

Association Between Suicide Donors and Outcomes in Heart Transplantation: A Retrospective Cohort Study

Álvaro Perazzo^{1,2,3,4}, MD, MSc; Samuel Padovani Steffen^{1,2}, MD, PhD; Aichah Ahmad El Orra⁵, MD; Shirlyne Fabianni Dias Gaspar^{1,2}, MD; Daniele Ronco^{3,4,6}, MD; Ronaldo Honorato Barros Santos^{1,2}, MD; Domingos Dias Lourenço Filho^{1,2}, MD, PhD; Luis Fernando Bernal da Costa Seguro¹, MD, PhD; Monica Samuel Avila¹, MD, PhD; Fabiana Goulart Marcondes-Braga¹, MD, PhD; Claudio Francesco Russo⁶, MD, PhD; Fernando Bacal¹, MD, PhD; Roberto Lorusso^{3,4}, MD, PhD; Fabio Antonio Gaiotto^{1,2}, MD, PhD; Fabio B Jatene^{1,2}, MD, PhD

¹Transplant Center, Instituto do Coração (InCor), Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HC-FMUSP), São Paulo, São Paulo, Brazil.

²Department of Cardiovascular Surgery, Instituto do Coração (InCor), Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HC-FMUSP), São Paulo, São Paulo, Brazil.

³Cardio-Thoracic Surgery Department, Maastricht University Medical Center+, University of Maastricht, Maastricht, The Netherlands.

⁴Cardiovascular Research Institute Maastricht (CARIM), University of Maastricht, Maastricht, The Netherlands.

⁵Faculdade de Medicina, Hospital Israelita Albert Einstein, São Paulo, São Paulo, Brazil.

⁶Cardiac Surgery Unit, ASST Grande Ospedale Metropolitano Niguarda, Milan, Italy.

This study was carried out at the Transplant Center, Instituto do Coração (InCor), Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HC-FMUSP), São Paulo, São Paulo, Brazil.

ABSTRACT

Introduction: The use of organs from suicide donors in heart transplantation is controversial due to potential concerns about graft function and recipient outcomes. This study investigates the association between heart transplantation using suicide donors related with the incidence of primary graft dysfunction (PGD) and mortality within 30 days after transplant.

Methods: A retrospective analysis was conducted on 97 adult heart transplant recipients at the Instituto do Coração of São Paulo between 2020 and 2021. Data on donor characteristics (age, sex, mechanism of brain death), recipient preoperative status (age, sex, cardiomyopathy etiology, body mass index, comorbidities, use of intra-aortic balloon pump, extracorporeal membrane oxygenation [ECMO]), intraoperative variables (ischemia time, cardiopulmonary bypass time, implantation time), and postoperative outcomes (use of ECMO, mortality) were analyzed.

Results: Of the 97 transplants analyzed, six were from suicide donors (6.2%). Recipients of hearts from suicide donors had a significantly higher need for ECMO (33.3% vs. 4.4%, $P = 0.036$), increased PGD (66.7% vs. 19.8%, $P < 0.05$), and higher 30-day mortality (50% vs. 3.3%, $P < 0.05$) compared to non-suicide donors. No significant intraoperative time differences were found between the groups.

Conclusion: This study is the first to identify a significant association between heart transplantation from suicide donors and adverse outcomes, including higher rates of PGD and early mortality. These findings suggest possible psychological and biological influences on organ quality and transplantation outcomes. Further research is needed to clarify these associations and inform donor selection criteria.

Keywords: Heart Transplantation. Donors. Primary Graft Dysfunction. Organ Preservation. Inflammatory Markers.

Abbreviations, Acronyms & Symbols

CPB	= Cardiopulmonary bypass
ECMO	= Extracorporeal membrane oxygenation
IABP	= Intra-aortic balloon pump
IL	= Interleukin
InCor	= Instituto do Coração
ISHLT	= International Society for Heart and Lung Transplantation
PGD	= Primary graft dysfunction
TBI	= Traumatic brain injury
TNF- α	= Tumor necrosis factor alpha

INTRODUCTION

Suicide is a complex phenomenon with a rising incidence in the Americas, according to the World Health Organization (or WHO)^[1]. It is estimated that for every death by suicide, there are at least 20 attempts^[2]. In Brazil, between 2000 and 2017, suicide rates gradually increased across all regions and in both sexes (75% for men and 85% for women), making it the fourth leading cause of death from external factors in the country and, therefore, a public health issue^[3].

According to an American study^[4], the use of organs from suicide victims constitutes a minority of donations. Although families are more inclined to consent to organ donation compared to those

Correspondence Address:

Álvaro Perazzo

 <https://orcid.org/0000-0001-9854-2788>

Transplant Center, Instituto do Coração (InCor), Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo (HC-FMUSP)

Av. Dr. Enéas Carvalho de Aguiar, 44, São Paulo, SP, Brazil

Zip Code: 05403-900

E-mail: alvaro.perazzo@hc.fm.usp.br

Article received on August 30th, 2024.
Article accepted on December 7th, 2024.

after traumatic brain injury (TBI) from motor vehicle accidents or cerebrovascular diseases^[5], candidates are often deemed unsuitable due to the prolonged ischemic time or the manner of death that compromises the integrity and function of the organ. Additionally, suicide encompasses complex psychosocial factors, where psychological essentialism leads to the act being perceived as immoral or as contaminating the soul. A New Zealand study showed that when choosing between donors who died by accident, suicide, or homicide, participants avoided hearts from suicide victims, believing that the donor's heart would transfer negative traits to the recipient^[6].

Despite these concerns, there is growing evidence that organs from donors who died by suicide may not necessarily result in inferior outcomes. A 14-year English study involving renal donors who had died by hanging found no difference in graft survival and dysfunction post-transplant compared to other causes of brain death^[7]. Similarly, a French study demonstrated comparable outcomes for liver transplants^[8], and an English study on lung transplants under similar circumstances indicated no significant differences in outcomes^[9]. These findings suggest that using organs from suicide victims could be a valuable contribution to addressing organ shortages^[10].

However, specific data on heart transplantation involving donors who died by suicide remain scarce. Current definitions of marginal donors include those with previously contraindicated characteristics^[11], such as age over 65 years, valvular dysfunction, hepatitis B or C positive status, coronary artery disease, or substance abuse/intoxication^[12]. Given the limited data available, the aim of this study is to evaluate whether heart transplantation using a donor who died by suicide is associated with higher rates of primary graft dysfunction (PGD) and mortality compared to heart transplants from non-suicide donors. Understanding these potential differences is crucial for refining donor selection criteria and improving outcomes in heart transplantation.

METHODS

A retrospective analysis was conducted on 105 adult heart transplant recipients at the Instituto do Coração (InCor) of São Paulo, Brazil, between 2020 and 2021. Due to incomplete records, eight patients were excluded, resulting in a final cohort of 97 patients for analysis. Data on donor characteristics (age, sex, mechanism of brain death), recipient preoperative status (age, sex, etiology of cardiomyopathy, body mass index, comorbidities, use of intra-aortic balloon pump [IABP], use of extracorporeal membrane oxygenation [ECMO]), intraoperative variables (total ischemia time, cardiopulmonary bypass [CPB] time, implantation time), and postoperative outcomes (use of ECMO, mortality) were collected and analyzed.

PGD was defined based on the 2014 International Society for Heart and Lung Transplantation (ISHLT) Consensus as severe biventricular and/or left ventricular dysfunction requiring ventricular assist device or ECMO within the first 24 hours after transplant. Moderate PGD was defined as an ejection fraction $\leq 40\%$ combined with an inotropic score > 10 . Hemodynamic parameters were excluded from the criteria due to incomplete data availability. Only cases where the IABP was used postoperatively as a support measure were considered for moderate PGD classification. Cases where the balloon was maintained without evidence of PGD were not classified as having PGD^[13].

The study was conducted in compliance with the ethical standards of the institutional research committee and the 1964 Helsinki Declaration and its later amendments. The protocol was approved by the institutional ethics committee at the InCor of the Faculdade de Medicina, Universidade de São Paulo (CAAE: 86764218.1.0000.0068). All patients provided informed consent before participation in the study.

Statistical Analysis

Continuous variables were described by mean and standard deviation, and categorical variables by number and proportion. Baseline characteristics related to intra and postoperative variables were compared between the group that received organs from suicide donors and the group that received organs from non-suicide donors using analysis of variance or the Mann-Whitney test and the Chi-square test, as appropriate. Statistical significance was considered for P -values < 0.05 . All analyses were conducted using the R statistical software.

RESULTS

The baseline characteristics of the donors are presented in Table 1 and Figure 1 — of the 97 heart transplants analyzed, six were from suicide donors (6.2%), and 91 were from non-suicide donors (93.8%). Young male donors (50.5%) with a mean age of 29.9 ± 9.3 years, with TBI (58.7%) and cerebrovascular diseases as the leading causes of brain death, were predominant. Regarding the recipients' baseline characteristics, Table 2 and Figure 2 show that our sample was mostly composed of male patients (62.9%) with a mean age of 49.2 ± 10.6 years, who were eutrophic (67%) and primarily suffered from dilated cardiomyopathy (39.8%) and Chagas disease (33.7%).

In terms of comorbidities, 22.7% had diabetes mellitus, 32% had systemic arterial hypertension, and 27.8% were former smokers. All patients were prioritized and hospitalized pre-transplant. Only 11.3% used ECMO, and 66% were prioritized for mechanical circulatory support with an IABP.

When comparing groups that received hearts from suicide donors vs. non-suicide donors, as shown in Table 3 and Figure 3, there was no statistically significant difference in intraoperative times. However, our sample does not suggest longer CPB times in patients who received transplants from suicide donors, which could suggest a confounding bias.

Significant statistical differences were observed in postoperative variables: patients who received transplants from suicide donors required ECMO more frequently (33.3% vs. 4.4%; $P = 0.036$). Also, there were higher rates of dysfunction, leading to a greater anticipated need for ECMO following the transplant.

Additionally, patients who received heart transplants from suicide donors exhibited a higher incidence of PGD (66.7% vs. 19.8%; $P < 0.05$) and a higher incidence of death within 30 days (50% vs. 3.3%, $P < 0.05$).

DISCUSSION

Among the 97 heart transplants analyzed, six (6.2%) involved donors who died by suicide, while 91 (93.8%) were from non-suicide donors. This distribution reflects global trends, where suicide accounts for only a small fraction of organ donations^[4]. The data

Table 1. Baseline characteristics of suicide and non-suicide donors.	
Characteristics	Mean ± standard deviation or absolute frequency (%)
Age (years)	29.9 ± 9.3
Recipient sex (male)	49 (50.5)
Mechanism of death	
Traumatic brain injury	57 (58.7)
Cerebrovascular disease	28 (28.9)
Suicide	6 (6.2)
Others	6 (6.2)

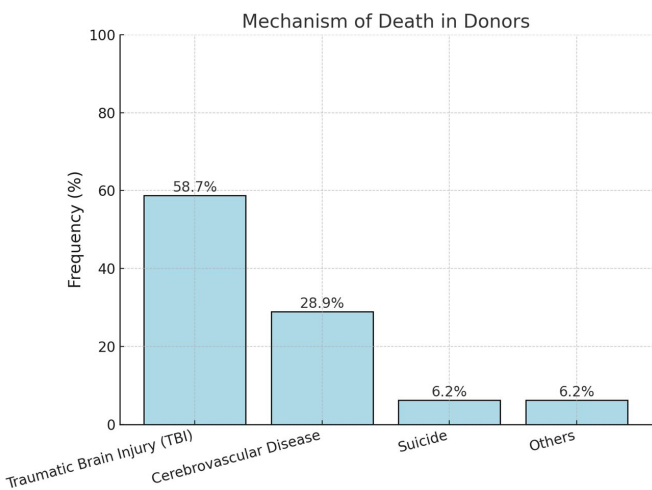


Fig. 1 - Mechanism of death in donors.

indicate a potential risk associated with using hearts from suicide donors in transplantation, particularly regarding higher rates of PGD and early mortality. These results are in contrast with findings from other organ transplants (lung, liver, and kidney), where the use of organs from suicide donors did not show significant differences in survival rates or dysfunction compared to non-suicide donors^[7-9]. This discrepancy could be due to the unique physiological and psychological considerations involved in heart transplantation. Our sample consisted predominantly of young male donors (50.5%) with a mean age of 29.9 ± 9.3 years, with TBI (58.7%) and cerebrovascular diseases as the leading causes of brain death, consistent with data from the 37th ISHLT report^[14]. According to a retrospective study conducted at InCor in 2020, prolonged CPB time is associated with the occurrence of PGD^[15]. CPB time is also responsible for several physiological alterations and can act as a complicating factor in the postoperative course of cardiac surgeries. Even though the safety of CPB has improved in recent years, the prevention of the systemic inflammatory response following cardiac surgery has not yet been adequately achieved. The activation of various inflammatory cascades triggered by the release of mediators is believed to contribute to parenchymal organ dysfunction, as well as to the detrimental

effects of CPB on the immune system, thereby increasing the risk of postoperative multiorgan failure and infectious complications. These inflammatory responses and cascades may also play a role in the increased incidence of PGD in such cases^[16]. Postoperative variables showed significant statistical differences: patients receiving transplants from suicide donors required ECMO support more frequently (33.3% vs. 4.4%; *P* = 0.036). This observation aligns with a retrospective English study involving 18,250 cases, which reported higher ECMO utilization among recipients of hearts from suicide donors who died by drowning or asphyxiation^[17]. However, in contrast to the previous study, our findings also indicate higher rates of dysfunction, contributing to an increased anticipated need for ECMO after transplantation. According to the first study to investigate intuitive thinking about organs donated by suicide victims^[6], organs from suicide victims are less frequently chosen, reflecting psychological essentialism — beliefs that suicide is an immoral act and contaminates the soul. This perception may lead to biases against using such organs for transplantation. Essentialism posits that an invisible internal essence determines a person's psychological characteristics and behaviors, and that this essence can be transmitted through various types of physical contact, including transplants. A manifestation of this belief is cardiopsychism — the theory that the heart is central to our mental functions and responsible for the seat of emotions and the true self^[18]. Consequently, heart transplantation might have a greater potential to reinforce these beliefs, potentially influencing clinical decisions and public perception. Furthermore, recent analyses highlight the role of the immune system in vulnerability to suicide, independent of psychiatric conditions. Studies show that patients with suicidal ideation or attempts have elevated levels of inflammatory biomarkers such as interleukin (IL)-6 and tumor necrosis factor alpha (TNF-α), suggesting that immune system dysregulation may contribute to suicidal behavior's pathophysiology^[19,20]. A Swedish study^[21] found that depressive patients with suicidal tendencies had higher concentrations of IL-6 and TNF-α and lower IL-2 levels in peripheral blood compared to depressive patients without suicidal tendencies and healthy controls. Moreover, it is known that the expression of certain genes may be reduced in individuals who die by suicide, including KCNJ2 (potassium inwardly rectifying channel subfamily J member 2), A2M (alpha-2-macroglobulin), AGT (angiotensinogen), PMP2 (peripheral myelin protein 2), and VEZF1 (vascular endothelial zinc finger 1). In addition, astrocytes, the stress response, the immune system, and microglia are also

Table 2. Baseline characteristics of the recipients.

Characteristics	Mean ± standard deviation or absolute frequency (%)
Age (years)	49.2 ± 10.6
Recipient sex (male)	61 (62.9)
Body mass index	
Underweight	4 (4.1)
Eutrophic	65 (67)
Overweight	18 (18.6)
Obesity grade I	8 (8.3)
Obesity grade II	2 (2)
Etiology	
Dilated	39 (39.8)
Chagas	33 (33.7)
Ischemic	9 (9.2)
Others	17 (17.3)
Cerebrovascular accident	14 (14.4)
Dyslipidemia	15 (15.5)
Diabetes mellitus	22 (22.7)
Former smoker	27 (27.8)
Atrial fibrillation	25 (25.8)
Systemic arterial hypertension	31 (32)
Use of intra-aortic balloon pump	64 (66)
Use of extracorporeal membrane oxygenation	11 (11.3)

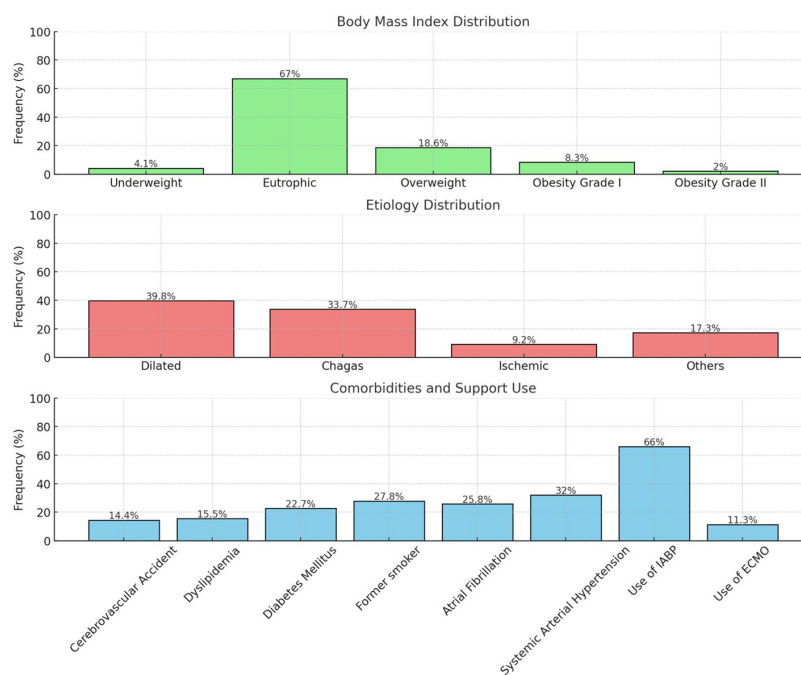
**Fig. 2** - Recipient characteristics: body mass index, etiology, and comorbidities. ECMO=extracorporeal membrane oxygenation; IABP=intra-aortic balloon pump.

Table 3. Comparison of intra and postoperative characteristics between recipients of suicide and non-suicide donors.			
	Suicide (n=6)	Non-suicide (n=91)	P-value
Intraoperative			
Implantation time (min.)	49.2 ± 4.5	56.5 ± 14.3	0.2
CPB time (min.)	70.3 ± 17.5	91 ± 29.9	0.1
Total ischemia time (min.)	192.3 ± 59.3	205.8 ± 46.8	0.5
Postoperative			
Need for ECMO	2 (33.3)	4 (4.4)	0.036
PGD	4 (66.7)	18 (19.8)	0.008
Severe PGD	2 (33.3)	11 (12.1)	0.14
Mortality within 30 days	3 (50)	3 (3.3)	0.016

CPB=cardiopulmonary bypass; ECMO=extracorporeal membrane oxygenation; PGD=primary graft dysfunction

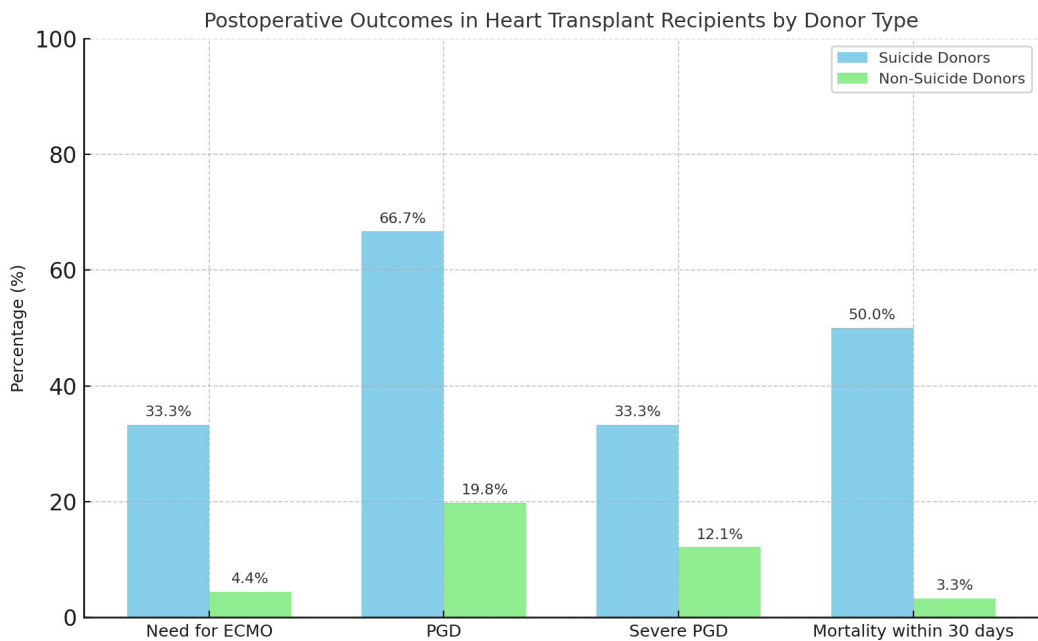


Fig. 3 - Postoperative outcomes in heart transplant recipients by donor type. ECMO=extracorporeal membrane oxygenation; PGD=primary graft dysfunction.

involved in the etiopathogenesis of suicide. Therefore, further studies are needed to investigate whether these same factors are also present in PGD^[22]. This suggests that immunological factors could potentially influence the outcomes of transplants from suicide donors, although further research is needed to explore this connection fully.

In conclusion, while our findings suggest caution when considering heart transplants from suicide donors due to increased risks of PGD and early mortality, the lack of substantial data in the literature on this specific topic calls for more comprehensive studies to better understand these associations and refine donor selection criteria for heart transplantation.

Limitations

The lack of detailed data regarding the method of suicide is a limitation, as previous studies have analyzed patients with the same mechanism (e.g., hanging) and its relationship to outcomes. We do not know if there is a difference concerning the method used for self-harm and the occurrence of higher rates of PGD and mortality. Additionally, the absence of comprehensive hemodynamic data within the first 24 hours after transplant makes it impossible to identify cases of mild PGD, and therefore, to determine the total prevalence of PGD. Associated with this factor is the common continuation of IABP use post-heart transplantation, which may

not necessarily be a result of PGD, thereby presenting a partial limitation concerning the classification of moderate PGD.

CONCLUSION

This is the first retrospective study to demonstrate an association between heart transplantation using a suicide donor and the outcomes of (PGD) and mortality within 30 days. Could beliefs rooted in essentialism somehow be related to these adverse outcomes? Could the intense suffering experienced by the patient who commits suicide affect the organ in a way that contributes to dysfunction and, consequently, to death? Is it possible that the impact of this mental suffering arises from the elevation of inflammatory markers that could significantly alter the quality of the organ to be donated? The lack of robust literature indicates the need for further research in this field to better understand such relationships.

ACKNOWLEDGMENTS

We would like to extend our gratitude to the entire team at the Transplant Center of InCor, Hospital das Clínicas, Faculdade de Medicina, Universidade de São Paulo, for their invaluable support and assistance throughout the research process. Special thanks to all the patients and their families for their participation and cooperation, which made this research possible.

No financial support.

Conflict of interest: RL is consultant for Medtronic, Getinge, and LivaNova; Advisory Board Member of Eurosets and Xenios (honoraria paid as research funding).

Authors' Roles & Responsibilities

AP	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or reviewing it critically for important intellectual content; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published	SFDG	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or reviewing it critically for important intellectual content; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published
SPS	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or reviewing it critically for important intellectual content; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published	DR	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or reviewing it critically for important intellectual content; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published
AAEO	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or reviewing it critically for important intellectual content; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published	RHBS	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or reviewing it critically for important intellectual content; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published
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		FGMB	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or reviewing it critically for important intellectual content; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published
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		FB	Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or reviewing it critically for important intellectual content; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published

- RL Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or reviewing it critically for important intellectual content; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published
- FAG Substantial contributions to the conception or design of the work; or the acquisition, analysis, or interpretation of data for the work; drafting the work or reviewing it critically for important intellectual content; agreement to be accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved; final approval of the version to be published
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