Analysis of contributors to possible organ donor discards in Chile

Francisca Del Rocio Gonzalez Cohens

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Mae Dirac

Lisa Force

Fernando Gonzalez

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Francisca Del Rocio Gonzalez Cohens

University of Washington

Abstract

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Francisca Del Rocio Gonzalez Cohens

Chair of the Supervisory Committee:

Mae Dirac

Department of Health Metrics Sciences

Organ transplantation is the best therapeutic option for several end-stage diseases. Nonetheless, there is an organ shortage due to lack of organ donation. Chile's low organ donation rate of 7.8 donors per million population is due to high familial refusal to donation, lack of possible organ donor referral, but most importantly, high number of discarded possible organ donors. To understand the factors that contribute to discarding possible donors, we used multi-level multivariate logistic regressions using individual-level and hospital-level explanatory variables. The statistically significant variance among hospitals and Local Procurement Coordinations (LPC) explains whether a patient is being discarded as well as the patient's gender, the population-level of poverty, rurality, and years of schooling where the hospitals are located. We propose standardizing the procurement process and implementing monitoring and evaluation technology tools to reduce variation across hospitals and LPCs, and thus, increase the number of effective organ donors in Chile.

To all the people that have and will become organ donors.

To all the patients that have and will receive a transplant.

To all the teams that work every day to improve our organ donation system.

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Glossary

Possible organ donor: A patient that meets the criteria of having a severe neurological condition that is out of neurosurgical reach and without sedation. They should have a Glasgow Coma Scale (GCS) of 7 or less and be between 6 months and 78 years old.

Potential organ donor: A possible organ donor who is certified as brain dead.

Discard: A possible organ donor that is not considered as possible donor anymore because of a medical condition or the presence of a barrier that hinders or makes it impossible for the patient to be certified as brain dead or to become an organ donor.

Contraindication: A potential donor that, after their brain death certification, can't become an organ donor because of a medical condition or a barrier that hinders or makes it impossible for the patient to become an organ donor.

Familial refusal to donation: When the family of a patient does not agree to donate the organs of the potential donor. Patients that in life stated their denial to become an organ donor will be considered under this category too.

Effective organ donor: A potential donor that is compatible with donation (i.e., was not contraindicated) whose family agreed to donation and enters a surgical ward for organ extraction.

Multiorgan donor: A patient that effectively donated more than 1 organ (paired organs, like kidneys are considered as one organ for this definition).

Procurement process: The process that all possible organ donors "follow" with the aim of becoming an organ donor.

Procurement follow-up: Another way of saying that a possible donor is following the procurement process.

Possible donor detection and referral: First stage of the procurement process where a health professional (typically a physician or a registered nurse) realizes that a patient meets the criteria for being considered as a possible donor (detection) and refers them to the local procurement coordination (LPC) to start procurement follow-up.

Local procurement coordination (LPC): Also called Procurement Unit. Is the clinical unit in charge of the organ procurement activity. They coordinate the procurement process from entering to follow-up until the process ends, whether because the patient is discarded, contraindicated, not donated, or becomes an effective organ donor. Each LPC serves a specific area that has at least 1 hospital. The unit is located in the largest hospital of the area it serves.

Health Service: In Chile, the territory is divided in "health services" as healthcare areas. Each health service comprises different municipalities and serves their population with all the healthcare level services. There is one LPC for each health service, and they are in charge of the procurement activity in all the tertiary (high complexity) and secondary (medium complexity) level hospitals.

Abbreviations

pmp: per million population

NCDs: Non-communicable diseases

CKD: Chronic kidney disease

ESRD: End stage renal disease

EHG: Explicit Health Guarantees

OECD: Organization for Economic Co-operation and Development

PD: Possible donor

ER: Emergency room

ICU: Intensive care unit

CPU: Critical patient unit

NCPT: National Coordination of Procurement and Transplantation

MOH: Ministry of Health

CC: Central Coordination

LPC: Local procurement coordination

HS: Health service

SIDOT: System of Organ Donation and Transplantation

FONASA: National Healthcare Fund

RGD: Related groups by diagnosis

BD: Brain death

CPA: Cardiopulmonary arrest

CPR: Cardiopulmonary resuscitation

NRND: National Registry of Non-Donors

WT: Withholding treatment

OR: Odds ratio

CNS: Central nervous system

CI: Confidence interval

1. Introduction

Organ transplantation has been proven to be the best (1,2) and most cost-effective (3–5) therapeutic option for several chronic non-communicable diseases. Nonetheless, uptake of this therapy has been limited by organ shortage (6). In the world, the average organ donation rate is 13.2 donors per million population (pmp) (7), serving fewer than 10% of patients who need a transplant each year (8).

While kidneys are the most needed organ and the most frequently transplanted (65%) (8,9), patients waiting for one may stay alive with access to dialysis, which serves as a kidney replacement therapy, albeit less cost-effective and with lower survival rates (2,4). Dialysis at least can provide relief for kidney disease, while those with seriously compromised organs other than kidneys have few other options (10), meaning that those patients are less likely to survive (11).

This is a growing problem since non-communicable diseases (NCDs) have been increasing in disability burden and mortality during the last 30 years, representing 72.3% of deaths worldwide (12). In particular, chronic kidney disease (CKD) and diabetes mellitus are the eighth leading cause of disability and the fifth leading cause of death in the world (12), and the prevalence of CKD has increased 29.3% in the last 30 years (13). The incidence of end-stage renal disease (ESRD) - the last CKD stage, where patients would need kidney replacement therapy - has increased by 43.1% for dialyzed- and 34.4% for transplanted-patients (13). Even though NCDs are more prevalent in High and Middle Income Countries, CKD has been found to be concentrated in lower income countries (13) that have less access to treatment (14), which increases the burden and the costs in the whole world (14) and furthers health inequities.

Chile is a Latin American country that is considered High Income by the World Bank, but also ranks high in inequality, with the highest Gini coefficient of the OECD and the seventh-

highest Gini coefficient in the world (15). Treatment for ESRD is covered by Chilean law in the "Explicit Health Guarantees'' (EHG) (16), a program that covers at least 80% of the healthcare cost of 85 diseases (17). While this disease represents the fourth cause of death in the country (12), it is the most expensive one to treat, accounting for the 22% of the entire EHG budget (18), leaving the remaining 78% of resources to be distributed among the other 84 diseases covered by the program.

Chile has a very low organ donation rate of 7.8 donors pmp on average over the last 10 years (19), one of the lowest in the OECD (1st quartile) (7,20). This allows the system to perform only 371 transplants on average per year (21), which results in growing transplantation waiting lists, long waiting times, increased morbidity and mortality, and increasing costs (14). This low donation rate has persisted for more than 20 years, despite the "opt out" nature of the donation system. In Chile, familial consent is 50% on average (22) despite having an opt-out legislation since 2010 (23), meaning that every adult is considered as an organ donor unless they register as a non-organ donor. This system was established with the aim of increasing organ donation consent that, at the time, was 65% (24). Albeit this barrier seems to be the largest one, it is indeed, the smallest (25).

Every country, in particular Chile, would benefit from increasing their organ donation rates. How to increase organ donation rates has been a never-ending question, and although there are countries that have succeeded in increasing their donation rates, such as Spain and USA, among others (26), Chile has always been failing to improve (27).

1.2 The organ donation problem

Organs can be obtained from living donors (kidney and liver section) or from deceased donors (multiorgan) (28). Deceased donors represent more than 74% of all donations (9,29), and a patient can become an organ donor after brain death or after circulatory death (28) (77% and

23% around the world (9,29)). Because of the large proportion that deceased donors represent, we will focus on that type of donation. We will specifically focus on brain-dead donors, because Chilean law does not allow performing organ donation after circulatory death (27,30).

To obtain organ donors after brain death in Chile, a long and complex process must be followed, the Organ Procurement Process. This process can be simplified as (27)[1]:

i. Detection of the possible donor in emergency rooms (ER), intensive care units (ICU), or critical patient units
ii. Referral of the patient to the local procurement coordination
iii. Transfer of the possible donor (for those detected in ER) to an ICU for hemodynamic and metabolic stabilization, and maintenance
iv. Diagnosis of brain death
v. Request of donation consent to the patient's family
vi. Coordination and logistics of the extraction surgery and transfer of organs and tissues to the implantation institutions.

This process is controlled and organizational oversight is provided by the National Coordination for Procurement and Transplantation (NCPT), which falls under the Undersecretary of Healthcare Networks of the Ministry of Health (MOH). The NCPT has 1 Central Coordination (CC) that coordinates the extraction and allocation of the procured organs. The allocation of all organs is done centrally by the Public Health Institute, using organ specific allocation algorithms that consider clinical variables (mainly HLA and PRA for kidney), size, and waiting time. The NCPT also has 27 public local procurement coordinations (LPCs) distributed in 27 of the 29 sub-

[1] To see a diagram of the procurement process, go to Appendix 1.

regions of the country, which are called “Health Services” (HS). These units are in charge of coordinating the procurement process inside the hospitals that belong to their HS (27).

Barriers to obtaining organ donors can be divided in three groups, by order of contribution:

1. Obtaining familial consent (fifth stage)
2. Patients never enter the procurement process (failure of the first stage)
3. Large number of patients are discarded among those who enter the process (process problems in all stages, and system problems).

A large body of literature explains the first barrier and reasons why people refuse to consenting to donation or have a negative attitude towards donation, such as not understanding brain death concept (31,32), or the satisfaction of the family with the care received at the hospital or the approach of the procurement team (31). Myths persist around organ donation and the system (33,34), such as the belief that famous or rich people will access a transplant faster, or that doctors will let patients die to extract their organs (35). Literature also suggests that familial consent can be associated with education, socioeconomic status, race, and age of the patient (34,36–43), and confidence with the entire health system (44).

The González Cohens et al. study conducted in Chile between 2013 and 2017, showed 87% of possible donors - defined as all patients who were admitted to a hospital because of a severe neurological condition that can end in brain death and subsequently discharged as dead (such as head trauma, stroke, hypoxia, anoxia, Central Nervous System tumor and infection, and medication intoxication, among others (45)) - never entered the procurement process (27). This problem has been also studied and shown to be particularly relevant in other countries (46–49), making it the second largest barrier. Reasons for possible donors not entering the procurement process that were identified in the Chilean study by Gonzalez Cohen and colleagues included having an unreliable referral method (phone call), unknown referral method, and lack of

knowledge of the conditions a patient must meet to be considered as a possible donor (27). To help solve that problem, the same group of researchers developed and implemented a smartphone application for making possible donor referral easier and faster, which was demonstrated to be efficacious in increasing referrals by 93% compared to the two previous years (50); solution that is aligned with the importance of early donor identification described in the literature (14,51,52).

The large number of possible donors discarded after entering the procurement process, the third barrier, can happen because of two main reasons: procurement process failures (53), and poor clinical condition of patients. Procurement process failures include maintenance issues (like local procurement coordination inexperience (54), lack of hospital support (51,55), size of the ICU (56,57), non-admission to the ICU (49), and unprepared clinical teams for treating a possible donor (52,58,59)), and coordination issues (14) (like unavailability of surgical ward, surgeons, other staff, or transportation for organs) (60). Factors contributing to poor clinical condition of possible donors include late referral (the patient lacks support in a crucial moment for organ maintenance), comorbidities, age, the admission cause, or socio-demographic factors.

Procurement process failures contributing to potential donor discards have been studied in the US and have been shown to respond to system and geographic factors (61,62) and local procurement coordination variability (63). Aspects of the clinical condition of possible donors that are associated with discards have been studied in some countries. Several studies describe the epidemiology of brain death (25,48,56,57,64–67), relating the cause of death (or cause of admission if the patient doesn't die) with the probability of becoming an organ donor. Thomson's study related the age of the donor, or the comorbidities they had before dying (68), and other demographic and social factors with the probability of becoming an organ donor, with the number (63) or quality of the organs retrieved (69,70), and transplantation outcomes (71,72).

Only Thomson's study analyzed how comorbidities, cause of death, and age relate with the probability of not becoming a donor (excluding familial refusals) (68), finding that non-donation

was significantly associated with situations where the potential donor had both brain death and another problem, including circulatory death, history of cardiac disease, chronic or liver disease, malignancy, absence of cerebrovascular disease, and ≥65 years of age (68).

Thomson's findings have somewhat limited application in the Chilean context, where donation after circulatory death is not permitted (30). This raises the question of whether patient characteristics still largely explain the probability of being discarded as a potential organ donor, or if procurement process failures dominate in this setting. Furthermore, if the diseases and injuries that can lead to brain death, mainly stroke and trauma (64–66), disproportionately affect low socioeconomic statuses (73–76), as well as the main causes for being discarded, such as malignancy and other pathologies, and these low socioeconomic status populations have a larger burden because of system inequities (access to education, segregation, access to healthcare, etc.), how much of the lack of organ donors is explained by structural inequities?

Patient socioeconomic status, other demographic variables, and comorbidities have been studied as determinants for becoming an organ donor, as well as the epidemiology of brain deaths. Most of the literature, however, fails to consider how all of these variables interact to determine whether patients become suitable candidates for certifying brain death and thus, having the possibility of becoming organ donors, which indeed can be an important source of inequity for that patients, but mostly for patients who need a transplant (77). Nonetheless, merging clinical and socio-demographic data at an individual level is not trivial, even less when those socio-demographic characteristics were not originally considered relevant at the moment of the establishment of the organ donor registry, which is the case in Chile.

Since the ideal scenario to understand how baseline patient characteristics explain the probability of being discarded as a possible organ donor is not feasible, we decided to approach the problem from a different perspective.

The distribution of different pathologies, age distribution, and social inequities in the population are some variables at the individual level that can introduce variability, but there are also other sources of variability that come from the LPC performance, and from the hospital where patients are procured. The relative importance of the variability contribution from each level of the system towards discarding possible organ donors is unknown and it has never been studied. If we consider municipal socio-demographic variables as proxies for the type of population served by each hospital and maybe the type of services each hospital provides, together with other structural variables, like level of complexity, and use them at the hospital level, we can account for much of the unmodifiable portion of the system. The variation found that is not explained by this unmodifiable portion could potentially be the portion that could be tackled with interventions.

The proposed study is innovative in two aspects. It moves one step back in the procurement process and describes the determinants for discarding possible donors who enter procurement follow-up, and does so by introducing a multilevel approach to account for variability in 3 structural levels, the individual, the hospital, and the LPC levels. This final approach is key to understanding the variables that explain the probability of being discarded as a possible donor, as well as from which level the largest source of variation comes from. Only understanding this makes proposing interventions for improving one of the main problems in the Chilean organ procurement and donation system possible.

2. Research question

To what extent do baseline patient, population, and hospital characteristics, and unknown sources of variation explain the probability of being discarded as a possible organ donor in Chile?

3. Methods

3.1 Study Design, participants, and setting

We conducted a multi-level study of all possible organ donors who entered the procurement process for organ donation (procurement follow-up) in all the public hospitals and private clinics in Chile from January 1st 2013 to December 31st 2022, clustered by 2 levels, hospital as level 1 and heath service (or LPC area) as level 2.

The National Coordination of Procurement and Transplantation (NCPT), which falls under the Ministry of Health, provided the database for analysis. This database was extracted from the Interconnected System of Organ Donation and Transplantation (SIDOT by its acronym in Spanish) and was anonymized to protect the identity of the patients. We considered all possible donors, regardless of their outcome (survived or died, and donation status), individual, or group characteristics.

This study was waived consent by the UW IRB (FWA #00006878).

3.2 Variables

Our primary outcome variable was being or not being discarded as a possible donor. To understand which patients fall in each category, we will explain the different final donation outcome or status. The final status, or organ donation outcome that a patient can have can be organ donor, familial refusals, contraindication, or discard. Out of these four organ donation outcomes, "discard" and "contraindicated" were considered as the dependent variable (taking the value of 1 in a binary variable), whereas "organ donor" and "familial refusals"[2] were considered as non-discard (taking the value of 0 in a binary value).

[2] It is worth noting that we chose to consider familial refusals in the same group as effective donors because most patients classified as familial refusals would have been effective donors if donation would

Besides the binary outcome described above, we also did an analysis of categorical outcome. In this case, we used the causes of discard and contraindication available in the database, and we proposed new classifications in order to improve the current one. Finally, we grouped those causes of discard and contraindication into four categories for further analysis.

The data cleaning process was particularly important because of the evolution of the causes of discard and contraindications, and the changing criteria for selecting each of them. In concrete, in the early years of the analyzed period there were less causes of discard and contraindications. We read all the "*observations*" field of the database (a variable where LPCs could further explain with words the reasons why the patient could not become an organ donor) to match previous causes to the new ones. While doing that process, the team noticed that there were a lot of misclassified patients, so a complete review of all the records was performed to ensure a unified standard criterion on the causes of discards and contraindications.

Beyond the outcome variables, our database contained potentially explanatory ecological and individual socio-demographic variables. We obtained information from the Department of Health Statistics and Information (78), the 2017 Census (79), a Social Development Index report from the *Universidad Autonoma* (80), the Observatory of the Ministry of Social Development (81), and the National Healthcare Fund (FONASA) (82). The independent ecological variables assigned to the hospital level were: municipality of site, % rural population, Municipality Development Index, % of poverty, average years of schooling, and % of native population. The structural hospital variables were: hospital complexity, public or private status, and whether it is a beneficiary of the Related Groups by Diagnosis (RGD) program.

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have been accepted. It could happen that a familial refusal could have been contraindicated if donation was accepted since we know about accepted cases that were contraindicated afterwards. Nonetheless, those are exceptional cases, so the possible dilution or exaggeration of findings these cases could introduce to the models are considered minimal.

The independent individual variables used were:

- **Socio-demographic[3]:** Gender (male=1).
- **Clinical[4]:** No data was accessed.

We decided to use these explanatory variables because they describe aspects of the population and setting that are unmodifiable or minimally modifiable and may limit how much impact interventions can have in improving the organ procurement system.

3.3 Data analysis

3.3.1 Evolution of organ procurement

We started by analyzing the relationship between the dependent and independent variables by using linear correlations, and their evolution throughout time by using descriptive statistics: frequencies, time trend graphs, averages and standard deviations, and rates. For analyzing changes over time, we used linear regression. For analyzing differences across LPCs we used ANOVA for normally distributed variables (addressed by Shapiro-Wilk test of normality) and Kruskal-Wallis for non-normally distributed variables (at a confidence level of 95%), with years as a time unit. We used Google Sheets, Google LLC, for data exploration, and R statistical software, version 4.0.2 (R Foundation), for statistical analysis.

3.3.2 Demographic and socioeconomic burden

To assess the primary outcome of discarded or non-discarded organ donation status (a binary outcome) we fitted multivariate logistic regressions for clustered data, considering each

[3] At the beginning, the ideal scenario was including Municipality of residence, Type of health insurance, and Nationality as part of the individual variables, but those data were not collected in the national organ procurement database, so they couldn't be included.
[4] Although there are clinical variables collected in the database, such as Cause of admission, biomarkers, comorbidities, blood type, and several laboratory tests, none of these were accessed due to technical issues with the database.

hospital as a level 2 cluster, and LPC as a level 3 cluster. To assess each discard as a category, we also fitted multivariate logistic regressions for the same clusters described above, but for each of the 4 groups of categories as a dichotomous variable. We used the technique of fitting univariate models first, and then fitting multivariate models by including all significant variables on their univariate models (at a confidence level of 95%) and removed them stepwise backwards if they were not significant (at a confidence level of 90%), until reaching a model with significant variables at a 95% confidence level.

The final model chosen for each outcome variable was the best significant model (lowest AIC/BIC, using ANOVA) with all significant independent variables (at a confidence level of 95%) and significant random effects for clustering levels. In the case where there were not significant differences between two models, the less complex was chosen. Finally, to reduce bias[5], we excluded private clinics and observations with missing data[6] only for these univariate and multivariate analyses. All these analyses were made in R statistical software, version 4.0.2 (R Foundation).

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[5] Expected bias comes from the fact that private clinics are located in wealthier settings but have worse organ donation outcomes.
[6] We only excluded 35 observations that had the sex variable missing.

4. Results

4.1 Data cleaning and findings

Between 2013 and 2022 there were 21,192 possible organ donors who entered procurement follow-up. Out of which 1,417 (6.69%) became effective organ donors, and 19,774 (93.31%) did not. Table 1 shows the different outcomes for all possible donors, and their percentages regarding the total number of possible donors and the total number of non-donors.

Table 1: *Number of possible organ donors by outcome and %.*

	N	% of Total	% of Non-donors
Total Possible Donors	21,192	100%	-
Donors	1,418	6.69%	-
Non-donors	19,774	93.31%	100%
Discards	18,115	85.48%	91.61%
Contraindications	296	1.40%	1.50%
Familial refusals	1,363	6.43%	6.89%

Out of the total non-effective organ donors (i.e., the sum of familial refusals, contraindications, and discards), the majority (13,492, 68.23%) had an "*observations*" field in the database with a description of the reason why they didn't become effective organ donors. This description, as well as all the patient data, are filled by the procurement nurses at the LPC level or less frequently at the CC level. We used this "*observations*" field to determine whether the cause and classification of non-effective outcomes were well assigned, and also to match previous causes to current available ones. We found that 194 (0.98%) patients were misclassified (for example, classified as a contraindication when they were, indeed, a discard). For re-classifying these patients we used the following definitions:

- **Discard:** A patient who does not meet the criteria for becoming an organ donor and **was not** certified as brain dead.
- **Contraindication:** A patient who does not meet the criteria for becoming an organ donor after **being certified** as brain dead.
- **Familial refusal:** A patient who was certified as brain dead whose family was interviewed for organ donation, but refused, whether because the patient's will while alive was to not become an organ donor, or because the family didn't authorize the donation.

After re-classifying the former 194 patients in their real outcome, we realized that 1,675 (8.47%) patients were misclassified in their cause that lead to that outcome (discard, contraindication, or familial refusal[7]). On the other hand, the cause "other" (658), which is used for causes not listed in the platform, was more frequent during the first years because not all the modern causes existed in the system. After matching them to the more modern causes of discard, 549 (83.43%) were re-classified. If we consider them in the previous total, we would have that 2,225 (11.25%) patients were misclassified. Table 2 shows the detail of misclassifications for both outcomes and causes of outcome.

Table 2: *Number of non-donors misclassified, and their %.*

	N	**% of Non-donors**	**% of Observations**
Non-donors	19,774	100.00%	-%
Observations field	13,492	68.23%	100.00%
Misclassified outcome	194	0.98%	1.44%
Misclassified cause w/o *other*	1,675	8.47%	12.41%
Misclassified cause w/ *other*	2,225	11.25%	16.49%
Correctly classified	11,073	56.00%	82.07%

[7] It is important to note that the number of misclassified patients in their cause of outcome is underestimated since we did not correct the causes of familial refusal because it was beyond the scope of this project (they are not discards nor contraindications). We expect this number to increase substantially if including them in future work.

We must highlight that 31.77% of non-donor observations did not have information in the "*observations*" field. Since we used that field to reclassify misclassified patients, there is still a probability of having more misclassified patients that we can't reclassify with the available information. This means that we can't assure having the correct classification in almost 1/3 of the observations. In other words, those observations could follow the same misclassification pattern observed in the "*observations*" field group, or they could have been correctly classified by the LPCs. Expecting an upper limit of 1,036.

Finally, we exclude 490 observations because 24 were duplicated and 466 were not referred to LPC and thus, never entered procurement follow-up as possible organ donors.

4.1.1 Original and new classifications for causes of outcome

4.1.1.1 Original classification

The original classification, including those for familial refusal, had 34 causes (by the end of 2022), where 5 of them were for familial refusals, and the rest for discards and/or contraindications (with some differences between causes of discard and contraindication). Since there were causes that had too few observations, had different spelling between discard and contraindication, or changed their name over time, we standardized their names, definitions, and to what types of outcome they could be assigned.

Table 3 shows all the causes by outcome with the criteria to inform the decision for reclassification.

Table 3: *Causes of outcome available at the database, displayed by outcome, and with criteria for reclassification.*

	Discards	Contraindic.	Refusals	Criteria
1	No recipient	No recipient	-	-
2	Sub-optimal donor	-	-	-
3	Age	-	-	-
4	Hemodynamic failure	-	-	-
5	Multi-organ failure	Multiorgan failure	-	Even though this cause is the same, it is spelled differently in both outcomes.
6	Stationary GCS	-	-	-
7	Unavailability of ICU bed	-	-	Should all be classified as maintenance care because of its broader implication.
8	Unavailability of maintenance care	-	-	-
9	Can't diagnose brain death (BD)	-	-	-
10	Withholding treatment	-	-	-
11	Neurological improvement	-	-	-
12	CPA (Cardiopulmonary arrest)	CPA	-	-
13	Uncontrolled septic process	Uncontrolled sepsis	-	Even though this cause is the same, it is spelled differently in both outcomes.
14	Underlying pathology	Underlying pathology	-	-
15	Transfer to another healthcare center	-	-	-
16	No family available for donation interview	No family available for donation interview	-	-
17	Hemodilution	Hemodilution	-	-
18	No forensic authorization		-	-

19	-	-	Judicial denial	This refers when a prosecutor does not allow the procurement because of legal issues. As it is not the family who denies, shouldn't be classified as Refusal, but as discard or contraindication.
20	Unknown CPA cause	-	-	Having unknown causes can happen to any diagnosis, not only CPA, an inclusive definition should be considered.
21	Refusal while alive	-	Refusal while alive	Should always be classified as Refusal because the donation interview was performed.
22	Registered as non-donor in national registry (NDNR)	-	Registered as NDNR	This shouldn't be included in both discard and refusal.
23	Family doesn't recognize donor status	-	Family doesn't recognize donor status	Should always be classified as Refusal because the donation interview was performed.
24	Familial refusal	-	Familial refusal	Should always be classified as Refusal because the donation interview was performed.
25	Parents or legal tutors don't authorize donation	-	-	Should be classified as Refusal because the donation interview was performed.
26	COVID-19 (5 classifications)	COVID-19 (1 classification)	-	As we are not interested in understanding the sub-causes due to COVID-19, we decided to group everything under one cause.
27	Without referral to LCP	-	-	Shouldn't be considered as a possible donor, and be under another outcome if the aim of this cause is to show the number of patients not referred.
28	-	Unavailable critical care bed for possible recipient	-	This was used just once, so we decided to move it as a sub-cause for other.
29	-	Lack of clinical history	-	This could happen at any point throughout the process, should be included as a cause of discard. Currently, in discards these patients are classified whether as suboptimal or underlying pathology.
30	-	Family retracts	-	Should be classified as Refusal because the donation interview was performed.
31	-	Family retracts due to logistic issues	-	Should be classified as Refusal because the donation interview was performed.

32	-	Positive serology for transmissible infections (HIV, Hepatitis B and C, Chagas, and others)	-	This could happen at any point throughout the process, should be included as a cause of discard. Currently, in discards these patients are classified whether as suboptimal or underlying pathology.
33	-	No transplantation teams available	-	This was never used correctly, so we decided to move it as a sub-cause for other.
34	Other	Other	-	-

After standardizing all existing causes by following the previous criteria, we ended up with 20 “new” causes of discard/contraindication. Table 4 shows them, and whether they could be used as cause of discard and/or contraindication. From now on, causes for familial refusal are excluded.

Table 4: Causes of outcome from database used for analysis.

	Cause	Discard	Contraindication
1	No recipient	✓	✓
2	Sub-optimal donor	✓	×
3	Age	✓	×
4	Hemodynamic failure	✓	✓
5	Multiorgan failure	✓	✓
6	Stationary GCS	✓	×
7	Unavailability of maintenance care	✓	×
8	Can't diagnose brain death	✓	×
9	Withholding treatment (WT)	✓	×
10	Neurological improvement	✓	×
11	CPA	✓	✓
12	Uncontrolled septic process	✓	✓
13	Underlying pathology	✓	✓
14	Transfer to another healthcare center	✓	×
15	No family available for donation interview	✓	✓
16	Hemodilution	✓	✓
18	No forensic authorization	✓	✓
19	Registered as NDNR	✓	✓
19	COVID-19	✓	✓
20	Other	✓	✓

4.1.1.2 New classification

When reviewing the classifications, we noticed that some patient or process characteristics were repeated, which were not accurately described by the original causes. To further improve the original classification and better inform the real cause of discard/contraindication, we included and propose adding 8 new causes of discard/contraindication. Table 5 shows them, including whether they could be used for discards and/or contraindications.

Table 5: *New causes of outcome proposed from database analysis.*

	Cause	Discard	Contraindication
21	Unspecified etiology	✓	✓
22	Attending physician talks about organ donation	✓	✓
23	Familial refusal before brain death	✓	×
24	No center accepts organs	✓	✓
25	No patient identification	✓	×
26	GCS > 7	✓	×
27	Neurosurgical solution	✓	×
28	Without neurological cause	✓	×

We also propose including 39 new **sub-causes** to the actual causes to have a more granular definition of why a patient was discarded or contraindicated, which are shown in Table 6. Albeit these sub-classifications will not be used for statistical analysis, the main reason for proposing them is that we would like to know which patients did not continue because of their underlying conditions, and which because of process inefficiencies. There are also other sub-causes that, even though they could be major causes by themselves, had too few observations to

be considered as a single cause for this analysis. The definitions for the new causes and sub-causes can be found in Appendix 2.

Table 6: *Sub-causes proposed by outcome and cause.*

	Sub-Cause	Discard	Contraindication	To use under cause
1	Central coordination does not validate patient	✓	✓	Age, Underlying pathology, Suboptimal donor, other
2	Transplantation team does not validate patient	✓	✓	
3	Risk behavior (drug use or convicts)	✓	✓	
4	No potentially removable organs	✓	✓	
5	Lower than minimum weight	✓	✓	Age
6	No neurosurgeon or neurologist	✓	×	Can't diagnose brain death
7	Ventilatory movements	✓	×	
8	Has reflects	✓	×	
9	Complementary test shows brain activity	✓	×	
10	Half-life of CNS depressant too long	✓	×	
11	Triggers ventilator	✓	×	
12	Hypernatremia	✓	×	
13	Hypercapnia	✓	×	
14	Hypothermia	✓	×	
15	Hypotension	✓	×	
16	Hemodynamic instability	✓	×	
17	Metabolic instability	✓	×	
18	Spontaneous ventilation	✓	×	
19	Non conclusive Apnea Test	✓	×	

20	Negative Apnea Test	✓	×	
21	Sedated patient	✓	×	Can't diagnose brain death, Stationary GCS, Neurological improvement
22	Absence or deficiency in maintenance / handling	✓	✓	All
23	Absence or withdrawal of LPC	✓	✓	
24	Lack of resources	✓	✓	
25	Treating physician discards patient	✓	×	
26	Unavailable critical care bed for recipient	✓	✓	Other
27	No transplantation teams available	×	✓	
28	Family doesn't understand BD concept	×	✓	
29	Possible medical negligence (legal)	✓	×	Mainly other
30	Without CPR	✓	×	CPA
31	Patient referred after dead	✓	×	
32	GCS=3 with some neurological activity	✓	×	Stationary GCS, Can't diagnose BD
33	Familial or patient will	✓		WT
34	Without antibiotic treatment	✓	×	Uncontrolled septic process
35	Decision is not communicated to LPC	✓	×	CPA, WT, Transfer to other healthcare center
36	Unavailable bed due to COVID contingency	✓	×	Mainly Unavailability of maintenance care
37	COVID contingency infeasibility	✓	✓	Mainly suboptimal donor
38	ICU physician doesn't provide bed	✓	×	Mainly Unavailability of maintenance care
39	Neurologist or neurosurgeon says patient will not fall to BD	✓	×	Many

4.1.1.3 Classification for statistical analysis

Finally, we grouped all the new discard and contraindication causes (not including sub-causes) into 4 groups according to their source:

- **Social:** Causes that are explained by social background, whether at an individual or at a higher level.
- **Patient:** Causes inherent in the patient, where clinical intervention can't interfere with the discard.
- **Process:** When a patient is discarded due to a process failure, like lack of resources, delays, or human errors.
- **Other (Patient, Process, or Social):** All the causes of discard where their sub-cause or underlying reason can belong to one of the previous 3 groups, but because of lack of further information, we couldn't assess their true classification. An example of this is *Withdrawal of treatment*, that can happen upon familial request (social), because clinicians decided it without informing the procurement team (process), or because of specific health issues of the patient (patient).

Table 7 includes all 28 causes[8] included in each group[9] and their frequency.

[8] To see a table with sub-cause frequency, go to Appendix 3.
[9] To see the full criteria used to group these causes, go to Appendix 4.

Table 7: Causes of discard and their frequency by group.

	Social	Patient	Process	Other
No family available for donation interview	75			
No patient identification	9			
Transfer to another healthcare center	809			
Familial refusal before brain death	36			
Stationary GCS		1,644		
COVID-19		510		
GCS > 7		21		
Neurological improvement		4,258		
Registered as NDNR		179		
Neurosurgical solution		74		
Without neurological cause		27		
Attending physician talks about organ donation			27	
Hemodilution			31	
Unavailability of maintenance care			494	
Can't diagnose brain death				438
Withholding treatment				702
No center accepts organs				20
Other				124
Underlying pathology				2,531
CPA				2,130
Uncontrolled septic process				431
No forensic authorization				34
Sub-optimal donor				874
Age				1,111
Unspecified etiology				179
Hemodynamic failure				1,033
Multiorgan failure				527
No recipient				83
Total	929	6,713	552	10,217
% Total discards	5.05%	36.46%	3.00%	55.49%

4.2 Evolution of organ procurement

4.2.1 Time trends

The total number of patients that entered procurement follow-up as possible donors remained stationary from 2013 to 2018 but started to grow afterward. The most important contributor for that possible donor growth is the increase in discarded patients. Figure 1 shows the temporal evolution of all possible donor outcomes for the studied period.

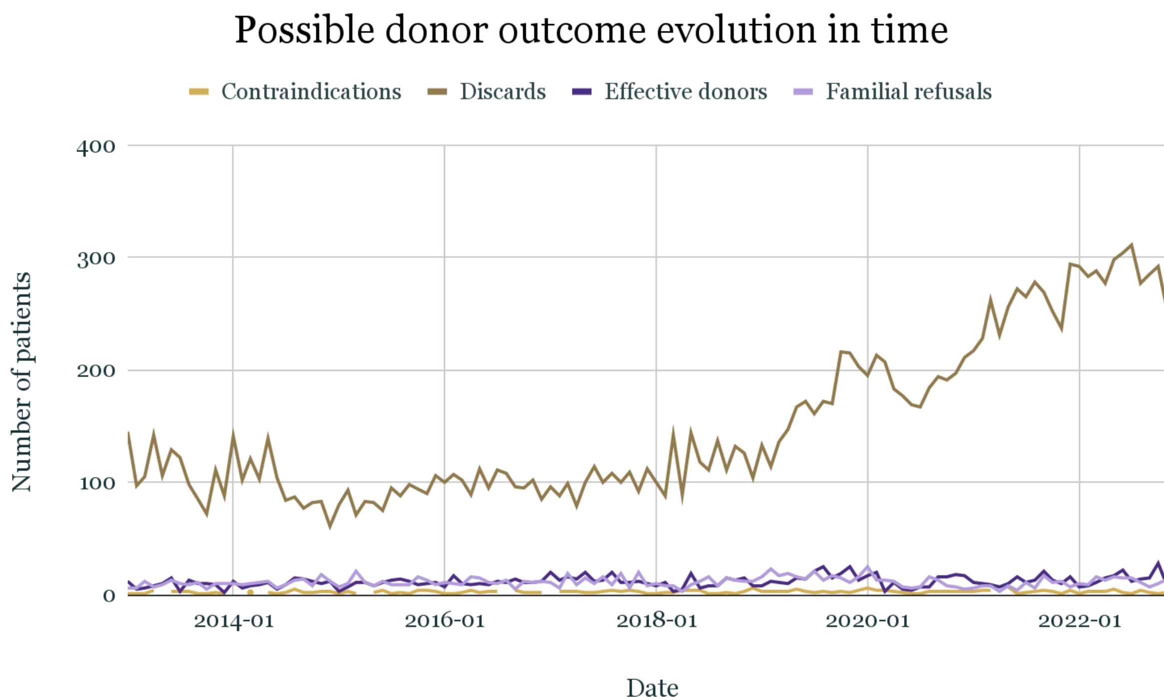

Figure 1: *Possible donor time trends between 2013 and 2022 for each of the possible outcomes: discarded, contraindicated, familiar refusal, and effective donor.*

We can notice that while discarded patients tend to grow over time, the other 3 outcomes (contraindications, familial refusals and effective donors) have been stable.. To compare the periods before and after the turning point for Discards, Table 8 shows the slopes for linear regressions against time, Figure 2 shows the evolution from 2013 to 2017, and Figure 3 shows it for 2018-2022, both with linear trends for each series.

Table 8: *Slope estimators and p-values of linear regressions for each outcome variable, for the whole and for the first and second half of the period.*

	2013-2022		2013-2017		2018-2022	
Outcome	Slope	p-value	Slope	p-value	Slope	p-value
Total possible donors	1.78	< 0.0002*	0.002	0.99	3.51	< 0.0002*
All outcomes						
Contraindications	0.01	0.0146*	0.02	0.05	0.0006	0.955
Discards	1.71	< 0.0002*	-0.18	0.168	3.49	< 0.0002*
Effective donors	0.05	0.0003*	0.10	0.00015*	0.07	0.105
Familial refusals	0.01	0.243	0.06	0.027*	-0.04	0.289
Dichotomous						
Discarded	1.72	< 0.0002*	-0.16	0.223	3.48	< 0.0002*
Non-discarded	0.06	0.00169*	0.16	0.0001*	0.03	0.625

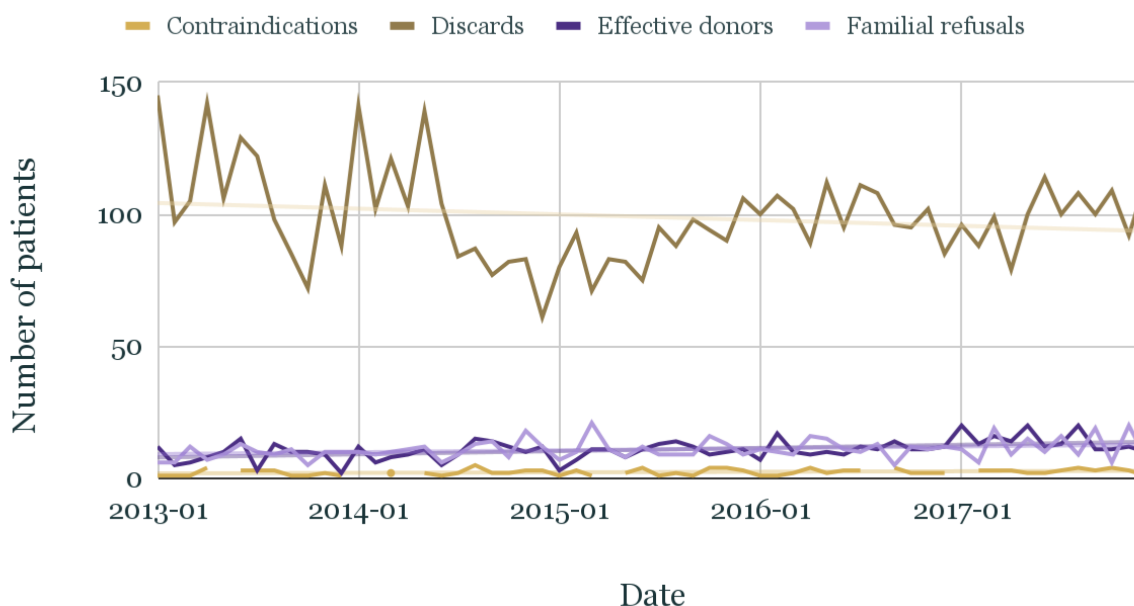

Figure 2: *Possible donor time trends between 2013 and 2017 for each of the possible outcomes: discarded, contraindicated, familiar refusal, and effective donor, and linear trends.*

As shown in the linear trends, and evidenced by the slopes in Table 8, during the first 5 years of analysis, the slope of all curves remain close to zero, meaning that there was no growth

in any of the outcomes of the patients (excepting familial refusals and effective donors that had significant growing slopes, albeit tending to zero). Whereas in the second half of the period there is a significant positive slope for discarded patients, but not for the rest of the outcomes, which remained close to zero and non-significant.

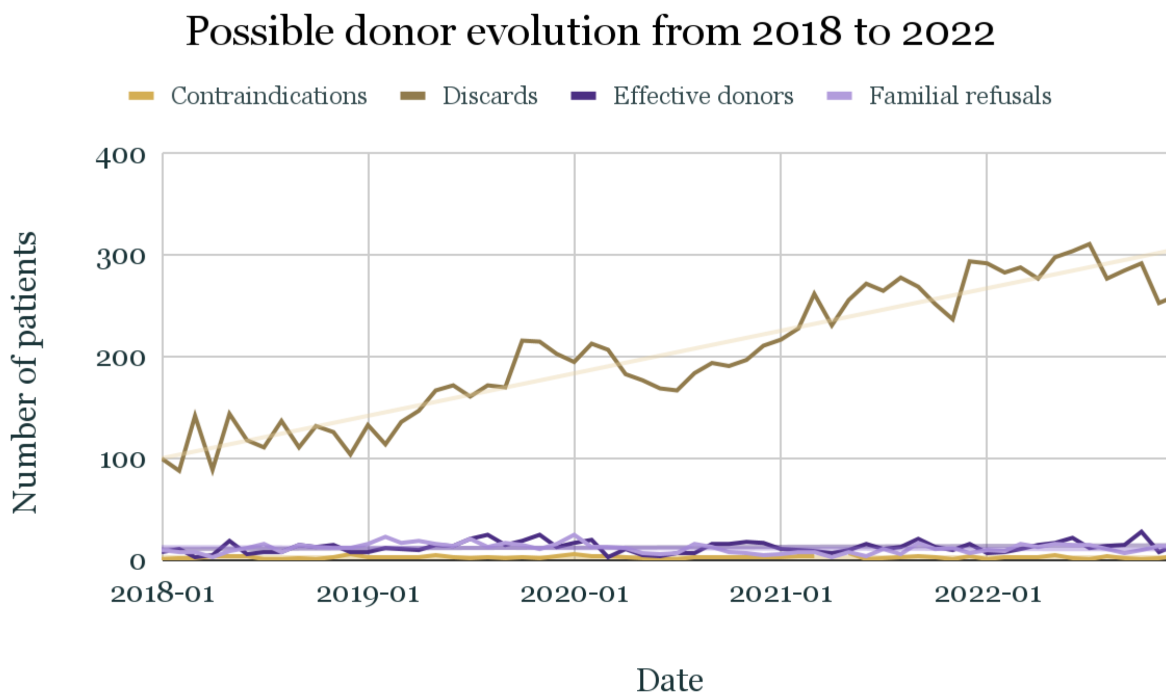

Figure 3: *Possible donor time trends between 2018 and 2022 for each of the possible outcomes: discarded, contraindicated, familiar refusal, and effective donor, and linear trends.*

To see the issue from another perspective, we converted the number of discards and non-discards into rates, by using Chile's 2017 census population, where we used the standard rate for organ donation, per million population (pmp). Figure 4 shows the time trend of both outcomes throughout the years, where we can see that while discards grow in time (slope = 14.23, p-value = 0.0007), non-discards remain unchanged (slope = 0.45, p-value = 0.164), just as in the previous analysis.

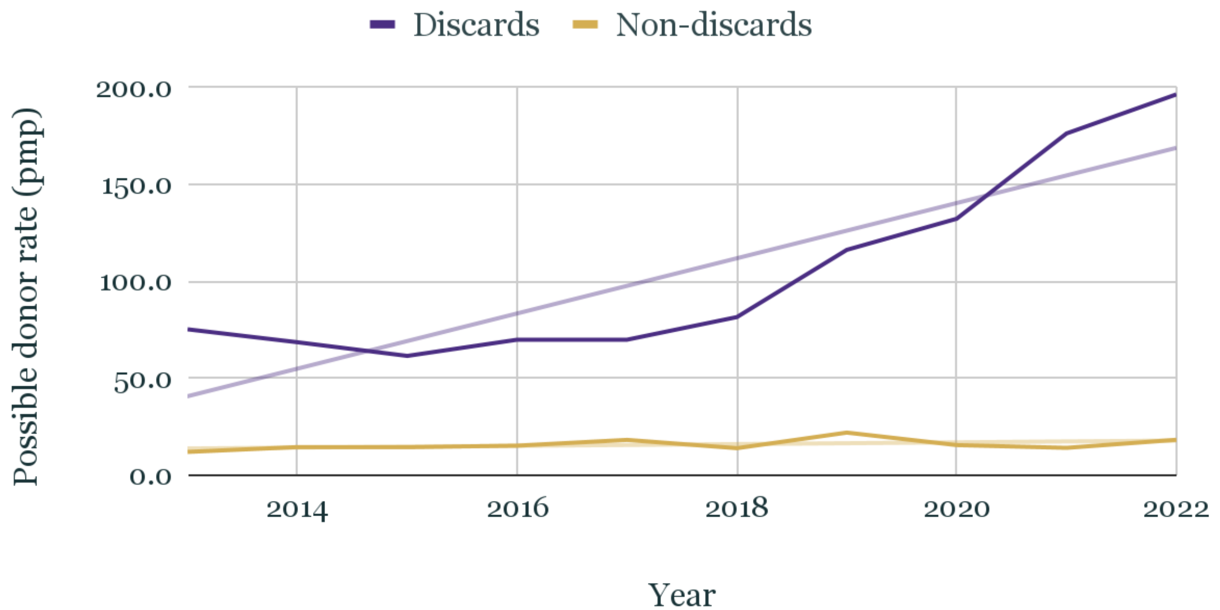

Figure 4: *Possible donor rates time trends between 2013 and 2022 for the dichotomous outcome (per million population) and their respective linear trends.*

If we look at the evolution of donors and non-donors in time and compare them with the number of healthcare centers (hospitals and private clinics) that entered the procurement system (by reporting possible donors in procurement follow-up) in Figure 5, we can see that there is a correlation between the number of discarded patients and the number of hospitals and clinics in the system (correl. = 0.95). Correlation that is insignificant for non-discards (correl. = 0.28).

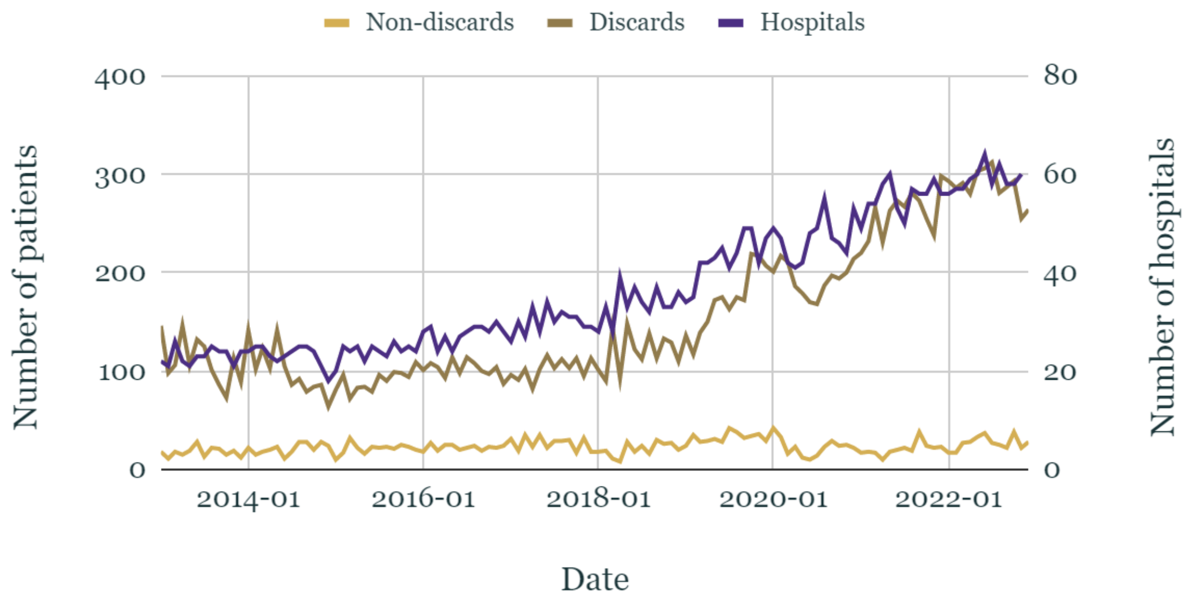

Figure 5: *Possible donor time trends between 2013 and 2022 for the dichotomous outcome (left vertical axis), and its comparison with the number of procuring hospitals in the system (right vertical axis).*

4.2.2 Local Procurement Coordinator (LPC) analysis

We analyzed the 28 health services that have a LPC, and at least 1 hospital participating in the procurement activity. We used their codes to facilitate a blind analysis, albeit coding all private centers as health service 0. A list of all codes and names can be found in Appendix 5.

Figure 6 shows a large variability in the number of discarded and non-discarded patients, as well as in the percentage of discarded patients. In fact, we found significant differences among LPCs for all possible donors, discards, and non-discards (p-values < 0.000026[10]).

[10] It may be common to find this p-value for different tests because it is the lowest p-value provided by R.

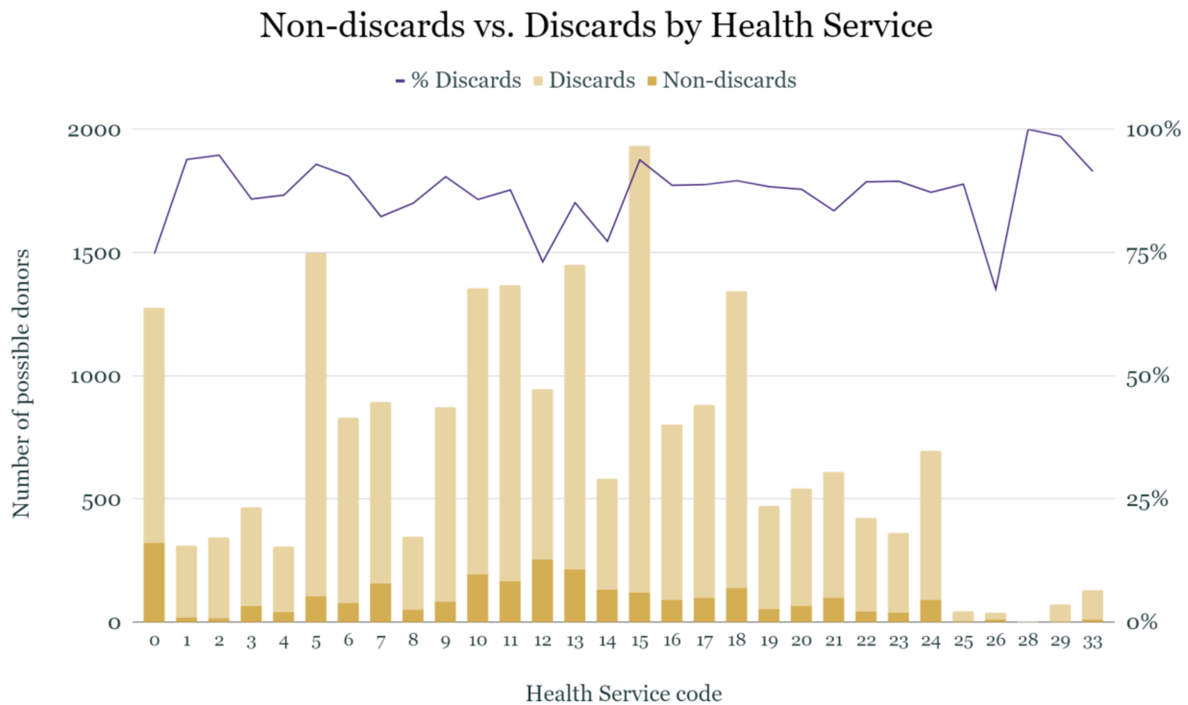

Figure 6: *Aggregated number of discards and non-discards for each Health Service, and percentage of discards*

If we normalize by population, this is, building rates pmp for each LPC, we would observe that, even though there are some changes for certain Health Services, the overall differences remain the same for possible donors (p-value < 0.000026), discards (p-value < 0.00001), and non-discards (p-value < 0.000015). Figure 7 shows the former, but in it we did not consider the private centers anymore because it is not possible to calculate their population size due to how the private sector in the country is structured.

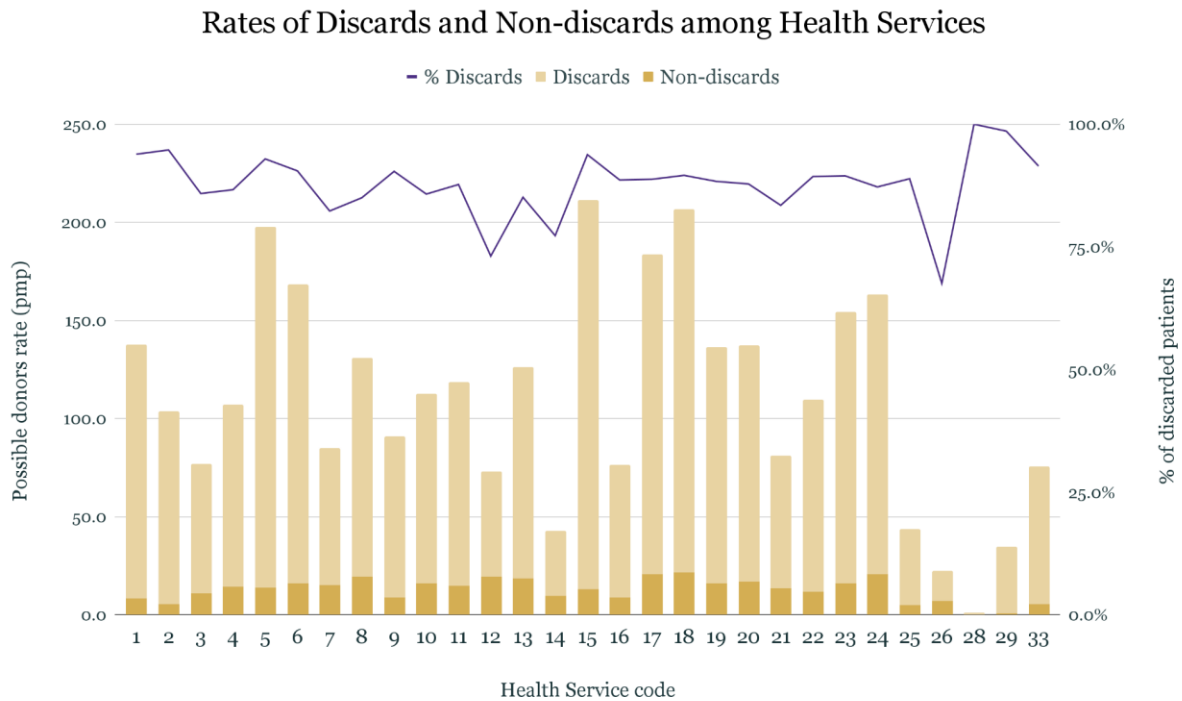

Figure 7: *Aggregated rates per million population (pmp) of discards and non-discards for each Health Service, and percentage of discards.*

Respecting the four groups of causes of discard we created and analyzed, we can also observe a large variation among LPCs, as shown in Figure 8, suggesting that each group of cause has its own relative weight depending on the LPC.

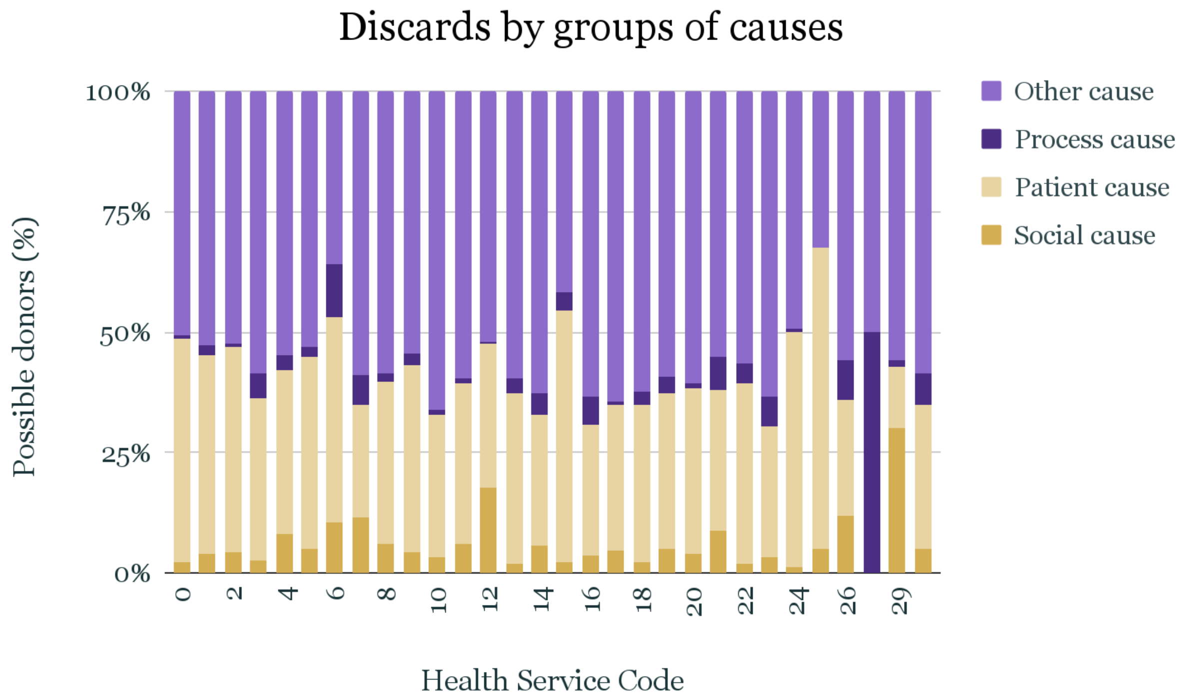

Figure 8: *Distribution of groups of causes of discard among Health Services represented as a percentage of the total possible donors in each Health Service.*

4.2.3 Description of other variables

Most patients who entered procurement follow-up were male (63.43%), something that maintained for all outcomes: discards, contraindications, familial refusals, and effective donors (64%, 64.53%, 57.23%, and 61.92%, respectively).

The total number of healthcare centers that have had possible organ donors was 111, where 67 (60.36%) are public centers, and 44 (39.64%) are private. The total average number of hospitals by LPC is 2.3 ± 1.37 (range 1 - 6), and the median number of private clinics by region is 1.0 (range 0 - 22), where the maximum is reached in the Metropolitan Region.

Regarding the complexity of the healthcare centers studied, 93 (83.78%) were classified as high complexity, and 18 (16.22%) as medium complexity, where the “Araucanía Sur” LPC has

the least proportion of high complexity hospitals, serving 4 medium complexity hospitals out of a total of 5 (80%).

Regarding the RGD participation status, 94 healthcare centers participate in the RGD reimbursement program, and all the hospitals in the North Macro Region of the country don't participate in the program.

Finally, Table 9 shows the descriptive statistics for the socioeconomic variables we included in the analysis, and Table 10 shows the correlation between all the variables, where all of the correlations were significant, except the ones with the circle.

Table 9: *Average, standard deviation, minimum and maximum of socioeconomic variables at the hospital level, separated as all hospitals and only public hospitals.*

	All healthcare centers		Only public hospitals			
	Average	St. Dev.	Average	St. Dev.	Min.	Max.
Muni. Development Index (0,1)	0.59	0.085	0.54	0.084	0.389	0.818
Poverty (%)	9.92%	3.05%	10.84%	3.08%	4.80%	17.60%
Rurality (%)	7.38%	9.61%	10.16%	9.68%	0.00%	37.90%
Years of Schooling (N)	11.9	1.1	11.2	1.1	9.3	14.7
Native population (%)	5.92%	4.78%	7.32%	4.84%	2.40%	20.20%

Table 10: *Correlations between all variables.*

	Discard	Public	High Comp.	RGD	MDI	Poverty	Rurality	Y. school.	Natives	Gender
Discard	1	0.09	-0.01°	-0.04	-0.06	0.1	0.06	0.12	0.04	0.03
Public		1	0.05	-0.1	0.03	0.25	0.15	-0.32	0.13	0.03
High Comp.			1	-0.02	0.01	-0.1	-0.35	0.14	-0.24	0°
RGD				1	0.05	-0.16	-0.02	0.13	-0.18	0.01°
MDI					1	-0.09	-0.09	-0.07	0.02	0°
Poverty						1	0.41	-0.7	0.29	0.02
Rurality							1	-0.56	0.34	0.02
Y. school.								1	-0.35	-0.02
Natives									1	0.02
Gender										1

4.3 Demographic and socioeconomic burden

We started with a total of 21,192 possible donors, 18,411 discarded and 2,781 non-discarded. Nevertheless, we decided to exclude private centers because of the possible introduction of bias due to differences in socioeconomic variables since private clinics are located in wealthier settings but have worse organ donation outcomes[11]. So, for the dichotomous outcome variable of being discarded, we included a total of 19,915 possible donors, 17,456 discarded and 2,459 non-discarded patients. Our final model included all three levels: the individual, the hospital, and the LPC level. From all the explanatory variables explored, three reached a significant level ($p<0.05$) on the multivariate model: the patient's gender, and the poverty and rurality levels of the municipality where the hospital is located. Table 11 shows the odds ratios (OR) for those significant variables with their respective p-value, both for the univariate and multivariate models. As well as the variance introduced to the model by the random effects of the hospital and LPC levels and confidence intervals for the multivariate model.

We can see that the poverty level has a much larger weight in the model than rurality, and even more than the gender of the patient. For each extra percent of poor population in the municipality, a patient is 28,160 times as likely to be discarded. Similarly, for each extra percent of rural population, a patient is 14.65 times as likely to be discarded, whereas a male patient is just 1.2 times as likely to be discarded as a female. The large intercept provides the information that a patient will always have large odds of being discarded. Finally, the two significant random effects indicate that there is a significant variation among both hospitals and LPCs.

[11] To be published: The kidney distribution system for transplantation in Chile explained according to Game Theory: How theoretical generosity transforms into selfishness. González Cohens F., González Bulboa C., González Fuenzalida F.

Table 11: *Results for the univariate and multivariate logistic regressions for 3 level clustered data, for discarded as dependent variable*[12].

	Univariate models		Multivariate models	
	Fixed Effects			
Independent Variable	OR	p-value	OR	p-value
Intercept	8.66	<0.0002	2.12	0.00373
Gender (male)	1.21	<0.00023	1.21	<0.000298
High Complexity	0.53	0.131	-	-
RGD	0.77	0.28	-	-
MDI	0.9998	0.0493	-	-
Poverty	418,730	<0.00081	28,160	<0.00015
Rurality	50.6	0.000223	14.65	0.00728
Years of schooling	0.76	<0.00015	-	-
Natives	193.4	0.0191	-	-
	Random Effects			
Level			Variance	CI (95%)[13]
Hospital Level	-	-	0.1326	(0.212 , 0.569)
LPC level	-	-	0.1243	(0.0998 , 0.57)

When we conducted four additional analyses, with each of the four groups of causes for discard as the outcome variables, we found different effects. In all of them, the only consistent result was the significant variation between hospitals. The gender of the patient was significant in all models, except in the group Other, whereas rurality was significant just for the group Other and Social. Interestingly, poverty, which was the most significant variable in the global model,

[12] All models were fit with 3 levels, though, for simplicity, we report variance and CIs only for the multivariate model.

[13] The CIs for the random effects must not contain 0 to be significant. But, since variance is not an estimator, it not will not necessarily be included in its CI.

was not significant for the group Process, which instead had Years of Schooling as a significant inversely related predictor. For the Social and Other groups, the variation among LPCs was not significant. Table 12 shows a summary of the OR and Variances of the significant variables in the multilevel models for all groups to facilitate comparison[14].

Table 12: *Results for the multivariate logistic regressions for 3 level clustered data, for the 4 groups of discards, each one as a dependent variable.*

	Social Cause		Patient Cause		Process Cause		Other Cause	
	Fixed Effects							
Independent Variable	OR	p-value	OR	p-value	OR	p-value	OR	p-value
Intercept	0.0057	<0.0021	-	-	31.94	0.00507	-	-
Gender	1.45	<0.0201	1.38	<0.0337	1.31	0.008	-	-
Poverty	1,448,342	0.0054	2,575	<0.0102	-	-	663,187	<0.0002
Rurality	231.8	0.0012	-	-	-	-	9.85	0.041
Years of Schooling	-	-	-	-	0.64	<0.0029	-	-
	Random Effects							
Level	Variance	CI	Variance	CI	Variance	CI	Variance	CI
Hospital	0.78	(0.68 , 1.17)	0.125	(0.203 , 0.56)	0.226	(0.16 , 0.9)	0.2897	(0.41 , 0.72)
LPC	-	-	0.233	(0.29 , 0.72)	0.48	(0.31 , 1.05)	-	-

[14] To see the full tables of univariate and multivariate models for each group, go to Appendix 6.

5. Discussion

It is interesting to see the evolution of possible donor outcomes throughout the time, where there was a notorious change in the trends since 2018, where just discarded patients started growing, and in fact, erased the trends that the other outcomes were having before. We attribute that change to several things.

In 2018, Gonzalez Cohens et al. (27) showed that the largest bottle neck in the procurement process was the lack of detections and referrals of possible donors (i.e., patients entering procurement follow-up), which indeed was the problem between 2013 and 2017. Three changes occurred which may have increased referrals. A new key performance indicator was introduced to the Balanced Scorecard of public hospitals[15] in the end of 2017 and the beginning of 2018, which started measuring referrals of possible organ donors, which might explain part of the observed growth. A technological tool for easing the referral of possible organ donors was sequentially implemented in 6 hospitals of the country between 2019 and 2022 (50), increasing the overall number of patients who entered procurement follow-up, which could also have influenced the observed increase. An increase in the number of participating hospitals. We observed a large correlation between the number of discards (and patients entered for follow-up) with the number of hospitals that started having procurement activity throughout time. This correlation suggests that the increase in possible donors is largely explained by the number of procuring hospitals and not necessarily by an increase in referrals by participating hospitals. These three changes were partially offset by a national audit of the procurement activity that showed that patients registered as non-donors in the National Registry of Non-Donors (NRND) had become donors despite their former decision. As a consequence, the National Audit Office

[15] According to the American Society for Quality, the Balanced Scorecard is a management system that provides feedback on both internal business processes and external outcomes to continuously improve strategic performance and results.

mandated discarding all patients that were registered in that list (83), something that needed to change the law to reverse that mandate (84). This mandate may explain at least part of the growth in discards, and the steadiness in effective donors. The net effect was a steady line in possible donors (slope = 0) who entered follow-up between years 2013 and 2017, which was "replaced" by a growing trend (slope = 3.51) in the 5-year period after. It would be interesting to study to what extent all of the possibilities we mentioned above, explain the increase of possible organ donors and thus, discards.

Chile faced a shift on the reason why it has been hard to improve organ donation rates. From the lack of possible organ donor referrals mentioned above, it moved to the large number of patients discarded as possible donors. Our main findings suggest that the underlying reasons for this huge bottleneck in the procurement process are the huge differences among hospitals and LPCs. Something that we showed both by describing the huge disparity among LPCs (in terms of number of possible donors entered to procurement follow-up, number of non-discarded patients, rates, and percentage of discards) and by the significant variation found in the multivariate regressions. This suggests that one of the main sources of variability among LPCs are indeed, those same LPCs themselves. In other words, the way each LPC approaches and performs their duty is not standardized at all, and varies from place to place, having as result completely different organ donation outcomes across LPCs. Things that might explain this situation are the different composition of the units, for example, the different levels of experience each nurse has (within and between LPCs), their technical knowledge, the number of nurses, how they relate with other clinicians, or even the relative support they receive from both the hospitals and the health service (54).

The only patient variable we could access from the national database and that we included in the analysis was significant, showing that in almost all models a male patient had higher odds to be discarded. Which could mean that the male population has worse conditions both physical

and social, than the female counterpart. Nonetheless, this variable was not significant for the Other group, suggesting that it may be significant just because it is the only characterization available for the patient level, or because the male population is overrepresented in the database.

The significant variance introduced by the hospitals where patients are procured, which was significant in all the models studied, suggests that the different way in which procurement is shaped at the hospital level is one of the most important sources of variability in the procurement activity. This is challenging in that variability could come from several different parts. For example, it could come from the knowledge of physicians or other clinicians in how to maintain possible donors, of the organ transplantation and donation law, of their role in the procurement process, or even unawareness of the procurement process at all. It could also come from lack of resources of the hospital, like not having neurologists or neurosurgeons available for evaluation or brain death certification, unavailability of complementary brain activity or organ status tests, or even unavailability of therapeutic drugs. It could also come from the relative power the LPCs have on each hospital, which could be really low in hospitals that are not the one where they are located. It is crucial to understand to what extent these possible sources of variability can jeopardize the procurement activity because they are targets that can be modified to improve the organ donation activity.

It is worth noting that the largest causes of discard are *Stationary GCS* and *Neurological Improvement*, even though their frequency has maintained relatively stable throughout the years. Would this be because the professionals who refer possible donors are not well trained for doing so or for measuring the GCS? Or maybe because the definition of a possible donor is not completely correct and could be improved? For example, the most important condition a patient must meet to be considered as a possible donor is having a GSC lower than 7 points. While GCS was developed in 1974 for predicting outcomes of patients with head trauma (85), there are other instruments that better predict survival or death as outcomes of patients with other neurological

conditions. The Full Outline of Unresponsiveness (FOUR) (86) includes the essential parts of the GSC and adds brainstem reflexes and respiration (45), making it useful for patients with trauma and stroke (86). The National Institutes of Health Stroke Scale (NIHSS) is widely used to evaluate acuity of stroke patients and works also well on intracerebral hemorrhage patients (87). While Ossama et at. found that all three scores similarly predicted outcomes at 24 hours for acute ischemic stroke, they found that NIHSS better predicts after 72 hours (88). If GCS was replaced or complemented by one or both of these alternative measurements, some of the patients discarded as *Stationary GCS* or *Neurological Improvement,* wouldn't have entered procurement follow-up because they would have been classified as not meeting possible organ donor criteria. The inclusion of one or both of these scores should be further studied to improve the procurement activity and better target the efforts made to obtain effective organ donors. Including the cause of admission to the analysis could help in recognizing which types of causes of admission are being discarded the most due to *Stationary GCS* or *Neurological Improvement,* which could in turn, help studying the inclusion of the scores.

The most interesting part of our findings is how important other "external" socioeconomic factors are for the procurement activity. Rurality, for example, was an unexpected significant variable. We must note that despite the average rurality in the studied hospitals is very low (because large and complex hospitals are usually located in urban areas), it greatly predicts if a patient would be discarded, this is, the more rural the area were the hospital is located, the more likely the patients to be discarded. Similarly, and even worse, was the absurdly large odds found for the variable poverty. In all the models where poverty was significant, the odds of discarding a patient were more than two thousand, twenty-eight thousand, sixteen thousand, and even 1 million. This suggests that there is an enormous inequity in the country, which is noticeable even in the organ donation system. What is even more uncomfortable about these two significant variables is that with the information we have it is not possible to know at what level they influence. Do they influence at the individual level? If poverty, rurality, and many other variables

influenced by these two are considered social determinants of health, are they a predictor of social issues and patient diseases that are not compatible with donation? If we look that poverty was indeed significant for the social, patient, and other models, we could assume they do. Or do they influence at the hospital level too/instead? For example, in the accessibility to resources, professionals, and state of the art care? And here we can mention the other variable that was significant just for the process model: years of schooling. Since we found that the more years of schooling in the municipality of the hospital the less likely a patient will be to be discarded, we can ask ourselves: Does this variable influence at an individual level as the other determinants of health? This is, by considering that the more educated the patient, the better their health status is. Or does it influence at the hospital level? As years of schooling was significant only in the process model, this could suggest that it affects only the hospital level, suggesting that the professionals that work in each hospital are influenced by the education level of the area where they work. This is, hospitals located in a more educated municipality would have "better" education, and thus be less likely to discard patients because of their intervention in the process, maybe because they make better choices about whom to refer, or they conduct better processes once the referral is made. Lastly, it is also interesting to mention our interpretation of the intercepts. For the social model the intercept shows that a patient would always be less likely to be discarded because of a social cause. And the opposite, a patient will always be more likely to be discarded due to a process issue.

Even though the results we show might look very discouraging for the country, the truth is that there is large room for improvement. Even though we found that social disparities greatly affect the procurement activity, some concrete actions can be taken to reduce variability in both the hospital and LPC level. First of all, it is crucial to have monitoring tools to know, hopefully in real time, how each LPC is doing, what decisions they are taking, under what criteria, and

understanding those hidden bottlenecks that might be hindering them from doing better (which can also differ by hospitals at a same LPC). Similarly, the national authority must conduct periodic process evaluations to understand the macro issues that might be preventing the country from improving its organ donation figures. Monitoring and evaluation are widely known and effective techniques to diagnose and improve implementation of interventions, programs, and policies (89,90). Using information technologies able to automatize these techniques could be a cost-effective way of boosting the procurement activity and achieving good results.

Despite the socioeconomic conditions could not be improved with an intervention for the procurement process, because they would require improvement of all the national social policies, introducing a monitoring and evaluation technology could also be able to show the inequities the hospitals are facing (like what resources are scarce in each place), what process steps are failing and why, that are jeopardizing the procurement activity, and also what education gaps should be reduced in clinicians for each hospital.

6. Recommendations

During the data cleaning process, we unexpectedly found that there was an important number of patients that were misclassified, not only in their causes, but also in their outcome. This is, under our point of view, a worrisome issue since these classifications are the ones that will allow informing policy and decision makers and providing an understanding of the results the policy is having, and to make changes to improve those results.

While reading the "*observations*" field of all patients that had data on it, we realized that there was not a unified criteria for choosing one cause of discard over another. There were patients that had different causes of discard while having a similar description in the "*observations*" field. However, we must disclaim that, since we couldn't access other variables (like cause of admission, test results, or known comorbidities), we couldn't have the full picture of the real causes of discarding each patient. But something that supports our concern is the fact that there is no official document with the definitions of all the causes nor description of borderline scenarios for when to choose each cause when in doubt. The problem with not having a standardized definition is that procurement nurses can interpret the causes at their will, something that we observed not only at the LPC level, but also at the central level, where the Central Coordinators had different criteria among themselves. This introduces a huge amount of variation and bias on the data, which highly hinders the analysis capacity and of course, may bias results; which, in the end, translates into misleading policy improvement suggestions.

Moreover, the main discard cause was "Other cause" (>50%) that highlights lack of standardization between LPC and even central coordinators, suggesting that also incorrect/unethical behaviors could be happening.

The causes of discard that had conflicting understood definitions were:

- **Discard and contraindication:** It is not clear for all LPCs when a patient should be classified as discarded and contraindicated. Some of them use contraindication as a condition which couldn't be accepted for donation, like an active cancer. Some others used them as a discard but after brain death certification (our definition). Some others don't have distinguishable criteria.
- ***Hemodynamic failure, multiorgan failure*, and *CPA:*** These are intrinsically related in a lot of cases, causing misclassification of the patients who suffer all of the three conditions. The cascade of events and when to choose from one cause over the other is not defined.
- ***Stationary GCS* and *neurological improvement:*** These have a "gray area", where it is not clear if the patient improved their condition, or if they would remain in the same condition, nor the implications for the procurement process. Moreover, if the patient reaches GCS=3, but doesn't meet all the criteria for brain death certification, it is not clear if they should be discarded because of *Can't diagnose brain death*, or *Stationary GCS*.
- ***Can't diagnose brain death:*** When certifying brain death, there are several conditions the patient must meet. If any of them are not met, brain death can't be certified. It could happen that a patient dies from a CPA during the apnea test, or while waiting to meet the criteria for the test. It is not clear whether to discard that patient because of *Can't diagnose brain death* or *CPA*.
- ***Suboptimal donor:*** This classification emerged during the first months of the COVID-19 pandemic and its ICU bed availability shortage, despite that Chile did not suffer a critical care bed unavailability and the 2020 effective organ donation was not significantly affected by SARS CoV-2 like other countries (19). It was included to respond to the contingency of choosing just those patients who were believed could reach brain death certification and have potentially good quality organs for donation, with the aim of not over-utilizing a scarce resource, the ICU bed. Nonetheless, its conflicting name, the lack

of definition, and diverse ways of understanding it, induced a large variability in the classification of these patients. When it was introduced, the already fine line between *age, underlying pathology, multiorgan failure, hemodynamic failure, Uncontrolled septic process,* and *Positive serology for transmissible infections*, was completely blurred. The problem with it is that all those different causes may respond to different underlying issues, like the conditions at which the patient arrived, or how they were managed inside the hospital. And the critical point about that, is that the introduction of this cause made it completely impossible to elucidate whether a patient was discarded because of their underlying conditions (the process can't be improved to convert those patients into donors), or because of a process failure (room for improvement).

- ***Unavailability of ICU bed / maintenance care:*** At the beginning it was defined as just "unavailability of ICU bed". This confused coordinators when discarding patients who could not access a critical bed in their hospital but could be transferred to another hospital. These aforementioned patients were classified under those 2 causes (*unavailability of ICU bed* and *Transfer to another healthcare center*). Nonetheless, *unavailability of ICU bed* was changed for *Unavailability of ICU bed / maintenance care,* which made the difference between those two causes in that borderline scenario clearer. In fact, this new cause evidenced that the procurement work should be done within a network, and if a hospital can't provide maintenance, there should be another hospital with the availability to do so, and only in the cases where there is no availability in the network, the patient should be discarded. Moreover, this change recognized that there are hospitals that can maintain the possible donor at the ER or other units.
- ***Transfer to another healthcare center:*** It is not clear when to discard a patient because of this cause or the cause that precipitated the transfer of the patient, like *Withholding treatment, Neurological improvement,* or for neurological surgery, among

others. This highlights a horizontal problem found in most causes of discard: how to choose a cause of discard given the temporality in which events occur.

- **Possible organ donor criteria:** It was widely known and accepted that the criteria for introducing a patient to procurement follow-up were: neurological cause, GCS≤7, no sedation, age over 6 months and less than 80 years, and out of neurosurgical reach. However, we found an important number of patients who were included as possible donors and started follow-up who did not meet one, more than one, or even any of these criteria. This situation not only questions the definition of a possible donor and where is the dividing line for those patients who have unknown conditions (that could or could not end in brain death), but it also points out that there is a huge variability in the criteria each LPC uses for defining a possible donor.

To improve this situation and all the problems mentioned above, we propose the following solutions:

- **Define outcomes:** Clearly define when a patient should be classified with each non-donor outcome, this is, familial refusal, contraindication, or discard. We propose using the definitions provided at the results section:
    - **Discard:** A patient who does not meet the criteria for becoming an organ donor and **was not** certified as brain dead.
    - **Contraindication:** A patient who does not meet the criteria for becoming an organ donor after **being certified** as brain dead.
    - **Familial refusal:** A patient who was certified as brain dead whose family was interviewed for organ donation, but refused, whether because the patient's will while alive was to not become an organ donor, or because the family didn't authorize the donation.

- **Define the process flow:** Clearly define the process to understand when and how a patient can be discarded or contraindicated to build standard criteria.
- **Build a guide with definitions:** Include all causes of discard, contraindications, and familial refusals. Together with the definition, provide examples, borderline cases, and define possible cascades of events and how to choose in those scenarios.
- **Train procurement nurses at the LPC and CC levels:** Train the people who will classify patients in how to classify them correctly. Nowadays, the LPCs don't know the definitions of the causes of discard, nor receive any training for how to use the classifications, nor receive the information when a new cause is added to the platform. Training to have a common understanding is crucial to ensure standard classifications.
- **More than one cause:** Consider the possibility of choosing more than one cause of discard in the case the cascade of events is not clear.
- **Include the new proposed causes of discards:** Since they can provide useful insights of the effectiveness of the process in different healthcare centers.
- **Add the new proposed sub-causes:** Since they can be useful to make decisions of process improvement.
- ***Lack of clinical history:*** Even though we did not consider this existing cause because of time issues (we realized it existed when most of the database was already classified), we do believe that it should be included in the causes of discard, not only for contraindications as it exists now, but also in discards. This is especially important when there is suspicion of cancer, and the result of a biopsy would take longer than the standard follow-up period (possible recipients should be protected when in doubt).
- ***Positive Serology:*** Even though we considered it under *Underlying Pathology* because it didn't exist as a discard cause (only as a contraindication cause), and it was easier to turn the serologies into pathologies for simplicity, we believe that this cause should be considered separately for both contraindications and discards. We also suggest including

the type of reactive serology into the sub-causes. In the near future, it is possible that some HIV or HCV positive patients could be accepted as organ donors, at least in some pilot and controlled initiatives (91).

- ***Underlying Pathology:*** Similarly, we recommend including all possible underlying pathologies as sub-causes to improve the understanding of the diseases that are being considered as exclusion for donation.
- ***Does not meet criteria:*** We recommend clearly defining what are the conditions a patient must meet to be considered a possible donor, and which ones could be relaxed and included as causes of discard. We recommend including a new outcome called *Does not meet criteria* to show the willingness of clinicians to refer patients to the LPC, but, at the same time, define the line between a patient who enters follow-up and a patient who does not. For that we propose:
    - **Neurological cause:** If the patient doesn't have a neurological cause, consider as *Does not meet criteria*. It could be possible that the reason for the altered level of consciousness be unknown when the patient arrives and discovered later.
    - **GCS≤7:** If the patient is referred with a GCS>7, consider as *Does not meet criteria*.
    - **No sedation:** If the patient is referred when sedated (CNS depressants), begin follow-up and discard because of *Stationary GCS, Neurological improvement,* or *Can't diagnose brain death*. This is because sedation may be part of the treatment of a critical patient, and there are patients who enter or receive sedation while in procurement follow-up that can become organ donors afterwards. Including them in the follow-up could increase the number of effective donors.
    - **Age over 6 months and less than 80 years:** If the patient is not in this age range, discard with cause *Age*. This, because the definition of an acceptable age is constantly changing.

- **Out of neurosurgical reach:** If the patient is referred after it is known it has neurosurgical reach, consider as *Does not meet criteria*. But if it is referred before the neurological evaluation, discard as *Neurological reach*. This is because there are a lot of patients that are referred before the neurological evaluation happens in order to have a timely referral (referring after the evaluation can end up with a discard or a referral after CPA). This classification can improve the understanding of how the process is done in the different hospitals.

- ***Suboptimal donor:*** We recommend no longer considering *Suboptimal donor* as a cause of discard. This because of the following reasons:
  - **Definition:** The concept of "optimum" has 2 definitions[16]:
    - Most conducive to a favorable outcome; best.
    - The most favorable conditions or level for growth, reproduction, or success.

    We understand that this cause was built under the COVID-19 contingency trying to follow the first definition, in the sense that a patient with any comorbidity or possibility of not being a good candidate, would be discarded because of resource scarcity. Nonetheless, the definition of optimum, and thus, suboptimal, is not clear. In math, an optimum is reached at a maximum or a minimal level, and since we want to focus on the maximum level, an optimum donor should be the "perfect" one for organ donation (i.e., a young person with no comorbidities, and all removable organs in perfect conditions). Since this is not the case in most organ donors, a patient will, most of the time, be a suboptimal donor. Indeed, given the average age (43.8 ± 16.25) of effective donors in Chile, most of them are not optimum donors, and thus, suboptimal from the beginning.

[16] Definitions from Oxford Languages, available on Google.com

- **Unclear:** Given that the definition of suboptimal is not clear, that any of the causes of discards are not defined, and that anything could be considered as suboptimal, LPCs and CCs started relaxing their own definitions of suboptimal and increasing the misclassified patients.
- **Boundaries with other causes:** Since this condition was included, the boundaries between *age, underlying pathology, multiorgan failure, hemodynamic failure, Uncontrolled septic process,* and *Positive serology for transmissible infections*, were completely blurred, leading to a large number of misclassifications that was not even included in this analysis because it was impossible to establish boundaries with the available information.
- **Remain broad:** The pandemic is over, and this cause no longer works for the purpose it was created, it furthers the misunderstanding of the borderline cases, and thus, it should be deleted.

7. Limitations

The lack of definitions of the patients' outcomes and causes of discard introduced huge unknown variability into the models, which is a big limitation of the study. We tried to address this situation by re-classifying the patients and clustering the causes of discard in believed social, process, or patient derived discards, albeit aware of the still introduced variation due to poor classification.

Data availability was one of the main issues encountered in this project. Even though we were able to fit relatively good models with the available data, the ambition of the project was larger. The current database that gathers all the Chilean organ donation and transplantation records, SIDOT, didn't have an adequate design for extracting and analyzing data. The first ambition was to include known comorbidities and several daily biomarkers to study the evolution of the patient, and other underlying unknown diseases. The second less ambitious plan was to include just the cause of admission, age, and blood type of the patient. Both analyses were discarded due to the infeasibility of accessing the data on time. Moreover, even the Ministry of Health hasn't had access to the data at the date this manuscript was written, nor during the 12 years of existence of the system, and a change in the contract with the provider company is actually taking place to access all the national records.

Albeit all the challenges we mentioned, our study has important strengths. It is the first study of this kind performed in Chile, which tried not only to describe the variables that better predict a patient to be discarded, but also considering hospital and LPC variability, something inherent of the Chilean healthcare system. We hope that, in the future, when we access the missing records, we will be able to include new variables to improve the predictions we have got in this study.

8. Future work

As we stated before, this study should be repeated when accessing more patient-level variables, especially causes of admission and age, since they have been shown in other studies to be important predictors of discards and effective organ donation. At the same time, it would be interesting to fit the same models but considering familial refusals as discards, or even not considering familial refusals at all, and see how predictors change or not with that switch of outcome variable. Finally, it is important to incorporate other hospital-level and LPC-level variables that might explain part of the variation found in the models. Some variables of interest could be number of beds in the hospital, level of knowledge of and/or participation in the procurement process of the clinicians in ER and ICU, relative importance of organ donation and/or transplantation in the hospital, number of procurement nurses in the LPC, years of experience of those nurses, relative support those nurses receive from each hospital, and training they've received, among many others.

9. Conclusion

This study has large implications for the organ donation policy in Chile. The results we obtained reflect an organ donation system unexpectedly impacted by the underlying social inequities in the country, which should also inspire other countries to add socioeconomic variables to study their organ donation systems.

The large variation found in discarded patients is highly explained by variance among hospitals and LPCs, evidencing a complete lack of standardization of the procurement process. If the process is not standardized, it would be impossible to obtain better results and subsequently, more effective organ donors. Even worse, if the process is not monitored nor evaluated, it is impossible to even demand better results from LPCs.

LPC nurses and all the people that work at the procurement system do their best to obtain good and better results, but if the central level can't monitor, understand, and propose improvements for their different realities, all their efforts would always be wasted. It is time to honor their efforts and, at least collect good quality information that can help monitoring, evaluating, and improving every day, not every 12 years.

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11. Appendix

11.1 Appendix 1: Procurement process diagram

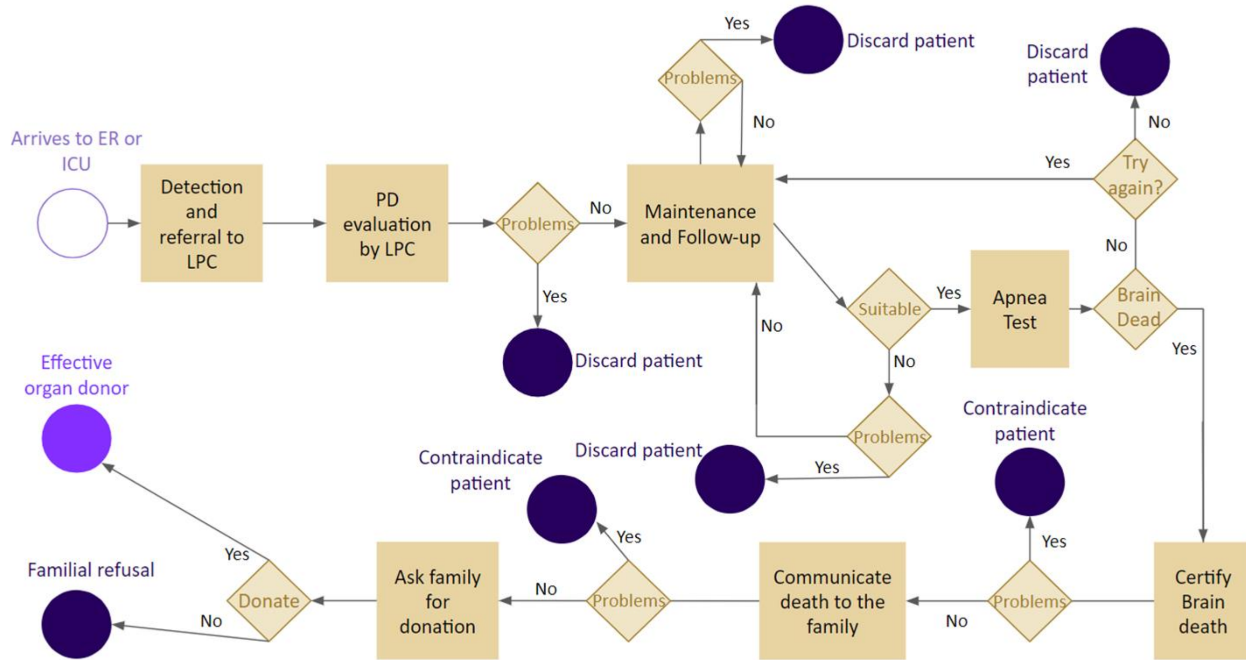

Figure 9: *Systems engineering process diagram of the procurement process.*

11.2 Appendix 2: Definitions for new causes and sub-causes of discard

11.2.1 New causes:

Unspecified etiology: Use when the etiology that led the patient unconscious couldn't be specified. One of the requisites for certifying brain death is knowing the exact cause that led the patient unconscious, not knowing this cause, is a cause of discard.

Attending physician talks about organ donation: If someone else, especially physicians, mention the possibility of organ donation, or whether the patient is under study for organ donation, both before or after the BD certification. By law, the LPC teams are the only ones empowered to talk about organ donation with the family after BD has been certified and the family is aware of the death.

Familial refusal before brain death: When the family of the patient spontaneously mentions the patient did not or they do not consent organ donation.

No center accepts organs: When the potentially removable organs were not approved or neglected by all the transplantation centers because of their quality or other reasons.

No patient identification: When the patient could not be identified albeit all efforts were made.

GCS > 7: When a patient is referred with a GCS higher than 7, the criteria for entering procurement follow-up.

Neurosurgical solution: When the condition of the patient could be solved by neurosurgery. Being out of neurosurgical reach is one of the conditions to be considered as a possible donor.

Without neurological cause: When the etiology that led the patient unconscious is discovered to be non-neurological (for example, metabolic).

11.2.2 New sub-causes:

Central coordination does not validate patient: When the patient is explicitly asked to be discarded or contraindicated by the CC on duty and is not a consensus by the CC and LPC.

Transplantation team does not validate patient: Before even offering the organs, the local transplantation team stated that the condition of the patient/organ/organs is/are not good enough for transplantation, and thus, the patient is discarded or contraindicated.

Risk behavior (drug use or convicts): When part of the clinical background of the patient is single or multiple drug use, and/or being or have been a convict. Even though these are not necessarily risk behaviors for donation, this classification can give a sense of the different perception of them in the healthcare teams.

No potentially removable organs: After doing laboratory and/or imaging studies the organs that were candidate for donation were confirmed to be low quality.

Lower than minimum weight: When the age discard is because the patient is too young (not old).

No neurosurgeon or neurologist: When the process is halted because there are no neurosurgeons or neurologists available for evaluating the patient or certifying BD.

Ventilatory movements: When the apnea test is negative, should be stopped, or can't be initiated because the patient presents ventilatory movements during it.

Has reflects: When the apnea test is negative, should be stopped, or can't be initiated because the patient presents reflects.

Complementary test shows brain activity: When brain death can't be certified because the complementary imaging test to the apnea test, shows the patient still has brain activity.

Half-life of CNS depressant too long: When the apnea test can't be initiated because the patient was sedated with a depressant which half-life is too long to wait until it fades without damaging the potential organs (2 half-lives).

Triggers ventilator: When the apnea test is negative, should be stopped, or can't be initiated because the patient triggers the ventilator.

Hypernatremia: When the apnea test is negative, should be stopped, or can't be initiated because the patient presents hypernatremia.

Hypercapnia: When the apnea test is negative, should be stopped, or can't be initiated because the patient presents hypercapnia.

Hypothermia: When the apnea test is negative, should be stopped, or can't be initiated because the patient is hypothermic.

Hypotension: When the apnea test is negative, should be stopped, or can't be initiated because the patient presents hypotension.

Hemodynamic instability: When the apnea test is negative, should be stopped, or can't initiate because the patient is hemodynamically unstable.

Metabolic instability: When the apnea test is negative, should be stopped, or can't initiate because the patient is metabolically unstable.

Spontaneous ventilation: When the apnea test is negative, should be stopped, or can't initiate because the patient shows spontaneous ventilation.

Non conclusive Apnea Test: When the apnea test has an inconclusive lab result.

Negative Apnea Test: When the apnea test shows a negative lab result.

Sedated patient: Patient who could not tolerate sedation removal, and thus, could not be considered as a possible donor.

Absence or deficiency in maintenance / handling: Patients that had an unfavorable outcome because they did not receive the best care they could have had.

Absence or withdrawal of LPC: In the case patient follow-up could not continue because LPC members were not present for it, whether because of health issues, system problems, other urgencies, or duty abandonment, among others.

Lack of resources: In the case the discard of the patient precipitated because some resource was not available, whether lab tests, imaging tests, life support machines, medication, or other.

Attending physician discards patient: Without considering the LPC opinion, nor recognizing its authority, the attending physician arbitrarily stops follow-up and maintenance.

Unavailable critical care bed for recipient: In the case the patient is contraindicated because there is no bed available to take care of the potential recipient/s of all potential removable organs after transplantation surgery.

No transplantation teams available: If all donated organs are assigned to a recipient/s but they are not harvested because there are no transplantation teams that could perform the harvesting surgery, thus the patient never becomes an organ donor, and is contraindicated.

Family doesn't understand BD concept: Understanding that the patient is dead is fundamental for doing the donation interview. If the family does not understand it, and still thinks the patient is alive, the interview can't be done and thus, the patient is contraindicated.

Possible medical negligence (legal): In the case where there is suspicion of medical negligence and the family could take legal action, the procurement process must be halted to protect its credibility.

Without CPR: A patient that suffered a CPA and is deliberately not reanimated, and thus discarded.

Patient referred after death: A patient that despite all efforts died in an extremely short period of time and referral could not take place before death. It is important to note that this sub-cause can only be used if the patient would have died in that same extremely short period of time even if the referral was done before the lifesaving maneuvers.

GCS=3 with some neurological activity: This sub cause should be use for disambiguation of the discards *stationary glasgow* and *can't diagnose BD,* when the patient that is discarded due to any of those reasons, was in GCS=3, but had some activity that impede them becoming potential donor. In the future, the dividing line between those 2 causes should be better defined and this sub-cause should be considered just for one of those 2.

Familial or patient will: When the withdrawal of treatment was done because the family spontaneously asked for it before any conversation with the attending physician. It could be because they want the patient to die because of the ominous projection, or because the patient explicitly stated to withdraw treatment when alive.

Without antibiotic treatment: A patient facing a septic process that does not receive the required antibiotic treatment to stop it from spreading.

Decision is not communicated to LPC: In the case the withdrawal of treatment or transfer to another unit or healthcare center is not communicated to the LPC, and thus the process is halted without the LPC knowing nor participating in the decision.

Unavailable bed due to COVID contingency: Just to understand how many patients could not follow the procurement process because of ICU bed scarcity during the pandemic. In future pandemics or contingencies (like earthquakes) could be used but erasing the word "COVID".

COVID contingency infeasibility: If the process was stopped because of some other resource other than critical maintenance care, or sub-process could not be done because of the contingency. For example, no ambulances available to transfer a patient, not enough medication, or closed transplantation programs, among others.

ICU physician doesn't provide bed: In the case the patient can't access maintenance care because they were denied bed at the ICU without any logical reason, or because the physician states that "they take care of patients that will live".

Neurologist or neurosurgeon says patient will not fall to BD: In the case the patient is discarded, and it is explicitly said by the neurologist or neurosurgeon, or the attending physician, that the patient will not cephalically die, and thus it should not continue in procurement follow-up.

11.3 Appendix 3: Sub-causes of discard frequency distribution

Table 13: *Sub-causes of discard frequency distribution.*

Name of sub-cause	Frequency
No neurosurgeon or neurologist	18
Absence or deficiency in maintenance / handling	23
Absence or withdrawal of LPC	8
Lower than minimum weight	11
Central coordination does not validate patient	100
Risk behavior (drug use or convicts)	41
COVID contingency infeasibility	16
Transplantation team does not validate patient	70
Unavailable critical care bed for recipient	1
Lack of resources	38
Triggers ventilator	11
GCS=3 with some neurological activity	28
Hypercapnia	1
Hypernatremia	22
Hypotension	4
Hypothermia	8
Family doesn't understand BD concept	4
Hemodynamic instability	37
Metabolic instability	1
Ventilatory movements	6
Attending physician discards patient	15
Neurologist or neurosurgeon says patient will not fall to BD	33
Possible medical negligence (legal)	17
Has reflects	8
Complementary test shows brain activity	22
Patient referred after death	5
Sedated patient	65
Unavailable bed due to COVID contingency	54

Decision is not communicated to LPC	18
No transplantation teams available	2
No potentially removable organs	15
Without CPR	25
Without antibiotic treatment	3
Negative Apnea Test	2
Non conclusive Apnea Test	6
ICU physician doesn't provide bed	11
Spontaneous ventilation	6
Half-life of CNS depressant too long	3
Familial or patient will	195
TOTAL PATIENTS WITH SUB-CAUSE	953

11.4 Appendix 4: Criteria for grouping the causes of discard

11.4.1 Social

Causes that have a social root, whether at the patient level, or a higher level. They may have to do with resources, willingness, or identification background.

11.4.1 Patient

Causes that are inherent to the patient's condition, and that could not be modified with any enhanced care at the moment.

11.4.1 Process

Causes that happen exclusively because of process failures, non-effectiveness, or inefficiencies. They could happen at the provider, LPC, hospital, Health Service, or system levels.

11.4.1 Other

Causes that, due to the original lack of definition and lack of variables accessed for this analysis, could not be assigned to an exclusive group among the previous ones. In fact, considering the proposed sub-causes could further improve the classification of the causes in this group.

11.5 Appendix 5: List of Healthcare Services and codes

Table 14: *Healthcare services by code.*

Code	Health Service Name
1	Arica
2	Iquique
3	Antofagasta
4	Atacama
5	Coquimbo
6	Valparaíso San Antonio
7	Viña del Mar Quillota
8	Aconcagua
9	Metropolitano Norte
10	Metropolitano Occidente
11	Metropolitano Central
12	Metropolitano Oriente
13	Metropolitano Sur
14	Metropolitano Sur Oriente
15	Del Libertador B.O'Higgins
16	Del Maule
17	Ñuble
18	Concepción
19	Talcahuano
20	Biobío
21	Araucanía Sur
22	Valdivia
23	Osorno
24	Del Reloncaví
25	Aisén
26	Magallanes
28	Arauco
29	Araucanía Norte
33	Chiloé

11.6 Appendix 6: Tables for univariate and multivariate models by group of outcomes

Table 15: *Results for the univariate and multivariate logistic regressions for 3 level clustered data, for social cause of discard as dependent variable.*

	Univariate models		Multivariate models	
	Fixed Effects			
Independent Variable	OR	p-value	OR	p-value
Intercept	0.52	0.00153	0.0057	<0.0021
Gender (male)	1.46	<0.00163	1.45	<0.0201
High Complexity	0.17	0.00569	-	-
RGD	0.60	0.251	-	-
MDI	0.9996	0.10308	-	-
Poverty	25,304,960,000	<0.00112	1,448,342	0.0054
Rurality	2,654	<0.00547	231.8	0.00116
Years of schooling	0.59	<0.00152	-	-
Natives	1,069	0.077405	-	-
	Random Effects			
Level			Variance	CI (95%)
Hospital Level	-	-	0.781	(0.68 , 1.17)
LPC level	-	-	-	-

Table 16: *Results for the univariate and multivariate logistic regressions for 3 level clustered data, for patient cause of discard as dependent variable.*

	Univariate models		Multivariate models	
	Fixed Effects			
Independent Variable	OR	p-value	OR	p-value
Intercept	2.68	<0.00541	-	-
Gender (male)	1.39	<0.00146	1.38	<0.0337
High Complexity	0.58	0.216204	-	-
RGD	0.68	0.112	-	-
MDI	0.9998	0.0723	-	-
Poverty	1.23	0.000809	2,575	<0.0102
Rurality	17.43	0.0125	-	-
Years of schooling	0.80	0.000298	-	-
Natives	546.26	0.01063	-	-
	Random Effects			
Level			Variance	CI (95%)
Hospital Level	-	-	0.125	(0.203 , 0.56)
LPC level	-	-	0.233	(0.29 , 0.72)

Table 17: *Results for the univariate and multivariate logistic regressions for 3 level clustered data, for process cause of discard as dependent variable.*

	Univariate models		Multivariate models	
	Fixed Effects			
Independent Variable	OR	p-value	OR	p-value
Intercept	0.23	<0.00541	31.94	0.00507
Gender (male)	1.32	0.00747	1.31	0.00799
High Complexity	0.35	0.106	-	-
RGD	1.41	0.442	-	-
MDI	0.9999	0.779	-	-
Poverty	8.57	0.00512	-	-
Rurality	103.36	0.00559	-	-
Years of schooling	0.64	<0.00268	0.64	<0.0029
Natives	3,592	0.0351	-	-
	Random Effects			
Level			Variance	CI (95%)
Hospital Level	-	-	0.226	(0.16 , 0.9)
LPC level	-	-	0.48	(0.31 , 1.05)

Table 18: *Results for the univariate and multivariate logistic regressions for 3 level clustered data, for other cause of discard as dependent variable.*

	Univariate models		Multivariate models	
	Fixed Effects			
Independent Variable	OR	p-value	OR	p-value
Intercept	4.83	<0.0002	-	-
Gender (male)	1.09	0.0701	-	-
High Complexity	0.59	0.225	-	-
RGD	0.80	0.355	-	-
MDI	0.9998	0.061	-	-
Poverty	274,230	0.00175	663,187	<0.0002
Rurality	44.53	0.000473	9.85	0.0412
Years of schooling	0.77	<0.00587	-	-
Natives	106.2	0.0555	-	-
	Random Effects			
Level			Variance	CI (95%)
Hospital Level	-	-	0.2897	(0.41 , 0.72)
LPC level	-	-	-	-