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## The importance of preventing infections related to the implantation of a cardiac implantable electronic devices in the population of Bydgoszcz

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### Abstract:

Cardiac implantable electronic device (CIED) infection, despite significant developments in medicine, is still a significant source of morbidity and mortality, occurring in the range of 1% to 4% of all implantation cases. A modern approach to reducing the risk of CIED infection is the use of an absorbable antibacterial coating, also known as an envelope in which the device is placed. The material from which the envelope is made is completely absorbed by the body approximately nine weeks after implantation, simultaneously releasing antibiotics. The presented manuscript discusses the importance of preventing infections related to CIEDs implantation and presents partial data on implanted CIEDs in the population of Bydgoszcz.

Research into infections associated with CIED implantation is highly important as it can significantly reduce the risk of complications and improve treatment outcomes. Continued research in this field is essential to refine prevention strategies and enhance the quality of care for CIED patients.

The presented data on implanted CIEDs in the population of Bydgoszcz represent a crucial step in understanding the prevalence of these devices and may provide valuable insights for further research into preventing CIED-related infections. Further analysis of this data can help develop more effective prevention strategies and improve healthcare in this area.

**Key words:** implantation, cardiac implantable electronic devices, Bydgoszcz

## 1. Introduction

Cardiac implantable electronic devices (CIEDs) are divided into: pacemakers (PMs)/ implantable pulse generators (IPGs), implantable cardioverter-defibrillators (ICDs) and cardiac resynchronization therapy (CRT) devices - with the function of defibrillation or stimulation only. CIED infection, despite the great development of medicine, is still a significant source of morbidity and mortality, occurring in the range of 1% to 4% of all implantation cases [1–3]. Table 1 presents the terminology associated with CIED infections [4].

Table 1. Terminology related to CIED infections.

		Lead or valvular vegetations on echocardiogram?			
		Yes	No		
Signs of pocket infection?	Yes	Pocket infection with lead/valvular endocarditis	Isolated pocket infection	-	blood cultures?
			Pocket infection with bacteremia	+	
	No	CIED-related endocarditis without pocket infection	Occult bacteremia with presumable cardiac implantable electronic device (CIED) infection		

The table is based on the article by N.O. Palmeri, D.B. Kramer, A.W. Karchmer, P.J. Zimetbaum: A Review of Cardiac Implantable Electronic Device Infections for the Practicing Electrophysiologist, JACC Clin. Electrophysiol. 7 (2021) [4]

## 2. Medical and economic-social significance of complications related to the implantation of cardiac implantable electronic devices

Initially, it was believed that device infections occurred only as a result of contamination of the implant by the bacterial flora naturally present on the skin during its implantation [5]. It is now recognized that pathogens can spread in the body through the blood from distant metastatic foci of infection, which results in the colonization of CIED with gram-positive bacteria [6,7]. CIED infection by gram-negative bacteria is rare, although it can occur, even as a result of transient bacteremia with origin in the abdominal cavity or urinary tract [8–10]. Among the gram-positive bacteria, the most common are staphylococci: *Staphylococcus aureus* and *Staphylococcus epidermidis* [11]. Other gram-positive bacteria such as *Cutibacterium* and *Corynebacterium* species account for a smaller percentage of infections [8,9]. Nowadays, *Staphylococcus aureus* is responsible for the majority of CIED infections and is associated with higher mortality rates compared to coagulase-negative staphylococci, which are other frequently occurring etiological organisms [12–14]. The incidence of CIED

infections in patients with *S. aureus* bacteremia is estimated to range from 30% to 40% [15]. Methicillin-resistant *Staphylococcus aureus* (MRSA), constitute half of all CIED infections caused by *S. aureus* and are often associated with a worse prognosis [16, 17]. The presence of MRSA on patients' skin is an independent risk factor for CIED infection, suggesting that infection may occur during device implantation [11, 18]. Culture-negative CIED infections are a particular problem, occurring in approximately 6% to 20% of all CIED infection cases. This usually occurs when antibiotics are administered before the results of appropriate culture tests are available, but may also occur in infections caused by microorganisms that are difficult to culture [11,16,19–22]. From 1993 to 2008, the number of CIED implantations in the United States increased by 96%. At the same time, the incidence of CIED-related infections increased by 210%, going from 1.5% in 1993 to 2.4% in 2008 [23]. This association has been attributed to the increasing burden of comorbidities in CIED patients, a higher percentage of complex devices, and a concomitant higher reimplantation rate [24,25]. Effective treatment requires the cooperation of experts in cardiac electrophysiology, infectious diseases and other medical specialties. Among the number of complications associated with CIED, infections have the greatest impact on mortality and prolong hospitalization. In the study by Palmisano et al., the procedure with the highest risk of complications was CRT implantation. Complications mainly concerned displacement of the electrode placed in the coronary sinus and infection of the device. Patients with complications had significantly higher device-related hospitalizations ( $2.3 \pm 0.6$  vs.  $1.0 \pm 0.1$ ;  $p < 0.001$ ) and inpatient days ( $15.7 \pm 25.1$  vs.  $3.6 \pm 1.1$ ;  $p < 0.001$ ) compared to patients without complications. Device infection was the complication that had the greatest negative impact on patient treatment outcomes [26]. It is estimated that 5% to 10% of patients die during hospitalization, while within a year after the procedure the overall mortality rate increases significantly and ranges from 16% to 36% [23,27–30]. It has been observed that the rates of complications and infections are higher in re-intervention than in primary CIED implantation procedures, further emphasizing that primary prevention of infection is particularly important [24,25,31,32]. In the United States of America, hospitalization costs related to the treatment of CIED infection range from USD 45,000 to USD 55,000 [33,34]. Another concern is the effective management of CIED infection. It always requires complete removal of the existing system (which is not possible in all institutions implanting CIEDs and is associated with a number of complications), long-term antibiotic therapy and the need to reimplant the device [31,35,36]. The standard of care results from the need to remove infected electrodes on which biofilm develops [37]. The new system must be implanted on the opposite side from the previous one, which limits the possibility of using the same venous route in the upper part in the future. Reinfection after reimplantation may significantly complicate or even require sternotomy. Moreover, it may not be possible to recreate a CRT system with similar clinical effectiveness because the target vein containing the previous left ventricular lead may not be available for reuse and other vessels do not provide a similar effect [38]. A number of information related to CIED infections in Poland is provided in the study entitled: "How to reduce costs associated with infections of systems used for cardiac electrotherapy in Poland" [38]. In 2019, the number of CIED implantations or replacements amounted to 44,000. PMs accounted for over 71.4% of this number, ICD implantations 17.6% of the total, while in the case of patients with cardiac resynchronization therapy with defibrillator function (CRT-D) this percentage was 9.1%, and implantation of cardiac resynchronization therapy with pacemaker function (CRT-P) accounted for 1.8% of the total [38]. The ratio of the number of infections to implantations in the period 2016-2019 was on average 0.9%, while taking into account only the CRT-P and CRT-D infection rates, the average level was 1.9% and 1.7%, respectively, and the average cost of treating infections CRT-D in 2016-2018 amounted to almost PLN 50,000 [38]. The authors of the report by the Institute of Innovation and

Responsible Development INNOWO show that although complications related to cardiac electrotherapy procedures do not occur often (approximately 1% of all procedures performed in Poland annually, i.e. approximately 400 CIED infections), they may have serious consequences for the well-being of patients, and what is more, analyzes included in the INNOWO report showed that the actual cost of treating CIED infection may reach up to PLN 200,000 [38]. On average, treatment procedures for CIED-related infection bring losses of PLN 3,000 to hospitals, and each subsequent day of the patient's hospitalization results in a decline in the financial result center by an average of almost PLN 872 [18]. The INNOWO report emphasized that in the years 2016-2019 there was an increase in the costs of treating infections related to PLN 5.4 million to PLN 7.4 million. More than 2/3 of the total cost of treating CIED infections were expenses related to hospitalization of patients and the devices themselves. The third largest category of costs were expenses for drugs and medical devices necessary to perform the extraction procedure [38]. This highlights the growing financial challenge of treating CIED infections and the need to take action to control and reduce these costs.

### ***3. Modifiable and non-modifiable risk factors for infection associated with cardiac implantable electronic device implantation and methods of its reduction***

ESC Guidelines and Recommendations: The European Society of Cardiology (ESC) 2021 guidelines provide important recommendations for reducing the risk of cardiac implantable electronic device (CIED) infection. These guidelines emphasize the administration of prophylactic antibiotics before surgery, the choice of skin antiseptics, and specific considerations for venous access and coronary sinus leads. These recommendations are crucial for standardizing infection prevention practices during CIED implantation [39].

The European Society of Cardiology (ESC) 2021 guidelines on cardiac pacing and cardiac resynchronization therapy contain information and recommendations on CIED prevention, which are presented in Table 2 [39].

Table 2. Summary of ESC recommendations regarding specific aspects of device implantation and perioperative management. Based on ESC 2021 guidelines [39].

Recommendation	class of recommendations
It is recommended to administer prophylactic antibiotics preoperatively, at least 1 hour before skin incision, to reduce the risk of CIED infection	I
Chlorhexidine should be considered instead of povidone-iodine for skin antisepsis	IIa
For venous access, the cephalic or axillary vein should be considered as the vein of first choice	IIa
For implantation of coronary sinus leads, quadripolar leads should be considered as first choice	IIa
Multiple fluoroscopic views should be considered to confirm target ventricular lead placement	IIa
Rinsing the device pocket with normal saline solution before wound closure should be considered	IIa
In patients undergoing CIED reintervention, the use of an antibiotic-eluting envelope may be considered	IIb
Pacing of the mid-ventricular septum may be considered in patients at high risk of perforation	IIb

In pacemaker implantations in patients with possible pocket issues such as increased risk of erosion due to low body mass index, Twiddler's syndrome or aesthetic reasons, a submuscular device pocket may be considered	IIb
Heparin-bridging of anticoagulated patients is not recommended	III
Permanent pacemaker implantation is not recommended in patients with fever. Pacemaker implantation should be delayed until the patient has been afebrile for at least 24 h.	III

Class I - Scientific data and/or generally accepted opinion indicate that a particular treatment or procedure is beneficial, useful, effective (Recommended or advisable); Class II - Evidence or opinion regarding the suitability or effectiveness of a particular treatment or procedure is inconsistent (Class IIa - should be considered, Class IIb - may be considered); Class III - Scientific data or generally accepted opinion indicates that a particular treatment or procedure is not useful or effective and, in some cases, may be harmful (Not recommended)

The authors of the guidelines in the section regarding the device pocket also inform that the use of an antibiotic-eluting envelope may be considered in patients with a pacemaker and a high risk of CIED infection. Risk factors for CIED infection include end-stage renal disease, chronic obstructive pulmonary disease, diabetes and procedures related to the replacement, revision or expansion of the device [38]. However, it should be remembered that less than two years have passed since the publication of the above guidelines, so below we present mainly data published after the period when the guidelines were created.

**Risk Factors for CIED Infection: Understanding the risk factors associated with CIED infection is essential for risk stratification and implementing preventive measures. Modifiable risk factors such as procedure duration, device placement, and antibiotic choices, as well as non-modifiable factors like previous CIED-related procedures and comorbidities, were identified as significant predictors of infection [40][41].**

The aim of the 2021 analysis by El-Chami et al. was to estimate the incidence of infections in de novo implanted transvenous (TV) ICDs and to assess factors associated with the risk of infections in the population using the Medicare program [40]. Of 26,742 patients with newly implanted TV-ICDs, 519 (1.9%) developed infection within 720 days after ICD implantation. More than half (54%) of infections occurred within the first 90 days, 16% of infections occurred after 365 days. The analyzed potential risk factors were identified using the codes of the International Statistical Classification of Diseases and Related Health Problems (ICD-10), which are presented in the article's supplement. Multivariate analysis revealed several significant predictors of infection:

1. age under 70,
2. presence of a cardiovascular prosthesis (condition after implantation of a valve prosthesis and condition after intraluminal closure of the left atrial appendage),
3. kidney disease treated with dialysis therapy,
4. diabetes with chronic complications,
5. chronic obstructive pulmonary disease,
6. depression,
7. valve disease,

8. anemia,
9. drug addiction,
10. weight loss.

Patients were excluded if there was evidence of previous CIED infection within 6 months and/or signs of infection were observed on admission. Due to the lack of data, the analyzed risk factors did not include the need to use corticosteroids or anticoagulants, which the authors emphasize in the limitations of the study [40]. To identify risk factors for CIED infection after secondary CIED-related procedures, Tarakji et al. analyzed 2,803 control patients from the WRAP-IT (World-wide Randomized Antibiotic Envelope Infection Prevention trial) trial; some traditional patient-related risk factors, including: end-stage renal disease, immunocompromised state and recent CIED infection were exclusion criteria from the WRAP-IT study) who received standard preoperative antibiotic therapy but did not receive an antibacterial envelope (44 patients experienced serious infections throughout the observation period) [41]. The study identified 17 risk factors out of 81 variables analyzed. Of the selected variables, 6 were related to the patient and device characteristics (non-modifiable), while 11 were related to the procedure itself (modifiable). Of these 11 procedure-related risk factors, 8 were associated with an increased risk of infection: [in brackets: (the number of occurrences of a given factor; hazard ratio)]

1. Extended procedure duration >60 min (100; 1.09)
2. Placement of the device beyond the subcutaneous location on the left side of the sternum (36; 1.10)
3. Use of glycopeptide antibiotics in the perioperative period (vancomycin, teicoplanin) compared to an alternative perioperative antibiotic - mainly cephalosporins (11; 1.15)
4. Full capsulectomy (vs. partial or no capsulectomy) (14; 1.22)
5. Use of anticoagulants and antiplatelet drugs during the CIED implantation procedure (16; 1.05)
6. Use of antiplatelet drugs during the CIED implantation procedure (16; 1.15)
7. Use of an anticoagulant during the CIED implantation procedure (66; 1.08)
8. Use of an anticoagulant during the CIED implantation procedure other than warfarin or apixaban (52; 1.17)

The authors included the following non-modifiable factors associated with an increase in the risk of CIED infection (some traditional patient-related risk factors, including: end-stage renal disease, immunocompromised status and recent CIED infection were exclusion criteria from the WRAP-IT study): [in brackets: (the number of occurrences of a given factor; hazard ratio)]

1. Any increase in the number of previous CIED-related procedures (53; 1.03)
2. History of atrial arrhythmia (49; 1/08)
3. Type of CIED (CRT-D vs PM/ICD) (22; 1.09)
4. Geographic location of the implantation center outside North America and Europe (13; 1.30)

5. Type of CIED (CRT-P vs PM/ICD) (10; 1.21)

Factors reducing the risk of CIED infection were: [in brackets: (the number of occurrences of a given factor; hazard ratio)]

1. Increase in body weight by one BMI unit (body mass index) (16; 0.99)
2. Use of apixaban vs. other anticoagulant vs. no anticoagulant (51; 0.71)
3. Skin preparation with hexidine chloride (38; 0.87)
4. Rinsing the CIED pocket with an antibiotic vs. rinsing with another agent or no rinsing (15; 0.94).

Meta-analysis by Olsen et al evaluated consecutive Danish patients undergoing CIED implantation or reoperation and aimed to identify lifelong risk factors for CIED infection. The study included a cohort of 84,429 patients who underwent 108,494 CIED surgeries. A total of 1556 cases of CIED removal were classified as pocket infections (n=1022) or CIED infections with bacteremia (n=534).

Multivariate analysis performed for both types of CIED infections showed that the significant risk factors were:

1. CIED reoperations
2. CIED type (ICD, CRT-P, CRT-D)
3. age <60 years and age >70 years
4. severe kidney failure or dialysis
5. systemic lupus erythematosus
6. dermatitis and eczema
7. rose
8. previous valve surgery
9. surgical revision of the electrode
10. drugs used: beta-lactamase-resistant penicillins, direct oral anticoagulant inhibitors (DOAC), clopidogrel, insulin, warfarin, acenocoumarol

Heart failure, ischemic heart disease, malignant tumor, chronic obstructive pulmonary disease and the need for temporary cardiac electrical stimulation had no significant effect in multivariate analysis. The authors cited the lack of available microbiological data and the fact that only patients after CIED removal were included in the analysis as limitations of the study. In 2022, Ngiam et al. assessed the risk factors associated with increased mortality in CIED infections in their meta-analysis, and it was the first work of this type in the world [42]. 12 studies were included in the analysis, including 10 retrospective studies and 2 prospective cohort studies. The overall mortality rate after CIED infection was 13.7% (438 of 1398 cases). The meta-analysis found that male gender (OR 0.77, 95% CI 0.57–1.01) seemed to be associated with a lower risk of mortality, while diabetes seemed to be associated with a higher mortality (OR 1.47, 95% CI 0.67–3.26) – these trends did not reach statistical significance. Significantly higher mortality was associated with:

1. Staphylococcus aureus as the etiological factor of CIED infection (OR 2.71, 95% CI 1.76–4.19),
2. Heart failure as a complication of CIED infection (OR 1.92, 95% CI 1.42–4.19)
3. Pulmonary embolism and other embolic phenomena as a complication of CIED infection (OR 4.00, 95% CI 1.67–9.56)

Risk stratification for device infection is important because it increases awareness of risk factors that can be eliminated or minimized through various preventive measures. Many known risk factors for CIED infection are modifiable and preventive measures can be taken to reduce the risk of their occurrence [36,43–45]. Due to the significant implications associated with CIED infection, it is crucial to identify patients at higher risk of developing such infection in order to implement appropriate preventive strategies. In order to stratify the risk of infection, several clinical scales have been proposed, such as those developed by Shariff or Kolek, or the 'Prevention of Arrhythmia Device Infection Trial' (PADIT) scale. Only some risk factors occur together on different scales, with different definitions and significance. All available scales are easy to use and can be quickly calculated based on medical history, standard laboratory tests and procedure type. Due to the low predictive capacity of each of the popular scales, further research in this area is necessary [46,47].

#### ***4. Antibacterial envelope as a method of reducing the risk of infection associated with the implantation of an implantable cardiac electrotherapy device.***

A modern approach to reducing the risk of CIED infection is the use of an absorbable antibacterial coating, also known as an envelope, in which the device is placed. Currently available antibacterial envelopes are made of polypropylene fibers, which gradually release rifampicin and minocycline over approximately 1-2 weeks. The material from which the coating is made is completely absorbed by the body approximately nine weeks after implantation, while releasing antibiotics (The TYRX Absorbable Antibacterial Envelope; Medtronic, Mounds View, MN, USA). Their antibacterial activity is directed against pathogens such as *S. aureus* (both methicillin-sensitive and resistant), *S. epidermidis*, *S. lugdunensis*, *Acinetobacter baumannii* and *Escherichia coli* [48].

Meta-Analyses and Antibacterial Envelopes: Several studies and meta-analyses have assessed the effectiveness of antibacterial envelopes in reducing CIED infections. These envelopes, when used in high-risk patients, have shown a substantial reduction in major infections and pocket infections [50][51][52]. Moreover, cost-effectiveness analyses have indicated that the use of antibacterial envelopes is economically favorable, particularly in patients at high risk of infection [49][54].

Within the pouch, minimal inhibitory concentrations can be achieved as early as 2 hours after implantation and persist for at least one week [49]. In order to optimize the benefit-cost ratio, it is recommended to use an envelope based on the result of the PADIT scale used [80]. Published results of the randomized WRAP-IT (The Worldwide Randomized Antibiotic Envelope Infection Prevention Trial) study, which aimed to assess the safety and effectiveness of The TYRX antibacterial envelope in reducing CIED infections. Patients were randomly assigned in a 1:1 ratio to the study group in which an antibacterial envelope was used and to the control group in which the envelope was not used. The observation period lasted 12 months. The study included patients at increased risk of CIED infection, including those undergoing device battery replacement, CIED expansion, implant site or lead revision, and patients undergoing CRT-D implantation. The primary endpoint of the study was the occurrence of a serious local or generalized CIED infection requiring surgical treatment or long-term antibiotic therapy with recurrence of infection or death within 12 months of surgery. Secondary study endpoints were procedure- or device-related complications within 12 months of surgery, any CIED infections within 12 months, and major device infections throughout the



follow-up period [50]. The WRAP-IT study was conducted between January 2015 and July 2017 and included 7,075 patients from 25 countries. Of the total number of patients studied, 6,983 patients were randomized into two groups: 3,495 patients received an antibacterial envelope and 3,488 patients were the control group in which no envelope was used. The average age of the respondents was  $70.1 \pm 12.5$  years, and 28% were women. The basic characteristics of both groups of patients did not differ significantly, and the duration of the procedure was also similar. The average follow-up period was almost 21 months. Over the 12-month follow-up period, the number of device revisions was lower in the antimicrobial envelope group (153 envelope patients vs. 186 control patients; RR 0.79; 95% CI 0.65-0.96). Additionally, fewer major infections were reported in the envelope group (30 cases in 25 patients with the envelope vs. 45 cases in 42 patients in the control group; HR 0.60; 95% CI 0.36-0.98;  $P = 0.04$ ), the majority of which were pocket infections CIED and infective endocarditis or bacteremia. The incidence of pocet infection was lower in the envelope group (0.4% vs. 1.0% in the control group; HR 0.39; 95% CI 0.21-0.72). In summary, the use of an antimicrobial envelope in a population of patients at increased risk of CIED infection resulted in a 40% reduction in the occurrence of major infections over a 12-month follow-up period compared to standard care. Additionally, there was no increased incidence of procedure-related complications or CIED in patients using the envelope [50].

The study by Chaudhry et al. aimed to assess the effectiveness of an antibacterial envelope in a group of patients at high risk of infection vs. a control group without an envelope (PADIT total score  $5.9 \pm 3.1$  vs.  $3.9 \pm 3.0$ ,  $p < 0.0001$ ) [51]. There were no pocket infections in the envelope group, compared with 2.6% in the control group ( $P = 0.04$ ). When analyzing only the high-risk group for CIED-related infection, a much more noticeable difference was found (0% vs. 9.9% pocket infections in the control group,  $P = 0.01$ ). Investigators confirmed the clinical effectiveness of the antimicrobial envelope in preventing device pocket infections in patients at intermediate and high risk of CIED infection according to the PADIT score. In pursuit of a better cost-benefit ratio, the authors recommend rational use based on the PADIT score [52].

**Risk Stratification:** The identification of high-risk patients is a critical step in infection prevention. Risk stratification tools such as the PADIT score can help categorize patients into low, medium, and high-risk groups, enabling tailored preventive strategies [52].

The PADIT study identified 5 independent predictors of device infection: previous CIED-related procedures, age, impaired renal function, immunosuppression, and procedure type. A risk score was calculated for each patient by summing the points assigned to each predictor: number of previous procedures (1 point for 1 procedure, 4 points for  $\geq 2$  procedures), age (1 point for age 60-69 years, 2 points for age  $< 60$  years ; we chose age  $\geq 70$  years as the reference group because it had the lowest risk), impaired renal function (1 point), impaired immunity (3 points), and type of procedure (2 points for ICD, 4 points for CRT, and 5 points for revision/ update). According to the infection incidence rate, patients were divided into groups: low risk ( $< 1\%$ ), medium risk (1%–3%), and high risk ( $> 3\%$ ). Based on this classification, 13,828 patients had low risk (score: 0 to 4), 4,151 patients had intermediate risk (score: 5 or 6), and 1,406 patients had high risk (score:  $\geq 7$ ), with hospitalization rates due to infections being 0.51%, 1.42% and 3.41% respectively. Asbeutah et al. performed a meta-analysis of 6 studies covering a total of 11,897 patients (5,844 group with antibacterial envelope vs. 6,053 patients in the control group) [53]. Compared with the control group, the

use of an antimicrobial envelope during the procedure was associated with a significant relative risk reduction of 74% in the occurrence of major CIED-related infections (the primary outcome used in the meta-analysis was the occurrence of a major device-related infection, defined as systemic infection or endocarditis requiring systemic antibiotic therapy and/or device extraction). in patients at high risk of infection (RR: 0.26 [95% CI, 0.08–0.85]; P=0.03). No significant reduction was observed among patients at any risk of infection (RR: 0.53 [95% CI, 0.06–4.52]; P=0.56). Kay et al established a decision tree to evaluate the cost-effectiveness of the antimicrobial envelope compared with standard of care, which was defined as one dose of prophylactic antibiotic administered before surgery. Resource use included drug purchase and administration, hospitalization, adverse events, extraction, and device replacement. The incremental cost-effectiveness ratio (ICER) was calculated based on costs and quality-adjusted life-years (QALYs). Over a 12-month period, the Medtronic antimicrobial envelope was less expensive and more effective than standard care when used in patients with an ICD or CRT-D. It was associated with an ICER of £46,548 and £21,768 per QALY in patients consecutively with IPG or CRT-P. The antimicrobial envelope was cost-effective at the £30,000 threshold, with initial infection probabilities exceeding 1.65% (CRT-D), 1.95% (CRT-P), 1.87% (IPG) and 1.38% (ICD) ). The model predicted that 3.2% of patients at high risk of CIED-related infection receiving prophylactic antibiotics would require CIED extraction within the first year of use (vs. 0.5% of the antimicrobial envelope group), and 5.5% of patients in the control group ( vs 0.9% of the antibacterial envelope group) will be hospitalized due to reinfection or device extraction within the first 12 months [49]. To estimate the cost-effectiveness of using an antibacterial envelope in three European healthcare systems: Germany, Italy and England, in patients at increased risk of infection with CIED implantation, Boriani et al. developed a special model in which patients were divided into subgroups based on presence of factors increasing the risk of infection. [54]. The most favorable cost-effectiveness profile of the antibacterial envelope occurred in patients who: had a previous CIED infection, a history of immunosuppressive therapy, or had a PADIT score of  $\geq 6$ . Probabilistic sensitivity analysis indicated that the use of an antimicrobial bag would likely be cost-effective in patients with other risk factors (history of  $\geq 2$  prior procedures, including ICD/CRT-D replacement, device replacement with electrode modification, and PADIT scores indicating moderate risk of infection). The authors considered their model to be an update of the results presented by Kay et al [54].

### ***5. Cardiac implantable electronic devices in the population of Bydgoszcz***

CIEDs implantations in Bydgoszcz are shown in figures [1-4].

CIED Implantation Trends: The data on CIED implantations in Bydgoszcz in 2021 indicate a substantial number of procedures, with pacemakers being the most common type followed by ICDs and CRT devices. The increasing number of CIED implantations is likely due to population aging and improved access to these procedures. These trends highlight the importance of infection prevention measures to address the growing number of CIED recipients [1-4].

Figure 1. Pacemakers in the population of Bydgoszcz. National Health Fund data for 2021.

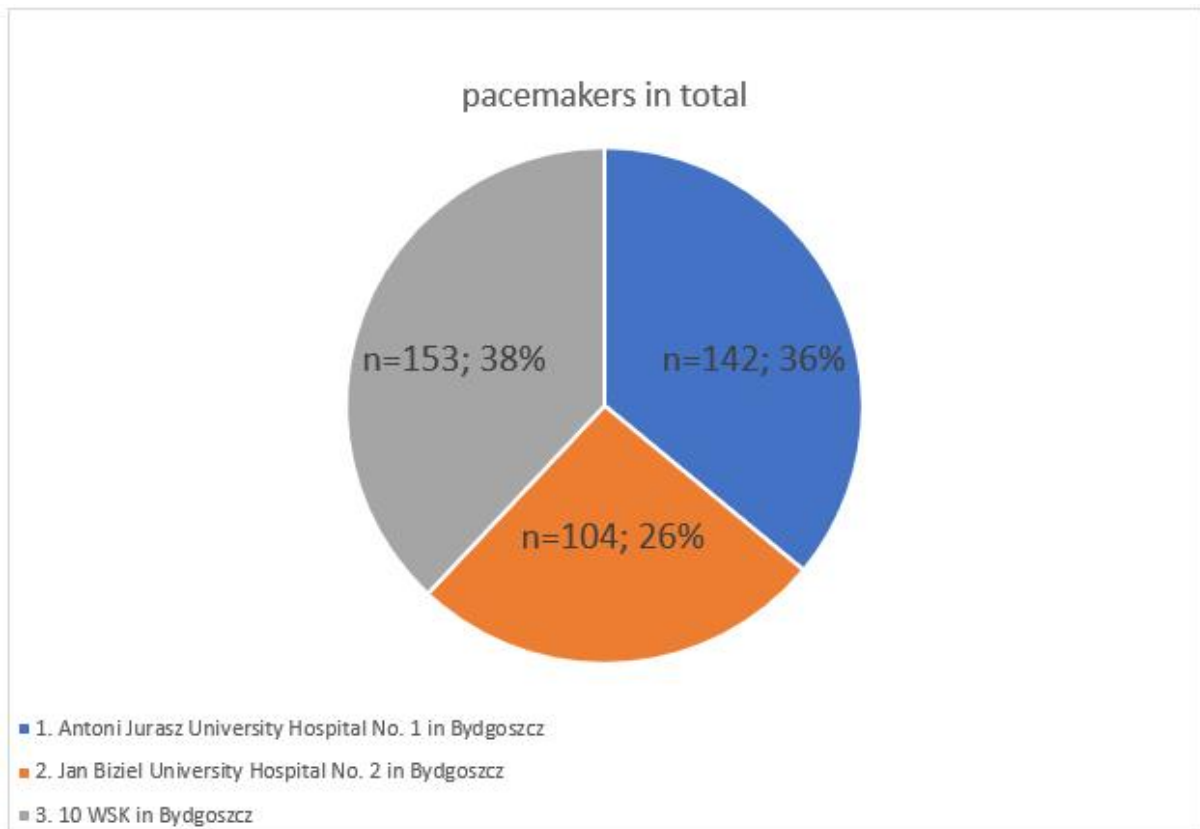


Figure 2. CRT-P in the population of Bydgoszcz. National Health Fund data for 2021.

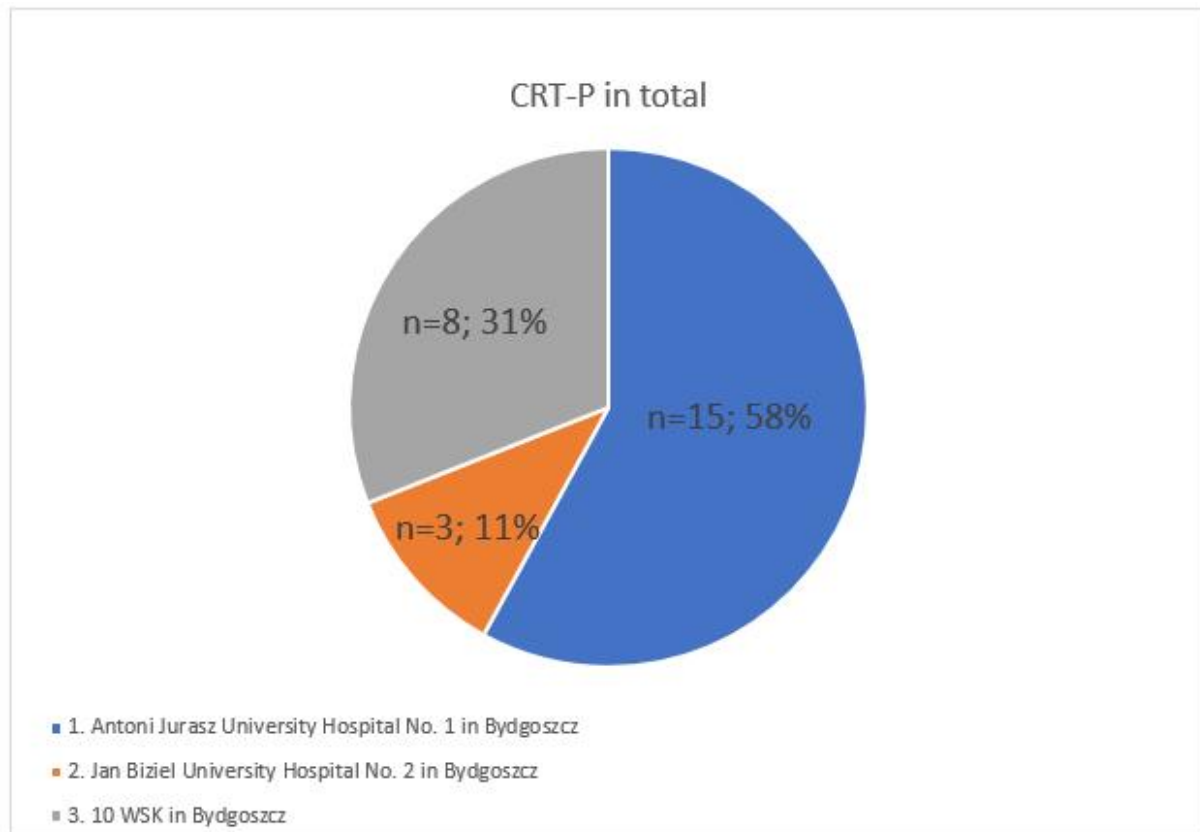


Figure 3. CRT-D in the population of Bydgoszcz. National Health Fund data for 2021.

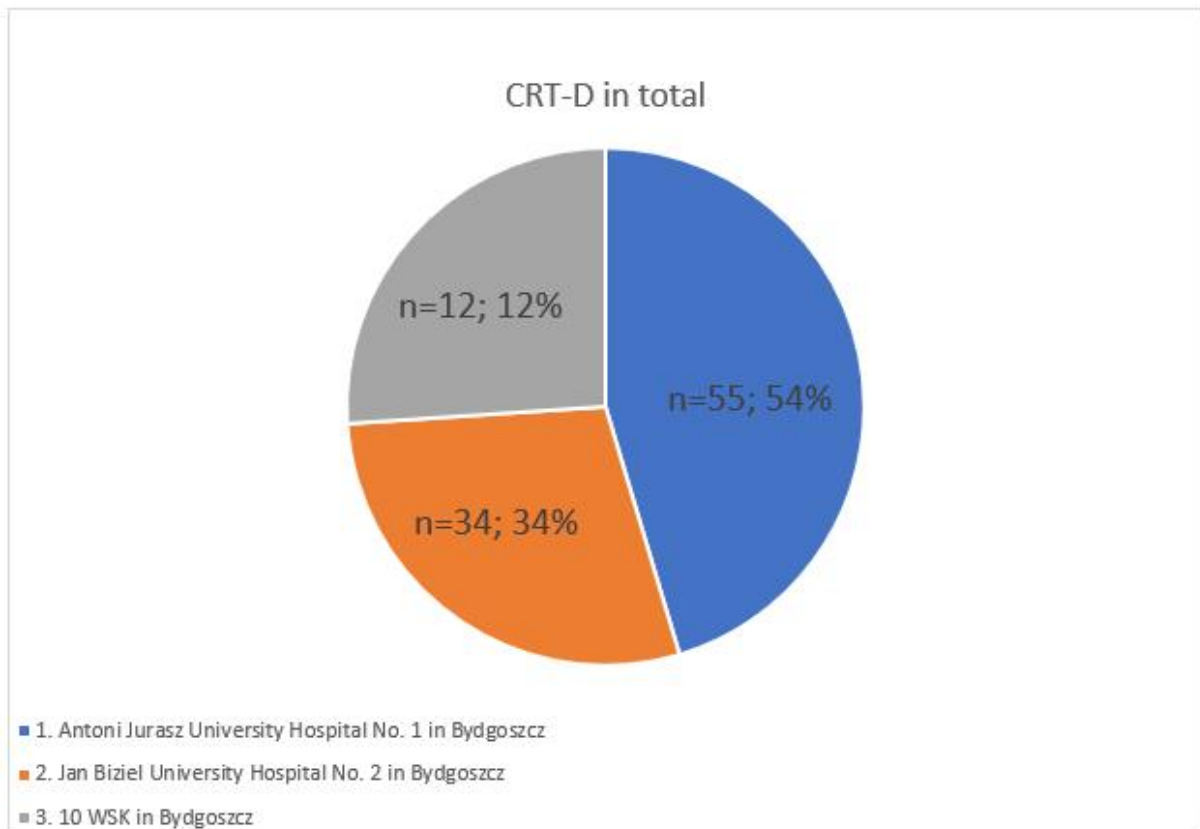
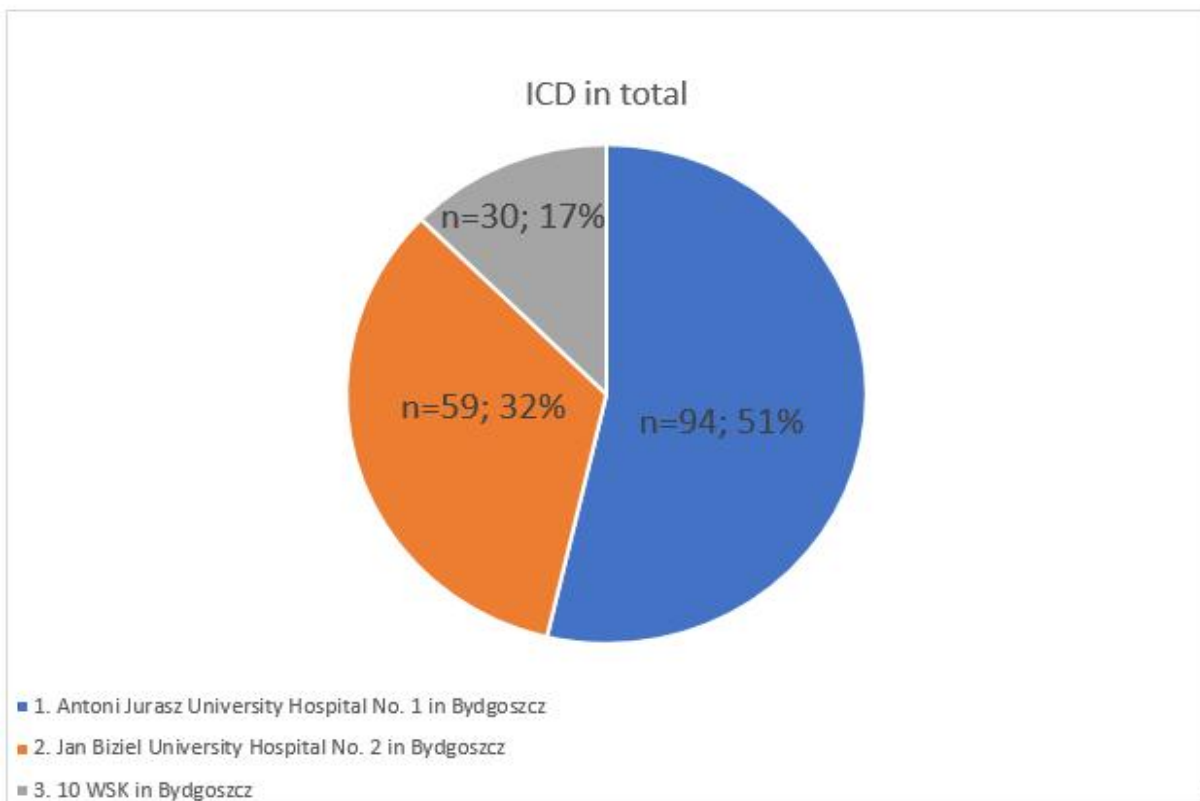


Figure 4. ICD in the population of Bydgoszcz. National Health Fund data for 2021.



The above data show that the number of implanted CIEDs in Bydgoszcz in 2021 was 706: PM - 399, ICD - 183, CRT-D - 101, CRT-P - 23. However, it should be emphasized that this number is growing every year, which is mainly related to the aging of the population and improved patient access to CIED-related procedures.

**Future Research:** While significant progress has been made in understanding and preventing CIED infections, ongoing research is necessary to refine risk stratification models, optimize preventive measures, and assess long-term outcomes. Future studies should also consider emerging risk factors and evolving technologies in the field of CIEDs.

## **6. Summary**

In conclusion, preventing infections associated with CIED implantation remains a crucial aim in cardiology. The ESC guidelines, along with risk factor identification and the use of antibacterial envelopes, provide effective strategies to reduce the incidence of CIED infections. Continuous research and vigilance are essential to further improve infection prevention practices and enhance the quality of care for patients receiving CIEDs.

Despite their relatively low incidence, CIED infections pose a significant challenge to healthcare systems. Methods of preventing this type of complications play a key role, and the most important of them is still antibiotic prophylaxis in the perioperative period. Increasing access to modern electrotherapy methods, such as wireless stimulators, or the use of modern preventive methods, such as antibacterial envelopes, will reduce the number of procedures related to CIED infections in the future, improve the quality of life of CIED patients and reduce overall costs for the payer.

### ***Author Contributions:***

Conceptualization: Ł.W.,S.S.,K.K.,A.J.; Methodology: Ł.W.,P.S.,G.G.; Formal analysis: Ł.W.,X.Z.,A.J.; Data curation: Ł.W.; Writing- original draft preparation: Ł.W., S.S.,K.K.,X.Z., P.S., A.J.,G.G; writing- review and editing: A.J.,P.S.,G.G.; Supervision: G.G.

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