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Evaluation of a critical care outreach service in a middle-income country: a stepped wedge cluster randomised trial and nested qualitative study

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Abstract: 215

Main text: 2976 (including abstract)

Keywords: Critical care outreach; stepped wedge randomised controlled trial; hospital mortality; cardiopulmonary resuscitation; length of stay; health service evaluation

Abstract

Purpose

This trial evaluates implementation of critical care outreach in a middle-income country.

Materials and Methods

Critical care outreach delivered by a team of intensive care nurses was implemented across general hospital wards in an Iranian university hospital. The order of implementation was randomised with wards stratified by predicted mortality rates. Effectiveness was evaluated using a stepped wedge cluster randomised controlled trial design, comparing outcomes between patients admitted before and after implementation. The primary outcomes were in-hospital mortality and cardiopulmonary resuscitation. A nested qualitative study explored challenges to implementation and contextualised the trial outcomes.

Results

Between July 2010 and December 2011, 13 wards were sequentially randomised to implement the critical care outreach: 7,802 patients were admitted before implementation and 10,880 after implementation. There were 370 deaths (4.74%) among patients admitted before implementation and 384 deaths (3.53%) after implementation. Adjusting for clustering and temporal trends, the odds ratio for mortality was 1.03 (95% CI: 0.68-1.53). Results for other outcomes were broadly similar. Focus groups revealed a lack of endorsement of the intervention by management and ward nurses.

Conclusions

This pragmatic evaluation of critical care outreach in a middle income country did not show a reduction in mortality or other outcomes.

Trial registration number IRCT201107187053N1

Introduction

Scientific background

Demand for intensive care beds is increasing in lower and middle income countries. [1, 2] Critical care outreach, comprising a system for identifying acutely ill patients in general wards and an outreach team, is widely implemented in developed countries. [3, 4, 5, 6, 7] However systematic reviews of randomised controlled trials have not found robust evidence that it reduces mortality, cardiac arrest, unplanned intensive care admissions or length of stay. [8, 9, 10] It has been suggested that the policy was not evidence based. [11, 12] Apart from one before and after study it is unevaluated in middle income countries. [13]

Explanation of rationale

Hospital managers decided to implement critical care outreach (CCO) across the general hospital wards of Shariati Hospital, Tehran. They agreed to a randomised roll-out, allowing robust evaluation as a stepped wedge cluster randomised controlled trial. [14]

Aim

This trial assessed the effects of CCO on hospital mortality and cardiopulmonary resuscitation. Secondary aims were to assess effects on length of stay and intensive care admissions.

Methods

Between July 2010 and December 2011 Shariati Hospital implemented and sequentially randomised CCO across 13 wards as an un-blinded stepped wedge cluster randomised trial. Outcomes were compared between admissions before (unexposed) and after each ward implemented CCO (exposed).

Trial Design

The trial was implemented in periods of four weeks: baseline data collection for three periods (12 weeks) ; roll out of the intervention to two wards every two periods (six steps of eight weeks each); post-intervention data collection for three periods (12 weeks) . This was a total of 18 periods (72 weeks). (Supplementary Figure 1) Each ward also had eight weeks transition phase of implementation, during which ward staff were trained to adopting the intervention.

Rationale for the trial design

Randomisation was at the cluster level to avoid issues of contamination. Because it was necessary to implement CCO sequentially in wards rather than introduce it to all wards at the same time, we randomised the roll out sequence. This allowed us to evaluate implementation as a stepped wedge cluster randomised trial.

Participants and setting

Shariati Hospital is a university and public teaching hospital with 800 beds, in 29 wards including five intensive care units (47 beds). It admits 20,000 patients annually. All thirteen adult general wards (general medical wards, orthopaedics, haematology, obstetrics, pulmonary, urology, surgery, and maxillofacial wards) served by three of the five intensive care units were selected for the new CCO team.

There were no patient exclusion criteria, everyone admitted to the thirteen wards over the duration of the trial was classified as belonging to one of the three exposure groups (unexposed, transition phase, exposed). Those admitted before the ward before was randomised to implement the intervention were unexposed; those admitted after were exposed; those admitted when the ward was undergoing training were in the transition phase.

Intervention

CCO was intended to respond to the needs of acutely ill patients and to share skills between intensive care and general ward staff. Implementation was overseen by a committee including representatives of management, nursing and medical teams. The CCO team included six experienced intensive care nurses who before the trial were introduced to the ward staff and underwent three months additional training in patient monitoring and clinical management. (Supplementary Appendix 1) Training of the critical care team included theory and management protocols followed by full-time practical training. The week the ward crossed over to the intervention, ward nurses began eight weeks of training on assessment, identification and management of acutely ill patients. (Supplementary Appendix 2)

The committee chose a single parameter system using routinely measured vital signs for ward staff to use to identify acutely ill patients for the CCO team. This was simple, avoided calculations and minimised false alerts. [15] Eligibility criteria included physiological criteria listed in Supplementary Appendix 3 (respiratory rate, oxygen saturation, pulse, blood pressure, temperature, urinary output, change in consciousness), ward staff concern, recent discharge from intensive care, or patients actively identified by the CCO team. Eligible patients showing no improvement after 30 minutes were referred to the CCO team. The CCO team assessed these patients using a composite scoring system. (Supplementary Appendix 4) The CCO team managed all high risk patients (score >5) and determined who should care for moderate risk patients (score 3 to 5). Ward staff managed all low risk patients (score <3).

Patients under CCO care were immediately evaluated by a team member and then either directly cared for by the CCO team or by ward staff under their instruction. Stable patients were discharged from CCO after 72 hours. Patients who remained acutely ill and haemodynamically unstable, or whose conditions caused concern, were transferred to the intensive care unit.

Before randomisation to the intervention arm (unexposed) wards usual care continued. Ward nurses cared for acutely ill patients under the supervision of ward physicians. Physicians could request transfer to intensive care but this was largely based on their individual judgement, rather than using scoring systems or formal referral criteria.

Outcomes

Primary outcomes were in-hospital mortality and number of patients undergoing cardio-pulmonary resuscitation (both expressed per patient). Secondary outcomes were length of stay and intensive care unit admission.

Data collection procedures

Data collection procedures were developed specifically for this evaluation. An independent data team was notified daily of new admissions to the study wards and on the same day reviewed patient records to collect information on patients' age, gender, reason for admission (medical, scheduled or unscheduled surgery, or ward transfer) and data required for the Simplified Acute Physiology score (SAPS II). [16] No additional investigations were undertaken, any missing SAPS II data items were assumed to be normal.

Mortality and length of stay data were obtained from the hospital electronic information systems. Data on cardio-pulmonary resuscitation and admissions to the intensive care unit were obtained from nursing office and CCO team records by the CCO team in exposed wards and by the independent data team in unexposed wards. For these outcomes data collection

was therefore not blind to exposure status. Where there was uncertainty, outcome data were rechecked by reviewing patient records.

Sample size

The sample size for this study was for the most part fixed by its design. That is to say, we used an opportunity to make a randomised evaluation of an intervention which was going to be rolled-out. Our study size was therefore constrained by the duration that it would take to roll-out the intervention to all wards. However, as preliminary power calculations suggested that this amount of data might only be able to detect larger differences, we added the 12 weeks pre and 12 weeks post periods worth of data (calculations showed that any additional data had no material impact on power). Over the 72 weeks of the trial expected 23,000 admissions to the wards. We used Hussey and Hughes methods to calculate the minimum detectable effect based on the mortality rate (primary outcome) in those unexposed to the intervention and the magnitude of the intra cluster correlation (ICC) of mortality rates. [17] With estimated in-hospital mortality of 3.5%, ICC from 0.01 to 0.05 and an average cluster size of 1,770 the study design would have 80% power (at 5% significance) to detect a decrease in mortality to 2.35 (a 35% relative risk reduction). This effect size is moderate to large but smaller than the effect found in a study of similar design in the U.K. [18]

Randomisation

The 13 wards were grouped into pairs (and one group of three) with similar expected ward mortality rates. The two wards with the highest expected mortality rate were paired the next two highest expected mortality wards were paired and so on. The two smallest wards had similar expected mortalities and were combined. For each pair, one ward was randomly allocated to initiate the intervention first in the first half of the study and the other second. The six pairs were then randomly allocated to their order in the sequence.

Allocation concealment and blinding

Randomisation was carried out at a fixed point in time independent of the trial team and the information on ward sequence was revealed 2 to 3 days before start of the transition period. Allocation concealment from individual patients was not important as there was neither individual patient recruitment nor consent. The intervention was delivered without blinding.

Statistical methods

Admissions to wards were categorized as unexposed, transition phase or exposed and baseline characteristics (age, gender, type of admission, chronic diseases, SAPS II score) summarised by category.

We tested the null-hypothesis of no difference in mortality rates before and after exposure using a mixed effect logistic regression model. In addition to other patient or ward characteristics, we adjusted for clustering (ward), calendar time (since the intervention is sequentially rolled-out) and exposure to the intervention for each ward at each time point. We report the odds ratio as the intervention effect. The primary analysis was unadjusted except for clustering and time effects. A secondary analysis adjusted for pre-specified patient covariates, age, sex, SAPS II score and type of admission (elective or emergency). Binary secondary outcomes were analysed in a similar way. Because length of stay, was markedly non-normally distributed, we used a log-linear model and report exponentiated coefficients which can be interpreted as the ratio of geometric means (or as a ratio of medians). These models were fitted using random effects models in STATA, using the meglm function. As there were convergence difficulties using STATA, we used the Laplace approximation. We report the latent ICC, as is recommended in settings with binary outcomes and use the STATA function loneway. [19]

All outcomes were considered significant at the 5% level and we report both unadjusted and adjusted treatment effects, along with estimates of the ICC. The primary analysis was by

intention to treat, with patients categorised on the basis of the exposure status of the ward to which they were admitted. For the fully adjusted analysis <2% of patients had incomplete data so missing data methods were not warranted.

Sensitivity analysis

Admissions during the transition phase are excluded from the main analysis. However in a sensitivity analysis for the two primary outcomes, admissions during the eight week transition phases were categorised as exposed to the intervention. Because patients transferring between wards might have been incompletely exposed to CCO, we also report outcomes subdivided by place of death.

Changes to methods after trial commencement

We had initially planned to fit the statistical models using population averaged models, using generalised estimating equation methods, in STATA because random effects models in cluster trials lack appropriate interpretation. [20] However when model fitting, the generalised estimating equation failed to converge or took a very long time to run. We therefore used random effects models. Where results did converge for both methods, overall conclusions were similar.

Qualitative evaluation

After implementation was completed a nested qualitative study explored challenges to implementation and contextualised outcomes of the trial. [21] Between February and April 2012, two focus groups were conducted with nurses delivering the intervention and health professionals on the wards and followed up with individual interviews to clarify issues arising from focus groups. Audio recording of the groups was transcribed and translated from Farsi. Data collection ended when no new information emerged. Data were analysed using an inductive content analysis approach. [22] AJ conducted the focus groups and translated the recordings; AL provided feedback on the developing thematic categories.

Results

Participant flow

Between July 2010 and December 2011, there were 22,919 admissions in the 13 wards: 1,890 could not be included because the patient was discharged or transferred to another ward within 24 hours of admission and before baseline data had been collected, leaving 21,029 patients contributing data to the trial. (Table 1) In the unexposed phase 7,802 were admitted, in the transition phase 2,347 and in the exposed phase 10,880. The CCO was implemented as intended under the randomisation schedule in all study wards. (Figure 1) On 1682 occasions took on the management of patients. On 46.2% of occasions they were called by ward staff, on 53.2% by members of the CCO team and on 0.7% following an emergency call. They also managed 879 patients after discharge from intensive care.

Baseline data

Age, gender and SAPS II scores were similar in patients admitted during the unexposed and exposed periods. There were some differences in the reason for admission. (Table 1) Small numbers of patients were transferred between the wards, 170 (2%), in both the unexposed and exposed periods.

Outcomes

There were 370 deaths (4.74%) among patients admitted to a ward during its unexposed period; and 384 deaths (3.53%) among patients admitted to a ward during its exposed period: totally unadjusted OR: 0.73 (95% CI: 0.64-0.85). (Table 2) However, after adjusting for time effects, covariate effects and clustering this effect became more uncertain (aOR: 1.02 95% CI: 0.68-1.55). Mortality appears to decline over time in patients admitted to unexposed wards. (Supplementary Figure 2) The secondary outcome followed a similar pattern: the proportion of patients receiving cardiopulmonary resuscitation decreased from 4.86% to

3.61% (totally unadjusted OR: 0.73 95% CI: 0.64-0.85). But this result became more uncertain after adjusting for clustering and time effects (aOR 1.00 95% CI: 0.69-1.48).

A similar proportion of patients was admitted to the intensive care unit in the two study periods (1.28% in the unexposed period and 1.23% in the exposed period) and the fully adjusted odds ratio was 1.15 (95% CI: 0.64-2.00). Length of stay declined from a median of 6 days in the unexposed wards to a median of 4 days in the exposed wards. We do not report an adjusted effect for length of stay as the model was unstable and the results unreliable. All temporal trends in outcomes in unexposed wards were similar. (Supplementary Figure 2) ICCs were higher than anticipated 0.013 (95% CI: 0.000-0.259) to 0.0979 (95% CI: 0.012-0.184).

Secondary analyses

Stratifying the results by the ward where the outcome event took place (i.e. either on the admitted ward or on a transferred ward), showed similar findings to the primary analysis: mortality and cardiopulmonary resuscitation rates declined in crude analyses but became uncertain after adjustment. (Supplementary Tables 3 and 4)

Qualitative evaluation

The focus group participants are shown in Supplementary Box 1. Structural (staff-patient ratio) and interactional (conflict between CCO teams and ward staff) challenges were identified to the implementation of the CCO. The intervention was delivered in the context of strongly embedded ward routines and high workloads; it therefore was perceived by many as interfering with routines and imposing additional work (Box 1 quotes 1, 2). There were some positive outcomes from the intervention through additional resources available to staff and an increase in understanding of optimal patient care. (Box 1 quote 3) However, some CCO team members and ward staff perceived a lack of endorsement from hospital management that made CCO appear to be ‘just another research project’ (Box 1 quote 4). There was lack of

consensus on whether intervention was appropriate in patients nearing the end of life, meaning that that some ward staff perceived the additional work mandated by the CCO team as potentially harmful to dying patients (Box 2 quote 5).

Discussion

Summary of findings

This stepped wedge cluster randomised trial of CCO in a teaching hospital in a middle-income country did not show reductions in mortality, proportions of patients needing cardiopulmonary resuscitation or admitted to the intensive care unit or in length of stay. The qualitative study revealed resistance to the CCO service by ward staff because of perceptions of conflict with existing ward routines and increased workload. Difficulties in implementation may explain the lack of effect. Alternatively it may be that this study was under powered because the intervention had a smaller than anticipated effect. We are uncertain whether this intervention is beneficial.

Qualitative evaluation suggests that both structural factors (existing staff workload, endorsement from hospital management) and attitudinal factors (willingness to change practice, understanding of end of life care) were not sufficiently in place for the intervention to succeed. There are particular ethical challenges in relation to end of life care in the context of following Islamic principles and there are no guidelines for do not resuscitate orders in Iran. [23] However do not resuscitate orders are found in other countries following Islamic principles. [24]

Strengths

This was a well-designed study, avoiding many of the problems of simple before and after studies through the use of a stepped wedge cluster randomised trial with wards matched on predicted mortality rates. Simple before and after designs do not adequately deal with confounding. [25] Uncertain conclusions under a robust design are preferable to an erroneous conclusion of effectiveness. [26, 27] As all admissions to the wards were included in the analysis we would identify effects of the CCO team on ward patients not under their care.

The nested qualitative evaluation may help explain why the intervention did not seem to change the outcomes.

Limitations

The stepped wedge cluster randomised trial is a novel study design and the design and analysis of these studies are still in development. ICCs were larger than expected, the effect of the intervention smaller and there were large changes over time in the unexposed clusters. These all added to the wider confidence intervals and the study's limited power to detect a small difference in mortality rates. The binary outcomes were modelled using the Laplace approximation which is not optimal and there was such instability with the convergence of the models for length of stay that it was unreportable. A further limitation of our analysis is that there was a considerable amount of missing covariate data, which meant that the fully adjusted estimate of the treatment effect was based on a relatively small subset of the observations. Multiple imputation is one commonly used method to allow for missing data in covariates. We did not use a multiple imputation the methods of analysis for stepped-wedge studies are in their infancy and no methodologicaly currently exist for a multiple imputation of missing data from a stepped-wedge study.

Because of the need for bespoke data collection methods the ascertainment of secondary outcomes was not blinded. We also lack quantitative data on important process measures such as numbers of patients reviewed by the CCO team. Ideally a second researcher would have reviewed the interview and focus group transcripts.

This evaluation considered four outcomes: mortality, admission to the intensive care unit, the need for cardiopulmonary resuscitation and length of stay. We did not consider resource costs or potential for harm, if diverting resources from other services affected other outcomes.

Comparison to existing literature

This is the only robust evaluation of CCO in a lower or middle income country. Our findings are consistent with the findings of evaluations of the effects of CCO teams in developed countries, which when considering all the evidence, found no overall reduction in mortality but also observed substantial heterogeneity between studies. [10] The design of this study was modelled on a study of CCO implementation in the UK. [18] However, unlike the UK study found a large and statistically significant reduction in mortality. Some studies have found that ward staff did not call or delayed calling outreach teams and this may explain low effectiveness.[28] In our study resistance to the intervention by ward staff suggests that contextual factors may have impeded effectiveness in a similar way. It has been suggested that ongoing education of ward staff and review of the use of the CCO team over several years may improve the effectiveness of the CCO by changing organisational behaviour, however our study was not of sufficient duration for this to happen.[29]

This pragmatic evaluation of implementation of CCO in a in a middle income country teaching hospital did not find evidence of a reduction in mortality or other outcomes. Changes in health services in middle income countries need robust evaluation. The stepped-wedge study design is a feasible method of evaluation.

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The authors have no conflicts of interest.

Trial registration

The trial was registered on 7th July 2015 on the Iranian Registry of Clinical Trials [Registration number IRCT201107187053N1]. [30]

Ethical approval

This research was approved by the Institutional Review Board of Tehran University of Medical Sciences and Digestive Diseases Research Institute in accordance with Iranian Ministry of Health and Medical Education guidelines.

List of abbreviations

CRT: cluster randomised trial; SW-CRT: OR: Odds Ratio; aOR: adjusted Odds Ratio; LOS: Length of Stay; CPR: Cardio Pulmonary Resuscitation; ICU: Intensive Care Unit; SAPS II score: Simplified Acute Physiology Score; SD: Standard Deviation; CI: Confidence Interval;

Competing interests

The author(s) declare that they have no competing interests.

Authors' contributions

AJ conceived the trial, and participated in its design, led its coordination and helped to draft the manuscript. KH helped design of the trial, developed the methods, carried out the statistical analysis and wrote the first draft of the paper. TM contributed to the design of the trial, the interpretation of the results and helped draft the manuscript. All authors read and approved the final manuscript.

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Figure 1: CONSORT flow diagram

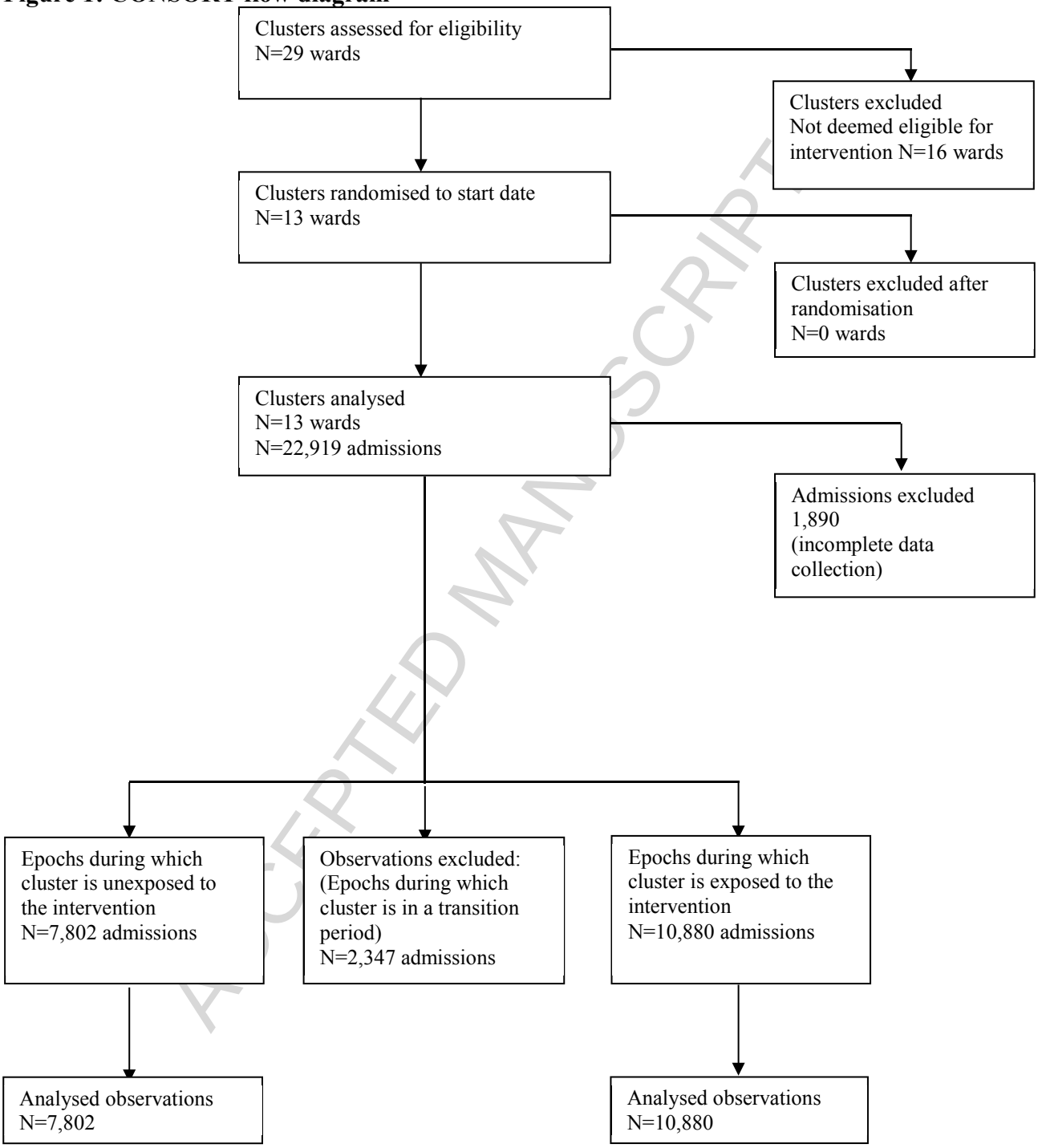

Table 1: Characteristics of study population stratified by exposure status

	Unexposed to intervention	Transition Period (training)	Exposed to intervention
Number patients	7,802	2,347	10,880
Age, years *	44 (20)	43 (19)	43 (19)
Male	3,732 (48)	983 (42)	4,266 (39)
SAPS II score*	13.0 (9.8)	12.3 (9.3)	12.2 (9.4)
Type Admission			
Scheduled surgery	2,113 (27)	739 (31)	3,849 (35)
Medical	3,689 (47)	969 (41)	4,124 (38)
Unscheduled surgery	1,684 (22)	621 (26)	2,855 (26)
Not known	316 (4)	18 (<1)	52 (<1)
Transferred Ward	170 (2)	29 (1)	170 (2)
Chronic Diseases			
AIDS	0 (0)	0 (0)	2 (0.02)
Haematological	107 (1.37)	59 (2.51)	235 (2.16)
Metastatic cancer	35 (0.45)	3 (0.13)	36 (0.33)
Month			
July 2010	578 (7)	0	0
August 2010	1,155 (15)	0	0
September 2010	1,145 (15)	0	0
October 2010	1,002 (13)	185 (8)	0
November 2010	1,013 (13)	220 (9)	0
December 2010	751 (10)	363 (15)	217 (2)
January 2011	716 (9)	372 (16)	297 (3)
February 2011	538 (7)	105 (4)	586 (5)
March 2011	276 (4)	74 (3)	309 (3)
April 2011	218 (3)	196 (8)	599 (6)
May 2011	275 (4)	286 (12)	833 (8)
June 2011	75 (1)	226 (10)	973 (9)
July 2011	60 (1)	196 (8)	1,134 (10)
August 2011	0	70 (3)	1,350 (12)
September 2011	0	54 (2)	1,277 (12)
October 2011	0	0	1,354 (13)
November 2011	0	0	1,303 (12)
December 2011	0	0	648(6)

Values are numbers and percentages, except for * where mean (Standard Deviation) are provided

Table 2: Outcome by exposure status

	Unexposed to intervention	Exposed to intervention	Treatment effect	P-value	Intra Cluster Correlation
Number of Patients	7,802	10,882			
Mortality					
Number (%)	370 (4.74)	384 (3.53)	OR (95% Confidence Interval)		0.059 (0.005, 0.113)
Unadjusted			0.73 (0.64, 0.85)	0.000	
Cluster adjusted			0.98 (0.79, 1.20)	0.817	
Fixed effects for time			1.21 (0.83, 1.76)	0.311	
Linear effect for time			1.04 (0.82, 1.31)	0.774	
Covariate adjusted*			1.02 (0.68, 1.55)	0.913	
Cardiopulmonary resuscitation					
Number (%)	379 (4.86)	393 (3.61)	OR (95% CI)		0.058 (0.004, 0.117)
Unadjusted			0.73 (0.64, 0.85)	0.000	
Cluster adjusted			0.97 (0.79, 1.19)	0.784	
Fixed effects for time			1.17 (0.82, 1.68)	0.381	
Linear effect for time			0.99 (0.79, 1.24)	0.920	
Covariate adjusted*			1.00 (0.69, 1.48)	0.999	
Length of Stay					
Median [IQR]	6 [3,10]	4 [2, 8]	RGM (95% CI)		0.098 (0.012, 0.184)
Unadjusted			0.86 (0.83, 0.89)	0.000	
Cluster adjusted			1.00 (0.97, 1.03)	0.971	
Fixed effects for time[$]					
Linear effect for time[$]					
Covariate adjusted*[$]					
Admission to intensive care unit					
Number (%)	100 (1.28)	134 (1.23)	OR (95% CI)		0.013 (0.000,0.259)
Unadjusted			0.96 (0.74, 1.25)	0.761	
Cluster adjusted			1.11 (0.78, 1.58)	0.558	
Fixed effects for time			1.28 (0.71, 2.31)	0.417	
Linear effect for time			1.21 (0.65, 2.26)	0.545	
Covariate adjusted*			1.15 (0.64, 2.09)	0.644	