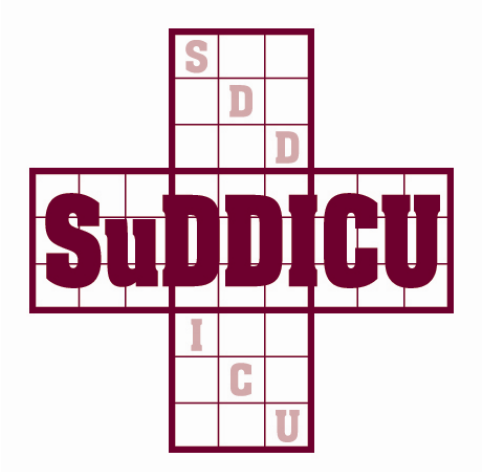
NETSCC, HTA

31st October 2011

Research Programme

The efficacy, cost-effectiveness and ecological impact of Selective Decontamination of the Digestive tract in critically ill patients treated in the Intensive Care Unit
The SuDDICU study

PHASE 2 - An exploratory study of the perceived risks, benefits and barriers to the use of SDD in UK critical care units



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1. BACKGROUND TO THE STUDY

Each year in the UK 140,000 patients are admitted to intensive care and of these almost 60,000 will die within a year of admission. Hospital acquired infections (HAI) are a major clinical problem for modern health services as they are associated with morbidity and mortality as well as high additional health care costs. Critically ill patients requiring ICU care are extremely susceptible to HAI and these infections are associated with high additional mortality, prolonged hospital stays and large health care resource utilisation. Between 20 and 50% of ICU patients suffer from such infections. Reducing the incidence and mortality from these infections is currently the focus of many intensive care quality improvement programmes and government initiatives in the UK and worldwide (1,2).

One intervention that has gained much attention in reducing HAI is selective decontamination of the digestive tract (SDD). SDD involves the prophylactic application of topical non-absorbable antibiotics to the oropharynx and stomach and a short course of intravenous antibiotics (3-13). The evidence base for SDD is strong with 12 meta-analyses of 28 randomised controlled trials (RCTs) in the literature enrolling over 7000 patients (3-13). Ten of these studies demonstrate a benefit in terms of reducing pneumonia rates and six studies show a specific mortality benefit in all ICU patients or in certain subgroups (14). A very recent large cluster randomised study from the Netherlands demonstrated a 3.5% reduction in adjusted mortality associated with SDD (15).

In the meta-analyses of SDD that have been published to date, clinical heterogeneity is a problem potentially resulting from combining studies using both topical and topical-systemic antimicrobials in the same analyses. The reports of primary studies included suffered from several methodological flaws, for example lack of blinding, lack of data on compliance with intervention, mixing of studies of diverse patient groups, only including sub-groups or no description of studies included. Evidence from these meta-analyses suggest that ventilator associated pneumonia (VAP) was reduced with both topical and topical-systemic SDD with an estimated odds ratio (OR) of 0.40 (95% confidence interval (CI) 0.15-0.60) (3-13). Mortality was also reduced in many studies, however there was considerable heterogeneity, particularly for meta-analyses of topical SDD, which is reflected in the imprecision of the estimated OR, 0.8 (95%CI 0.41-1.84). The Cochrane review of SDD demonstrated that SDD was associated with reduction in pneumonia, OR 0.32 (0.26-0.38) and death, OR 0.75 (0.65-0.87) (16). Since the Cochrane review, additional primary research has been published which also showed a mortality benefit, OR 0.63 (CI 0.46-0.87) (4). None of the published meta-analyses included the recent Dutch cluster randomised study (15). This mortality benefit was present in the more recent randomised studies and is of the magnitude of 3-6% absolute risk reduction (ARR) with

a number needed to treat (NNT) of 17 to save one life (14,15). If this mortality benefit could be realised in UK practice then it could save as many as 2-3000 lives per annum in the UK.

1.1 Evidence-practice gap- Despite this evidence base, the ICU community in the UK have not widely adopted this intervention with between 10-15 ICUs (out of 240) in the UK reporting that they actually undertake SDD (17,18). Existing limited surveys of practice and our preliminary investigations as to why this strategy has not been fully adopted suggest three main possibilities (17,18).

1. The strategy of giving prophylactic broad spectrum antibiotics to critically ill patients is counterintuitive to clinicians who have always believed that antibiotics need to be used in a rational and sparing way to prevent the development of multi-resistant micro-organisms.
2. The current evidence base is seen as inadequate in three ways. Firstly, there is a perception that the magnitude of the mortality benefit is not biologically plausible for such an intervention. Secondly, there is concern about the external validity and generalisability of the evidence. Most of the existing randomised studies of SDD come from countries where infections due to multi-resistant organisms are uncommon and the incidence of multi-resistant organisms, such as methicillin-resistant *Staph. Aureus* (MRSA) is low. Further, the recent widespread implementation of VAP bundles into UK practice may also reduce the generalisability of the evidence by reducing the baseline incidence of VAP, thereby reducing the impact of additional measures such as SDD.
3. It is commonly stated that implementation is difficult in practice due to the time consuming and awkward nature of administering SDD. This will undoubtedly become a secondary point if future high quality studies prove benefit.

However, these simple surveys fail to fully dissect the complex issues related to SDD use in the UK or internationally.

Many practitioners argue that the evidence needs to be replicated in a health care system where infections due to multi-resistant organisms are common and the incidence of multi-resistant organisms such as *MRSA* and *Clostridium Difficile* is comparatively high, such as in the UK. Further, they argue that none of the existing studies have had parallel high quality infection surveillance programmes analysing the long-term effects of SDD on the microbial ecology of the critical care unit in which it is applied. Existing data on the ecological impact of SDD is indeed limited with some studies suggesting an increase in the incidence of Gram positive organisms such as *Staphylococcus aureus* but others failing to show such effects (15,19-21). Finally, it is possible that this intervention is so counterintuitive that clinicians will not change their practice regardless of the evidence base or that one clinician group could

impede another group, who are in favour of the intervention, from implementing it. These issues are known to be similar in many regions around the world and this study will help to understand the specific issues in the UK.

1.2 Why this work is important- In summary, it seems that until we have further high quality evidence demonstrating efficacy, cost-effectiveness, ecological impact and the barriers to implementation for SDD he, this intervention is unlikely to be implemented more widely and, thus, patients will be denied a potentially lifesaving therapy. As an example, the recent large trial from the Netherlands is unlikely to change UK practice due to the perceived problems of lack of external validity and generalisability to the UK system (15). A current NICE/NPSA pilot on patient safety has made a strong research recommendation that SDD be subject to study including investigation of barriers to implementation (22). The current clinical focus on HAI, the move to making HAI a key target of patient safety initiatives, the political prioritisation of HAI and increased interest in this subject from research funding bodies makes this the ideal time to conduct this research. The study (known as the SuDDICU study) was also formally adopted in 2009 by the Intensive Care Society as its new UK national research study. This highlights the importance of this question to the UK ICU community.

Despite the clear importance of HAI in critically ill patients, and despite a national appreciation and prioritisation of the importance and urgency of this research topic, it remains unclear why SDD has not been implemented into routine practice. Despite the limited surveys undertaken to date, little is known about clinical staffs' beliefs about the existing evidence base, the perceived benefits and risks of SDD in clinical practice, the factors that influence current practice and likely barriers to implementation. . Further, it is also unclear whether there is a requirement for further high level evidence of effectiveness from within the UK before implementation would become acceptable and what sort of study would be feasible and acceptable to clinicians and trialists. The multi-method exploratory study presented in this protocol will attempt to address these issues. It will investigate the perspectives of a wide range of stakeholders in multiple settings, using observational, interview and questionnaire data analysed using both qualitative and quantitative approaches. This will result in a comprehensive and multi-faceted evidence base to inform a decision about the kind of research that is needed to address the SDD issue.

The variable uptake in SDD is also apparent in other countries outside of the UK, for example, in Canada, the US and in Australia/New Zealand. Reflecting the international importance of the topic, partner teams in Canada and Australia & New Zealand have also received funding to undertake parallel investigations into the reasons for low uptake in their settings (adopting the UK SuDDICU protocol). These partner projects have each been designed to stand

independently (and be funded independently). Prof Brian Cuthbertson (International Chief Investigator) and Dr Jill Francis (International methodological lead and Co-PI in the UK) are co-investigators on all the awarded grants ensuring cross-application learning and dissemination of best practice internationally.

2. SuDDICU- THE OVERALL PROGRAMME OF RESEARCH

The SuDDICU project is a programme of research to be undertaken across Canada, UK and Australia (see appendix 1). The programme of research consists of four *phases* including:

Phase 1- Evidence synthesis,

Phase 2- An exploration of risks, benefits and barriers to implementation of SDD (the application under consideration),

Phase 3- Pilot work for an effectiveness and / or implementation trial, and

Phase 4- An effectiveness and / or implementation trial. Phase 1 is already complete and Phase 2 (with four *stages*) is the focus of this protocol.

3. PHASE 2 OF THE OVERALL PROGRAMME OF RESEARCH

This study has four ***stages*** (see Figure 1 below) including

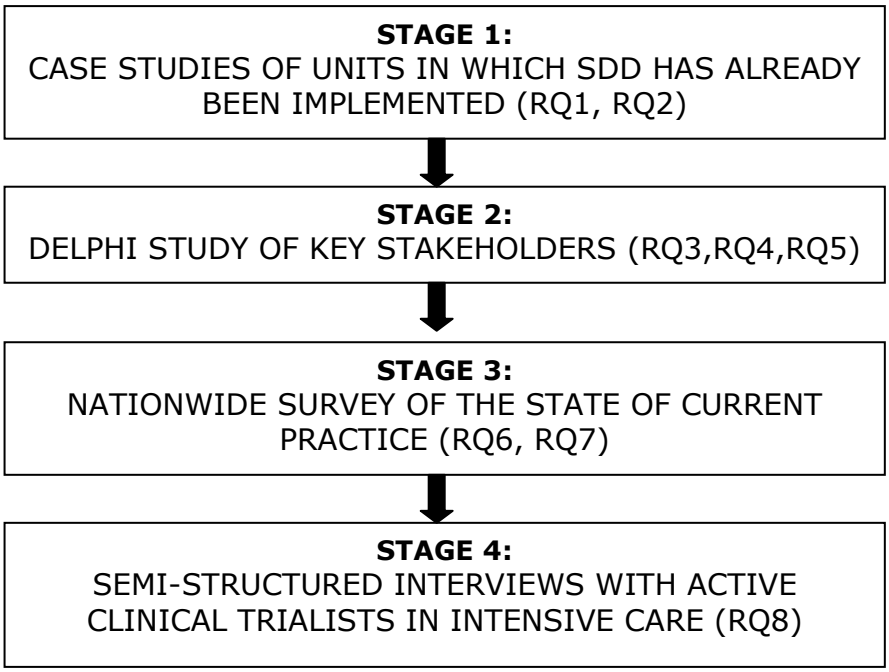
Stage 1- case studies in units using SDD (this study will be performed in the UK only as the UK is the only country in this study with units that use SDD),

Stage 2- a Delphi study of key stakeholder beliefs in relation to SDD (Canada, UK and Australia),

Stage 3 – A nationwide survey of the state of current practice (Canada, UK and Australia),

Stage 4- semi-structured interviews with trialists (Canada, UK and Australia) and

Figure 1: Design of exploratory study showing links to research questions:



Note. RQ = Research Question, for a more detailed outline of the four stages see appendix 2.

4. AIMS AND RESEARCH QUESTIONS

The overall aim of this study is to identify the perceived risks, benefits and barriers to the use of SDD in critical care units. The aims of the Canadian arm of this phase of SUDDICU are:

The overall aim of this study is to identify the perceived risks, benefits and barriers to the use of SDD in UK critical care units. To achieve this aim, the following objectives are proposed:

Aim 1- To identify and precisely describe the clinical intervention in units and hospitals that deliver SDD:

a) ***Research Question 1-*** What are the components of the intervention of SDD?

b) ***Research Question 2-*** How has SDD been implemented and delivered into practice?

Aim 2- To identify the range of beliefs, interpretations and views about the current evidence base relating to the use of SDD in key stakeholder groups:

c) ***Research Question 3-*** What are the views of key decisional authorities of the internal/external validity of the existing evidence base for SDD?

d) ***Research Question 4-*** What are the views of key decisional authorities about the likely positive and negative consequences of implementing SDD in critical care units?
e) ***Research Question 5-*** What are the views of key decisional authorities about the likely barriers to implementing SDD in critical care units?

Aim 3- To identify current practices nationally and assess the acceptability of further RCTs in the field of SDD among a wide group of intensive care clinicians and medical microbiologists:

f) ***Research Question 6-*** If there are uncertainties in the evidence base, do physicians believe they could be addressed in a clinical trial. What research questions, trial design(s) and interventions would be optimal and what predicts these beliefs?
g) ***Research Question 7-*** What are the stated current practices and intentions to implement amongst critical care and infectious disease physicians with regard to SDD?

Aim 4- To assess the feasibility of a proposed effectiveness RCT comparing SDD against a control group in ICUs, or a proposed implementation study to increase uptake in ICUs, among international intensive care clinical trialists.

h) ***Research Question 8-*** What are the likely challenges in undertaking a large multi-national randomised controlled study of SDD in ICU?

5. DETAILED PLAN OF INVESTIGATION

The study presented in this protocol will attempt to address the issues identified above. We will adopt a 'multi-lens' approach by investigating the perspectives of a wide range of decisional authorities in multiple settings, using observational, interview and questionnaire data analysed using both qualitative and quantitative approaches. This will result in a comprehensive and multi-faceted evidence base to inform a decision about the kind of research that is needed to address issues identified in this area. The findings will be analysed and synthesised using hypothesis generation and hypothesis testing strategies, as described below. The full international investigation will involve four inter-related *stages* (see Figure 1 above for details) and will culminate in an assessment of the need for and acceptability of an effectiveness and/or implementation trial of SDD. If a trial is deemed appropriate, the evidence from this investigation will then be used to design the trial and to specify (or, for an implementation trial, to develop) the intervention to be evaluated. From this point onwards this proposal will only discuss the study under funding request from CIHR (the Canadian Delphi and national surveys).

6. CASE STUDIES

6.1. Aim- To identify and precisely describe the clinical intervention in units and hospitals that deliver SDD *(addressing aim 1, Research Question 1 and 2, see above)*
Two case studies will be conducted in units in which SDD has been implemented. These will focus on a behavioural analysis of the processes of implementation, based on a modification of Michie and Johnston's (23) advice for specifying clinical behaviour (who, what, to whom, when, how). It will identify the "A,B,C" (antecedents, behaviour, consequences) (24) of each action that is taken in the sequence of behaviours between identifying a patient who may be eligible for SDD, prescribing, supplying, storing, communicating, administering (to the patient) and so on, and the factors associated with the 'flow' between these actions. This will involve observational visits, interviews with a range of clinical staff (e.g. consultants, registrars, pharmacists, nurses etc) and documentary analysis, which will be used to identify the actions required from all staff to (a) introduce SDD to the ICU and (b) maintain, regulate and optimise the delivery of SDD over time. These case studies will inform the practical issues around implementation of SDD in ICUs either in the context of a trial intervention or to inform implementation strategies.

6.2 Target units- The two SDD units will be purposively sampled from an existing database from a national survey of SDD in the UK. This survey, undertaken by Bastin and Ryanna (18), identified all units in the UK which delivered SDD as a routine part of clinical care. Dr Anthony Bastin, custodian of the survey results, has agreed that we can use the survey data for this purpose. One Unit that has recently implemented SDD and one that has used SDD over a longer period will be identified**.** When identified, SDD Units will be contacted and asked to take part in the study.

6.3 Methods- From multiple visits to each site, structured observations of the administration of SDD in the ICU will be followed by semi-structured interviews with nursing staff, clinical leads and other decision makers to elicit accounts of the processes of change, including decision making, documentation and resource issues. Retrospective accounts will be elicited, describing how the Unit decided to introduce SDD, factors that triggered change, barriers experienced (i.e., interruptions to the 'flow' of actions), and the strategies used to overcome them. The perceived consequences of the SDD policy for the unit (and the hospital more generally) will be documented. The case studies will identify:

- Accounts of implementation of SDD in practice, in terms of the behaviours performed by the full range of individual clinicians (e.g. nursing staff, intensive care consultants,

consultant medical microbiologists, pharmacists, clinical leads / directors and ICU pharmacists);

- Accounts of how SDD was first introduced into the Unit, including the trigger factors to change and the ways in which barriers were overcome at each site;
- Specific content that may be used to populate the content of behaviour change techniques to be used in an implementation intervention (if study findings suggest such an intervention should be designed and evaluated);
- Procedures to consider in order to deliver an implementation trial (if study findings suggest such a trial should be undertaken).

7. DELPHI STUDY

7.1 Aim To identify the range of beliefs, interpretations and views about the current evidence base relating to the use of SDD in key stakeholder groups (*addressing aim 2, Research Question* 3 to 5*, see above*).

7.2 Target groups- We will target the key decisional authorities who have the greatest influence on the decision to implement SDD in an ICU. Our investigations suggest these decisional authorities are critical care physicians, critical care pharmacists, infectious disease physicians and Medical and Nursing managers for ICU. This final group is identified as the key staff within a unit who would have decisional authority at a unit level for the implementation of a new intervention (such as SDD) and would also have the greatest experience in leading and conducting clinical implementations in critical care practice. Although a heterogonous group, they will develop the range of beliefs that is required in a Delphi study. It should be noted that critical care nurses who deliver direct clinical care were identified by our nurse collaborators as not being a key decisional authority due to their current lack of exposure to the evidence base or the delivery of SDD in practice.

7.3 Sampling and sample size- There is a broad range of estimates of suitable sizes for a Delphi panel, but smaller sizes (such as 10 for each stakeholder group) have been deemed appropriate where panel members have similar training (25). Four key decisional authority groups (as below) will be sampled. The total UK sample size will be approximately 40 (This arrangement is mirrored in the international partner studies.). Participation in this study will be fairly demanding, involving a 40-minute telephone interview and three subsequent email responses (taking approximately 15 minutes to complete). Assuming a 50% response rate, we plan to sample 20 decisional authorities in each group with a view to recruiting 10. Purposive diversity sampling will be used in all groups to identify as wide a range of initial views as

possible, based on a range of variables: Academic-affiliated or not; years of experience; gender and size of critical care unit (i.e. number of critical care beds), and current practice (routinely perform SDD or not). During the interview phase, we will track (diversity variation) on these factors using a diversity sampling table (appendix 3). We will invite additional participants to participate, if required, to maximise variation. Proposed sampling within the different key decisional authority groups is as follows:

1. *Critical care physicians*- We propose to use lists of intensive care physicians held by the Intensive Care Society of UK. Permission to access these lists for this purpose has already been received. This database contains contact details on over 2000 practising clinicians in the UK. It also contains the range of variables listed above regarding academic affiliation etc. Stakeholders will be sampled according to the purposive diversity sampling stated above and 20 stakeholders approached to take part in the study.
2. *Critical care pharmacists*- We propose to use the UK Clinical Pharmacists Association (UKCPA) Critical Care Group e-mail network which has access to 360 critical care pharmacists in the UK (over 75% of the UK's critical care pharmacists). Dr Rob Shulman is the Research Lead for the UKCPA Critical Care Group and is a co-applicant on this application. Through the network we will be able to identify the range of variables listed above regarding academic affiliation etc. Stakeholders will be sampled according to the purposive diversity sampling strategy described above and 20 stakeholders approached to take part in the study.
3. *Medical microbiologists*- There is no specific critical care group for UK medical microbiologists so we will sample this population in two ways. We will contact ICU clinical leads (identified through the Intensive Care Society membership database) and identify who is the lead microbiologist locally for each of these. Secondly Dr Peter Wilson (co-applicant) is on the editorial board of the British Society of Antimicrobial Chemotherapy (BSAC) and they have given permission to approach their membership through the Society, using a survey monkey (online survey facility). Using this we can establish critical care affiliation and other required variables and from these two approaches a valid database will be generated of UK practising microbiologists working in the critical care field. Stakeholders from this group will be sampled according to the purposive diversity sampling strategy described above. Twenty stakeholders will be approached to take part in the study.
4. *Clinical managers/leaders from critical care*- The Intensive Care Society lists will also be used to identify ICU directors / leads. We will also identify ICU nurse managers / nurse consultants through contact with the British Association of Critical Care Nurses and ensure that these stakeholders are well represented in the sample. Twenty stakeholders will be approached to take part in the study.

7.4 Methods- Using an adaptation of the Delphi technique (26) comprising an initial exploratory 'round', followed by three iterations, we will sequentially build a picture of respondents' beliefs and views on SDD (see appendix 4 for greater detail on Delphi methods). We will thus assess the likely factors influencing the acceptability of a proposed RCT comparing SDD against a control group in critical care units and/or a proposed RCT comparing implementation strategies for SDD in critical care units. A Delphi approach has previously been used for this purpose. For example, a Delphi study was conducted to identify potentially relevant determinants of innovation in health care organisations (27) and, similarly, to develop a national survey about medical instrumentation (28).

The aims and objectives of this phase require an exploratory approach to data collection in the first round, so that the full range of views may be elicited and subsequently considered by all participants in later rounds. The rounds of the Delphi study will be as follows:

- *Round 1. Initial exploration.* Semi-structured one-on-one interviews to generate a full range of views of key decisional authorities (item generation phase).
- *Round 2.* Email-administered questionnaire in which the authorities rate their strength of agreement (on a 9-point scale) with the listed beliefs and concerns elicited in Round 1.
- *Round 3.* Quantitative data (frequency distributions and measures of location and spread) from Round 2 fed back by email to these authorities, who are asked to either confirm or revise their initial views.
- *Round 4. A multi-national comparison* of data from each setting presented to all key decisional authorities (by email), who will be asked to re-rate their views in the light of this feedback. This will enhance the generalisability of the results.

The first three rounds will be performed in parallel but the final will be across all groups.

7.5 Initial exploratory interviews (Round 1)–

Semi-structured one on one interviews conducted by telephone (to enable efficient use of clinical staff's time and ensure adequate geographical coverage) will elicit relevant beliefs and concerns about SDD in clinical practice and about participating in an effectiveness or implementation trial of SDD. These interviews will use a broad theoretical basis, based on "theoretical domains" reported by Michie et al 2005 (29) (appendix 5), to ensure coverage of the full range of potential barriers to use of SDD. A topic guide based on the Theoretical Domains Interview (TDI) has been developed and includes consideration of:

- Factors that might influence the use of SDD, such as decisional authorities' knowledge of the evidence base, perceptions that using SDD will result in good/poor clinical outcomes, ecological factors that are barriers to the use of SDD.
- Factors that might influence participation in an effectiveness trial, e.g. beliefs about the strengths and weaknesses of the evidence base (including equipoise), areas where the

evidence base is regarded as inadequate, barriers to participating in a trial (including aspects of trial design).

- Factors that might influence participation in an implementation trial, e.g. beliefs about the barriers and facilitators that might influence the uptake of the evidence about SDD (if the evidence is regarded as positive and adequate).

Transcribed interviews will be content analysed based on the theoretical domains framework using methods previously employed by the research team in the context of critical care (30).

7.6 Initial ratings of agreement with identified beliefs and concerns (Round 2)- Based on findings from the first round of the Delphi study, we will develop an initial list of beliefs and concerns (a) about using SDD in clinical practice, (b) about participation in an effectiveness trial to evaluate SDD, and (c) participation in an implementation trial to evaluate strategies to facilitate uptake of SDD for presentation to the same group of participating clinical staff by email. We will attempt to balance the number of negative and positive items (unless this would distort the original meanings). All views from Round 1 will be included, to ensure that minority views are considered by all participants. Participants will be asked to rate the strength of their agreement (on a 9-point Likert scale) with the listed beliefs and concerns as well as the importance of the item (31). For (b), we will cover the factors that would influence trial design (e.g. nature of intervention, control group care, outcome measures) together with their overall ratings of trial acceptability (willingness to participate) and feasibility (ability to participate) if their concerns were to be addressed in the trial design. Data will be summarised as frequency distributions together with a measure of central tendency (i.e., median, unless distributions symmetrical). The level of overlap of distributions between groups will be noted but will not be fed back to the groups.

7.7 Further ratings of agreement with identified beliefs and concerns (Round 3)- Quantitative data (frequency distributions) from Round 2 will be fed back to all participants within the respective groups by email and they will be asked to either confirm or revise their initial views, again on a 9-point scale. These data will again be summarised as frequency distributions. Again, all rarely mentioned beliefs will be discussed by the research team before any are discarded. We will note differences between clinician groups, and in particular, whether the views of the groups show trends to diverge or converge between Rounds 2 and 3.

7.8 Multi-national feedback and further ratings (Round 4)- In Round 4, data from Canada, UK and Australia will be presented to all participants in all groups by email. If there are differences in the data (e.g. between clinical specialties or between nations) these differences will be represented in this feedback. Participants will be asked to re-rate their views. Data will be analysed (a) within countries and (b) for all settings combined. The Delphi

study report will present (i) the perceived importance of each specific belief about the use of SDD in critical care units; (ii) the acceptability and feasibility of conducting an effectiveness trial; and (iii) the acceptability and feasibility of conducting an implementation trial. The international comparisons in this round are vital to increase the generalisability of the results and of any future study result, since lack of generalisability has been cited as a major factor limiting the uptake and implementation of SDD in the past. This round will require that the investigations conducted in each country use a broadly parallel time frame, so that the feedback is presented to all participants with similar time intervals. Thus, the full Delphi results will allow us to consider how best to elaborate the key findings from the nationwide survey of the state of current practice, described below.

8. NATIONWIDE SURVEY OF THE STATE OF CURRENT PRACTICE

8.1 Aim- To identify current practices nationally and assess the acceptability of further RCT in the field of SDD in a wide group of intensive care clinicians and medical microbiologists (*addressing aim 3, Research Question* 6 and 7*, see above*).

8.2 Target group- This study will be a large-scale online questionnaire survey of intensive care clinicians and medical microbiologists. These groups were chosen as investigations suggests that these two groups are the most cognisant and influential with regard to the current use, barriers to implementation and willingness to participate in a subsequent effectiveness or implementation study.

8.3 Sampling- (i) We propose to use lists of intensive care clinicians held by the UK Intensive Care Society (ICS). Permission to access these lists for this purpose has been given by the UK ICS. This database contains contact details on over 2000 practising clinicians in the UK. All consultants on this database will be surveyed by an online questionnaire. (ii) Microbiologists involved in critical care in the UK will be identified first through responses from critical care clinical leads identifying their local microbiology leads and secondly from members of the British Society of Antimicrobial Chemotherapy involved in critical care, using the methods described in 3.3.2 above. These methods will enable us to survey the majority (approximately 180) of medical microbiologists practising in critical care.

8.4 Methods- The development and validation of the questionnaire will follow guidance developed and used by members of this research team (32).

Item generation - Questionnaire items will be developed using standard guidance (33) to assess the theoretical domains (29) identified in the Delphi study as relevant to implementation of SDD. The exact content of the questionnaire will be informed by the specific

beliefs and views identified as important in the Delphi study, thereby ensuring maximum relevance. Within the constraints of a relatively brief questionnaire (to maximise response rate), the items will cover intentions (willingness to deliver SDD in practice; willingness to participate in a randomised trial) and the factors likely to influence these intentions (e.g. views about current evidence regarding effectiveness and risk; complexity of the procedure; resources required to deliver SDD; views about clinical factors regarding which patients would be likely to benefit). Response options will be decided following the Delphi study but are likely to follow guidance for questionnaire design (7 options for a well-educated sample) (33). Participants will also be given the opportunity to make open-ended comment. These open data will be used to check the content validity (coverage) of the questionnaire. Brief demographic data will also be requested in order to describe the sample and assess representative of the responder group.

Pre-testing- The questionnaire (and cover email) will be pilot tested, to assess wording, acceptability and length, using personal interviews with 4 clinical collaborators (i.e. individuals not in sampling frame so data from all physicians can be used in the analysis). Each question will be evaluated by the research team in the light of the pilot test findings and the appropriate course of action will be agreed (i.e. accept original question, accept question with changed meaning, change question but retain meaning, eliminate question or develop new question (34).

Administration- Questionnaire links will be emailed to all clinicians in the two sampling frames described above. Reminder emails (up to a maximum of two) will be emailed to non-responders at two-week intervals after the first invitation. Study participant codes and ICU codes will be used to target reminders to the appropriate clinicians and to identify responses from the same Unit. All records linking contact details with study identification numbers will be kept secure and will be securely destroyed as soon as the data set is complete, to preserve participant confidentiality. From our previous research with health care professionals we understand that achieving acceptable response rates can be challenging. We will use clinical networks to try to achieve 'buy-in' from the relevant clinical disciplines and will use appropriate timing of the online survey, and reminders, to ensure as representative a sample as possible.

8.5 Sample size- Depending on the response rates achieved in the professional surveys, we will be able to assess respondent views with increasing levels of accuracy. For example, assuming we receive at least a 60% response rate from each professional group (previous surveys in this field, conducted by members of our team (37), have shown that this response rate is achievable); if we achieve approximately 110 responses in the microbiologist group we will be able to estimate all underlying proportions to within 9% with 95% confidence (and with greater precision as underlying proportions get nearer 0% or 100%); and this precision

increases to estimating proportions to within 3% in the ICU consultant survey assuming we receive over 1000 responses. We will also seek to boost the response rate by informing members about the study through the Intensive Care Society journal and the Intensive Care Society bi-annual meetings, and will also adopt the principles put forward by Edwards et al to promote questionnaire response (38).

8.6 **Analysis-** Analysis will include simple descriptive statistical methods and statistical prediction techniques. First, we will summarise responses to each question using frequency distributions. Second, we will use multiple regression techniques (including multi-level modelling to adjust for any observed clustering due to consultants being clustered within ICUs) to identify the theoretical constructs (e.g., attitude including perceived likely benefits and harms, perceived control over delivery of SDD) and characteristics of responders that best predict willingness (or 'intention') to implement SDD. Any differences between intensivists and microbiologists will be explored. The strongly predicting constructs and variables will be targeted for change if this programme progresses to an implementation trial, using systematic methods for intervention development.

Members of the study team have extensive experience in the design, delivery, analysis and interpretation of wide scale questionnaire surveys for health care professionals (32,35,39,40). This includes expertise in item development and piloting (JF, MJ, ME), psychometrics (CR, GM, MJ, JF) and statistical analysis (CR, GM, MC, MJ, JF). Furthermore, the content of the questionnaires will be guided by theoretical considerations and will therefore measure not only intuitively important ideas but also well-specified theoretical constructs. This will enable us to understand the drivers of intention to provide SDD at a more generalisable level than previous surveys have achieved.

9 INTERVIEWS WITH INTENSIVE CARE TRIALISTS

9.1 ***Aim***- To assess the feasibility of a proposed effectiveness RCT comparing SDD against a control group in ICUs, or a proposed implementation study to increase uptake in ICUs, among international intensive care clinical trialists (*addressing aim 4, Research Question* 8*, see above*).

9.2 **Target group-** We will interview expert national and international clinical trialists in the critical care area (including trialists with experience in SDD) to identify challenges and barriers to undertaking research in the field of SDD research. condition).

9.3 **Sample**- Clinical trialists from intensive care with experience in undertaking clinical trials research in this field, as well as researchers with specific experience in clinical trials in SDD research will be invited to participate. We will seek to recruit up to 10 international experts to participate. Experts will be identified from authorship of large randomised trials in critical care and international research groupings in critical care.

9.4 **Methods-** Semi-structured one-to-one face-to-face or telephone interviews, using a topic guide developed from the previous phases as well as from expert experience, will be used to study this area. Questions will address potential trial design issues (e.g. cluster randomisation), specification of the SDD intervention and of control group care; outcome measurement; recruitment; ethical considerations and other issues raised in the observational and Delphi studies. The stimulus materials for these interviews will include the relevant findings from the Delphi study. Specifically, we will identify problems with feasibility and acceptability (including ethical issues), views about trial design and beliefs about practical barriers to recruitment and intervention delivery. We will ask the trialists to comment on potential ways to overcome these problems and to make further recommendations about trial design (including eligibility criteria and the nature of the control

9.5 **Analysis-** Data will be transcribed and analysed using content analysis (41). A full description of the design and measurement issues to consider when planning a possible effectiveness/implementation trial will be produced.

10. ASSESSMENT OF NEED FOR AND ACCEPTABILITY OF AN SDD EFFECTIVENESS TRIAL AND/OR AN SDD IMPLEMENTATION TRIAL (see also appendix 6)-

The results of the four stages of research outlined above will lead to an evidence-based decision about whether to proceed to an effectiveness trial to evaluate SDD or an implementation trial (i.e., development and evaluation of an intervention to increase uptake of SDD in critical care units). The applicant team/project steering group will make an assessment of whether a trial is necessary, justifiable, acceptable and feasible based on a set of decision rules informed by the results of the national surveys. For example:

- If intention to implement SDD is low (median <6 on a 7-point scale) or variable, and predicted by attitude scores and/or scores for specific beliefs about the consequences (benefits and harms) of implementing SDD, it may be judged appropriate to proceed to a clinical trial. Such a pattern of results would suggest that dissatisfaction with the current evidence base explains the lack of implementation.

- If intention to implement SDD is low or variable and predicted by scores relating to social influence (e.g., pressure from colleagues in other disciplines), this would suggest that an implementation intervention could be effective if delivered by an identified opinion leader, clinical lead or local 'champion' through team meetings. We would likely proceed to an implementation trial to evaluate such an intervention.

1. If intention to implement SDD is low or variable and predicted by beliefs relating to lack of capacity to implement SDD (e.g., resource issues), this would suggest that an implementation intervention could be effective if it focuses on barrier identification and generation of strategies to overcome barriers, known as 'coping planning' (42). In this case we would proceed to an implementation trial to evaluate such an intervention. Six of the investigators (ME, JF, MJ, MC, CR, GM) have worked together for many years in the field of implementation research and have developed and streamlined effective methods for designing appropriate implementation interventions.

- If intention to implement SDD is low or variable and predicted (in the multi-level model) at the Unit level, rather than by individual clinical staffs' views of the evidence, we would design an intervention directed at critical care units rather than individual clinicians. This would be informed by the behavioural analysis of SDD implementation in critical care units where it is currently practised. We would likely proceed to an implementation trial to evaluate such an intervention.
- By contrast, if intention to implement SDD is high (i.e., if there are ceiling effects and restricted variance), then the current low level of implementation will be attributable to an 'intention-behaviour gap', suggesting that external barriers prevent clinical staff from translating their intentions into action. This pattern of results would suggest that an implementation trial to test strategies for facilitating uptake may be appropriate.
- Finally certain patterns of results may indicate that other studies might be needed. For example, if the research shows that beliefs about the effectiveness of SDD in hospitals with high levels of HAIs are a major barrier to implementation then further primary or secondary research exploring whether this belief is true might be justified.

Findings about acceptability and feasibility of a clinical trial will also inform the decision of how to proceed. Specifically:

- If willingness (intention) to participate in a trial is low we are unlikely to proceed to a clinical trial.
- If willingness (intention) to participate in a trial is high this will indicate that the trial is sufficiently acceptable to proceed. We will also take into account scores for perceived ease or difficulty of participating).

We will also use the consensus data from the Delphi study (and from the UK investigation of two critical care units where SDD has been implemented), to inform the:

- Behavioural (practical, organisational and management) issues that would need to be addressed in order to mount a trial;
- Ethical issues relating to informed acceptance of trial entry among eligible patients;
- Trial design issues including measurement of outcome and process variables.

If any one stakeholder group seems to be uniformly of the opinion that there are no design features that would make a trial acceptable, and/or if a third (or more) of the members of two (or more) groups deem any such trial unacceptable, the clinical trial should not be pursued. Depending on the views expressed about the existing evidence base (i.e. if treatment is viewed as potentially beneficial) we will consider an implementation trial to change clinical practice. If appropriate, the change techniques that would form the components of such a trial will be selected using methods previously reported by members of the research team (43). The final decision on trial continuation will be made by the project steering group.

The ethical permissibility of a clinical trial will also inform the decision about how best to proceed. Even if intention to participate in a trial is high, apparent ethical obstacles to a trial with a placebo or control must be analyzed carefully. The evidence supporting SDD is substantial. The *Declaration of Helsinki* requires that "the benefits, risks, burdens and effectiveness of a new intervention must be tested against those of the best current proven intervention" (a). While this provision seems on its face to preclude the possibility of an effectiveness trial of SDD, deeper exploration of conceptual foundations are required. In particular, we will explore the applicability and implications of the ethical concept of clinical equipoise to the permissibility of an effectiveness trial or implementation trial in this context (b). Clinical equipoise requires that at the start of a trial there must be a state of honest, professional disagreement in the community of experts as to the preferred treatment (c). How ought data regarding physician opinion, for instance from the Delphi study, inform whether clinical equipoise obtains? What is the relationship between clinician opinion and the evidence supporting SDD? That is, how do we determine whether an observed division in clinical opinion is *warranted* by the evidence? Finally, while the applicability of clinical equipoise to effectiveness trials is well understood, how does it inform the decision whether to initiate an implementation trial? This analysis will both inform the decision about how best to proceed and provide information useful to research ethics boards reviewing a future trial protocol of SDD.

The project will be coordinated by a Study Office in the Health Services Research Unit, University of Aberdeen. The University of Aberdeen is committed to the highest standards of research governance and seeks to conform to all relevant governance guidelines and codes of

practice as detailed in the Research Governance Framework and ICH guidelines for Good Clinical Practice (GCP). As well as ensuring that research is conducted according to the requirements set out in these documents, the project will be conducted with the written agreement of the relevant Multi-Centre Ethics Committee(s), and NHS Research and Development departments.

A full application for ethical approval is currently being prepared. We predict no problems with this application. We have permission to use the databases of clinicians for the study and this agreement is compliant with appropriate privacy agreements and regulations. There are very few risks for study participants and society in this study but the potential for increased understanding is marked. We will obtain informed consent from participants in all occasions. We will retain study documents in line with HTA regulations.

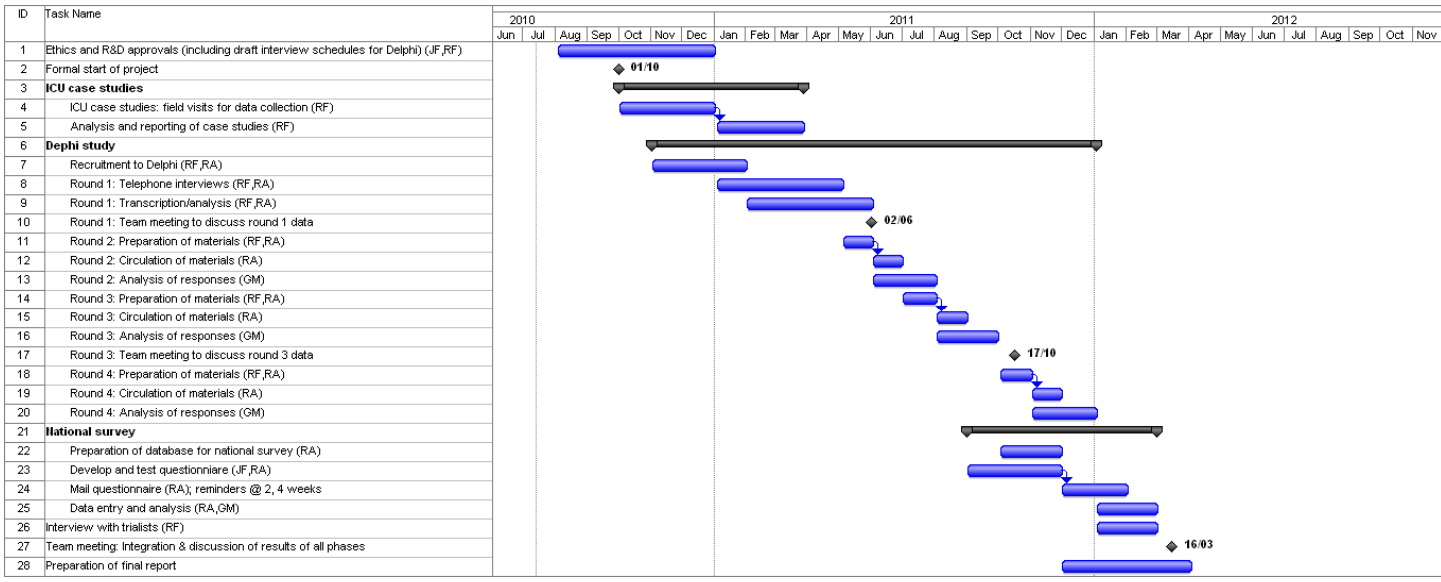
11. STUDY OUTPUTS-

The primary output of this research will be a summary report listing the following key domains:

- Precise specification of the SDD intervention as recommended by Davidson (44) for reporting interventions, including evidence to identify the relevant decisional authorities and strategies that appeared to overcome barriers to the implementation of SDD.
- Decisional authorities' views about the current evidence base relating to the use of SDD, with respect to clinical benefit, clinical risk, ecological risk and cost-effectiveness.
- Additional potential clinical-level factors associated with the clinical implementation and utilisation of SDD in critical care units and with failure of clinical implementation.
- Acceptability and feasibility data relating to an RCT of SDD in critical care units.
- The theoretical constructs and beliefs that predict intentions to implement SDD (or not).
- The theoretical constructs and specific beliefs that predict acceptability of a randomised controlled trial of SDD in critical care units.

11.1 Project timetable– Total duration 1st November 2010 to 30th March 2012

Delphi survey	1st November 2010	-	31st August 2011
Survey development	1st September 2011	-	30th September 2011
National survey	1st October 2011	-	28th February 2012
Analysis and write-up	1st March 2012	-	30th April 2012



(Note - Gantt chart key: RF=research fellow; RA=research assistant; JF=Jill Francis; GM=Graeme Maclennan)

11.2 Prior experience and skills- The applicants are a multidisciplinary team including clinical experts, experienced health psychologists, methodologists and implementation researchers. Geoff Bellingan (GB; lead clinical applicant) is an experienced intensive care physician, director of intensive care with a strong track record of undertaking clinical research in critical care including especially in the field of infection control. Jill Francis (lead methodological applicant) is a highly experienced health psychologist with extensive experience of behavioural approaches to implementation research including the proposed methods. Together with GB she will supervise the research staff and co-ordinate the inputs of the research team to ensure that the intellectual contributions of all grantholders are well integrated. Brian Cuthbertson is a professor of critical care and an experienced critical care physician with a strong track record of undertaking clinical research in critical care including many randomised trials. Marion Campbell is a professor of health services research and expert clinical trialist and methodologist. Craig Ramsay is a highly experienced health services researcher and clinical trialist with an expert interest in implementation research methodology. Peter Wilson is an honorary senior lecturer and consultant microbiologist with a research interest in the epidemiology of health care associated infections and antimicrobial use as they relate to antimicrobial resistance in community and health care associated infections. Rob Shulman is an experienced critical care pharmacist and honorary senior lecturer in pharmacy practice and leads research at the UKCPA Critical Care group. Marie Johnston is a professor of health psychology with a wealth of experience in studying health professional behaviours in clinical practice. Kathy Rowan is a hugely experienced health services researcher and trialist who is the Director of the Intensive Care National Audit and Research Centre. Martin Eccles is a professor of clinical effectiveness and general practitioner who is one of the leading researchers in implementation research in the UK. Graeme MacLennan is a senior statistician,

highly experienced in the use of the proposed analytic techniques including multi-level modelling.

The quality of the project will also benefit from the collaboration with partner teams conducting parallel research (adopting the SUDDICU protocol) in Canada, Australia and New Zealand. These projects are independently funded as described in section 3.2 above, with Prof Brian Cuthbertson and Dr Jill Francis as co-investigators on the grants in all countries, ensuring cross-application learning and high quality. The collaborator teams include extremely experienced and prominent clinical researchers and trialists. In Canada, Prof Brian Cuthbertson is PI. Collaborators include: Jeremy Grimshaw (trials, implementation); John Marshall (trials, surgery); Deborah Cook (critical care); Richard Hall (anaesthesiology, pharmacology); Lynn Johnston (infectious diseases), Merrick Zwarenstein, (trials, health services research); Niall Ferguson (Delphi methodology in critical care); Charlies Weijer (bioethics) and Lauralyn McIntyre (critical care). Collaborators in Australia include: John Myburgh (critical care), Simon Finfer (critical care), Jeffrey Lipman (critical care), David Paterson (infectious diseases); Parisa Glass (applied science); Ian Seppelt (critical care and Australian PI).

11.3 Role of the Principal Applicant and Co-Applicants- The two main groupings that will contribute to the governance arrangements for this study are the Project Management Group (PMG) and the Project Steering Group (PSG). The PMG will consist of the two Co-PIs and research staff with other grantholders co-opted as required. It will undertake to communicate promptly and effectively with the sponsor to satisfy and reassure the sponsor that the sponsor's obligations on the authorisations, financing and reporting of the study are being met. The PSG will consist of the two Co-PIs with an independent Chair and two further independent members. Professor Tim Walsh (Consultant & Honorary Professor in Critical Care, Chairman of the UK NIHR CRN Critical Care Specialty Group and Chairman of the Scottish Critical Care Trials Group) has agreed to chair the PSG. Independent members are Professor Robbie Foy (Professor of Primary Care) and Mr Barry Williams (Chair, CRITpal group). The PSC will meet by telelink as required and for three face-to-face meetings during the project.

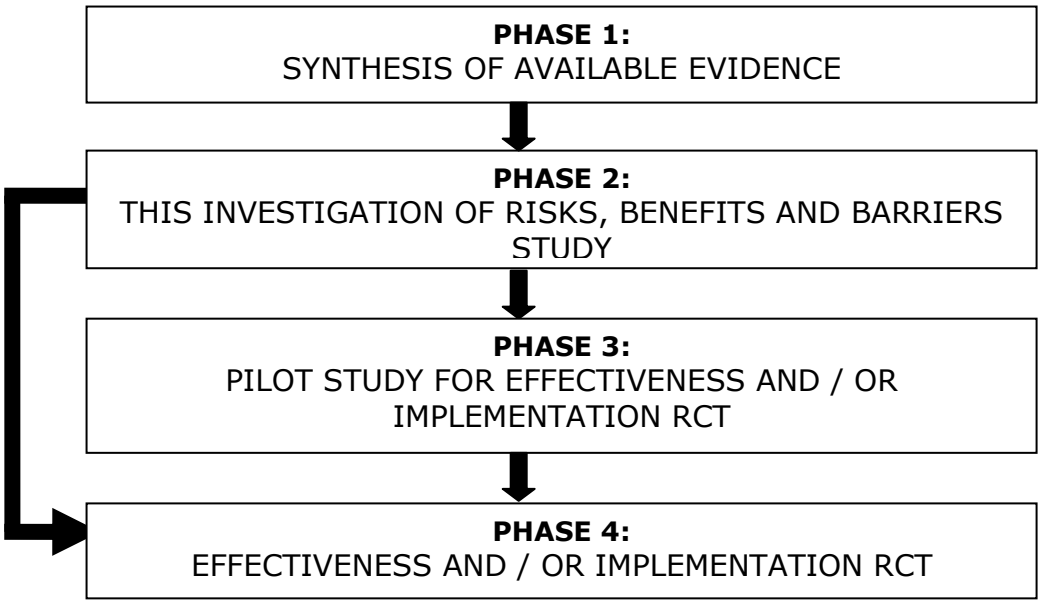
In addition an International Project Collaborators Group representing the parallel studies in Canada and Australia/New Zealand has already been formed (Chair: Professor Marion Campbell, a co-applicant on the UK application). It will meet by videoconference at the end of the study to discuss the appropriate steps for taking this programme of research forward.

11.5 Presentations at clinical meetings and conferences and publication in peer-reviewed journals- The results of this study will be presented at local, national (in all study areas) and international meetings and conferences. The protocol will be published before study

commencement and the final results will be published in a peer-reviewed journal.

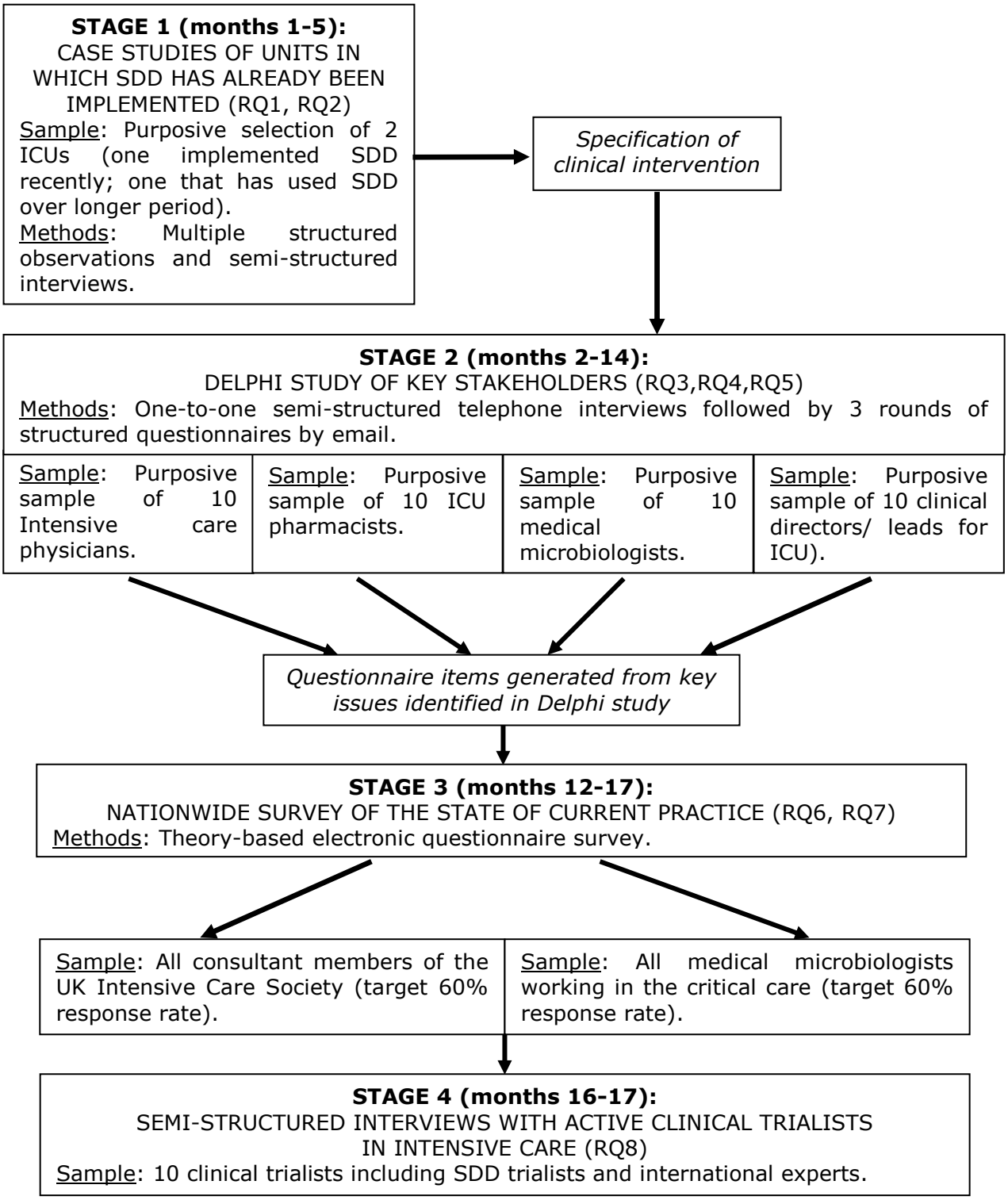
Appendix 1 THE FOUR *PHASES* OF THE SUDDICU PROGRAMME OF RESEARCH

The SuDDICU project is a programme of research to be undertaken across Canada, UK and Australia/New Zealand. The programme of research consists of four **phases** - from evidence synthesis to effectiveness/implementation trial.



We have formed a multidisciplinary research group to design the proposed series of investigations. These collaborators bring expertise and skills from clinical and non-clinical disciplines in Canada, the UK, Australia and New Zealand (representing the Canadian Critical Care Trials Group, UK Intensive Care groups and the Australian New Zealand Intensive Care Society Trials group respectively), and they have given support for conducting the studies in each country. However, the individual country results need to, and have been designed to, stand in their own right in each country. The primary role of any multi-national comparisons will be to enhance the worldwide understanding of these issues.

APPENDIX 2 FLOW DIAGRAM OF THE FOUR STAGES OF UK SUDDICU PHASE 2



APPENDIX 3 DIVERSITY SAMPLING PROCEDURES

The Delphi phase of the SuDDICU study employs “purposive diversity sampling” to select participants from 4 different groups of relevant stakeholders (i.e. intensive care physicians, ICU pharmacists, medical microbiologists, clinical directors/clinical leads for ICU).

Purposive diversity sampling is a non-probability sampling method that aims to assess heterogeneity in opinion by including all opinions or views. Proportionate representation of population is not important for this sampling method. The aim is to identify a broad spectrum of ideas, not identifying the "average" or "modal instance“. Sampling will thus look for diversity with regards to key criteria, which can be set a priori or will emerge as the study is being undertaken.

Purposive diversity sampling will be used in all groups to identify as wide a range of initial views as possible, based on a range of variables, including:

- Academic-affiliated or not;
- Years of experience (time since commencing as consultant/other professional grade);
- Size of ICU (i.e. number of ICU beds);
- Current practice (routinely perform SDD or not).

During the interview phase, diversity on these factors will be tracked using a diversity sampling table and additional participants will be invited to participate, if required, to maximise variation. In practice, diversity sampling is undertaken by identifying key experts in the four key stakeholder groups, who are likely to know something about the SDD evidence base and who would be prepared to engage with the project. As recruitment continues, the interviewer would populate the diversity table (see below) and report back to the team periodically to take advice about how to keep the sample balanced in terms of the factors named in the column headings. In addition, the interviewer would look for variation in key opinions – e.g. if everyone in the sample is against the use of SDD you would actively look for people who are in favour. Moreover, if further criteria emerge throughout the sampling process variation on these variable would also need to be assured.

The key objective of this sampling procedure is to ensure that we develop a questionnaire that includes the key issues and opinions. Whether these opinions are representative or not will be assessed in the nationwide questionnaire study, not in the Delphi. ... Does this all make sense?

DIVERSITY SAMPLING MATRIX (to be populated on an ongoing basis during the interview round of the Delphi study). This will inform the purposive sampling strategy.

Participant number	Clinical discipline	Gender	Years of experience	Academic-affiliated or not	Number of ICU beds	SDD delivery or not	Other relevant criteria
01							
02							
03							
04							
05							
…							
40							

APPENDIX 4 THE DELPHI STUDY- FURTHER BACKGROUND AND METHODOLOGY

The second stage of this study will use an adapted Delphi approach. Delphi approaches have been used for over four decades for solving problems in health and medicine (26,45,46). Although the approach was originally used to *establish* expert consensus (e.g., deciding appropriateness of clinical actions, where there was a lack of evidence) (46), it has developed into a method for *identifying* levels of agreement (or disagreement) within an expert group (47), using a structured, iterative process including anonymised feedback, in a series of sequential questionnaires or 'rounds'. The Delphi approach additionally has the benefit of few geographical limitations. This approach has good fit with a major objective of this study: to identify the range of clinician opinion and other clinician level factors, within and across settings, to assess the current balance of evidence and whether an effectiveness trial is advisable and feasible. It has been noted that the outputs of a Delphi process are merely opinion and should be treated as such (26). However, in this study, it is important for our purposes to conduct a systematic assessment of a full range of clinician opinion as this is likely to drive the use of SDD in practice and to identify whether a trial is feasible.

There are two further advantages of using this technique, compared with face-to-face group discussion. First, it operationalises the principle that good decision making first involves the generation of multiple alternatives, leaving a critique of those alternatives to a later stage (48). Second, it avoids the problems that may occur in face-to-face (or 'nominal') group discussions, e.g. 'groupthink' (in which individuals reach premature consensus through 'normative' influence (49) arising from the early or strong views of influential individuals such as senior colleagues) or 'group polarisation' (49) (in which individuals express opposing views because of competition within the group). By contrast, the Delphi approach uses virtual groups and feeds back group opinions anonymously in a series of iterations, or 'rounds'. It is designed to use 'informational' influence (50), in which novel ideas may be introduced and considered by individuals in the group without being contaminated by the effects of group dynamics (51). The appropriate number of rounds will vary according to the complexity of the issues discussed and the diversity of the sample, but there is evidence that four rounds are appropriate (52,53).

Critics of the Delphi approach argue that it may lead to superficial change of opinion (from 'normative' influence based on social pressures rather than 'informational' influence based on considering new views) and that pressure to agree will lead to 'lowest common denominator' consensus (26). In this study, no pressure to agree will be applied. Four 'rounds' (described below) will be used to identify agreement, if it exists, or stable disagreement, using criteria specified in advance, in the manner reported by Park and colleagues (47). The Annex to this appendix lists the criteria Park used to identify the levels of agreement among nine clinicians about appropriate indications for three medical procedures.

A further criticism of the Delphi approach is that, although its reliability increases with the size of the group and the number of rounds, participants sometimes become fatigued after two or three rounds (45) To minimise this possibility we propose to adapt the Delphi method in the following ways:

1. The first round of a Delphi study usually asks participants to complete open questions in a paper-based questionnaire. The data are analysed qualitatively using content analysis and identify the issues to be addressed in later rounds. The adaptation will consist of replacing the written questionnaire with open questions delivered via telephone interviews. We feel that this will involve a lesser burden on participants, who have high work demands.
2. The second and subsequent rounds of a standard Delphi process involve structured questionnaires using ranking or rating response formats. The items are generated from the Round 1 analysis. Data are analysed quantitatively. Third and subsequent rounds indicate to participants the central tendency and dispersion of scores from the previous round. Our proposed methods replicate the standard methods in every detail (for Rounds 2 and 3) and the questionnaires will be delivered and returned by email, thereby again ensuring appropriate geographical coverage.
3. Rounds 1 to 3 will be conducted in parallel, independently, in the three collaborating settings (Canada, Australia/New Zealand, and UK).
4. The final adaptation of the method will involve a multi-national round (Round 4). This will feed back the central tendency and dispersion data from Round 3 of each national setting. This comprises the final adaptation of a standard Delphi approach.

The later phases of this study, in turn, will be influenced by the results of the Delphi study. First, we will interview trialists to identify their views about the challenges and barriers to undertaking research in the field of SDD. The stimulus materials for these interviews will consist of the results of the Delphi study with respect to trial feasibility (i.e., stakeholders' views about trial feasibility). Second, a nation-wide survey of critical care consultants in each setting will be conducted. This will establish current patterns of SDD practice, beliefs about the evidence and about barriers to implementation and willingness to recruit patients to an effectiveness trial or to participate in an implementation trial. The questionnaire will be theory-based but the actual content of items will be based on the beliefs and views identified as most relevant from the Delphi study. It is particularly important to select the most relevant views in this way, as questionnaire length will be kept to a minimum to encourage a high response rate. Members of the team have used this kind of sequential process for questionnaire design in previous studies (30,39,54).

APPENDIX 5 INTERVIEW TOPIC GUIDE (TEMPLATE) based on "theoretical domains" reported by Michie et al 2005 (29)

Topic guide for telephone interviews (29), including theoretical domains, component constructs and questions for investigating the implementation of evidence based practice (Column 3). Column 3 will be adapted to be appropriate to SDD and to the clinical staff to be interviewed. In particular, questions about the knowledge domain will be expanded to cover a range of views about the evidence base and questions relating to 'guidelines' will be re-worded.

(1) Knowledge	Knowledge	Do they know about the evidence relating to SDD?
	Knowledge about condition/scientific rationale	What do they think the evidence indicates?
	Schemas, mindsets & illness representations	Do they think evidence is sufficient?
	Procedural knowledge	Do they know what provision of SDD involves?
(2) Skills	Skills	Do they know how to do SDD?
	Competence/ability/skill assessment	How easy or difficult do they find performing SDD to the required standard in the required context?
	Interpersonal skills	Do they have appropriate communication skills for liaising with colleagues about provision of SDD?
(3) Social/ professional role and identity	Identity	What is the purpose of the guidelines?
	Professional identity/ boundaries/role	What do they think about the credibility of the source?
	Group/social identity	Do they think guidelines should determine their behaviour?
	Social/group norms	Is doing SDD is compatible or in conflict with professional standards/identity?
	Alienation/organisational commitment	Prompts: moral/ethical issues, limits to autonomy
		Would this be true for all professional groups involved?
(4) Beliefs about capabilities	Self-efficacy	How difficult or easy is it for them to do SDD?
	Control – of behaviour and material and social environment	What problems have they encountered?
	Perceived competence	What would help them?
	Self-confidence/professional confidence	How confident are they that they can do SDD despite the difficulties?
	Empowerment	How capable are they of maintaining SDD?
	Self-esteem	How well equipped/ comfortable do they feel to do SDD?
	Perceived behavioural control	
	Optimism/pessimism	

(5) Beliefs about consequences	Outcome expectancies Anticipated regret Appraisal/evaluation/review	What do they think will happen if they do SDD? (prompt re themselves, patients, colleagues and the organisation; positive and negative, short term and long term consequences)
	Consequents	What are the costs of SDD and what are the costs of the consequences of SDD?
	Attitudes	What do they think will happen if they do not do SDD?
	Contingencies	Do benefits of doing SDD outweigh the costs?
	Reinforcement/punishment/ consequences	How will they feel if they do/don't do SDD?
	Incentives/rewards	Does the evidence suggest that doing SDD is a good thing?
	Beliefs	
	Unrealistic optimism	
	Salient events/ sensitisation/critical incidents	
	Characteristics of outcome expectancies – physical, social, emotional; sanctions/ rewards, proximal/distal, valued/not valued, probable/ improbable, salient/not salient, perceived risk/threat	
(6) Motivation and goals	Intention; stability of intention/certainty of intention	How much do they want to do SDD?
	Goals (autonomous, controlled)	How much do they feel they want to do SDD?
	Goal /target setting	Are there other things they want to do or achieve that might interfere with SDD?
	Goal priority	Does the guideline conflict with others?
	Intrinsic motivation	Are there incentives to do SDD?
	Commitment	
	Distal and proximal goals	
	Transtheoretical model and stages of change	
(7) Memory, attention and decision processes	Memory	Is SDD something they usually do?
	Attention	Will they think to do SDD?
	Attention control	How much attention will they have to pay to do SDD?
	Decision making	Will they remember to do SDD? How?
		Might they decide not to do SDD? Why? (prompt: competing tasks, time constraints)
(8) Environmental context and resources	Resources/material resources (availability and management)	To what extent do physical or resource factors facilitate or hinder SDD?
	Environmental stressors	Are there competing tasks and time constraints?
	Person x environment interaction	Are the necessary resources available to those expected to undertake SDD?
	Knowledge of task environment	

(9) Social influences	Social support Social/group norms	To what extent do social influences facilitate or hinder SDD? (prompts: peers, managers, other professional groups, patients, relatives)
	Organisational development	Will they observe others doing SDD (i.e. have role models?)?
	Leadership Team working Group conformity Organisational climate/culture Social pressure Power/hierarchy Professional boundaries/ roles Management commitment Supervision Inter-group conflict Champions Social comparisons Identity; group/social identity Organisational commitment/alienation Feedback Conflict – competing demands, conflicting roles	
	Change management Crew resource management Negotiation Social support: personal/ professional/organisational, intra/interpersonal, society/ community Social/group norms: subjective, descriptive, injunctive norms Learning and modelling	
(10) Emotion	Affect	Does doing SDD evoke an emotional response? If so, what?
	Stress	To what extent do emotional factors facilitate or hinder SDD?
	Anticipated regret	How does emotion affect SDD?
	Fear Burn-out Cognitive overload/tiredness Threat Positive/negative affect Anxiety / depression	
(11) Behavioural regulation	Goal/target setting	What preparatory steps are needed to do SDD? (prompt re individual and organisational)
	Implementation intention	
	Action planning	Are there procedures or ways of working that encourage SDD?
	Action planning Self-monitoring Goal priority Generating alternatives Feedback	

	Moderators of intention-behaviour gap Project management Barriers and facilitators	
(12) Nature of the behaviours	Routine/automatic/habit	What is the proposed behaviour (SDD)?
	Breaking habit	Who needs to do what differently when, where, how, how often and with whom?
	Direct experience/past behaviour	How do they know whether the behaviour has happened?
	Representation of tasks	What do they currently do?
	Stages of change model	Is this a new behaviour or an existing behaviour that needs to become a habit? Can the context be used to prompt the new behaviour? (prompts: layout, reminders, equipment) How long are changes going to take? Are there systems for maintaining long term change?

APPENDIX 6 CRITERIA USED TO SPECIFY AGREEMENT

Pre-specified criteria reported by Park et al (47) and used to identify the levels of agreement, using nine-point rating scale, among **nine** clinicians about appropriate indications for three medical procedures. This kind of specification will be adapted to suit the larger sample sizes and used to identify levels of agreement and disagreement in this study.

Agreement

A9S: All nine of the ratings fell within a single three-point region—1 to 3, 4 to 6, or 7 to 9.

A9R: All nine of the ratings fell within *any* three-point range.

A7S: After discarding one extreme high and one extreme low rating, the remaining seven ratings all fell within a single three-point region—1 to 3,4 to 6, or 7 to 9.

A7R: After discarding one extreme high and one extreme low rating, the remaining seven ratings all fell within *any* three-point range.

Disagreement

D9S: Considering all nine ratings, at least one was a 1 and at least one was a 9.

D9R: Considering all nine ratings, at least one fell in the lowest three point region (1 to 3) and at least one fell in the highest (7 to 9).

D7S: After discarding one extreme high and one extreme low rating, at least one of the remaining seven ratings was a 1 and at least one was a 9.

D7R: After discarding one extreme high and one extreme low rating, at least one of the remaining seven ratings fell in the lowest three point region (1 to 3) and at least one fell in the highest (7 to 9).

D5R: After discarding two extreme high and two extreme low ratings, at least one of the remaining five ratings fell in the lowest three point region (1 to 3) and at least one fell in the highest (7 to 9).

APPENDIX 7 COMPOSITION OF RESEARCH TEAM

Investigators located in the UK:

- Jill Francis (Lead Methodologist and UK Co-Principal Investigator; Chartered Health Psychologist)
- Marion Campbell (Director, Health Services Research Unit)
- Marie Johnston (Professor of Health Psychology, Chartered Health Psychologist)
- Craig Ramsay (Director Health Care Assessment Programme, Health Services Research Unit)
- Graeme MacLennan (Senior Statistician, Health Services Research Unit)
- Martin Eccles (Professor of Clinical Effectiveness, University of Newcastle)
- Geoff Bellingan, UK Clinical lead and UK Co-Principal Investigator, Director, Intensive Care Unit, UCL
- Peter Wilson, Senior Lecturer in Medical Microbiology, UCL

Investigators located in Canada:

- Brian Cuthbertson (International Study Chief Investigator and Canadian Principal Investigator, Professor and critical care specialist, Sunnybrook Health Sciences Centre, Toronto)
- Lauralyn McIntyre (Canadian Principal Investigator, Scientist, Clinical Epidemiology, Ottawa Hospital Research Institute, Ottawa)
- Jeremy Grimshaw (Director, Clinical Epidemiology Program, Ottawa Hospital Research Institute, Ottawa)
- John Marshall (Professor of Surgery, University of Toronto and Attending Surgeon, St Michaels Hospital, Toronto)
- Karen Burns (Attending Physician, St Michaels Hospital, Toronto, Canada)
- Deborah Cook (Canada Research Chair in Critical Care, McMaster University, Hamilton, Canada)
- Peter Dodek (Center for Health Evaluation and Outcome Sciences, St. Paul's Hospital, 1081 Burrard Street, Vancouver, B.C, Canada)
- Richard Hall (Professor of Anesthesiology and Pharmacology Associate Professor of Surgery Dalhousie University and The Queen Elizabeth II Health Sciences Centre Halifax Nova Scotia Canada)
- John Muscedere (Associate Professor of Medicine, Queen’s University and Intensivist, Kingston General Hospital, Kingston, Canada)
- Joe Pagliarello (Clinician Scientist, University of Ottawa, Ottawa, Ontario, Canada)
- Lynn Johnston, (Professor of Medicine, Chief of Infectious Diseases, Dalhousie University, Halifax, Nova Scotia, Canada)
- Salman Kanji (Pharmacist, Critical Care Unit, Ottawa, Ontario, Canada)

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