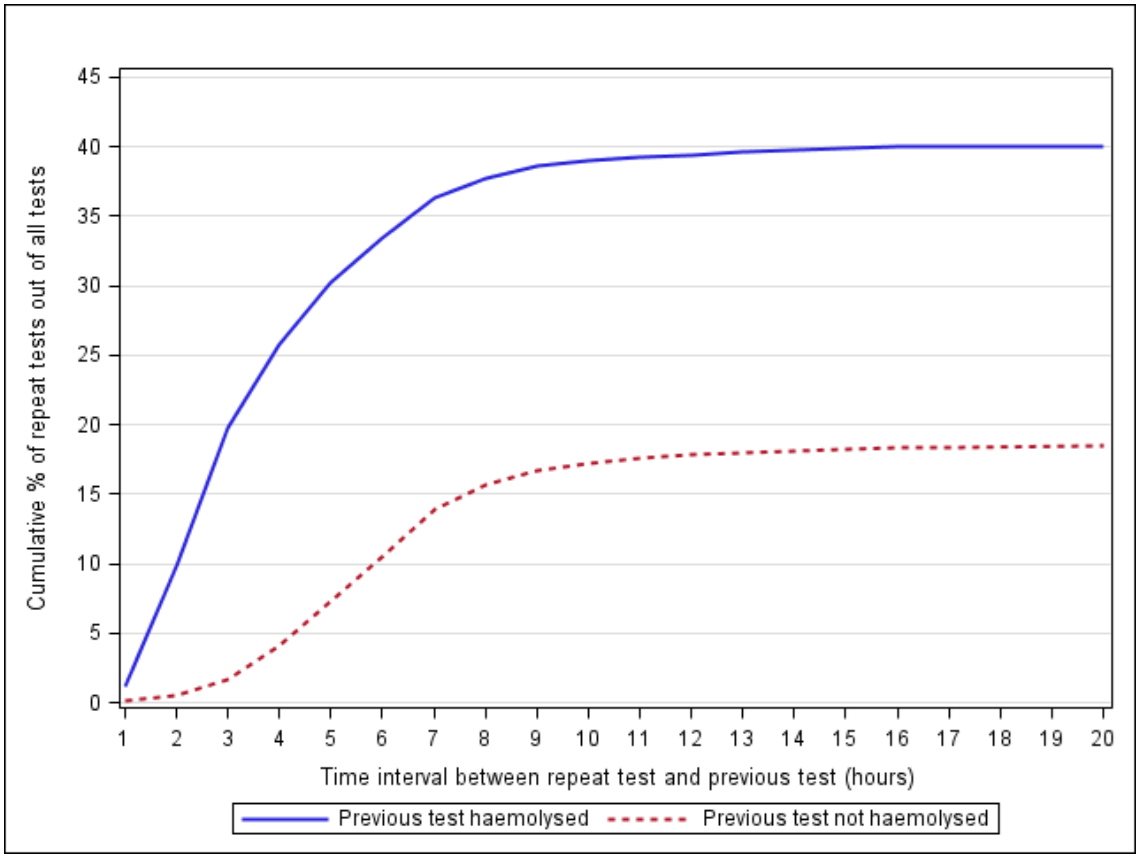

Figure 20. Cumulative percentage of repeat Troponin tests over time, in the ED.

HOSPITAL INPATIENTS

There were 75,077 specimens collected for Troponin testing for 35,390 hospital inpatients at the five study hospitals. About half of these admissions (52.8%) had only one Troponin test ordered. The maximum number of Troponin tests in a single hospital inpatient admission was 52 tests. In total, 938 of the specimens collected for a Troponin test (1.2%) were found to be haemolysed. There were 39,687 repeat Troponin tests. Figure 21 compares the mean and median and variability in the time interval between the previous Troponin test and the repeat Troponin test for when the previous test specimen was not found to be haemolysed (upper bar) and for when the previous test specimen was found to be haemolysed (lower bar).

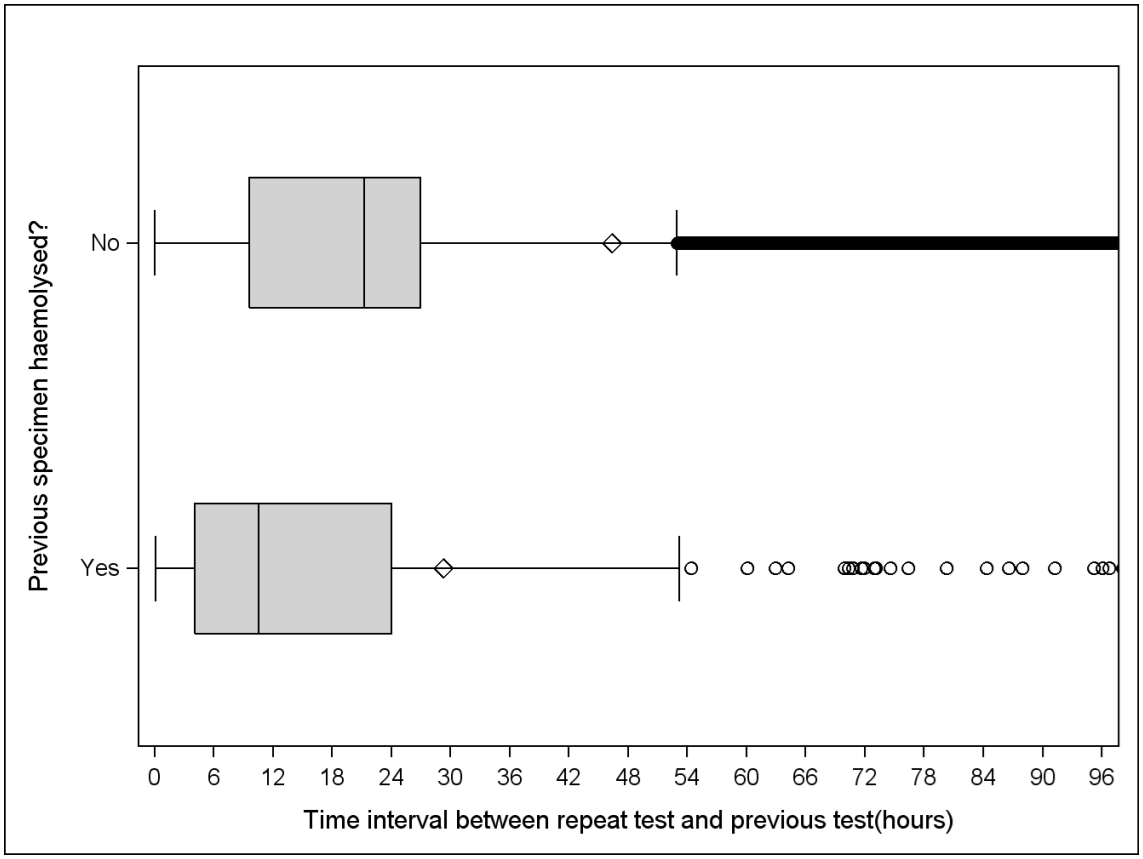

Figure 21. Time intervals between the previous Troponin test and the repeat Troponin test (hours), for hospital inpatients.

Table 24 shows that 629 repeat Troponin tests (1.4%) occurred after the preceding Troponin test was haemolysed, and in these cases there was a median interval of 10.6 hours between the previous test and the repeat Troponin test. In comparison, when the previous Troponin test was not haemolysed (98.6%), there was a median interval of 21.3 hours between it and the repeat Troponin test. The difference between these median repeat test intervals was significant ($p<0.0001$ from the Wilcoxon Rank Sum test).

Table 24. Time intervals between the previous Troponin test and the repeat Troponin test (hours), for hospital inpatients.

Previous specimen haemolysed?	N (%)	Mean time interval in hours (95% CIs)	Median time interval in hours (IQR)	Maximum time interval in hours
No	39,058 (98.4%)	46.3 (44.4-48.3)	21.3 (9.6-26.9)	19702.4
Yes	629 (1.4%)	29.3 (23.7-34.9)	10.6 (4.1-24.0)	769.5

Figure 22 shows the cumulative proportion of repeat Troponin tests, out of all Troponin tests, that occurred up to 36 hours after the previous Troponin test in hospital inpatient wards, when the specimen for the previous test was haemolysed (blue solid line) and when the previous specimen was not haemolysed (red dashed line). At all time points indicated on the graph, a larger proportion of Troponin tests was accounted for by repeat tests when the specimen for the preceding Troponin test was haemolysed than when the previous specimen was not haemolysed.

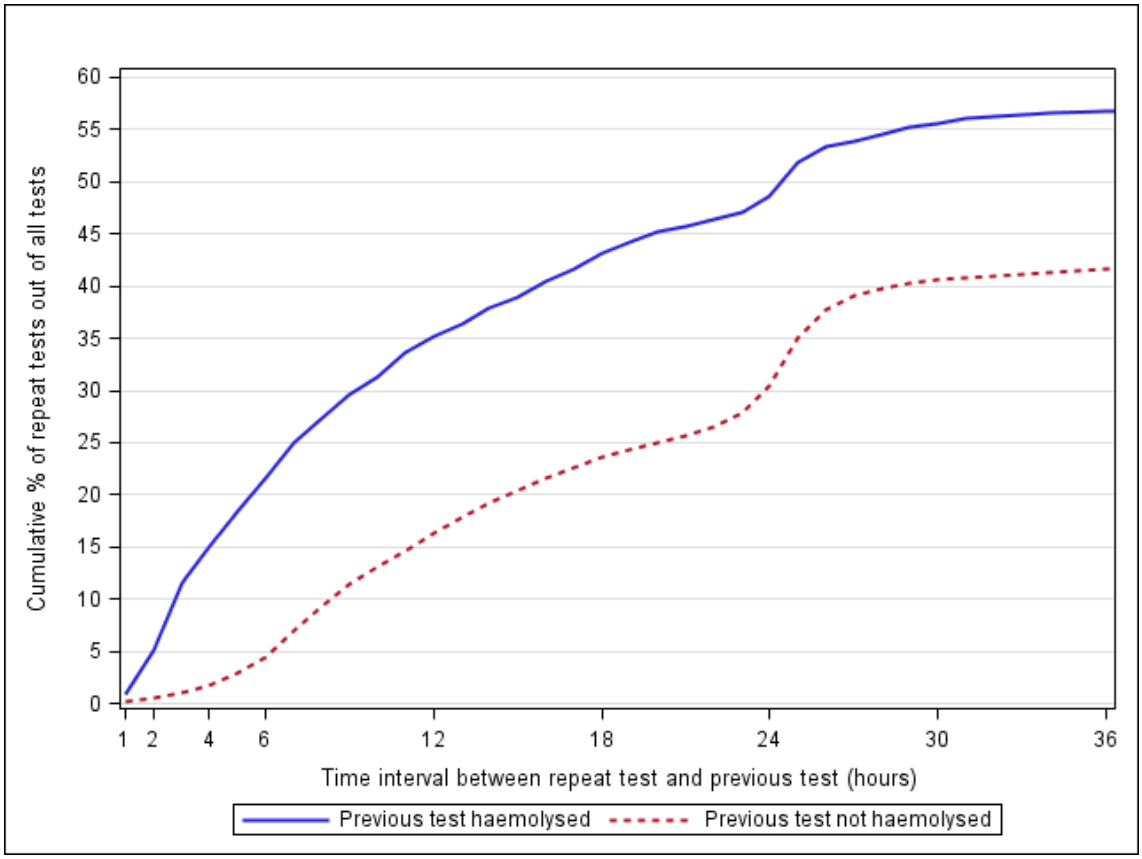

Figure 22. Cumulative percentage of repeat Troponin tests over time, for hospital inpatients.

In this section, we examined the impact of haemolysis on repeat testing of Potassium and Troponin at EDs and in the hospital inpatient setting. For both tests, in both settings, repeat tests were more likely to be ordered within a shorter interval from the previous test if the previous specimen was haemolysed than when the reference specimen was not haemolysed. Repeat testing also accounted for a greater proportion of all Potassium and Troponin tests in the ED setting than for hospital inpatients.

SECTION 2.7: IMPACT OF HAEMOLYSIS ON EMERGENCY DEPARTMENT LENGTH OF STAY

Haemolysis can lead to disruptions in the laboratory process which can delay the clinician's diagnostic decision and their treatment plan for the patient. Haemolysed blood specimens can thus impact the duration of a patient's stay in the ED (their Emergency Department Length of Stay [ED LOS)]. This section aims to use advanced statistical modelling techniques to assess the impact of a haemolysed specimen on patients' ED LOS while controlling for other confounding variables.

ED LOS

Figure 23 shows the distribution of ED LOS in the five study EDs (ED LOSs above the 99th percentile, 1440 minutes or 24 hours, are not shown). The median ED LOS was 343 minutes (IQR: 236-496). The ED LOS was skewed to the right.

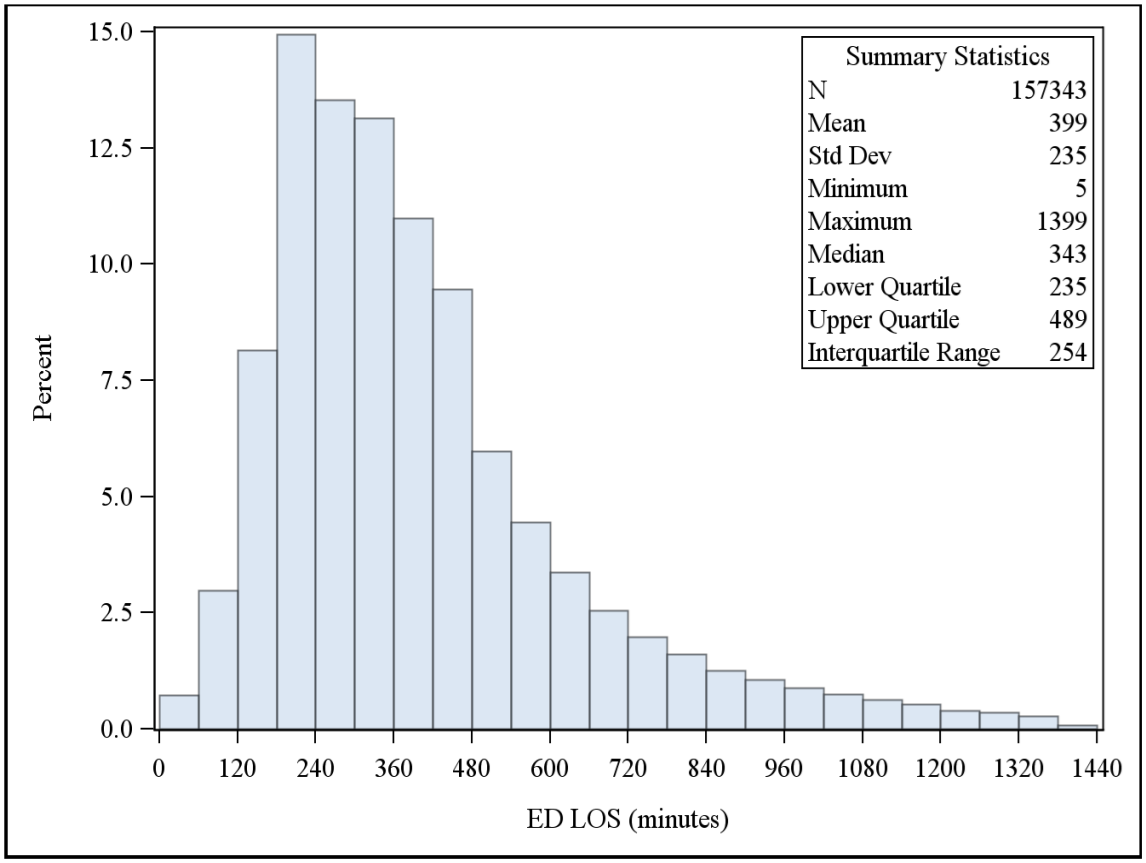

Figure 23. The distribution of ED LOS up to the 99th percentile. Note: inset box legend also describes ED LOS up to the 99th percentile; not all ED LOS.

BASELINE CHARACTERISTICS

Table 25 compares the ED LOS of ED presentations at the study EDs where at least one specimen was haemolysed ("Yes" column) with the ED LOS of ED presentations where none of the specimens were haemolysed ("No" column). The overall ED LOS of the two groups were compared first, and then the difference in ED LOS between the two groups is shown for sub-groups of ED presentations using multiple

univariate comparisons belonging to different age groups, gender, triage category, day of the week and time of day that the ED presentation began, mode of separation from the ED, the season of the year, the year within the study period, and for each of the study EDs.

Overall, 10,904 (6.9%) of ED presentations had at least one haemolysed specimen and the median ED LOS for these was 371 minutes. On the other hand, 148,030 ED presentations did not have any haemolysed specimens and had a shorter median ED LOS of 332 minutes. Apart from patients who were allocated to the "Immediately Life Threatening" triage category (Triage 1), where the median ED LOS was 9 minutes shorter when there was a haemolysed specimen (255 minutes compared to 264 minutes), ED presentations where a blood specimen was found to be haemolysed were associated with longer ED LOS than ED presentations that did not have any haemolysed specimens. The causal direction of this relationship, however, is uncertain.

Table 25. Baseline characteristics of ED patients and presentations according to the haemolysis experience during ED stay

	Haemolysed?					
	No			Yes		
	ED LOS (minutes)			ED LOS (minutes)		
	N	Col %	Median (IQR)	N	Col %	Median (IQR)
Overall (row %)	148030	93.1	343 (235-493)	10904	6.9	371 (253-538)
Age (years)						
<18	10845	7.3	332 (246-446)	492	4.5	353 (257-464)
18-34	21633	14.6	293 (203-437)	1345	12.3	317 (218-472)
35-49	21519	14.5	308 (212-460)	1466	13.4	326 (228-495)
50-64	22602	15.3	326 (223-477)	1721	15.8	357 (239-519)
65-79	28787	19.4	358 (241-511)	2334	21.4	383 (259-551)
>79	42644	28.8	390 (274-548)	3546	32.5	411 (293-584)
Missing	42	<0.1	480 (243-2481)	2	<0.1	381 (319-442)
Triage						
Imminently life threatening (2)	31808	21.5	330 (225-483)	2281	20.9	359 (239-524)
Potentially life threatening (3)	63112	42.6	351 (240-500)	4685	43	382 (262-546)
Potentially serious (4)	46928	31.7	350 (238-499)	3448	31.6	377 (262-547)
Less Urgent (5)	3883	2.6	297 (205-439)	265	2.4	317 (209-445)
ED arrival time						
1AM - 7AM	14802	10	414 (280-560)	1047	9.6	452 (311-600)
7AM - 1PM	47763	32.3	338 (234-463)	3564	32.7	363 (251-486)
1PM - 7PM	52615	35.5	324 (230-446)	3871	35.5	349 (245-479)
7PM - 1AM	32850	22.2	364 (235-682)	2422	22.2	417 (252-744)

	Haemolysed?					
	No			Yes		
	ED LOS (minutes)			ED LOS (minutes)		
	N	Col %	Median (IQR)	N	Col %	Median (IQR)
Day of week						
Sun	20032	13.5	334 (231-490)	1478	13.6	372 (249-562)
Mon	22850	15.4	357 (239-517)	1654	15.2	381 (257-559)
Tue	21451	14.5	351 (237-507)	1664	15.3	378 (259-552)
Wed	21106	14.3	348 (237-498)	1554	14.3	378 (260-534)
Thu	21256	14.4	340 (234-486)	1532	14	355 (243-508)
Fri	21399	14.5	343 (235-483)	1545	14.2	373 (252-522)
Sat	19936	13.5	331 (232-471)	1477	13.5	359 (250-519)
Season						
Summer (Dec-Feb)	35700	24.1	338 (234-482)	2773	25.4	361 (250-522)
Autumn (Mar-May)	37506	25.3	334 (231-479)	2597	23.8	362 (248-519)
Winter (Jun-Aug)	38610	26.1	356 (239-521)	2650	24.3	391 (257-581)
Spring (Sep-Nov)	36214	24.5	345 (237-493)	2884	26.4	371 (256-533)
Year						
2010	33993	23	370 (254-538)	2609	23.9	408 (280-577)
2011	35995	24.3	362 (250-518)	2508	23	387 (268-561)
2012	37071	25	355 (243-504)	3750	34.4	370 (251-533)
2013	40971	27.7	297 (215-434)	2037	18.7	316 (226-453)
ED						
ED A	26672	18	371 (260-518)	1661	15.2	401 (280-556)
ED B	20030	13.5	279 (209-418)	1792	16.4	305 (225-449)
ED C	20466	13.8	352 (240-527)	2034	18.7	380 (265-577)
ED D	60544	40.9	358 (245-515)	4133	37.9	395 (271-565)
ED E	20318	13.7	318 (218-454)	1284	11.8	344 (235-474)

MODELLING

DATA AND METHODS

Excluding those presentations with missing triage categories and unknown gender, there were 158,883 presentations for modelling. We used Generalised Estimating Equation (GEE) Modelling to take into account the correlation of the multiple presentations from the same patients with a log-link function and gamma distribution to fit skewed ED LOS data. All the patient demographics and visiting characteristics in Table 26 were adjusted in the models and interactions between haemolysis, year and ED were also considered in the models.

IMPACT OF HAEMOLYSIS ON ED LOS AFTER ADJUSTMENT

After adjusting for all the baseline characteristics, we estimated the ED LOS for patients who experienced haemolysed specimens and for those who did not. The ED LOS was on average 18 minutes longer for patients who experienced one or more haemolysed specimens, than for those who did not.

Table 26. Comparison of the estimated ED LOS between ED presentations with one or more haemolysed specimens and those that did not, from GEE model after adjusting for the baseline characteristics.

Haemolysed?	Estimated ED LOS in minutes (95% CIs)
No	319 (313-325)
Yes	337 (329-344)
Additional ED LOS associated with haemolysis	18 (13-22)

SECTION 2.8: RISK FACTORS ASSOCIATED WITH HAEMOLYSIS IN HOSPITALS

In this section, we aimed to identify the risk factors associated with haemolysis in hospitals. The 974,963 blood specimens collected from the five study hospitals and the five nearby hospitals were used for this analysis.

The initial descriptive statistics showed the haemolysis rates for each of the baseline characteristics including patient and clinical characteristics without taking into account any correlations between factors. A subsequent multilevel modelling approach assessed the relationship between those same patient and clinical characteristics and the probability of a haemolysed specimen while controlling for the effect of the other factors in the model.

BASELINE CHARACTERISTICS

Haemolysis rates and their 95% CIs for different risk factors are shown in Table 27. Younger patients (<5 years) and older patients (>80 years) had higher haemolysis rates (1.50% and 1.10%, respectively) than patients aged between 5 and 80 years of age (0.67%). Females had a higher rate of haemolysis (0.90%) than males (0.78%). Specimens collected by clinical staff had a higher rate of haemolysis (0.87%) compared to laboratory phlebotomists (0.80%). The haemolysis rate was higher for specimens that were transported (i.e. where the test was processed in a laboratory that was not co-located with the hospital where it was collected) than when it was not transported (1.00% and 0.83%, respectively). The haemolysis rate was higher on weekends (0.92%) than on weekdays (0.81%). The haemolysis rate was also higher in winter and spring (0.88% and 0.90%, respectively) than in summer or autumn (0.74% and 0.83%, respectively).

Table 27. Haemolysis rates for different risk factors

Risk factor	N	Col %	% of haemolysed specimens (95% CIs)
Overall	974963	100	0.84% (0.82%-0.85%)
Age group (years)			
<5 years	32789	3.4	1.50% (1.40%-1.60%)
5-80 years	657700	67.5	0.67% (0.65%-0.69%)
>80 years	281898	28.9	1.10% (1.10%-1.20%)
Gender			
F	475523	48.8	0.90% (0.87%-0.93%)
M	496978	51	0.78% (0.75%-0.80%)
Laboratory phlebotomist			
No	506540	52	0.87% (0.84%-0.89%)
Yes	468423	48	0.80% (0.77%-0.82%)

Risk factor	N	Col %	% of haemolysed specimens (95% CIs)
Transportation			
No	926228	95	0.83% (0.81%-0.84%)
Yes	48735	5	1.00% (0.93%-1.10%)
Day of week			
Weekends	211359	21.7	0.92% (0.88%-0.96%)
Weekdays	763604	78.3	0.81% (0.79%-0.83%)
Season			
Summer (Dec-Feb)	267676	27.5	0.74% (0.71%-0.77%)
Autumn (Mar-May)	231751	23.8	0.83% (0.80%-0.87%)
Winter (Jun-Aug)	253122	26	0.88% (0.84%-0.92%)
Spring (Sep-Nov)	222414	22.8	0.90% (0.86%-0.94%)
Year			
2010	241913	24.8	0.82% (0.78%-0.85%)
2011	225779	23.2	0.85% (0.82%-0.89%)
2012	242819	24.9	1.20% (1.20%-1.20%)
2013	264452	27.1	0.50% (0.48%-0.53%)
Hospital			
F	71718	7.4	0.54% (0.49%-0.59%)
G	35928	3.7	0.33% (0.27%-0.39%)
H	382	<0.1	0.52% (0.00%-1.30%)
A	120392	12.3	0.89% (0.83%-0.94%)
B	80457	8.3	1.40% (1.30%-1.50%)
C	76744	7.9	1.50% (1.40%-1.60%)
D	503262	51.6	0.70% (0.68%-0.73%)
I	6199	0.6	0.61% (0.42%-0.81%)
E	72405	7.4	0.87% (0.80%-0.94%)
J	7476	0.8	0.60% (0.43%-0.78%)

MODELLING

DATA AND MODELS

After having excluded presentations where age and gender were not reliably recorded, there were 972,298 specimens for modelling. Multilevel modelling was adopted to take into account the correlation of the multiple specimens taken from the same patient. The model included hospital and year as fixed factors to adjust for the temporal and hospital effects on haemolysis. The final model also included the following factors to assess any association with haemolysed specimens: patient age group and gender, whether a specimen was transported to a laboratory at a different site, whether the specimen was drawn by a laboratory phlebotomist or clinical staff, whether the collection occurred on a weekday or the weekend, and the season.

RISK FACTORS

Table 28 shows the patient and specimen collection characteristics that were associated with significantly higher probability of haemolysis while controlling for the study hospital and study year. Patient age, gender, whether the specimen was collected by a clinical staff, and whether the collection occurred during a weekend, were all significant risk factors associated with haemolysis. A higher chance of haemolysis was associated with very young and very old patients (<5 years and >80 years), female patients, specimens collected by non-laboratory staff and specimens collected on weekends.

Table 28. The Odds Ratio estimates for different patient and collection characteristics compared to a reference group.

Risk Factor	Odds Ratio (95% CIs)	P-value
Age category		<0.0001
5-80 years	0.50 (0.45-0.56)	
>80 years	0.75 (0.67-0.83)	
<5 years (reference group)		
Gender		0.0008
Female	1.11 (1.05-1.17)	
Male (reference group)		
Laboratory phlebotomist		<0.0001
No	1.40 (1.33-1.47)	
Yes (reference group)		
Day of week		0.0002
Weekday	0.92 (0.87-0.97)	
Weekend (reference group)		

STAGE 3: HAEMOLYSIS: DETECTION AND REPORTING PRACTICES ACROSS THE PATHOLOGY SERVICE

INTRODUCTION

This project has provided a description of both the overall rate of haemolysed specimens in the study pathology service and a detailed analysis and comparison of the haemolysis rates for different clinical contexts and different patient characteristics. However, it is critical that a description of the rates of haemolysis is accompanied by an understanding of what criteria the laboratories are using for identifying haemolysis (e.g. what severity of haemolysis would result in a specimen being labelled as haemolysed). This stage of the project was designed to assess the policies and practices for identifying and measuring haemolysis throughout the pathology service laboratories.

METHODS

A literature search was conducted to generate a pool of potential questions for the structured interviews that would then constitute the data collection tool for this study. The source of potential questions included existing international surveys of haemolysis detection practices [3,10,44,60,75-78] and existing RCPAQAP materials.[79,80]

Sixty-four questions were identified from ten different sources.[3,10,44,60,75-80] Duplicate questions, that targeted the same laboratory characteristic, were removed from the pool. This was followed by the removal of additional items, in consultation with biochemistry and quality management experts, that were deemed to be too broad in their scope or whose responses would do little to aid understanding of haemolysis in the study laboratories. The wording of the final subset of questions for inclusion was modified to improve clarity and minimise the potential for confusion. Finally, project steering committee members who were biochemistry and quality management experts used their familiarity with the issues leading to haemolysis and the potential impact of haemolysis on the effectiveness of the pathology service to assess the relevance and clarity of the final subset of questions.

The final version of the structured interview questions contained nine questions. When including all of the sub-items, there were a total of nineteen questions / sub-items in the structured interview document. Appendix A shows a copy of data collection tool for the structured interview.

Structured interviews were conducted in-person at five biochemistry laboratories belonging to the same pathology service and hospitals which have already been described. The interviews were conducted by two members of the research team, one of whom had an extensive background in pathology testing, the other was an experienced researcher. At each biochemistry laboratory, two staff members were present: the team leader (or their representative) and the local laboratory manager. At the biochemistry laboratory for Hospital D, only one staff member was present: a senior pathologist very familiar with the haemolysis issue and

detection and recording practices within the laboratory. A copy of the data collection tool for the structured interview (see Appendix A) was provided to all participants at least one day (but often many days) before the structured interview was to occur so they could ensure they had the necessary information on-hand during the interview. Each structured interview was conducted on-site within each laboratory in an office or room away from the day-to-day operations of the laboratory. Each interview lasted for approximately one hour and, in addition to responding to the prepared questions, the laboratory staff were encouraged to express their own views of the actual practices within their laboratory.

Subsequent to the in-person structured interviews, two laboratories belonging to the same pathology service but located in regional cities in New South Wales were contacted by telephone and a telephone interview using the same structure was conducted by the same two members of the research team and an appropriate staff member at the laboratory. One additional laboratory responded to the same structured interview questions via email (including responses to follow-up and clarification questions).

RESULTS

The laboratories belonged to smaller independent pathology services before being conglomerated into a single large pathology service. Therefore, historically, the different laboratories used a variety of biochemistry analysers and LIS. Once the laboratories were joined together under the umbrella of the single pathology service, considerable standardisation occurred, mainly in 2013 and 2014. New analysers from the same manufacturer (Abbott Architect series) were installed in all the interviewed laboratories. The laboratories in the five study hospitals implemented a new Analyser Management System [4] middleware and there was also standardisation for the LISs around the AUSLAB system (although communication between LISs could still only occur effectively for laboratories that had previously belonged to the same pathology service). The implementation of AUSLAB and AMS was more recent (during 2014) for the regional laboratories. One of the regional laboratories was still using a LRS Health MediPATH LIS in conjunction with Abbott Architect analysers but was planning to move to AUSLAB and AMS systems in early 2015.

One laboratory was recognised by all the other laboratories as being the main co-ordinator of the haemolysis policy for the entire pathology service. This laboratory had conducted its own internal study to assess the effect of various grades of haemolysis on the results of different analytes by spiking specimens whose properties were already known, with predetermined amounts of haemoglobin and measuring the extent of the resulting deviation that the spiked specimen exhibited compared to the control specimen.[73,74] The co-ordinating laboratory was involved in the setting up of the biochemistry analysers, and writing the procedures for haemolysis, and implementing the haemolysis cut-off values in the middleware of all the other interviewed laboratories.

When the research team asked the interviewees at each laboratory to provide the haemolysis cut-off values that would result in either (a) a "specimen haemolysed" comment being added to a result, or (b) the result being suppressed altogether, the interviewees that had already implemented AUSLAB and AMS responded with the same haemolysis cut-off values, and they provided the same document (written at the co-ordinating laboratory) which specified the cut-off values that had been determined by the internal study. The laboratory that was still using MediPATH LIS was operating with a different set of haemolysis parameters, and also used a different policy of using the same cut-off value to add a comment and to suppress a result (i.e. if a comment was added, the result was also suppressed and the comment indicated this). Apart from this final laboratory, there was a high degree of consistency between the responses received from the pathology service laboratories interviewed. However, of the non-co-ordinating laboratories, only the regional laboratory operating with MediPATH LIS was able to definitively say that the HI index parameters had been checked since the implementation.

The responses to the structured interview questions were also consistent between the laboratories for items that asked whether haemolysis was determined using an aided or unaided visual check or the HI index from the laboratory instrumentation (all laboratories reported using the latter); whether there was a systematic process for ruling out intravascular / in vivo haemolysis (only informal methods were reported by the laboratories); and what types of information the laboratory recorded when a specimen was found to be haemolysed: (a) the collector identification number was recorded for all blood specimens collected, but was only recorded within the LIS at the five Sydney study laboratories; (b) the blood draw instrument and method was not routinely recorded at any of the laboratories; (c) the blood draw site was not routinely recorded at any of the laboratories; (d) the regional laboratory using MediPATH LIS recorded (on the tube and request form, but not in the LIS) whether pre-transport centrifugation had occurred but none of the other laboratories recorded this; and (e) the transport method or temperature were not routinely recorded for any blood specimens at any of the laboratories, but the AS ISO 15189-2013 standard requires that accredited laboratories monitor specimen temperatures during transport.[81]

The main qualitative finding is that the smaller labs saw their small-size as an advantage when it came to haemolysis because they are multidisciplinary and there is a more holistic approach to the patient, while the larger laboratories' (such as the co-ordinating laboratory) size means things are more automated and the specimen is not even really accessible once it enters the automated "Track" system.

Most interviewees indicated that they believed that many haemolysed specimens were caused by the blood draw technique and that blood specimens drawn by a laboratory phlebotomist would be rarely haemolysed, even in more difficult clinical situations or if they were to use a method or equipment that would normally have a higher risk of haemolysis. Some laboratories indicated that they thought clinical staff have inadequate training in conducting blood draws and advocated for some formal training and accreditation system for any

staff member before they are given responsibilities for blood draws. They also argued that the quality of the laboratory process would be improved with respect to ED patients if a laboratory phlebotomist was deployed to conduct blood draws within EDs. They suggested that this would result in reduced costs by reducing the number of unnecessarily repeated tests, the administrative resources required to organise and source a replacement specimen, and the ED resources being freed up sooner by reducing the duration of ED LOS.

DISCUSSION AND IMPLICATIONS

The occurrence of haemolysed specimens in pathology laboratories, especially biochemistry laboratories, is one of the most frequent preanalytical errors and can interfere with the integrity of the specimen and the results of some test analytes.[31] This can in turn disrupt the laboratory process because a replacement specimen needs to be found to conduct the requested tests, which takes laboratory staff time and resources and delays the availability of the test results.[65] In some cases, a new specimen needs to be collected which not only requires additional laboratory / hospital staff time and resources but subjects the patient to a repeat blood draw and an increased risk of iatrogenic injury such as infection [82] while also contributing to slower diagnoses, longer hospital episodes of care, and increases in laboratory costs.[65]

The present project employed a mixed-methods research strategy using data from a variety of RCPAQAP KIMMS, hospital, laboratory, and pathology service sources to investigate the issue of haemolysis, its procedural causes, how it is detected and counted, its prevalence, and its impact on laboratory processes and patient care.

This project began with an evidence scan of the existing international literature to explore the rates of haemolysis that existing studies have reported and how these rates differ depending on various clinical factors. The evidence scan revealed four main groups of clinical factors that were the basis for comparisons of haemolysis rates across the literature: (1) hospital / laboratory characteristics such as the location within the hospital or staff type conducting the blood draw; (2) patient characteristics such as sex and age or diagnosis; (3) phlebotomy characteristics such as the draw site, site preparation method, tourniquet time, and whether it was a difficult collection; and (4) equipment characteristics such as blood specimens drawn using an IV catheter or venepuncture aspirated via syringe or evacuated tube system (such as BD Vacutainer™) and the size of the needle or catheter.

In collaboration with the RCPAQAP KIMMS project we investigated the pathology practice profile of 68 KIMMS participant groups spread across all Australian states and territories which processed in excess of 80 million accessions in the three year data collection period. That section of the report described pathology practice profiles of KIMMS participants, their methods for identifying and counting haemolysis rejections, and changes in the haemolysis rate for KIMMS participants over a three year period.

The next goal of the project was to undertake an extensive linkage of data coming from the pathology service computer systems and key hospital sources, to assess the incidence rate of haemolysed specimens in five different hospitals supported by the one pathology service and describe differences in haemolysis rates in different clinical contexts. We provided detailed comparisons of the haemolysis rates between the five hospitals, between patients in the ED, the inpatient setting, and other sources, whether the blood collection was performed by a laboratory phlebotomist or a clinical staff member, and how the haemolysis rate changed

over a four year study period coinciding with changes to haemolysis detection parameters. Using the same detailed linked dataset we examined the impact of haemolysis on repeat testing of Potassium and Troponin at EDs and in the hospital inpatient setting and used multilevel modelling to estimate the impact of a haemolysed specimen on the duration of a patient's ED LOS. Lastly, we used multilevel modelling methods to estimate the increased risk of haemolysed specimens occurring according to various patient and collection characteristics.

In the final stage of the project the goal was to investigate what measures were employed by pathology service laboratories to identify and measure haemolysed specimens and their impact on the quality and effectiveness on their services. We conducted a number of on-site structured interviews with the laboratories associated with the five study hospitals in metropolitan Sydney, followed by structured telephone and email interviews with laboratories in regional NSW, to provide complementary explanatory data for the results reported earlier in the report. The structured interviews revealed not only the types of biochemistry analysers, middleware, and LISs in use in the different laboratories, but also their practices for identifying haemolysis, including whether visual identification or HI index was used, how the haemolysis parameters had been selected, what the cut-off values were for various analytes, whether they had been checked after implementation of new systems, and the laboratory policies for dealing with haemolysed specimens including what conditions would lead to a comment being added to a result, or a result being suppressed and a new specimen being requested.

LIMITATIONS

Stage 1 of the project utilised data from the RCPAQAP KIMMS project. While these data were a rich and valuable source of information for the prevalence of a number of preanalytical errors across Australia, including haemolysis rejections, the lack of harmonisation in practices between laboratories resulted in the following issues:

Differences in accessioning practices in laboratories (whether accessions represented episodes or specimens) and how haemolysis rejections were counted (whether they were counted according to the tests that were rejected, the specimens that were rejected, or the episodes that were rejected) meant that it was inappropriate to report an overall rate of haemolysis rejections for all participants and detailed analyses could only be conducted for a subset of participants who all used the same method for assigning accessions and counting haemolysis rejections.

KIMMS participant laboratories report their activity by the number of accessions for all types of specimens (including tissue specimens, urine, faeces, etc.) where haemolysis is not necessarily relevant. They do not report the number of accessions processed on blood specimens, which would provide a more appropriate denominator for the calculation of haemolysis rates. We do not see this introducing any systematic bias in

how haemolysis rates were calculated, but the proportion of laboratory activity accounted for by blood specimens will influence the apparent haemolysis rate.

KIMMS participant laboratories did not report their operational haemolysis cut-off parameters including the criteria for haemolysis rejections and this will influence the rate of haemolysis rejections that they report.

Stage 2 of the project provided a number of detailed analyses of the rates of haemolysed specimens according to different clinical contexts and patient characteristics. However, because different analytes had different sensitivity to free haemoglobin (and different cut-off values recorded) not all specimens flagged as haemolysed in the LIS necessarily impacted on the laboratory process. For example, there may have been minimal impact on the laboratory or patient if a test request resulting in haemolysed specimen did not contain any analytes sensitive to free haemoglobin, because it would have been unnecessary to request another test or conduct a repeat phlebotomy. It was not possible to assess a direct relationship between all haemolysed specimens and repeat test orders or specimen collections.

CONCLUSION

The outcome of this project was to produce a detailed analysis of the prevalence and variation of haemolysis at an international level by performing an evidence scan and reporting the incidence rates found in the existing literature, then conducting analyses of the haemolysis rejection rates at a broad national scale using the KIMMS dataset, and finally, at a more specific level, assessing the rate of haemolysis according to clinical and patient characteristics, within five study hospitals, and the impact that haemolysis had on patient outcomes such as ED LOS. These quantitative analyses were supplemented by structured interviews with a number of laboratories to understand variation in laboratory practices for identifying and measuring haemolysis and policies for dealing with haemolysed specimens.

This resource can potentially benefit a range of different stakeholders in the healthcare system:

PATIENTS/CONSUMERS:

Patients and consumers benefit from having the highest quality pathology services. The occurrence of haemolysed specimens can result in invalid or unavailable test results which necessitate follow-up phlebotomies which can be unpleasant and increase the risk of iatrogenic injuries.[82] There can also be delays in diagnosis and treatment caused by repeat phlebotomies and this can lead to longer stays in the ED.

CLINICIANS:

The evidence scan provided in this report describes the clinical and patient characteristics associated with higher rates of haemolysis, particularly how different phlebotomy methods, draw sites, and equipment can result in a higher probability of a specimen being haemolysed. These findings can inform harmonised phlebotomy practices and the development of an evidence-based best-practices model for blood collection.

HOSPITAL PATHOLOGY LABORATORIES:

Haemolysis is a disruptive event in pathology laboratories and results in laboratory resources being spent on communicating with clinicians and processing additional repeat tests. Having a better understanding of the phlebotomy and patient characteristics associated with haemolysed specimens can facilitate the adoption of an evidence-based best-practices model for blood collection. Measuring, benchmarking, and comparing the rates of haemolysis in different clinical and patient contexts, in different laboratories and across time, is a critical process in monitoring and quality improvement. Performance benchmarks can enhance harmonisation, with the potential to improve quality of practice across sites.

HOSPITAL MANAGEMENT:

The analyses of haemolysis rates across sites and different clinical contexts, in particular differences in haemolysis rates between the ED and inpatient settings and between specimens collected by laboratory phlebotomists and clinical staff, can inform hospital decisions regarding the allocation of resources and responsibilities in patient care. In particular, hospital management can consider the clinical contexts where laboratory staff can be deployed to conduct phlebotomies.[40]

GOVERNMENT DEPARTMENTS OF HEALTH AND LHDS:

This report revealed that there is variation in practice in how phlebotomies are conducted and that these methodological differences result in different rates of haemolysed specimens. The results of this report can inform the creation and adoption of evidence-based best-practice training and mentorship programs for clinical staff and for protocols for equipment and procedures used during phlebotomies.

APPENDIX A: STRUCTURED INTERVIEW FOR HAEMOLYSIS PRACTICES

HAEMOLYSIS Identification and Measurement Practices Interview Questions-v8dA-clean.docx

HAEMOLYSIS

Identification and Measurement Practices Interview

This short list of questions being asked of Pathology North laboratories is designed to assess how haemolysis is identified and measured across the organisation.

We know you are busy so we have minimised the number of questions.

Please select the single response that most closely describes practices at your laboratory. You may also write additional free-text notes to clarify your responses.

We appreciate your time in responding to these questions.

(i) Biochemistry analyser manufacturer/model, installation date (if known):

_____

(ii) Laboratory Information System software/version, installation date (if known):

_____

(1) Since the installation of the analyser, has somebody checked that the Haemolysis Index parameters* in your analyser have been setup correctly?

(a) Yes (laboratory employee) **(b)** Yes (external organisation employee) **(c)** No **(d)** N/A

* the mapping of haemoglobin concentrations to HIL levels, and rejection criteria for analytes

(2) How did you determine the haemoglobin concentration levels at which you add a 'haemolysed' comment to a result, or suppress a result altogether?

(a) based on parameters supplied by manufacturer	**(b)** based on results of an internal study of the impact of varying degrees of haemolysis on analytes	**(c)** based on results of an external study of the impact of varying degrees of haemolysis on analytes

(3) How does your laboratory determine if a sample is haemolysed?

(a) Haemolysis Index – as per laboratory instrumentation	**(b)** Visual check – comparison to a colour chart	**(c)** Visual check – unaided	**(d)** No formal method in place	**(e)** I do not check

(4) Does your laboratory record **any of the following** collection characteristics for haemolysed specimens

collector (at least pathology staff or not)	(a) Yes	(b) No	(c) N/A
blood draw instrument/method*	(a) Yes	(b) No	(c) N/A
blood draw site	(a) Yes	(b) No	(c) N/A
pre-transport centrifugation	(a) Yes	(b) No	(c) N/A
transport method/temp	(a) Yes	(b) No	(c) N/A

* e.g. vacuette / vacutainer system vs needle and syringe vs via cannula vs via butterfly needle

(5) Does your laboratory have systematic process for ruling out in vivo / intra-vascular haemolysis (haemolysis due to a patient illness: eg several infections by bacteria, autoantibodies, autoimmune haemolytic anaemia, HELLP syndrome)?

(a) Yes **(b)** No **(c)** N/A

Please outline the process:	

(6) Which of the following policies does your laboratory follow? (you may choose more than one answer if applicable)

(a) Rejects ALL haemolysed SAMPLES, i.e. all tests on a haemolysed sample (please specify how this criterion is determined)	**(b)** Rejects ALL haemolysed SAMPLES (as (a)), except precious or irreplaceable samples	**(c)** Reject INDIVIDUAL TEST results from a sample depending on instrument Haemolysis Index or other assessment of haemolysis interference for particular tests	**(d)** Perform the test and report TEST RESULTS, WITHOUT QUALIFYING statement
(e) Perform the test and report TEST RESULTS, WITH QUALIFYING statement that the sample was haemolysed	**(f)** Haemolysed comment and SINGLE ESTIMATE of analytical result reported	**(g)** Haemolysed comment and ESTIMATED RANGE of analytical result reported	**(h)** Haemolysed comment and MATHEMATICAL CORRECTION applied to result according to the degree of haemolysis

Comments or explanation of multiple selections:	

(7) At what haemoglobin concentration (g/L) does your laboratory **(a)** add a 'haemolysis' comment to a result, and **(b)** suppress a result altogether, for <u>at least one analyte</u>?

(a) add a comment _____ **(b)** suppress result _____

(8) At what haemoglobin concentration (g/L) does your laboratory **(a)** add a 'haemolysis' comment to the results, and **(b)** suppress the results altogether, for <u>all analytes</u>?

(a) add a comment _____ **(b)** suppress results _____

(9) What are your laboratory's haemolysis rejection criteria for: (in haemoglobin concentration [g/L]; write N/A if not haemolysis not assessed for this analyte, or "don't know" if you don't know)

Troponin (specify which analyte)	Potassium (specify which analyte)	Direct Bilirubin	Lactate dehydrogenase (LDH)	Aspartate aminotransferase (AST)
_____	_____	_____	_____	_____

Thank You!

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