Selective decontamination of the digestive tract in critically ill patients treated in intensive care units: a mixed-methods feasibility study (the SuDDICU study)

Jill J Francis,[1,2,3]* Eilidh M Duncan,[1,2] Maria E Prior,[1,2] Graeme S MacLennan,[2] Stephan U Dombrowski,[2,4] Geoff Bellingan,[5] Marion K Campbell,[2] Martin P Eccles,[6] Louise Rose,[7] Kathryn M Rowan,[8] Rob Shulman,[5] A Peter R Wilson[5] and Brian H Cuthbertson[9]

[1]Health Psychology Group, University of Aberdeen, Aberdeen, UK
[2]Health Services Research Unit, University of Aberdeen, Aberdeen, UK
[3]School of Health Sciences, City University London, London, UK
[4]Department of Psychology, Stirling University, Stirling, UK
[5]University College Hospital, London, UK
[6]Institute of Health and Society, Newcastle University, Newcastle upon Tyne, UK
[7]Lawrence S. Bloomberg Faculty of Nursing, University of Toronto, Toronto, ON, Canada
[8]Intensive Care National Audit and Research Centre (ICNARC), London, UK
[9]Department of Critical Care Medicine, Sunnybrook Health Sciences Centre, Department of Anaesthesia, University of Toronto, Toronto, ON, Canada

*Corresponding author

Declared competing interests of authors: Jill Francis has a number of research projects funded by research councils and charities, and funds for travel for dissemination purposes are included in some research grants. Geoff Bellingan has received SuDDICU grant funding from University of Aberdeen for investigator travel to research meetings. He is the principal investigator in a HTA-funded trial of enteral vs. parental nutrition in intensive care units, and has spoken on the SuDDICU study at other related meetings, for example Scottish Intensive Care Society, and received travel support to attend these meetings. Martin Eccles's institution received money for his efforts on this study. Peter Wilson received support for travel to meetings for the study from Aberdeen University. He has received payment for his work as a member of the Drug Safety Monitoring Board, Infection Control Services, for medico-legal work, and for Henry Smith professional lectures.

Published April 2014
DOI: 10.3310/hta18250

Scientific summary

The SuDDICU study

Health Technology Assessment 2014; Vol. 18: No. 25
DOI: 10.3310/hta18250

NIHR Journals Library www.journalslibrary.nihr.ac.uk

Scientific summary

Background

Hospital-acquired infections (HAIs) are a major cause of morbidity and mortality and markedly increased health-care costs. Critically ill patients who require management in an intensive care unit (ICU) are particularly susceptible to these infections. Selective decontamination of the digestive tract (SDD) may reduce these infections and improve mortality. Recent meta-analyses based on 36 randomised studies demonstrate a benefit in terms of mortality and reducing pneumonia rates; however, SDD has not been widely adopted into practice.

Objectives

The overall aim was to identify the perceived risks, benefits and barriers to the use of SDD in UK.

Objectives with matching research questions:

Objective 1: To identify and precisely describe the clinical intervention in ICUs and hospitals that deliver SDD.

Research question 1: What are the components of the SDD intervention?

Research question 2: How has SDD been implemented and delivered into practice?

Objective 2: To identify the range of beliefs, interpretation and views about the current evidence base relating to the use of SDD in key stakeholder groups.

Research question 3: What are the views of key stakeholders about the internal/external validity and adequacy of the existing evidence base for SDD and how willing are they to participate in further research?

Research question 4: What are the views of key stakeholders about the likely positive and negative consequences of implementing SDD in ICUs and what is the relative importance of these beliefs in influencing overall views about SDD?

Research question 5: What are the views of key stakeholders about the likely barriers to implementing SDD in ICUs?

Objective 3: To identify current practice and assess the acceptability of further randomised controlled trials in the field of SDD in a wide group of intensive care consultants and clinical microbiologists.

Research question 6: What are the stated current practices and intentions of intensive care consultants and clinical microbiologists with responsibility for critically ill patients about SDD?

Research question 7: If there are uncertainties in the evidence base, do these clinicians believe they could be addressed in a clinical trial? Which research questions, trial design(s) and interventions would be optimal, and what predicts these beliefs?

Objective 4: To assess the feasibility of a proposed effectiveness randomised controlled trial comparing SDD against a control group in ICUs, or a proposed implementation study to increase uptake in ICUs, among international clinical triallists.

Research question 8: What are the likely challenges in undertaking a large multinational randomised controlled study of SDD in an ICU?

Methods

We used a 'multilens' approach comprising four stages:

Stage 1: In case studies of two ICUs in which SDD is routinely delivered, we used observations of SDD delivery at the bedside, interviews with staff involved in SDD policy, monitoring or delivery, and documentary analysis (e.g. of SDD protocols, training materials) to identify and describe how SDD has been adopted and implemented.

Stage 2: A three-round Delphi study was designed to assess consensus (rather than to achieve consensus). Participants were professionals from four stakeholder groups with a potential interest in SDD: intensive care consultants, clinical microbiologists, hospital pharmacists and ICU clinical leads or nurse managers/educators. We used semistructured interviews based on a theoretical framework of health professional behaviour change and structured questionnaire instruments to identify the range of stakeholders' beliefs, views and perceived barriers to the use of SDD. A topic guide was developed for round 1 (semistructured interviews). Questions about barriers to SDD delivery were based on a framework of 'theoretical domains' that describe barriers to clinical behaviour change and other questions focused on participants' views about the need for, and acceptability of, further SDD research. Interviews were audio recorded, transcribed verbatim and analysed using content analysis. The identified beliefs were used to populate a questionnaire instrument for rounds 2 and 3. These further rounds were conducted using online materials. Round 3 materials included group-level feedback of the round 2 responses (frequency distributions) and individualised reminders of participants' response to each question in round 2. We assessed the stability of views across rounds 2 and 3 at the within-person level (individual change scores) and the group level (changes in group means). We also assessed the importance of the identified views using multiple indices and described the levels of consensus in the sample about the beliefs identified. Findings from the Delphi study were used to develop the questionnaire instrument for the next stage.

Stage 3: In a large-scale nationwide online questionnaire survey, we invited to participate (1) all intensive care consultant members of the UK Intensive Care Society (ICS) and (2) all clinical microbiologists with responsibility for patients in intensive care who were members of the Health Infection Society (HIS) and/or the British Society for Antimicrobial Chemotherapy (BSAC). We used multiple regression techniques to identify the factors that predict three key outcomes: support for, or opposition to, SDD; ethical acceptability of an effectiveness trial; and willingness to participate in further SDD research.

Stage 4: The research team identified expert international triallists with known expertise in intensive care trials and/or implementation trials based on their professional profile and the research team's knowledge of the field. Twenty expert triallists were initially approached by personal e-mail from a clinical member of the research team, followed by another e-mail, information sheet and consent form from the project manager. Semistructured telephone interviews were conducted with international clinical triallists. Participants were selected on the basis of their research profiles in intensive care, clinical trials and/or implementation trials. The triallists discussed the feasibility of either a randomised controlled effectiveness trial or a randomised controlled implementation trial. They were asked to identify challenges and barriers to undertaking further research in the field of SDD.

Findings from the four stages of this study were compared and contrasted in order to address the overall research objectives. Findings were then compared with a series of decision rules (developed a priori) that facilitated the formulation of recommendations for further research.

Results

Stage 1: The two case studies identified the clinical components (drug specification) and behavioural components (who does what, when and how) of SDD as delivered in practice. There was some complexity in the interplay and flow of the clinical and behavioural components of SDD, involving multiple staff. However, provision of SDD was simple from the perspective of individual staff and delivery was regarded as straightforward.

Stage 2: In the Delphi study (round 1, $n = 47$; round 2, $n = 44$; round 3, $n = 42$), scores were stable at both the individual and group levels between rounds 2 and 3. The most important consequence of SDD was identified as the potential for SDD to increase antibiotic resistance. In terms of the theoretical domains framework (TDF), the domain *Beliefs about consequences* was regarded as the most important domain. Other important domains were *Knowledge* (of the evidence base) and *Motivation and decision processes* (around SDD adoption). We identified various levels of consensus, including patterns that signified (1) consensus around agreement with respect to a range of barriers to implementation of SDD, (2) consensus around uncertainty with regard to the effect of SDD on a number of key clinical outcomes and (3) bimodal distributions for key variables such as opposition to SDD and the generalisability of the current evidence base. Further effectiveness research in the field was reported to be both ethical and acceptable, and there was a high level of reported willingness to participate in future SDD research.

Stage 3: The national survey ($n = 419$ intensivists, $n = 49$ microbiologists) confirmed the general findings of the Delphi study, with reported uncertainty about the effect of SDD on antimicrobial resistance, infection rates, mortality, length of stay and cost-effectiveness. In terms of current SDD practice, we identified different stages of consideration, or adoption, of SDD. Approximately 10% of the sample reported currently delivering components of SDD whereas approximately 40% had not yet considered SDD. As with the Delphi study findings, the distribution of survey scores reflecting opposition to SDD was bimodal and this bimodality was evident among both intensive care consultants and clinical microbiologists. In other words, both groups included a substantial proportion (approximately 20%) who were not opposed to SDD. The other, primary, mode was at the mid-point of the scale (reflecting uncertainty) for intensivists and at the 'opposed' end of the scale for microbiologists. Level of opposition to, or in support of, SDD was significantly predicted by all the items in the questionnaire that assessed the beliefs about consequences [i.e. about whether or not SDD affects antibiotic resistance, HAIs, *Clostridium difficile* infections, ventilator-associated pneumonia (VAP) and mortality] but was not predicted by self-assessed knowledge of the SDD evidence base.

A large majority of the participating clinicians reported that uncertainties should be addressed in a new study and that further SDD research would be ethically acceptable. Seventy-eight per cent of participants reported that they would participate in a clinical effectiveness randomised controlled trial (RCT) and 94% of participants would support such a study if their colleagues were in favour. Sixty-three per cent reported being prepared to participate in a RCT to evaluate an intervention to promote the uptake of SDD (i.e. an implementation trial). There was strong support for the following design features in a clinical effectiveness trial: the measurement of antibiotic resistance as a major outcome measure, a control group to receive VAP bundles and/or chlorhexidine mouthwash.

As expected, current practice was associated with opposition to SDD. From the beliefs data, belief about whether or not SDD increases antibiotic resistance was the strongest predictor of two key opinions: opposition to SDD and further SDD research being ethically acceptable. The belief that current uncertainties in the evidence base should be addressed in a new study was the strongest predictor of

two intentions: willingness to participate in future effectiveness research and willingness to participate in future implementation research.

Stage 4: Within the triallist study ($n = 10$), several triallists accepted the current evidence about benefits of SDD for the individual patient, although most expressed uncertainty about its effects on antibiotic resistance. Reflecting this uncertainty, the triallists focused largely on the challenges of conducting an effectiveness trial. These challenges were seen as substantial. In particular, such a trial would need to be extremely large and multinational in nature. To adequately address the uncertainty about antibiotic resistance, a trial would need to use a cluster-randomised design. There was concern about the impact of the ethical and regulatory requirements within the various nations in the UK relating to patient consent in a cluster RCT. There was also considerable uncertainty about whether or not national funding bodies would be willing and able to fund a multinational trial.

Conclusions

Implications for health care

- There was a striking level of uncertainty about the effects of SDD on clinical outcomes that are regarded as important. This uncertainty suggests considerable potential for improvement in prevention of HAIs in critically ill patients, but further evidence is required to clarify the balance between potential individual-level benefits (e.g. infections, mortality) and potential society-level harms (e.g. antibiotic resistance) related to SDD.
- There was significant confusion apparent in clinicians' understanding and perceptions of the components that constitute SDD and related interventions, e.g. selective oral decontamination (SOD). The importance of detailed guidance on what constitutes different interventions was clear.
- For those units considering the adoption of SDD, it was apparent from our research that the delivery of SDD is feasible and can be adopted into unit practices. However, a detailed specification of the proposed clinical and behavioural components of the intervention should be developed.
- This study highlighted that the introduction of SDD, whether into routine practice or within a research context, requires consensus across a range of different stakeholders (including ICU colleagues, clinical microbiologists and medical directors/those with decisional authority within units). Our study also highlighted that microbiologists appear to be more opposed to SDD than intensivists, although a substantial minority are not opposed. Representatives of these stakeholder groups should be engaged early in any discussions around the use/introduction of SDD.
- A substantial minority of participants reported that SDD would be adopted (apparently quite straightforwardly) if adoption was mandated by regulatory bodies.

Recommendations for research

Further SDD research was viewed as important, acceptable and feasible to the key stakeholder groups who participated in this study. However, further effectiveness research would need to be on a scale that raises challenges for trial design and trial conduct. Research priorities are as follows:

1. A study within UK ICUs is required to model resistance patterns as a function of SDD use.
2. Further large-scale effectiveness trials of SDD in intensive care practice are required to answer remaining uncertainties, especially those issues relating to antimicrobial resistance.
3. There is general willingness to participate in a future effectiveness RCT of SDD; however, support for further research is time-sensitive (owing to the changing context) and is not unanimous. Future research needs to address the substantial barriers to acceptance and participation in any trial. These barriers should be addressed with reference to the study findings, for example (1) clinicians with lower self-assessed knowledge of the SDD evidence base shifted their opinions following feedback about

others' views, suggesting a role for discussion among clinical colleagues, (2) concerns about antibiotic resistance and other potential harms were of paramount importance, suggesting the importance of emphasising that a UK trial would assess antibiotic resistance patterns, (3) consensus between ICU colleagues was seen as important, suggesting that consensus building and development are key to acceptance and participation and (4) a substantial proportion of clinicians would be prepared to participate in a trial of SDD if their colleagues were in favour, suggesting that the presence of a SDD 'champion' in an ICU could influence participation.

4. Future trials should include (1) a primary mortality outcome, (2) pre-trial, during-trial and post-trial monitoring of antimicrobial resistance, (3) a control group that includes chlorhexidine and/or VAP bundles and (4) a cost–benefit analysis, and (5) a qualitative study to investigate the fidelity of the SDD intervention as delivered.
5. Groups proposing to undertake such a trial need to overcome the following challenges: (1) gaining sufficient acceptance of the trial, (2) gaining adequate participation in the trial, (3) the clear specification of the trial intervention, (4) major methodological issues relating to trial design and conduct, (5) clarification of the acceptability (to ethics committees) of cluster-level consent in the case of a cluster RCT and (6) major funding issues.
6. At this time, there is a much lower level of interest in adoption of SDD, or studies designed to encourage implementation of SDD, into practice.

Funding

This project was funded by the NIHR Health Technology Assessment programme and will be published in full in *Health Technology Assessment*; Vol. 18, No. 25. See the NIHR Journals Library website for further project information.

Health Technology Assessment

HTA/HTA TAR

ISSN 1366-5278 (Print)

ISSN 2046-4924 (Online)

Five-year impact factor: 5.804

Health Technology Assessment is indexed in MEDLINE, CINAHL, EMBASE, The Cochrane Library and the ISI Science Citation Index and is assessed for inclusion in the Database of Abstracts of Reviews of Effects.

This journal is a member of and subscribes to the principles of the Committee on Publication Ethics (COPE) (www.publicationethics.org/).

Editorial contact: nihredit@southampton.ac.uk

The full HTA archive is freely available to view online at www.journalslibrary.nihr.ac.uk/hta. Print-on-demand copies can be purchased from the report pages of the NIHR Journals Library website: www.journalslibrary.nihr.ac.uk

Criteria for inclusion in the *Health Technology Assessment* journal

Reports are published in *Health Technology Assessment* (HTA) if (1) they have resulted from work for the HTA programme, and (2) they are of a sufficiently high scientific quality as assessed by the reviewers and editors.

Reviews in *Health Technology Assessment* are termed 'systematic' when the account of the search appraisal and synthesis methods (to minimise biases and random errors) would, in theory, permit the replication of the review by others.

HTA programme

The HTA programme, part of the National Institute for Health Research (NIHR), was set up in 1993. It produces high-quality research information on the effectiveness, costs and broader impact of health technologies for those who use, manage and provide care in the NHS. 'Health technologies' are broadly defined as all interventions used to promote health, prevent and treat disease, and improve rehabilitation and long-term care.

The journal is indexed in NHS Evidence via its abstracts included in MEDLINE and its Technology Assessment Reports inform National Institute for Health and Care Excellence (NICE) guidance. HTA research is also an important source of evidence for National Screening Committee (NSC) policy decisions.

For more information about the HTA programme please visit the website: www.hta.ac.uk/

This report

The research reported in this issue of the journal was funded by the HTA programme as project number 09/01/13. The contractual start date was in October 2010. The draft report began editorial review in April 2012 and was accepted for publication in April 2013. The authors have been wholly responsible for all data collection, analysis and interpretation, and for writing up their work. The HTA editors and publisher have tried to ensure the accuracy of the authors' report and would like to thank the reviewers for their constructive comments on the draft document. However, they do not accept liability for damages or losses arising from material published in this report.

This report presents independent research funded by the National Institute for Health Research (NIHR). The views and opinions expressed by authors in this publication are those of the authors and do not necessarily reflect those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health. If there are verbatim quotations included in this publication the views and opinions expressed by the interviewees are those of the interviewees and do not necessarily reflect those of the authors, those of the NHS, the NIHR, NETSCC, the HTA programme or the Department of Health.

Published by the NIHR Journals Library (www.journalslibrary.nihr.ac.uk), produced by Prepress Projects Ltd, Perth, Scotland (www.prepress-projects.co.uk).