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Expert Review of Medical Devices

ISSN: (Print) (Online) Journal homepage: https://www.tandfonline.com/loi/ierd20

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To cite this article: Eliane Molina Psaltikidis, Eliana Auxiliadora Magalhães Costa & Kazuko Uchikawa Graziano (2021) Reuse of pacemakers and implantable cardioverter-defibrillators: systematic review, meta-analysis and quality assessment of the body of evidence, Expert Review of Medical Devices, 18:6, 553-567, DOI: 10.1080/17434440.2021.1927706

To link to this article: https://doi.org/10.1080/17434440.2021.1927706

EXPERT REVIEW OF MEDICAL DEVICES
2021, VOL. 18, NO. 6, 553–567
https://doi.org/10.1080/17434440.2021.1927706

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META-ANALYSIS

Reuse of pacemakers and implantable cardioverter-defibrillators: systematic review, meta-analysis and quality assessment of the body of evidence

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ABSTRACT

Background: Pacemakers (PMs) and implantable cardioverter-defibrillators (ICDs) have reduced mortality and improved the quality of life of cardiac patients. However, the high cost of these devices prevents their large-scale incorporation, particularly in low-income countries, where reusing explanted PMs/ICDs has become an alternative.

Methods: A systematic review and meta-analysis were conducted of studies that compare infection rates, device-related deaths, malfunction and premature battery depletion in patients with reused PM and ICD implants and those with new devices. The quality of the body of evidence was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework.

Results: The meta-analysis demonstrated no significant intergroup differences in infection rates (OR 0.98; 95% CI 0.60–1.60), device malfunction (OR 1.58; 95% CI 0.56–4.48) or premature battery depletion (OR 1.96; 95% CI 0.81–4.72) and no device-related deaths. Based on GRADE assessment, confidence in estimates for the outcomes infection rate and device-related death was rated as moderate.

Conclusion: The results of this analysis enabled us to conclude that PMs and ICDs can be safely and effectively reused. As such, every effort should be made to overcome regulatory, technical and ethical barriers to ensure implantation.

ARTICLE HISTORY
Received 7 February 2021
Accepted 6 May 2021

KEYWORDS
Pacemaker; artificial; cardiac pacemaker; cardiac resynchronization therapy devices; equipment reuse; reusability; equipment

1. Introduction

Cardiovascular diseases are an important global public health problem, accounting for 30% of all deaths worldwide. Although advances in treatment in this area have contributed significantly to lowering associated morbidity and mortality, this technological improvement in health care has not been reported in middle and low-income countries [1–3].

This disparity is clearly evident in care-related cardiac electrophysiology, specifically pacemakers (PMs) and implantable cardioverter-defibrillators (ICDs), which are costly devices. The estimated cost of a PM is from US$2,500 to US$8,000 and US $10,000 to US$18,000 for an ICD, making them impossible to supply in low-income countries [4–6]. For example, the cost of a basic PM in India, excluding hospital expenses, varies from US$2,200 to US$6,600, which is more than the annual income of most of the country's low-to-medium-income population [3].

In the United States, approximately 250,000 PMs and 100,000 ICDs are implanted every year, with a 20-fold increase in the last 15 years. Nevertheless, international aid organizations estimate that more than one million people die every year due to lack of access to pacemakers and other implantable cardiac electronic devices [1,4–7]. The number of PMs implanted annually per million inhabitants is 782, 518 and 767 in France, the United Kingdom and the United States, respectively, compared to only 30, 17, 5 and 5 in Peru, India, Bangladesh and Sudan. This disparity may be the result of demographic differences in population size and access to healthcare services; however, socioeconomic inequality is likely more important, indicating that many patients who could benefit from the device are unable to obtain it [1,6].

Although charity organizations donate new pacemakers, this is rarely sufficient to cover the number of patients in need of the device. The reuse of pacemakers and ICDs explanted from dead donors is an alternative for many patients in different countries, made possible by crematoriums and/or funeral homes that collect the devices [3,6].

In practice, many single-use products from different medical specialties are reprocessed and reused worldwide, largely due to the high cost of these materials. For example, catheters for cardiac ablation and electrophysiology studies have been reprocessed and reused for more than 25 years in the United States, India, several European countries, Brazil and other Latin American nations [8–13].

The results of research on PM and ICD reuse are described in a number of investigations, but few are prospective studies with a control group and none are randomized controlled trials. Another methodological limitation is the variability of outcome definitions, processing practices and functional assessment. However, most of these studies report that reusing explanted PMs and ICDs is not associated with increased infection or mortality rates and represents a significant saving [4,6,14,15].

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Article highlights

- Lack of resources in the populations and health systems of low-income countries have caused inequalities in the treatment of cardiac patients due to the inadequate supply of artificial PMs and implantable cardioverter-defibrillators (ICDs).
- Reuse of these devices has been reported since the 1970s in several case series and cohort studies, but no randomized controlled trials.
- Published systematic reviews indicate no significant difference in clinical outcomes between patients implanted with reused PMs/ICDs and those with new devices. However, arguments and health restrictions against this practice remain in place.
- This systematic review and meta-analysis included recent studies that analyze infection rates, device-related deaths, malfunction and premature battery depletion. The findings corroborate those of previous meta-analyses and concluded that reusing PMs and ICDs is a safe and viable option when new devices are inaccessible.
- This study differs from previous research in that the body of evidence on the topic was assessed using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) framework, which made it possible to classify the confidence in estimates for infection rate and device-related death as moderate.

A 2011 meta-analysis evaluated published and unpublished data on the safety of PM reuse over a period of 40 years. The 18 articles selected, totaling 2,270 patients, revealed a low incidence of adverse events with reused PMs, specifically 1.95% for infection and 0.68% device malfunction, and no significant difference in the rate of infection between reused and new devices (1.31%) [4]. Another meta-analysis on pacemaker and defibrillator reuse, with studies between 2009 and 2017 involving 2114 patients, established risk of infection, malfunction premature battery depletion and death as the primary outcome and found no statistically significant difference between new and reused devices (2.23% versus 3.86% respectively, p = 0.807, OR = 0.76, CI: 0.45 to 1.28) [15].

Despite evidence in favor of pacemaker reuse, the practice is currently only adopted in a few specialized services in low and middle-income countries, largely due to the significant legal and regulatory barriers that prevent its broader implementation [6].

In this respect, the present study aims to assess the quality of the body of evidence on the topic, under the following guiding question: are patients with reused PMs and ICDs at greater risk of infection, device-related death, malfunction or premature battery depletion than those implanted with new devices? The null hypothesis was adopted as an assumption, that is, that there would be no significant differences in outcomes between groups with new and reused PMs and ICDs.

2. Systematic review and meta-analysis methodology

2.1. Study registration

This systematic review and meta-analysis are part of the project entitled 'Reuse of cardiac pacemakers and implantable cardioverter defibrillators', registered on the Open Science Framework (OSF) and available at https://osf.io/zkg4w [101].

2.2. Information sources and search strategy

This study was conducted in line with the methodological recommendations of the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (Prisma)[16]. Searches were carried out in May 2020 on the following databases: Medline (via Ovid), Pubmed, Embase, Cochrane, Web of Science, BSV (Virtual Health Library) and Lilacs, using the MESH terms: 'Pacemaker, Artificial', 'Cardiac Pacemaker, Artificial', 'Cardiac Resynchronization Therapy Devices', 'Artificial Biventricular Pacemaker', 'Equipment Reuse', 'equipment recycling', 'Reusability, Equipment', as well as synonyms and free text, with the aid of the Boolean operators 'and' and 'or'. Manual searches were also performed to identify unpublished studies and check the references of the articles found. There were no restrictions for the year of publication or language.

The searches were carried out by the authors, with the assistance of a librarian specialized in Health Information (Dr. Rosana Evangelista Poderoso, Director of the Medical Sciences School Library at Unicamp). The complete strategy used for Pubmed is presented in Annex 1. The studies were selected independently by the three authors and disagreements resolved by consensus.

2.3. Eligibility criteria

Studies were selected based on the PICOS framework [16–19], whereby the population (P) were patients submitted to PM or ICD implantation, intervention (I) was the reuse of these devices compared (C) to implanting new ones, and the outcomes (O) were: infection, device-related death, malfunction and premature battery depletion. The inclusion criterion used for the studies (S) was the presence of a control group, even if only in retrospective analysis.

Articles were initially selected based on their titles and abstracts, and then read in full and independently by the three reviewers to confirm their eligibility. Disagreements between the reviewers were resolved by consensus and all exclusions justified.

2.4. Data extraction

Data were extracted by the three reviewers, using a standard instrument to obtain the following information: a) reference data for the study: title, authors, journal information; b) objectives; c) type of device (PM or ICD); d) patients' clinical characteristics; e) method; f) results with effect measures and g) conclusion. One of the reviewers checked the consistency of the data collected and compiled an electronic spreadsheet for the meta-analysis.

2.5. Quality assessment

The Newcastle-Ottawa Scale (NOS) [20] was used to assess risk of bias, considering three categories: selection, comparability and outcomes. Each reviewer applied the scale to all the studies and disagreements were resolved by consensus.

2.6. Data analysis

The meta-analysis was performed with the help of a statistician (Bernardo dos Santos MSc – Research Support Center of the USP Nursing School). A random effects model was used, estimated by restricted maximum likelihood, which groups all the studies together based on the assumption of heteroscedasticity. The odds ratio (OR) and 95% confidence interval were calculated for each variable. An OR < 1 indicated a smaller chance of the outcome with reuse and > 1 a greater likelihood. Forest plots were used to display the results of the individual studies and meta-analysis. The variability of the studies was estimated using the H^2 statistical measure and heterogeneity by I [2], with values ≤25%, 50% and ≥75% corresponding to low, moderate and high inconsistency, respectively [21]. The program used was R software version 4.0.3.

The quality of the body of evidence was assessed using the GRADE framework [22–25, 102], which analyzes risk of bias, inconsistency, indirectness, imprecision and publication bias, with ratings in four categories: high, moderate, low and very low. This methodology makes it possible to identify the confidence in estimates for adopting a recommendation in clinical practice or the health system, based on estimates of the effects for each outcome of interest. Outcomes of interest are categorized as critical, important but not critical or of limited importance to the decision process, using patient perspective as reference [22–25, 102]. The four outcomes of interest selected in the present study were classified as critical, due to their impact on the survival and quality of life of patients with PMs or ICDs. The baseline risk for the outcomes in patients with new PMs or ICDs was established based on the systematic review and meta-analysis by Sinha et al., as the most recent study that provides these data [15], and used to estimate the absolute increase in risk. Risk of publication bias was evaluated indirectly, since funnel plots are not recommended for meta-analysis containing a small number of studies [26]. The results obtained using the GRADE framework were analyzed and interpreted by an expert in the methodology (Dr. Taís Freire Galvão, Professor at the Faculty of Pharmaceutical Sciences of the State University of Campinas).

3. Results

3.1. Study selection

The manual and electronic database searches resulted in 291 files, 141 of which were simultaneously and independently selected by the reviewers based on their title and abstract, after excluding duplicates. Eleven articles were chosen to be read in full, nine of which complied with the PICOS framework [27–35]. The study selection flowchart is presented in Figure 1.

3.2. Overview of the studies

The main characteristics and results of the studies selected are shown in Table 1. All nine articles were cohort studies, but only two completely prospective, and were published between 1989 and 2020, with most concentrated in 2015 [27–31]. The methodological quality of the studies was assessed using the Newcastle-Ottawa Scale (NOS), with scores from zero to nine; four studies were attributed 8 points, another four 7, and one 6, demonstrating that high risk of methodological bias is not present in these observational investigations (Table 2).

The studies were conducted in three countries: three currently classified as high-income (Canada, Romania, Sweden), five upper middle-income (China, the Dominican Republic, Guatemala, Mexico, South Africa) and two low-income (India and Honduras) [103]. In only two studies, both carried out before the 2000s, were reused PMs implanted in populations from high-income countries [34,35], and in another four, Canada and France supplied PMs and ICDs to lower income nations [27–29,31].

Five studies evaluated the reuse of PMs and ICDs [27,29–32], one assessed only ICDs [28] and the remainder, which are older articles, analyzed only PMs [33–35]. However, the number of ICDs assessed was far lower than PMs: of the 2189 participants in the reuse groups across all nine studies, only 386 (17.6%) received an ICD. In most of the studies analyzed [27,29–32], the reused PMs and ICDs were generally extracted postmortem at funeral homes or hospitals. With respect to patient allocation into groups, none of the studies were blinded and in five, the individuals selected for reused devices were elderly or had a worse prognosis [29–31,34,35]. Ze et al. (2014) [34] used a different approach, whereby the reuse group consisted of patients whose devices were removed due to infection, reprocessed and then reused in the same patient.

All the articles used ethylene oxide sterilization; however, descriptions of the steps involved in cleaning and preparing the pacemakers were either very brief or incorrect, such as immersing the device in detergent for several days and applying chemical disinfectants before sterilization [27–30,32,33], both of which are contraindicated according to current best practices for processing health products.

3.3. Clinical outcome results

The average follow-up time was 29 months (varying from 6 to 48 months). Among the outcomes, infection and device malfunction were analyzed by all the studies, followed by premature battery depletion in seven articles and device-related death in four. The incidence of infection was 2.06% in the reused PM/ICD group and 1.58% for those with new devices, while malfunction and premature battery depletion obtained 0.23 and 1.37 for the reuse group and 0.06 and 0.55 for patients with new devices, respectively. No device-related deaths were reported in any of the groups. Five studies [27,29,30,32,35] reported the number of deaths unrelated to PMs or ICDs, caused by other underlying diseases or events. Considering only these articles, unrelated mortality in the reuse group was 5.55% (83 deaths/1494 participants) and 3.49% (140 deaths/4010 participants) in the group implanted with new devices. For all nine studies, the percentage of losses was 1.93% for patients with reused PMs/ICDs and 1.84% for those with new devices.

The conclusions of all the studies indicated that reusing PMs and ICDs is a viable strategy, with no significant differences in terms of worse clinical outcomes for patients.

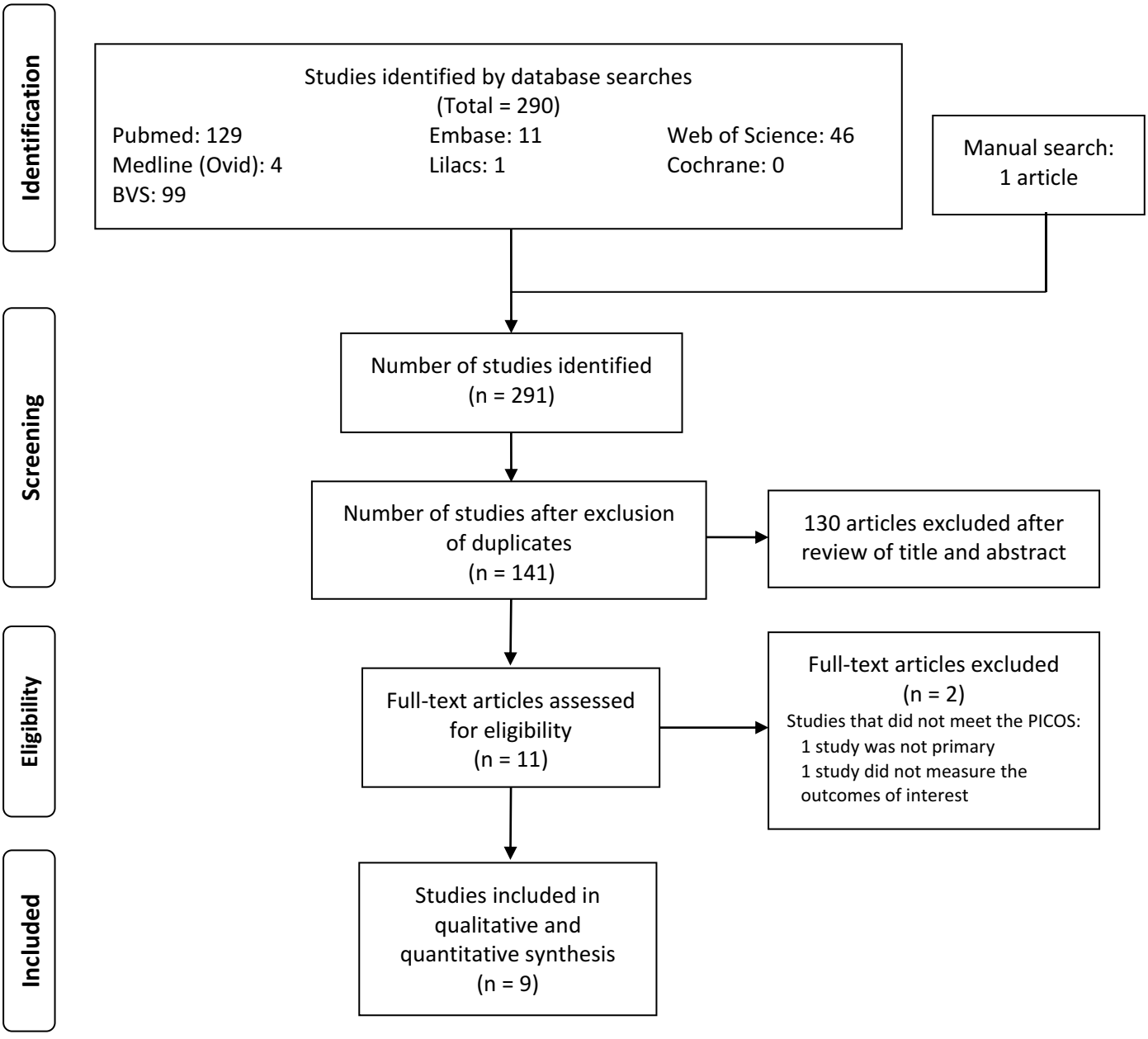

Figure 1. Flowchart of study selection.

3.4. Results of the meta-analysis and quality assessment of the body of evidence

The odds ratio (OR) was used as an effect measure in the meta-analysis and calculated for all the outcomes of interest except device-related death, which did not occur.

In regard to infection, the results of the individual studies showed no statistical significance, whereas pooled values were 0.98 for the OR (95% CI 0.59–1.62), heterogeneity (I [2]) of 23.04% and variability (H [2]) of 1.3. The forest plot is shown in Figure 2. The nine studies included also compared device malfunction between groups, with no statistical significance and, in most cases, a wide confidence interval, with a pooled OR of 1.58 (95% CI 0.56–4.48) (Figure 3), I^2 = 0% and H^2 = 1. Premature battery depletion was analyzed by seven of the articles, with OR = 1.96 (95% CI 0.81–4.72) and the relevant forest plot presented in Figure 4. Heterogeneity and variability results for malfunction were similar (I [2] = 0% e H^2 = 1).

The GRADE evidence table [102] is presented in Table 3,4. The outcomes of interest were classified as critically important from the patient's perspective, as a function of their severity. All the studies were observational and started from a low level of confidence in estimates.

The risk of bias of the body of evidence was classified as not serious for all the outcomes, inconsistency was low and there was no indirectness. For imprecision, all the effect measures and their confidence intervals indicated the null hypothesis, that is, no statistically significant difference between groups with new or used devices. Since the focus of the analysis was the absence of a significant intergroup difference in outcomes, the risk of imprecision was categorized as not

Table 1. Main characteristics and results of the selected studies.

Study and year of publication	Study reference	Country	Study methodology	Type of device	Method of obtaining device for reuse	Newcastle-Ottawa quality score	Follow-up period	Reuse Group						New Group						Effect measure adopted	Conclusion
								No. of participants	No. of infections	No. of device-related deaths	No. of malfunctions	No. of premature battery depletions	No. of losses	No. of participants	No. of infections	No. of device-related deaths	No. of malfunctions	No. of premature battery depletions	No. of losses		
Khairy et al. 2020	**27**	Canada, Dominican Republic, Honduras, Guatemala and Mexico	Prospective cohort	PM and ICD	Postmortem extraction	7	24	1051	21	0	0	NA	24	3153	38	0	0	NA	66	Relative risk	Among patients in underserved countries who received a resterilized and reused pacemaker or defibrillator, the incidence of infection or device-related death at 2 years was 2.0%, an incidence that did not differ significantly from that seen among matched control patients with new devices in Canada.
Enache et al. 2019[1]	**28**	Romania	Prospective cohort	ICD	Postmortem extraction or accidental contamination	8	33	157	3	NA	0	0	0	114	5	NA	0	0	0	Odds ratio	According to our data, properly verified and resterilized ICDs are as safe as new devices, when risk of infection or malfunction rates are assessed. Due to the high costs of new ICDs, their safe reuse has profound humanitarian and financial implications.
Selvaraj et al. 2017	**29**	India	Retrospective cohort	PM and ICD	Device exchange or postmortem extraction	7	6	260	0	0	0	NA	0	627	3	0	0	NA	0	Incidence	We found no difference in rate of infection or device malfunction among patients getting a reused device as compared with those with a new device. This study reinforces the safety of reusing devices for implant including cardiac resynchronization therapy deviceand implantable cardioverter defibrillator.

(*Continued*)

Table 1. (Continued).

Study and year of publication	Study reference	Country	Study methodology	Type of device	Method of obtaining device for reuse	Newcastle-Ottawa quality score	Follow-up period	Reuse Group						New Group						Effect measure adopted	Conclusion
								No. of participants	No. of infections	No. of device-related deaths	No. of malfunctions	No. of premature battery depletions	No. of losses	No. of participants	No. of infections	No. of device-related deaths	No. of malfunctions	No. of premature battery depletions	No. of losses		
Jama et al. 2015	**30**	South Africa	Retrospective cohort	PM and ICD	Postmortem extraction	6	15	63	0	0	1	0	0	63	0	0	0	0	0	Incidence	No significant differences were found in performance between re-used and new pacemakers and ICDs with regard to infection rates, device malfunction, battery life and device removal for complications. Pacemaker and ICD re-use is feasible and safe and is a viable option for patients with bradyarrhythmias and tachyarrthythmias.
Şoşdean et al. 2015	**31**	Romania	Retrospective cohort	PM and ICD	Device exchange or postmortem extraction	8	35	115	5	NA	0	1	0	146	7	NA	0	0	0	Odds ratio	Reuse of biventricular cardiac implantable electronics seems feasible and safe in both the general population and the elderly population, and it could be a promising alternative when new devices cannot be obtained in a safe period of time.
Ze et al. 2014	**32**	China	Rretrospective and prospective cohort	PM and ICD	Removal of infected device and reinsertion in the same patient	7	42	102	3	NA	2	0	3	115	2	NA	3	0	2	Relative risk	Reuse of infected cardiac rhythm management device in the same patients is noninferior to the implantation of new devices. In developing countries without full medical coverage, careful reuse of infected CRMDs can be considered.

(*Continued*)

Table 1. (Continued).

Study and year of publication	Study reference	Country	Study methodology	Type of device	Method of obtaining device for reuse	Newcastle-Ottawa quality score	Follow-up period	Reuse Group						New Group						Effect measure adopted	Conclusion
								No. of participants	No. of infections	No. of device-related deaths	No. of malfunctions	No. of premature battery depletions	No. of losses	No. of participants	No. of infections	No. of device-related deaths	No. of malfunctions	No. of premature battery depletions	No. of losses		
Nava et al. 2013	**33**	Mexico	Retrospective and prospective cohort	PM	Postmortem extraction	8	48	323	10	NA	1	11	16	316	11	NA	0	5	20	Relative risk	Pacemaker reuse is feasible and safe and is a viable option for patient with bradyarrhythmias. Other than the expected shorter battery life, reuse of pacemaker generators is not inferior to the use of new devices
Linde et al. 1998	**34**	Sweden	Retrospective cohort	PM	Postmortem extraction	7	24	100	2	NA	1	0	0	100	7	NA	0	0	0	Incidence	The re-use of pacemakers can be carried out without increased risk to the patients provided a proper routine for technical control and sterilization is followed. Re-use means substantial savings which possibly could make advanced pacemaker treatment available to all eligible patients irrespective of age. Whether re-use is feasible with implantable defibrillators remains to be determined.
Rosengarten et al. 1989	**35**	Canada	Prospective cohort	PM	Device exchange or postmortem extraction	8	36	18	1	0	0	0	0	52	1	0	0	0	0	Incidence	New and refurbished pacemakers are similar with respect to pacemaker related survival and complications. Refurbished pacemakers effect a major reduction in pacemaker costs while maintaining health care standards.

Table 2. Quality assessment of the studies using the new castle-ottawa scale [20].

	Khairy et al. 2020	Enache et al. 2019	Seravaj et al. 2017	Jama et al. 2015	Şoşdean et al. 2015	Ze et al. 2014	Nava et al. 2013	Linde et al. 1998	Rosengarten et al. 1989
A. Selection Study references	**27**	**28**	**29**	**30**	**31**	**32**	**33**	**34**	**35**
Representativeness of exposed cohort	⊛	⊛	⊛	⊛	⊛	⊛	⊛	⊛	⊛
Selection of non-exposed cohort	☒	⊛	⊛	⊛	⊛	⊛	⊛	⊛	⊛
Ascertainment of exposure	⊛	⊛	⊛	⊛	⊛	⊛	⊛	⊛	⊛
Outcome of interest absent at beginning	⊛	⊛	⊛	☒	⊛	☒	⊛	⊛	⊛
B. Comparability									
Study controls for the most important factor	⊛	⊛	⊛	⊛	⊛	⊛	⊛	⊛	⊛
Study controls for any additional factor	☒	☒	☒	☒	☒	☒	☒	☒	☒
C. Outcome									
Assessment of outcome	⊛	⊛	⊛	⊛	⊛	⊛	⊛	⊛	⊛
Sufficient follow-up for outcome occurrence	⊛	⊛	☒	☒	⊛	⊛	⊛	⊛	⊛
Adequacy of follow-up in cohorts	⊛	⊛	⊛	⊛	⊛	⊛	⊛	☒	⊛
Total number of stars	**7**	**8**	**7**	**6**	**8**	**7**	**8**	**7**	**8**

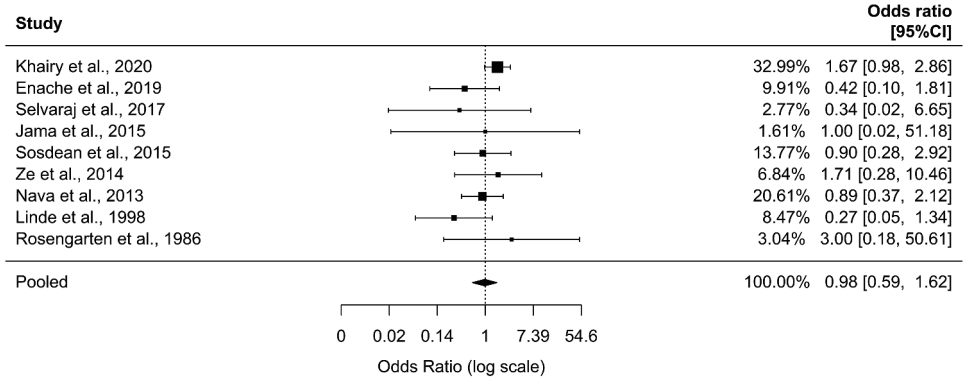

Figure 2. Forest plot for infection rate in studies that compare groups of patients implanted with reused versus new pacemakers and implantable cardioverter-defibrillators.

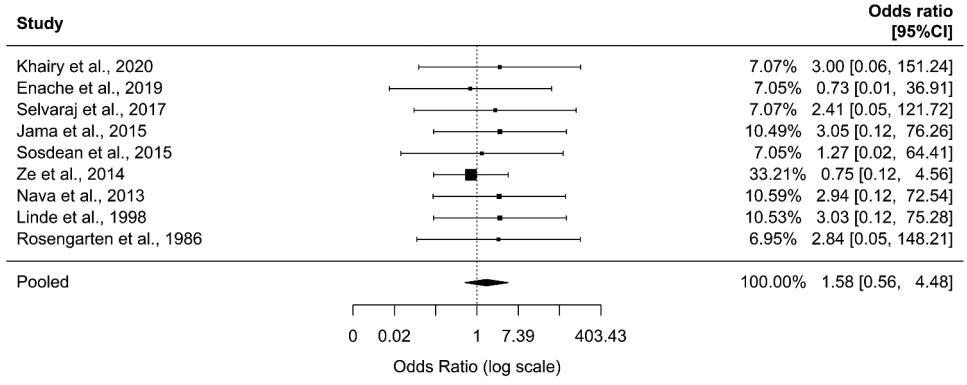

Figure 3. Forest plot for device malfunction in studies that compare groups of patients implanted with reused versus new pacemakers and implantable cardioverter-defibrillators.

serious. Additionally, the fact that several studies allocated older patients and those with a worse prognosis to the reused device group was considered a confounding factor. This favored better clinical outcomes in patients with new PMs/ICDs, who would be expected to exhibit lower rates of infection and device-related death, although this was not observed in any of these studies or the meta-analysis. As such, the confidence in estimates can be raised to moderate for infection and death.

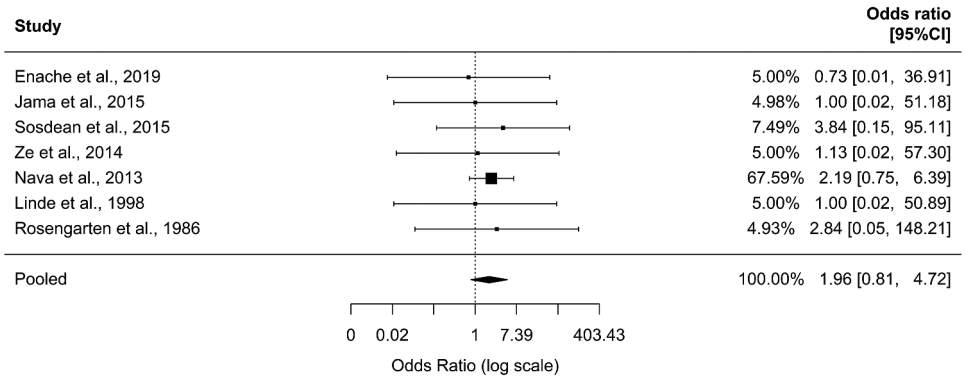

Figure 4. Forest plot for premature battery depletion in studies that compare groups of patients implanted with reused versus new pacemakers and implantable cardioverter-defibrillators.

Although the device malfunction and premature battery depletion outcomes were not statistically significant according to the meta-analysis, they enabled low confidence in estimates. Thus, further research is recommended with the implementation of functional controls for PMs and ICDs in order to strengthen the evidence for these outcomes.

The absolute effect is based on the relative magnitude of an effect and the baseline risk obtained by the control group in the study by Sinha et al. [15]. The absolute effect was 0 fewer per 100 (1 fewer to 1 more) for infection, 0 fewer per 100 (0 fewer to 0 more) for malfunction and 1 more per 100 (0 fewer to 2 more) for premature battery depletion. These calculations could not be performed for device-related death since no cases were reported.

4. Discussion

This meta-analysis contained 9 articles and included 6875 patients, 2189 of whom received reused PMs or ICDs. All the studies were either retrospective or prospective cohorts or a combination of both. Despite being the gold standard for robust evidence in the field of health, no randomized controlled trials were found, likely for ethical reasons. The primary outcomes infection, malfunction and premature battery depletion were identified both in patients who received new and reused PMs and ICDs, with no statistically significant intergroup differences. No studies reported any device-related deaths. The smaller number of ICDs analyzed in relation to PMs may be a limitation in this analysis, especially because of the risk of ventricular arrhyhthmia and shock events.

These results confirm the findings of two other meta-analyses [4,15] with the same focus, which concluded that PM and ICD reuse is a safe and viable alternative when these devices are inaccessible to patients with bradyarrhythmias and tachyarrhythmias. The authors also studied infection, premature or unexpected battery depletion, other device malfunctions and device-related death as primary outcomes. However, the present study differs in that the body of evidence on the topic was assessed using the GRADE framework, which made it possible to classify the confidence in estimates for infection rate and device-related death as moderate.

Publications on the reuse of PMs and ICDs date back to the 1970s, when the practice was already common in countries such as India, Romania, Sweden, Hungary, Israel, Australia, the Netherlands, Brazil, Italy and the Philippines [1,4], but has gradually been abandoned due to legal and ethical considerations [1,4]. The current European Cardiology Society guidelines, published in 2013, do not cover the issue and legislation varies between countries, since an existing legal and regulatory framework is a prerequisite for the reuse of implanted medical devices [3], which is banned in France, Portugal, the United States and Brazil, among others [9]. However, the regulatory restrictions identified in high-income countries such as the United States, Canada, France and other European nations do not prevent devices extracted postmortem from being donated to countries with no other alternative [27,31]. In 1983, records indicate the emergence of an organizational framework on the reuse of these devices, with multicenter programs aimed at donating explanted pacemakers and defibrillators to underprivileged countries after sterilization and functional testing.

The authors cite one such initiative, the Montreal Heart Institute, which created a program to retrieve pacemakers and defibrillators from 28 funeral homes and crematoriums in Canada and donate them to patients in poorer countries, thereby enabling greater access to these devices [27]. Another program cited in several articles is the Stimubanque organization in Nancy, France [28,29,31] which, since 2007, has partnered with STIM développement [104] to collect and distribute PMs/CDIs explanted postmortem at hospitals and funeral homes, with the verbal consent of family members, as well as those exchanged for more advanced models and devices whose packaging was inadvertently opened during implantation. In the United States, the University of Michigan Frankel Cardiovascular Center created the 'My Heart your Heart' project in 2009, which has since retrieved and distributed thousands of PMs and ICDs to patients in low-income countries [36], mainly South Africa, India, Mexico, the Dominican Republic, Guatemala, Honduras and Romania [29,31, 105]. Healthcare services and professionals interested in participating in these projects can obtain information from the organizational websites [104, 105].

Table 3. GRADE evidence table [102] on new versus reused pacemakers and implantable cardioverter-defibrillators.

Certainty assessment							No. of patients		Effect			
No. of studies	Study design	Risk of bias	Inconsistency	Indirectness	Imprecision	Other considerations	Reused pacemaker	New pacemaker	Relative (95% CI)	Absolute (95% CI)	Quality	Importance
Infection related to reused x new pacemaker (follow-up: average of 29 months; based on: no of cases of infection)												
9	observational study	not serious	not serious	not serious	not serious	Although all the potential confounding factors suggest a spurious correlation, no effect was observed.	45/2189 (2.1%)	74/4686 (1.6%) 1.8%	**OR 0.98** (0.59 para 1.60)	**0 fewer per 100** (1 fewer to 1 more) **0 fewer per 100** (1 fewer to 1 more)	□□□○ MODERATE	CRITICAL
Mortality related to reused x new pacemaker (follow-up: average of 20 months; based on: no. of deaths)												
4	observational study	not serious	not serious	not serious	not serious	Although all the potential confounding factors suggest a spurious correlation, no effect was observed.	0/1392 (0.0%)	0/3895 (0.0%) 0.0%	Not estimable		□□□○ MODERATE	CRITICAL
Malfunction related to reused x new pacemaker (follow-up: average of 29 months; based on: no. of cases of malfunction)												
9	observational study	not serious	not serious	not serious	not serious	none	5/2189 (0.2%)	3/4686 (0.1%) 0.0%	**OR 1.58** (0.56 to 4.48)	**0 fewer per 100** (0 fewer to 0 fewer) **0 fewer per 100** (0 fewer to 0 fewer)	□□○○ LOW	CRITICAL
Premature battery depletion related to reused x new pacemaker (follow-up: average of 33 months; based on: no. of cases of premature battery depletion)												
7	observational study	not serious	not serious	not serious	not serious	none	12/878 (1.4%)	5/906 (0.6%) 0.8%	**OR 1.96** (0.81 to 4.72)	**1 more per 100** (0 fewer to 2 more) **1 more per 100** (0 fewer to 3 more)	□□○○ LOW	CRITICAL

CI: Confidence interval; **OR**: Odds ratio

Table 4. Search strategy used for the Pubmed database. May, 2020.

((((((((‘Equipment Reuse’) OR (“Recycling	Equipment”)) OR (‘equipment recycling’)) OR (‘equipment reusability’)) OR (“Reusability	Equipment”)) OR (‘product recycling’)) OR (“Recycling	Product”)) OR (((((((refurshed) OR (resterilization)) OR (reusing))) OR (Reuse)) OR (Recycling)) OR (reusability)) OR (Reprocessing))) AND ((((((((((‘Equipment Reuse’[MeSH Terms]) OR (“Recycling	Equipment”[MeSH Terms])) OR (‘equipment recycling’[MeSH Terms])) OR (‘equipment reusability’[MeSH Terms])) OR (“Reusability	Equipment”[MeSH Terms])) OR (‘product recycling’[MeSH Terms])) OR (“Recycling	Product”[MeSH Terms])) OR (((((((refurshed [Title/Abstract]) OR (resterilization[Title/Abstract])) OR (reusing[Title/Abstract])) OR (Reuse [Title/Abstract])) OR (Recycling[Title/Abstract])) OR (reusability[Title/Abstract])) OR (Reprocessing[Title/Abstract]))) OR ((((((Infections[MeSH Terms]) OR (‘bacterial infections’[MeSH Terms])) OR (“Infection	Bacterial”[MeSH Terms])) OR (“Infections	Bacterial”[MeSH Terms])) OR (‘Bacterial Infection’[MeSH Terms])) OR (((((‘Cardiovascular Infections’[MeSH Terms]) OR (‘cardiovascular infection’[MeSH Terms])) OR (‘cardiovascular infections’[MeSH Terms])) OR (“Infection	Cardiovascular”[MeSH Terms])) OR (“Infections	Cardiovascular”[MeSH Terms]))))) AND ((((((((((((((((“Pacemaker
Artificial”[MeSH Terms]) OR (‘artificial pacemaker’[MeSH Terms])) OR (‘artificial pacemakers’[MeSH Terms])) OR (“Pacemakers	Artificial”[MeSH Terms])) OR (“Cardiac Pacemaker	Artificial”[MeSH Terms])) OR (‘Artificial Cardiac Pacemaker’[MeSH Terms])) OR (‘Artificial Cardiac Pacemakers’[MeSH Terms])) OR (“Cardiac Pacemakers	Artificial”[MeSH Terms])) OR (“Pacemaker	Artificial Cardiac”[MeSH Terms])) OR (“Pacemakers	Artificial Cardiac”[MeSH Terms])) OR (“Biventricular Pacemakers	Artificial”[MeSH Terms])) OR (‘Cardiac Resynchronization Therapy Devices’[MeSH Terms])) OR (‘Artificial Biventricular Pacemaker’[MeSH Terms])) OR (‘Artificial Biventricular Pacemakers’[MeSH Terms])) OR (“Biventricular Pacemaker	Artificial”[MeSH Terms])) OR (“Pacemaker	Artificial Biventricular”[MeSH Terms])) OR (“Pacemakers	Artificial Biventricular”[MeSH Terms])) OR ((((((Pacemaker[Title/Abstract]) OR (pacemakers[Title/Abstract])) OR (Biventricular[Title/Abstract])) OR (Resynchronization [Title/Abstract])) OR ((‘Cardiac Device’[Title/Abstract])) OR (‘Cardiac Devices’[Title/Abstract]))))	

Rosengarten et al. [35] report on a Canadian experience in reusing pacemakers at Montreal General Hospital, before the practice was banned in the province, in which the refurbishing costs for the hospital were very low compared to new devices. The estimated total cost of pacemaker refurbishment was 160 USD (Canadian dollars), with 50 USD for replacement parts, 10 USD for expenses related to refurbishment itself and 50 USD/h of sterilization; the device manufacturer (Medtronic®) charged 300 USD for functional testing, saving the hospital 33,000 USD/year. Functional assessment of the refurbished pacemakers by the manufacturer can be considered a standard of excellence and was not mentioned in any of the other studies analyzed.

Implanted PMs and ICDs must be removed after death to prevent explosions during cremation. Although an estimated 84% of these devices are still fully functional when explanted, they are typically discarded, contributing to the waste of a costly technological resource and exacerbating global environmental issues [3,5]. Additionally, data suggest that the average time between pacemaker implantation and the death of the recipient is 46 months (3.8 years), and given that the battery life of PMs varies from 7 to 10 years, the batteries in devices discarded after death still have a considerable shelf life [5,10].

The reuse of single-use devices (SUDs) is a global reality and not only in low-income countries. While only France strictly prohibits this practice, it is permitted in Brazil, the United States, Canada, Australia, Germany and several other European nations, subject to compliance with national health standards. The remaining countries have no specific legislation on the issue [9].

Despite the lack of national and international health standards aimed at improving patient safety and institutional liability, the practice remains controversial, with debate centering on technical feasibility, financial, legal and ethical aspects, as well of conflicts of interest on the part of manufacturers, healthcare personnel and funding agencies [6–14,37]. Although the reuse of SUDs, particularly implanted devices, is a contentious issue and prohibited by some national health authorities, such as the United States Food and Drug Administration (FDA) [13], it should be noted that more than one million people die annually worldwide as a result of lack of access to pacemakers, and effective reuse of these devices could be a viable option in countries whose health system is unable to supply them [1].

Several authors have reported that, if the reuse of implantable medical devices is in fact safe, as indicated by a number of studies, the practice can be justified, not only as an attempt to save lives, but to foster equality and recover the health and quality of life of patients in need of this technology [14,31]. However, there are still concerns regarding the safety and effectiveness of reuse protocols [4,11].

In terms of the technical feasibility of reusing material labeled as a single-use device by its manufacturer [13], the FDA clearly states that optimal and validated cleaning is key in decisions on safety by institutions proposing the practice, followed by functional testing. The basic guideline cited by the agency is that 'SUDs that cannot be cleaned effectively are impossible to sterilize properly'.

In this respect, the risk of reusing PMs and ICDs should be assessed against the obvious benefits to patients unable to access this technology. It is likely for this reason that in most of the studies, those deemed eligible to receive refurbished devices were older patients, those with a shorter life expectancy and chronic diseases such as cancer and degenerative pathologies. Nevertheless, variables not addressed by the authors of the studies selected for this meta-analysis should also be considered, including the possibility of transmitting prion diseases such as Creutzfeldt-Jakob Disease (CJD), since these agents are resistant to the ethylene oxide sterilization used in all the studies analyzed here. However, there are no reports of CJD cases related to the reuse of devices contaminated only with blood, since transmission of this agent results from exposure to tissue from the central or ocular nervous systems [38].

All the articles in the systematic review and meta-analysis showed flaws in the creation and validation of cleaning protocols, and focused on the occurrence of adverse outcomes (infection, premature or unexpected battery depletion, other device malfunctions and death) rather than emphasizing the importance of comparable safety between reused and new devices. Cleanliness was visually assessed when, at the very least, chemical tests should be conducted to detect the presence of residual protein, thereby ensuring more robust protocols.

German guidelines for cleaning SUDs stipulate up to 80 µg of protein residue on visibly clean devices, > 80 and < 150 µg as an alarm value indicating the need for review, and 150 µg as a limit value no to be exceeded [39].

The cleaning protocols presented for PMs and ICDs vary from unacceptable descriptions such as 'cleaned with alcohol and sterilized using ethylene oxide' [32] to some technically viable, albeit unvalidated, procedures. None of the studies mentioned concerns regarding the presence of biofilms, which are currently a global concern, particularly for implanted biomaterials [40,41].

Similarly, functional testing varied from minimal assessment based on visual inspection of device integrity, to outsourcing this practice to the manufacturer, as reported by Rosengarten [35]. The remaining battery life of the devices was part of functional testing in all of the studies analyzed, with the most common criterion adopted being a time period greater than or equal to half the maximum battery life, varying from 4 to 5 years. Some studies were more rigorous and stipulated a minimum 75% battery shelf life as a prerequisite for authorizing their reuse.

In this respect, there is an urgent need to improve the safety of processing PMs and ICDs for reuse. As such, it is essential to devise a processing method to transform contaminated used devices into fully functional (equivalent to new products), clean (no biofilms, endotoxins or residues of processing products) and sterilized material, in line with the principles of the FDA-validated protocol [13].

A group of experts in the field of processing medical devices could create a safe standard operating procedure to be followed worldwide by anyone who intends to reuse PMs and ICDs, including functional testing and ideally involving manufacturers.

From a financial perspective, there is no doubt that reusing these devices represents a huge saving for healthcare services and countries alike, but this should not outweigh safety concerns. Given the complexity of these products, steps must be taken to ensure that commercial and technological development measures enable them to be manufactured at affordable prices, giving everyone access to new devices, as has gradually occurred for catheters used in angiography. Providing different health care for patients who can afford it and those who cannot should be a thing of the past [1,15]. Equal access to health care requires quality and safety, regardless of the patient's socioeconomic status.

Linde et al. conducted a cost-benefit analysis in 1994 and found that implanting 317 reused pacemakers a year would represent an estimated national saving of US$ 919,300.00. Another study reported that the cost of implanting a reused ICD is 75% lower than that of a new device [28].

The dilemma regarding pacemaker reuse may not be a technical issue, since multiple studies, including this meta-analysis, confirm its safety, but instead a matter of agreement between regulatory authorities and manufacturers not only regarding these devices, but other costly SUDs. Thus, it is important to restructure regulatory frameworks for SUDs, initially in terms of manufacturer classification of these devices when registering them with regulatory agencies. Labels of multiple or single-use should be demystified and tests specified to confirm that SUDs can in fact be safely reused. This would definitively resolve the issue since, when registering these devices, manufacturers currently do not present evidence precluding their reuse. The conflicts of interest surrounding the issue should also be considered, since they motivate decisions regarding how these products are labeled as single-use devices.

Limitations of this meta-analysis are the small number of observational studies on the topic and lack of randomized controlled trials. A further limitation is the possibility of bias, given that in some studies patients selected for reused devices had more comorbidities and a shorter life expectancy, evident in the higher mortality unrelated to PMs or ICDs in the reuse group. This selection bias indirectly confirms that this practice does not pose an additional risk to the population studied.

5. Conclusion

The present study indicates that infection, malfunction and premature battery depletion are possible adverse events for PMs and ICDs, regardless of whether the devices are new or reused. It also confirms the findings of previous studies that this practice can be effective and clinically beneficial for patients in countries unable to sustainably supply these products and who cannot personally afford them.

It can be concluded that PM and ICR reuse is safe and feasible, provided that rigorous selection and processing methods are adopted by health services or reprocessing companies, in order to ensure the quality of the implanted device.

6. Expert opinion

The body of evidence on the clinical outcomes of patients who received reused pacemakers demonstrates the effectiveness of this practice, with moderate confidence for infection and device-related death. It is hoped that the scientific community will mobilize to produce new knowledge regarding the validation of processing protocols and acceptance parameters for reused devices, especially in countries with a limited supply of this important but costly therapeutic resource.

The main barriers to PM and ICD reuse can be categorized as regulatory, technical and ethical. Regulatory barriers require that the health authorities of countries unable to supply these devices have sufficient knowledge on the issue to satisfactorily address any conflicts of interest based on solid arguments. While the manufacturers of PMs and ICDs have legitimate reasons to advocate single use, not only to limit their liability and guarantee their product, but also due to financial and technological development issues, national health authorities have sole power to endorse the practice or not. This is essential in establishing quality control regulations and the traceability of these devices, balancing principles of equality and safety. Possible measures include establishing programs to collect explanted pacemakers, centralizing functional testing at public biomedical technology centers, providing accreditation for facilities capable of safely processing these devices and supporting the creation of clinical protocols and treatment guidelines on PM and ICD indication. This will certainly benefit patients and save public resources.

Another alternative to address regulatory barriers is market interference strategies, including public pricing, bulk buying from manufacturers and centralized distribution, in order to prevent intermediary costs and potential conflicts of interests on the part or prescribing professionals. These measures should be accompanied by clinical protocols and treatment guidelines based on the rational use of this costly technology.

With respect to technical barriers, the challenge lies in validating a selection, functional testing and processing protocol that allows traceability and can be safely applied by institutions that intend to reuse PMs and ICDs. The definition of clear and feasible device acceptance parameters is vital. With respect to cleaning the devices, methods must be available that can adequately remove dirt and measure organic residues before sterilization. There is significant scope for research in this area, including the identification of microbial activity on explanted devices, the presence of biofilms, microscopic analysis of the external surface of the pacemaker to check for structural damage that favors biofilm formation, and the application of chemical tests to assess cleanliness, among others.

Ethical barriers are relevant because even when pacemaker reuse is proved to be safe, transparent clinical criteria are needed to indicate when a new or refurbished device should be used. This decision cannot be based on the patient's financial status or savings for the health system. For example, young patients could be prioritized for new devices because their longer battery life would prevent the need for repeated surgeries. In cases of removal due to infection, reusing these devices in the same patients is a possible alternative, as proposed by Ze et al. [32]. The principles of evidence-based health and health technology assessment can help decision makers to conduct a broader analysis of the issue and create clinical protocols that optimize access to this precious resource, based on fairness and equality.

The authors of the present study form part of a work group aimed at examining PM and ICD reuse from the three above-mentioned perspectives. The meta-analysis that assesses the quality of the body of evidence is the first result of this group project and aims to provide support for arguments on the clinical outcomes of patients implanted with reused PMs and ICDs in order to encourage the Brazilian health authorities to review the ban on this practice in the country. A second systematic review is underway on ethical aspects and international health regulations on the topic, in addition to an experimental study to validate a processing protocol for these devices, which is currently in the methodological planning phase.

Furthermore, we hope that, armed with this evidence, health authorities will take the necessary steps to address the conflicts of interest that cause unequal access to the PMs and ICDs that cardiac patients need to survive.

Acknowledgments

The authors are grateful to Dr. Rosana Evangelista Poderoso (Librarian and Director of the Medical Sciences School Library at Unicamp), Dr. Bernardo dos Santos (Statistician at the Research Support Center of the USP Nursing School) and Dr. Taís Freire Galvão (Pharmacist, Professor at the Faculty of Pharmaceutical Sciences at Unicamp).

Declaration of interest

The authors have no relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript. This includes employment, consultancies, honoraria, stock ownership or options, expert testimony, grants or patents received or pending, or royalties.

Reviewer Disclosures

One peer reviewer is a consultant to Medtronic Inc., and is a member of Speakers Bureau Abbott Labs (SJM). Peer reviewers on this manuscript have no other relevant financial relationships or otherwise to disclose.

Author contributions

Conceived and designed the experiments: EM Psaltikidis EAM Costa KU Graziano. Performed the experiments: EM Psaltikidis EAM Costa KU Graziano. Analyzed the data: EM Psaltikidis EAM Costa KU Graziano. Contributed reagents/materials/analysis tools: EM Psaltikidis EAM Costa KU Graziano. Wrote the paper: EM Psaltikidis EAM Costa KU Graziano. Provided editorial advice: EM Psaltikidis EAM Costa KU Graziano.

Funding

This paper was not funded.

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