

# BMJ Open DONORS (Donation Network to Optimise Organ Recovery Study): Study protocol to evaluate the implementation of an evidence-based checklist for brain-dead potential organ donor management in intensive care units, a cluster randomised trial

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## ABSTRACT

**Introduction** There is an increasing demand for multi-organ donors for organ transplantation programmes. This study protocol describes the Donation Network to Optimise Organ Recovery Study, a planned cluster randomised controlled trial that aims to evaluate the effectiveness of the implementation of an evidence-based, goal-directed checklist for brain-dead potential organ donor management in intensive care units (ICUs) in reducing the loss of potential donors due to cardiac arrest.

**Methods and analysis** The study will include ICUs of at least 60 Brazilian sites with an average of  $\geq 10$  annual notifications of valid potential organ donors. Hospitals will be randomly assigned (with a 1:1 allocation ratio) to the intervention group, which will involve the implementation of an evidence-based, goal-directed checklist for potential organ donor maintenance, or the control group, which will maintain the usual care practices of the ICU. Team members from all participating ICUs will receive training on how to conduct family interviews for organ donation. The primary outcome will be loss of potential donors due to cardiac arrest. Secondary outcomes will include the number of actual organ donors and the number of organs recovered per actual donor.

## Strengths and limitations of this study

- This is the first randomised trial to evaluate whether a goal-directed checklist for the management of brain-dead potential organ donors may be useful in reducing cardiac arrests and contributing to increase organ availability for transplants.
- The preparation of the goal-directed checklist was preceded by the review of a clinical practice guideline following the Grades of Recommendation Assessment, Development and Evaluation system.
- Brazil is a country with a wide spectrum of demographic and socioeconomic scenarios; the diversity of institutions to be included in Donation Network to Optimise Organ Recovery Study will allow us to provide results in a broad range of demographic and socioeconomic scenarios.
- Main study limitations are the unblinded design and the high heterogeneity of care and outcomes expected among centres in the study.

**Ethics and dissemination** The institutional review board (IRB) of the coordinating centre and of each participating site individually approved the study. We requested a

waiver of informed consent for the IRB of each site. Study results will be disseminated to the general medical community through publications in peer-reviewed medical journals.

**Trial registration number** NCT03179020; Pre-results.

## INTRODUCTION

Organ transplantation is the only treatment option for many patients affected by end-stage organ failure. Despite advances in the field of organ donation, the disparity between the number of patients on transplant waiting lists and the availability of organs for transplantation is increasing. Several parameters determine the availability of suitable organs for donation, and many of these depend on a successful sequence of actions by several healthcare professionals, starting with the identification of a potential multi-organ donor and ending with surgical organ procurement.<sup>1–5</sup> In this process, important factors contributing to the gap between organ supply and demand include failure to identify and report brain death, lack of family consent for organ donation, inaccurate perceptions of contraindications to organ donation and haemodynamic instability that may compromise the quality of organs or even lead to loss of donors due to cardiac arrest.<sup>1–3</sup> A systematic application of clinical management strategies aimed at the haemodynamic stabilisation of brain-dead donors may contribute to an increase in the number of organs for transplantation by improving the quality of organs and reducing the loss of potential donors due to cardiac arrest.<sup>1 2 4</sup> In addition, other measures such as optimal ventilatory support and temperature control may improve the quality of organs, resulting in a higher organ recovery rate and better clinical outcomes for transplant recipients.<sup>6 7</sup>

Checklists have an established role in healthcare to prevent omissions while performing complex procedures. A series of studies have shown that the use of a goal-directed checklist may help the systematic application of clinical guidelines, leading to greater adherence to evidence-based clinical interventions and improving clinical outcomes. Examples include the World Health Organization (WHO) surgical safety checklist, the Keystone intensive care unit (ICU) project checklist to prevent catheter-related bloodstream infection and clinical checklists to ensure patient safety in the ICU.<sup>8–11</sup>

There is a lack of evidence for the use of checklists regarding the clinical aspects of improving organ availability for transplantation of brain-dead donors. Some observational studies have reported that the application of a goal-directed checklist to guide the management of brain-dead potential organ donors may reduce the rate of cardiac arrest and increase the number of organs recovered per donor.<sup>12–19</sup> However, given the relatively small number of studies, their observational design and inconsistency of findings, often related with barriers to carrying out studies in this scenario,<sup>5</sup> this literature cannot yet support the use of a goal-directed checklist in the current management of brain-dead potential organ donors.<sup>20</sup>

Our hypothesis is that supporting the management of potential organ donors with the use of an evidence-based bedside checklist may reduce the loss of potential organ donors due to cardiac arrest and increase the number of donors and organs recovered per donor. In this protocol, we describe the methods to be used in the Donation Network to Optimise Organ Recovery Study (DONORS).

## OBJECTIVES

### Primary objective

The primary objective is to evaluate the effectiveness of the implementation of an evidence-based bedside checklist, containing goals and recommendations of care as guidance for the management of brain-dead potential organ donors, in reducing potential organ donor losses due to cardiac arrest.

### Secondary objectives

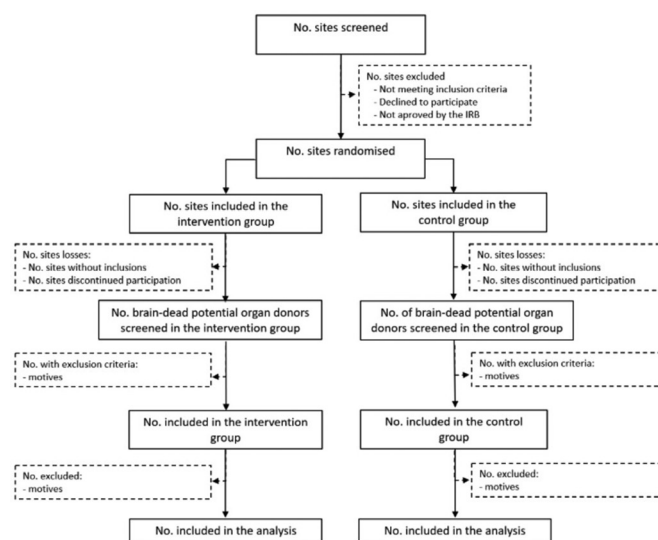
Secondary objectives are to assess whether the evidence-based, goal-directed checklist is effective in (a) increasing the number of actual organ donors and (b) increasing the number of organs recovered per actual donor.

## METHODS AND ANALYSIS

The protocol is registered at ClinicalTrials.gov (NCT03179020) and the present manuscript provides additional details regarding study design and methodology. The items from the WHO trial registration data set are described in the online supplementary file 1.

### Study design

DONORS is a parallel cluster randomised controlled trial involving ICUs of Brazilian hospitals. We will randomly assign hospitals to the intervention group, comprising the checklist implementation, or the control group, consisting of usual care in each ICU (figure 1).



**Figure 1** Study flow diagram. IRB, Institutional Review Board; No., number.

## Participants

### Cluster eligibility, recruitment and exclusion criteria

We will invite adult ICUs with an average of at least 10 annual notifications of potential organ donors in the prior 2 years. Information regarding notifications is provided by the Brazilian National Transplantation System.

Coronary care units, intermediate care units and emergency departments will not be included. We will also exclude institutions that already systematically use checklists as guidance for the management of potential organ donors supported by implementation tools, such as guidelines and clinical decision algorithms for bedside use, in print or digital form.

### Patient eligibility and exclusion criteria

We will screen and include consecutive brain-dead potential organ donors, as confirmed by the first clinical examination consistent with having brain death, within the age range of 14 to 90 years. Only ICU patients will be included; potential donors outside the ICU will be included in the study if admitted to ICU within 3 hours of initial assessment.

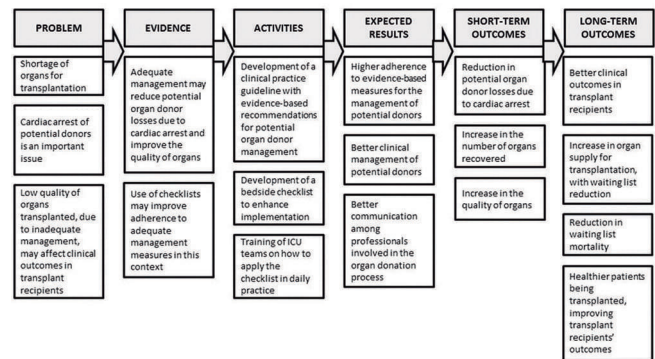
Diagnosis of brain death will be made according to the Brazilian Federal Board of Medicine guidance, consisting of: two clinical examinations performed by two different physicians, in an interval of at least 1 hour between the examinations, and one apnoea test followed by neuro-imaging (transcranial Doppler, cerebral arteriography, electroencephalography or brain scintigraphy).<sup>21 22</sup> We will exclude brain-dead patients who are not candidates for organ donation (online supplementary file 2).

## Interventions

### Checklist for brain-dead potential organ donors management

After a preliminary prospective study<sup>13</sup> that found a positive impact of a clinical goal-directed protocol on reducing irreversible cardiac arrests in brain-dead potential organ donors, an updated checklist was generated after drawing up a clinical practice guideline (CPG) for brain-dead potential organ donor management. The CPG recommendations were developed from July 2016 to March 2017, as a joint initiative of the Brazilian Ministry of Health, Brazilian Association of Intensive Care Medicine (AMIB), Brazilian Association of Organ Transplantation (ABTO)<sup>23</sup>, and Brazilian Research in Intensive Care Network (BRICNet). The recommendations were developed using the Grading of Recommendations, Assessment, Development and Evaluation system.<sup>24</sup> The following criteria were considered in the decision-making process: the risks and benefits of interventions, the quality of evidence for risks and benefits, resource use and costs and acceptability by healthcare professionals.

The checklist was designed to address CPG goals and recommendations that involve temperature control, mechanical ventilation, haemodynamic control, endocrine and metabolic control and use of antibiotics and blood products, as required, and hormone administration (hydrocortisone, vasopressin and/or desmopressin, insulin). Thyroid hormone was not recommended due to



**Figure 2** Logical model for the checklist intervention. ICU, intensive care unit.

lack of evidence to confirm the benefit of its use.<sup>25 26</sup> We tested the checklist in four ICUs with high volume in brain death notifications that participated in the preliminary study<sup>13</sup> and make minimal adjustments suggested by the professionals that tested the tool. The full checklist is available in online supplementary file 3. **Figure 2** describes the logical model for the intervention to be tested in this study. We will provide on-site training in each ICU for healthcare professionals to inform how to implement the checklist and how to apply the intended recommendations.

The checklist will be bedside applied immediately after the time of potential donor inclusion in the study and repeated every 6 hours until organ recovery or loss of the potential donor. A member of the intrahospital transplant coordination (IHTC) or a designated ICU professional will apply the paper-based checklist at the bedside. The same individual will be responsible for personally prompting the medical team to modify medical management if any inappropriate aspect of care is noted.

### Usual care

ICUs in the control group will continue with their usual management of potential organ donors. They will not be informed of the items assessed in the goal-directed checklist or the strategies to enhance compliance.

### Co-interventions

All ICU teams and IHTC members of the participating institutions will receive training in family interviews for organ donation. The training and interview process have been based primarily on the Spanish model of communication in critical situations (online supplementary file 4).<sup>27–31</sup> Training consists of two components: (1) face-to-face training of one ICU team representative and one IHTC member of each institution and (2) provision of an online, self-instructional course for all ICU team members and IHTC members participating in the study. These co-interventions aim to standardise ICU strategies in relation to family interviews, reducing variability between participating sites. This is important for the trial due to three main reasons: (a) inadequate interviews may result in a lower rate of effective donation (secondary outcomes of the study), independently of potential donor



**Table 1** Strategies to maximise adherence to study interventions and co-interventions**Strategies**

1. In-person training of two representatives (study coordinators) from each participating site on the conduct of family interviews.
2. Provision of an online course for the training of all ICU team members and IHTC members on how to prepare for and conduct a family interview. A family interview support guide will also be made available.
3. On-site training of ICU team members and IHTC members of all hospitals in the intervention group. The training aims to provide guidance on the methods for administration of the goal-directed checklist for the management of potential organ donors to as many ICU and IHTC professionals as possible.
4. Monthly reports with the number of potential donors screened and included will be sent by electronic message, in the form of a newsletter, to all members of the health team comprising of professionals from the ICU and IHTC.
5. The local co-ordinators of the participating sites will be contacted by the study central office co-ordinators whenever there is a failure to adhere to the protocol or to complete the patient's clinical record form.
6. The local coordinators of the participating sites will receive, whenever a patient is included, electronic messages to remind them of the need to administer the bedside goal-directed checklist and prompt the medical team on management during the stay of potential organ donors in the ICU.
7. Remote support from the study coordinators and central office will be made available to all local coordinators for any questions related to the study.

ICU, intensive care unit; IHTC, intrahospital transplant coordination.

management; (b) reducing variability between participating sites may have an impact on reducing the intra-cluster correlation of the study, increasing its power and (c) training strategies might enhance the engagement of the participating sites, especially those in the control group, thereby balancing a potential Hawthorne effect. [Table 1](#) shows the strategies to promote effective implementation of intervention and co-intervention.

**Sample size**

With 60 ICUs, we will need to include 19 brain-dead potential organ donors per site (1140 potential donors) to detect an absolute reduction of donor losses due to cardiac arrests of 10% (from 28% in the control group to 18% in the intervention group),<sup>13</sup> considering an intra-class correlation coefficient (ICC) of 0.05, power of 80%, and a two-sided alpha level of 5%. Therefore, considering a possible variation in cluster size and its impact on statistical power, we intend to include a minimum of 60 ICUs

with at least 1200 potential organ donors, not allowing more than 30 participants in each cluster.

**Randomisation**

We will randomly assign ICUs to the intervention group or control group with a 1:1 allocation ratio using blocks of variable sizes (2 and 4) and stratified by the estimated annual number of notifications of brain death in each site (sites with  $\leq 29$  and  $> 29$ ). ICUs from the same institution are not considered independent clusters to avoid contamination. We will randomise the ICUs consecutively as per the date of authorisation of the principal investigator to implement the study in the institution, obtained after the Institutional Review Board (IRB) approval. To ensure allocation concealment, a statistician from the study coordinating office will be responsible for the randomisation process, with all researchers involved in the trial blinded to the allocation sequence.

**Outcomes**

The primary outcome will be the number of brain-dead potential organ donor losses due to cardiac arrest, defined as any loss of brain-dead potential organ donors from irreversible or unreversed cardiac arrest that occurs after patient enrolment, while the subject remains eligible for organ donation (no contraindications, family approval or waiting family decision for donation). Losses of potential donors due to other factors (eg, family refusal or contraindication to organ donation after patient inclusion) will not be considered for this outcome.

The secondary outcomes will be:

1. Number of actual organ donors, indexed to brain-dead potential donors, defined as donors for whom the surgical procedure for organ recovery has been initiated (irrespective of organ recovery)<sup>3</sup>;
2. Number of solid organs recovered per actual donor (ranging from zero to seven organs per donor, as follows: liver, heart, pancreas, two lungs and two kidneys).

The tertiary outcomes will include:

1. The proportion of potential donors with adequate respiratory parameters (defined as arterial PaO<sub>2</sub> of oxygen/fraction of inspired oxygen ratio  $\geq 200$ );
2. The proportion of potential donors with adequate body temperature (defined as body temperature between 34°C and 35°C if haemodynamically stable and  $> 35^\circ\text{C}$  if mean arterial pressure (MAP)  $< 65$  mm Hg or use of norepinephrine or dopamine);
3. The proportion of potential donors with adequate circulatory parameters (inadequate parameters defined as MAP  $< 65$  mm Hg or dose of norepinephrine  $\geq 0.1$  mc/kg/min or dose of dopamine  $\geq 15$  mcg/kg/min);
4. Organ dysfunction score, assessed by the Sequential Organ Failure Assessment Score.

**Blinding**

Due to the nature of the intervention, it will not be possible to blind investigators or healthcare providers

in this study. However, we will not disclose details of the content of the checklist to the control group.

### Data collection

An ICU healthcare professional or an IHTC member will collect the data, which will be recorded at the patient's bedside using a printed case report form and subsequently transferred into an electronic data capture system (REDCap, Vanderbilt University, Tennessee, USA).<sup>32</sup> Investigators will receive training for these activities during the study initiation meeting.

### Data monitoring

The study statistician will be responsible for reviewing weekly data on all inclusions, checking data consistency and checking whether all forms have been completed correctly. Clinical research monitors will review all data collected and may require supplementation or correction of inconsistent data according to the Good Clinical Practices (GCP) recommended by the International Council for Harmonisation (ICH).<sup>33</sup> On-site monitoring visits will take place after the fifth patient inclusion in the site and when 100% of the projected number of inclusions for the site has been achieved. Additional monitoring visits will be performed as needed, based on the detection of data inconsistencies, errors in completing the forms or suspected fraud. Periodic remote follow-up will be performed via telephone or electronic messages with the participating sites according to patient recruitment. The data to be collected from each subject are summarised in [table 2](#).

### Statistical analysis

We will prepare a detailed statistical analysis plan before data analysis, which is intended to be published or made available online. We will perform the statistical analysis following the intention-to-treat principle, accounting for cluster design, with observations of the ICUs analysed according to the group to which they have been allocated. We will examine the normality of data by visual inspection of histograms and using the Shapiro–Wilk test for normality. Baseline characteristics of both the ICUs and potential organ donors will be presented as frequencies and percentages, means and SD and medians and IQR, whenever appropriate, for the intervention group and control group.

For the primary outcome, we will calculate HRs considering the time to the outcome, since patients will be subjected to management at different time intervals in the institutions. Patients will be considered at risk for the occurrence of the outcome of interest while under consideration as potential donors. If the outcome of interest does not occur, patients' follow-up will be considered to have ended at the time their management has been discontinued (family refusal or contraindication to donation). We will conduct predefined subgroup analyses, considering the following variables: age >60 years, cause of the injury leading to potential brain death (traumatic or non-traumatic) and patient severity on ICU admission defined by the Simplified Acute Physiology Score 3 (SAPS 3) with a

**Table 2** Data to be entered in the clinical record form of all potential organ donors included in the study

1.	Identification of the potential donor: research centre code and patient's hospital registration number, sex and date of birth.
2.	Screening: inclusion and exclusion criteria for definition of eligibility.
3.	History: date and time of hospital admission, date and time of ICU admission, reported and estimated weight, height, SAPS 3 on ICU admission, comorbidities prior to hospitalisation, cause of brain death, date and time of first clinical examination for the diagnosis of brain death.
4.	Respiratory variables: tidal volume, mL; respiratory rate, mpm; PEEP, cm H <sub>2</sub> O; plateau pressure, cm H <sub>2</sub> O; peak pressure, cm H <sub>2</sub> O (if volume is controlled); FiO <sub>2</sub> , % Blood gas variables: PaO <sub>2</sub> , mm Hg; SaO <sub>2</sub> , %; PaCO <sub>2</sub> , mm Hg; base excess, mmol/dL; PcvO <sub>2</sub> , mm Hg; ScvO <sub>2</sub> , %; PcvCO <sub>2</sub> , mm Hg; lactate, mmol/dL.
5.	Temperature and haemodynamic variables: temperature, °C; heart rate, bpm; systolic blood pressure, mm Hg; diastolic blood pressure, mm Hg; CVP, mm Hg and/or ΔPp, % and/or ΔSV, % and/or IVCCI, %; cardiac arrhythmias.
6.	Diuresis and fluid balance: infused volume; diuresis and fluid balance at different time intervals.
7.	Laboratory variables: haemoglobin, g/dL; creatinine, mg/dL; platelets, /mm <sup>3</sup> ; bilirubin, mg/dL; sodium, mEq/L; potassium, mEq/L; magnesium, mEq/L; phosphorus, mEq/L; calcium, mEq/L.
8.	Drug use: norepinephrine, dopamine, vasopressin, desmopressin, corticosteroids, antibiotics.
9.	Family interview: time, place and name of the professional communicating the establishment of a brain death protocol to the family; time, place and name of the professional communicating the death to the family; time, place and name of the professional conducting the family interview with the request for organ donation; experience and qualification of the professional conducting the family interview with the request for organ donation; family authorisation for organ donation; loss of potential donor due to family refusal; causes of family refusal.
10.	Protocol completion: date and time of second clinical examination for the diagnosis of brain death; date and time of a complementary test for the diagnosis of brain death; complementary test performed for the diagnosis of brain death.
11.	Occurrence of cardiac arrest, loss of potential donor due to cardiac arrest, completion of organ harvesting, number and type of organs recovered.

CVP, central venous pressure; FiO<sub>2</sub>, fraction of inspired oxygen; ICU, intensive care unit; IVCCI, Inferior Vena Cava Collapsibility Index; PaCO<sub>2</sub>, arterial partial pressure of carbon dioxide; PaO<sub>2</sub>, arterial partial pressure of oxygen; PEEP, positive end-expiratory pressure; PcvCO<sub>2</sub>, central venous partial pressure of carbon dioxide; PcvO<sub>2</sub>, central venous partial pressure of oxygen; SaO<sub>2</sub>, arterial oxygen saturation; SAPS 3, Simplified Acute Physiology Score 3; ScvO<sub>2</sub>, venous oxygen saturation; ΔPp, pulse pressure respiratory variation; ΔSV, stroke volume respiratory variation.

cut-off determined by its median. We will conduct sensitivity analyses of adherence to the intervention (compliance with checklist proposed measures) and of the time interval between the first clinical examination consistent with having brain death and inclusion in the study.



**Figure 3** Geographical distribution of the participating intensive care units in Brazil. (map base copyright obtained from [www.gettyimages.pt](http://www.gettyimages.pt)).

For secondary and tertiary outcomes, we will use models for correlated data, considering the ICU as a cluster and each outcome with its own probability distribution. We will conduct a sensitivity analysis of the outcome ‘number of solid organs recovered per actual donor’, considering the number of kidneys harvested. We will analyse secondary outcomes by adjusting for multiple hypothesis testing. For all statistical comparisons, we will adopt a statistical significance level of 0.05. An up-to-date version of the R programme (R Development Core Team) will be used to conduct analyses.

### Study planning and implementation schedule

We finalised the study design and protocol in March 2016. The National Study Investigators Meetings were held in two parts: 9 to 10 March 2017 and 8 to 9 June 2017. At the time of manuscript preparation, 63 ICUs representative of the Brazilian geopolitical territory are currently recruiting study subjects (figure 3). On-site training started on 1 June, 2017. We expect that the recruitment will be completed in December 2019. The list of sites included is available at [ClinicalTrials.gov](http://ClinicalTrials.gov) (NCT03179020).

### Organisational aspects of the study

The study is sponsored and co-ordinated by the Moinhos de Vento Hospital, Brazil, in partnership with the Brazilian Ministry of Health through the Programme of Institutional Development of the Brazilian Unified Health System and in association with the General Co-ordination Office of the National Transplant System and the Brazilian Research in Intensive Care Network. The study is supported by the AMIB Committee for Organ Donation for Transplant, ABTO, the Spanish National Transplant Organisation and the organ procurement

organisations of the states of Santa Catarina and Rio Grande do Sul. The study steering committee consists of intensivists, transplant coordinators and epidemiologists with expertise in conducting multi-centre studies. The committee is involved in the conception and design of the study, supervision of progress and procedures during the study and writing of the study report and any resulting study manuscript.

### Ethics and dissemination

The study was designed in accordance with resolution No. 466/2012 of the Brazilian National Health Council/Ministry of Health, the Declaration of Helsinki, the Document of the Americas and the ICH/GCP E6(R2) 2016.<sup>33</sup> The study was approved by the IRB of the coordinating centre (No. 53999616.0.1001.5330) and by the IRB of each participating site (online supplementary file 5). Participating in the intervention or control groups does not imply any risk for the subjects included, since the groups will not be deprived of the application of the most up-to-date recommendations. Because obtaining written informed consent from patients’ family members entails operational and methodological difficulties, and would have a potential negative impact on organ donation as well, we requested a waiver of informed consent for the IRB of each participating site.

This trial, regardless of the results, will be published in a peer-reviewed medical journal and presented in scientific conferences and scientific meetings involving the representatives of each participating hospital, of each Brazilian state transplant centre and of the Brazilian Ministry of Health.

### Patient and public involvement

Considering the characteristics of the study population, the patients were not directly involved in the research question, study design, study participants recruitment and study conduction.

## DISCUSSION

Despite the existence of CPGs that currently provide recommendations for a ‘standard of care’ in the management of potential organ donors,<sup>23 29</sup> they are not always implemented, resulting in the risk of loss of specific organs due to management failures or even multiple organ loss due to cardiac arrest of the potential donor.<sup>1–4 23 34</sup> CPGs usually do not have an impact on bedside practice in the short-term, as they rarely take into account clinical applicability.<sup>35</sup> Therefore, a CPG-based goal-directed checklist associated with a clinician prompting system may be an effective approach to improve physician adherence to CPG recommendations. Physician-centred healthcare can be associated with non-adherence to basic recommendations of care, especially in highly complex processes, such as the management of potential organ donors.<sup>34</sup> In this context, we expect that these organisational adjustments, supported by a checklist-based management strategy, will have a positive impact on organ donation.



Patel *et al*<sup>19</sup> published the results of 671 multi-organ donors managed using a goal-directed checklist in the USA. The predetermined goals were met in 45% of cases prior to organ recovery, and the use of the goal-directed checklist significantly increased the number of organs transplanted per donor.<sup>19</sup> Recently, we published a prospective observational study that involved 27 ICUs in a southern Brazilian state demonstrating that the use of a goal-directed checklist to guide the management of deceased donors reduces brain-dead potential organ donor losses due to cardiac arrest.<sup>13</sup> Compliance with the checklist increased after the start of the study from 52.1% to 85.8% ( $p < 0.001$ ). The use of the checklist was associated with a lower likelihood of occurrence of cardiac arrest (OR: 0.30, 95% CI 0.18 to 0.49,  $p < 0.001$ ) and an increase in the number of organs recovered per donor.<sup>13</sup> Although these results are encouraging and reproduce the observations of other authors, the observational nature of the studies provides only weak evidence on the subject.<sup>14-19</sup>

The study design and basis for the implementation of DONORS may provide new insights that can help overcome the weaknesses of previous observational studies, often related with barriers to conduct studies in deceased organ donors.<sup>5</sup> The cluster randomisation design will limit selection biases, and we will count on a large number of ICUs, which are responsible for a significant amount of brain death notifications throughout Brazil. The DONORS design will include the evaluation of the effectiveness of a goal-directed checklist strategy in different socioeconomic scenarios in Brazil, allowing us to provide real-world evidence to support the practical clinical applicability of the study findings. In addition, the trial is testing the effectiveness of the proposed intervention by means of an implementation strategy that may be considered feasible to replicate in different settings. Finally, the characteristics of the institutional quality improvement programme of this protocol will allow the potential benefits generated by the proposed study model to be incorporated into ICUs and ultimately transferred to other clinical areas for the care of critically ill patients.

The implementation of a goal-directed checklist for the management of potential donors is a complex intervention, with multiple components. It is important to state that, as in most quality improvement studies, how the intervention is implemented is crucial to the interpretation of the results. In this respect, through this protocol, we aimed to describe in detail all the interventions and co-interventions proposed in the study in order to allow reproducibility of our procedures in other settings. In addition, the logical model presented in the study (figure 2) is intended to explore the relationships between the activities proposed in the intervention and the mediators of the effect, such as improved clinical management of potential donors and enhanced communication with the ICU team about the expected outcomes. Also important is that, although the study focuses on assessing short-term outcomes in

potential donors (eg, cardiac arrest and number of organs recovered), potential beneficial outcomes are expected for transplant recipients, such as improved graft function, survival and quality of life.

Our study has some limitations. First, high variability in care and outcomes among institutions is expected. Although the chosen ICC may be considered conservative, there are no estimates in the literature for the proposed intervention, which may result in lack of power if the actual ICC is larger than the estimate. In spite of the procedures to avoid the transfer of information about the checklist to ICUs in the control group, although with low probability this possibility should be considered, thereby exposing the details of the content of the goal-directed checklist for the control group. Furthermore, although stratified randomisation is planned for this study, we must take into consideration the differences in the number of brain death notifications among ICUs, which will recruit patients at different rates, which in turn may generate learning curves that may have an impact on the final cluster randomisation trial results. In order to minimise this problem, we are allowing a maximum of 30 patients to be recruited per each study site; however, some ICUs may recruit a small number of patients. Inadequate adherence to the checklist may have an impact on the results observed in the intervention group, showing no effect that may be either due to lack of efficacy of the intervention or due to its suboptimal implementation. Another important aspect to highlight is that, although we expect to see an improvement in the quality of organs with the use of the checklist, therefore improving outcomes for organ-transplant recipients, we are limiting the data collection and study procedures to potential donors, not allowing direct assumptions about its possible effects. Finally, a possible variability in the care of patients with catastrophic brain injury (CBI), before its evolution to brain death, may occur among the study sites. On the other hand, the results may contribute as an indirect evidence for the management of patients who have a CBI.

## CONCLUSIONS

We expect that the results from DONORS will provide information regarding the practical use of checklist-guided management interventions for potential multi-organ donors that may contribute to reducing potential donor losses due to cardiac arrest or other relevant outcomes. At this time, with the increasing demand for organs for transplantation, standardised, evidence-based guidelines that may be adopted globally by ICUs and by transplant coordinators are needed to improve the availability and quality of organs available for donation. The evidence generated by this trial will have great potential to contribute positively to the donation of organs.

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