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ORIGINAL PAPER

DEVELOPING A MODEL OF INFORMATION TRANSFER PRACTICE BETWEEN INSTITUTIONS TARGETED AT PRIMARY HEALTH CARE PATIENTS WHO ARE ASYMPTOMATIC CARRIERS OF CARBAPENEMASE PRODUCING *ENTEROBACTERIACAE*

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Abstract

Background: Drug-resistant bacteria are one of the main reasons of deaths worldwide. A significant group of these bacteria are carbapenemase producing *Enterobacteriaceae* (CPE). The goal of this study was to develop a diagnostic and therapeutic model targeted at asymptomatic carriers of CPE. **Material and Methods:** A team of experts from different branches connected to health care, discussing the topic based on the data collected from previous research. Working sessions were dispersed between June and December 2022. The consensus has been reached via repeated discussion and literature search. **Results:** The facility where CPE are detected is required to create an alert pathogen note and to notify sanitary-epidemiological station and National Reference Centre for Antimicrobial Susceptibility of Microorganisms – neither these institutions, nor the patient are required to notify the primary care physician. In primary care clinics, it is possible to work towards breaking the transmission of CPE by educating patients with CPE and persons who were in contact with them, and to undertake actions in order to look for patients with risk factors for CPE colonisation. In order to improve communication between individual levels of the health care system, standardised information could be introduced to the discharge note about a case of CPE, which will be electronically transmitted to the primary care facility. It might contribute to effective combating of the spread of CPE, by serving as a source of knowledge and education for patients and by checking the patient's risk factors, which will improve the performance of tests for CPE colonisation. **Conclusions:** The established model of good practice requires a change of legal regulations and its implementation, which will reduce the spread of CPE in health care facilities and will enable its future improvement. Med Pr Work Health Saf. 2023;74(4):263–70.

Key words: ambulatory care, bacterial infections, drug resistance-bacterial, health communication, delivery of health care, bacteria anaerobic

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INTRODUCTION

The growing antimicrobial resistance of bacteria (bacterial AMR) is a real global hazard to human life and health [1].

Based on statistical model prepared by The Global Burden of Disease (GBD) the estimated number of deaths attributed to AMR globally in 2019 amounted to 4.95 million (third global cause of deaths after ischaemic heart disease and stroke), including 1.27 million of deaths caused by AMR, that is, ones where drug-resistant bacteria were a direct cause of death. In other words, if no infection would occur in situations where infections caused by drug-resistant bacteria actually occurred, 4.95 million of deaths could have been prevented. Whereas in a situation where instead of infections caused by drug-resistant bacteria, infections caused by drug-sensitive pathogens would occur, 1.27 million of deaths would have been avoided [1].

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The epidemiological problem related to drug resistance is related to unlimited and uncontrolled use of antibiotics. The group of antibiotics for which the antibiotic resistance problem occurs include carbapenems, which are a group of β-lactam antibiotics with the broadest spectrum of activity among all antibiotics [2,3].

When the strains of pathogenic bacteria develop antibiotic resistance, the mortality increases – it is caused by restriction of the possibility of treatment. This is one of the largest challenges of public health. This phenomenon demonstrates significant growth and is present worldwide, however the occurrence between countries and continents differs significantly [2–5].

Based on the data obtained by European Centre for Disease Prevention and Control (ECDC) in the years 2015–2019 from European Economic Area (EEA) countries (which include European Union countries, Iceland, Liechtenstein and Norway), the percentage of carbapenem-resistant strains isolated from the pathogenic strains of *Klebsiella pneumoniae* is increasing. In 2015 it constituted 6.8% out of the 22 063 notified cases, and in 2019 it increased to 7.9% of the 40 430 cases [6].

Enterobacterales order constitutes of 7 families – one of which is *Enterobacteriacae* with species such as *Escherichia*, *Salmonella*, *Shigella*, *Enterobacter*, *Klebsiella*, *Citrobacter* [7,8]. They are clinically significant Gram-negative bacteria, present in water, soil and gastrointestinal flora of humans and animals. Contagion of those strong pathogens may happen by contact with droplets, food and contaminated surface. Until recently, in treatment of those infections carbapenems were widely used, with good effect. Unfortunately, using carbapenems with negligence has led to the development of carbapenem-resistant *Enterobacteriacae* (CRE). Production of carbapenemase, deemed to be the cause for rapid global spread of CRE, is a trait of carbapenemase-producing *Enterobacteriaceae* (CPE). Carbapenemases are enzymes, that possess an ability to hydrolyse penicillins, cephalosporins and carbapenems – antibiotics called "drugs of last resort" [9].

Diagnoses of diseases caused by CRE are made in health care facilities – mainly in-patient treatment facilities. The presence of CPE is not always followed by typical symptoms, which creates problems with the diagnosis of CRE cases. They may be present in the organisms of their carriers without any symptoms. This condition is called being a carrier/colonisation [9]. In Polish National Antibiotic Protection Programme (Narodowy Program Ochrony Antybiotyków – NPOA) the duration of CPE colonisation observed from the time of CPE detection amounts to 6 months [10].

However, despite the serious nature of the problem there are no specific guidelines, which would enforce the communication of primary care facilities with hospitals in the context of exchange of data of sick patients and asymptomatic carriers. Frequently, primary care physicians do not receive information about the patient's asymptomatic carrier status, even though it was established in the hospital.

Primary care physicians do not directly encounter the issue of infections with drug-resistant bacteria, there are no statistical data concerning the primary health care, and what is most important, there are no established procedures in case of a visit by a patient with such a problem. Good practices exist, but they apply to hospitals and omit the primary care facilities. Even though the phenomenon of asymptomatic carrier of CPE status occurs rarely, the problem is socially important, due to the possibility of spread of antibiotic-resistant pathogens among the members of the patient's family. Additionally, the possibility of acquiring and transferring of drug-resistance to other bacteria causes this phenomenon to be extremely dangerous. What is more, the appearance and occurrence of multi-drug resistant organisms (MDRO) is closely related to the health care system [7].

MATERIAL AND METHODS

This study is a follow-up to a study analysing the risk factors of CPE colonisation. It has been found out that the connective tissue diseases are the most important variable in prediction of CPE colonisation – followed up by dementia, abnormal values of leukocytes, heart failure and stay at the orthopedics ward. During the data collection, the lack of communication and good practice model in terms of procedures for patients with positive CPE results has been observed [11]. The model has to be created in order to manage those infections better and limit their spread.

The main goal of the study was to establish a good practice model which includesprocedures for patients with a positive result for CPE and for patients from CPE asymptomatic carrier risk groups in primary health care facilities.

In order to create a viable model of communication, an expert method was applied. Four members have been chosen to form a panel of experts. Each of those

members was responsible for a following reason and they specialised in different, particular fields:

- family medicine specialist was responsible for documenting the problem and searching for variety of solutions that could be combined to fix it,
- voivoidship medical consultant handled all of legislation related problems, in order for the model to be ready to implement in real life,
- nosocomial infection specialist searched for the causes and effects of poorly and correctly managed communication models, in order to strengthen the claim of using them,
- information flow in logistics management specialist was responsible for creating the pathway of information between different health care facilities.

The experts based the preparation of the model, working on the results from the aforementioned study [11]. The meetings were conducted using Microsoft Teams software, as well as in person, in a time period June–December 2022. The panel of experts has reached conclusions via repeated discussion and literature search, until they have reached the consensus.

The study protocol has been approved by the ethics committee of Medical University of Lodz (Łódź, Poland) in accordance to the Legislation No. K.B.-34/19 from January 8, 2020.

RESULTS

Procedures intended to restrict the spread of drug resistant bacteria include detection, treatment, prevention and control. All these fields are related to the development of science, the use of new technologies, and also include multi-dimensional coordinated strategies, supervision and control over the perception of principles of infection prevention.

Infection management strategies focus on inhibiting the transmission of drug-resistant pathogens from patient to patient. The remaining issues concern the following of hand hygiene principles by medical personnel, appropriate use and cleaning of medical equipment, education of personnel, early detection through the active use of screening for CRE, in order to detect asymptomatic carriers of CRE at the moment of admitting a patient to a hospital, contact tracing, restricting the colonisation of the environment [12,13], notification on diagnosed cases, statistics [14].

There is no single model of combatting CPE, nor a single effective strategy. However, active supervision in order to break the chain of transmission should be a part of proactive approach to solving the issue of drug-resistance [15].

What is most important in combatting the spread of CPE seems to be conducting screening for the detection of asymptomatic carriers of CPE. It is worth considering which group of patients should be subjected to the screening. The subject of looking for common characteristics of colonised persons could enable establishing a list of these characteristics, which would facilitate catching the patients from risk groups. The importance of this problem, and at the same time the difficulty resulting from the selection of risk factors has been shown by studies conducted at an Emergency Department of a university in Denmark. Patients were qualified for screening for CPE after a survey created by the Danish National Board of Health was filled out. The CPE risk factors included:

- earlier CPE colonisation,
- contact with a person colonised with CPE in the household during the last 6 months,
- stay in a hospital outside of Scandinavian countries which lasted >24 h,
- antibiotic treatment during the last 6 months during a stay outside of Denmark,
- stay in a care home, homeless shelter, refugee centre, being present in a war zone,
- hospitalisation,
- dialysis, cancer treatment.

On the basis of a survey filled out by 5117 patients at ER departments, 163 cases of medical history at risk of CPE were found. Swabs for CPE were performed in all 5117 patients. It turned out that there were 4 positive results for CPE in the entire population. One of these results belonged to a patient from a group of 163 persons which met the criteria established by the Danish National Board of Health.

This study has identified only one 1 of 4 colonised patients, which means a sensitivity of 25% (95% CI: 1–81%) [15].

Global strategies for screening differ. In Japan, screening tests for CPE are performed on all patients admitted at an intensive care unit (ICU) [16], similarly in Vietnam [17].

In Poland NPOA, the National Reference Centre for Antimicrobial Susceptibility of Microorganisms (Krajowy Ośrodek Referencyjny ds. Lekowrażliwości Drobnoustrojów – KORLD) and National Health Inspectorate (Państwowa Inspekcja Sanitarna) have established recommendations for the performance of screening tests intended to detect CPE at hospital

admission, in cases considered to be burdened with a risk of being a CPE carrier, which include:

- hospitalisation during the last year in hospitals in areas with increased occurrence of CPE,
- stay in long-term care facilities during the last year,
- earlier infection/colonisation with NDM/KPC/OXA-48 (New Delhi metallo-β-lactamase/*Klebsiella pneumoniae carbapenemase*/*Klebsiella pneumoniae* OXA-48 type),
- contact with medical care in countries with high incidence of CPE infections (India, Pakistan, northern Africa, Greece, Italy) [18] and further procedures in case of detection of CPE.

DISCUSSION

The active screening algorithms established as part of the NPOA apply to patients admitted to hospitals and long-term care facilities. The aforementioned criteria, pursuant to analysis of studies, were considered by the NPOA to be the most important factors of CPE carrier status.

The strategy for controlling the spread of CPE recommended by the NPOA includes the area of actions within hospitals, directed towards CPE screening, and actions concerning the entire facility, such as, among others, hand hygiene, decontamination of the hospital environment, rational antibiotic therapy, and also actions coordinated by Voivoidship Sanitary-Epidemiological Station (Wojewódzka Stacja Sanitarno-Epidemiologiczna – WSSE) [18].

During surgical procedures, an infection of the medical personnel may also occur as a result of contact with blood after gloves tear, which happens most frequently to the primary surgeon [19]. Some surgeries, for example thyroidectomy, have an increased risk of this event – knowledge of a patient's CPE carrier status is a valuable information, which may increase the safety of surgeons [20].

The significant disproportion between the available knowledge about CPE and the recommendations of the NPOA is not conducive to limiting the spread of CPE.

Due to the increasing understanding of the problem of CPE it seems necessary to clarify and standardise the recommendations for screening for CPE colonisation [21].

Despite the above mentioned recommendations, which seem detailed, only 12% of CRE carriers are detected [22], and 37% of carbapenem-resistant *Klebsiella pneumoniae* remain undetected [23].

There are model procedures in Poland applicable to CPE carriers, supervised by the National Sanitary Inspection, KORLD, NPOA in accordance with the regulations of the Minister for Health. However, they apply in hospitals and in health care centres.

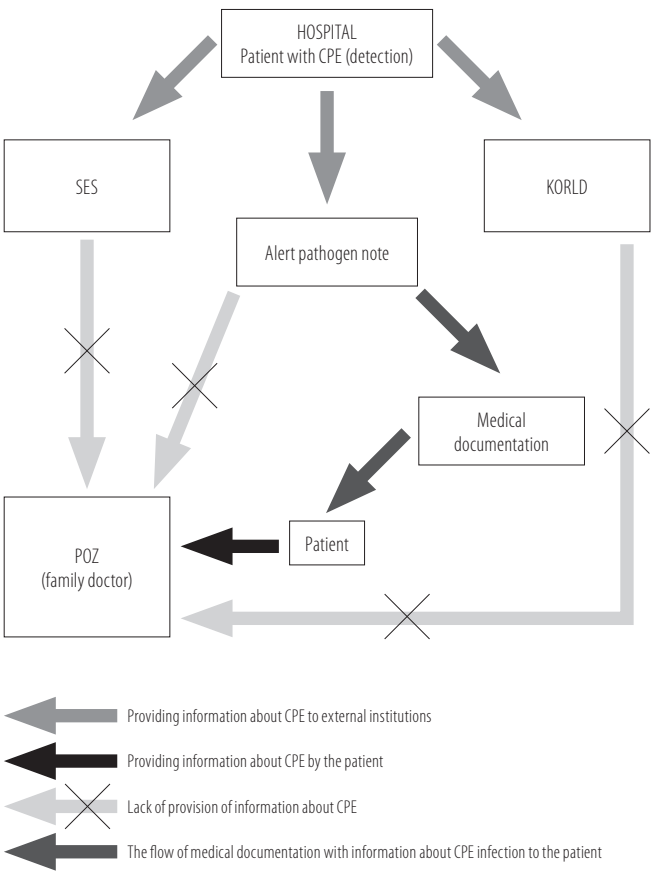
In case of CPE colonisation established during admission to a hospital, the procedures include:

- contact isolation until negative results are obtained (2, spaced 48 h apart) or until the end of hospitalisation;
- screening tests from patients from the room after 48–72 h and every week (a maximum of 3 tests), if antibiotic therapy is used tests after 3 days since it is introduced and every week thereafter;
- creating an alert pathogen note – "every individual registration note is marked with a sequential number and concerns the occurrence of a single case of a hospital-associated infection or of an alert factor, confirmed in a hospitalised patient during documented consultation referred to in article 15 § 2, 4 of the Act of 5 December 2008 on preventing and combating infections and infectious diseases in humans, hereinafter referred to as the Act" [24];
- notifying the National Sanitary and Epidemiological Station (SES) on a form for notification of a positive result of a test for the presence of biological pathogens (form ZLB-1);
- verification of the principles of isolation by the hospital associated infections control team and a monthly report to SES should more than one case occur.

In case of establishing of a CPE case during the hospital stay (>48 h since admissions), the following is recommended:

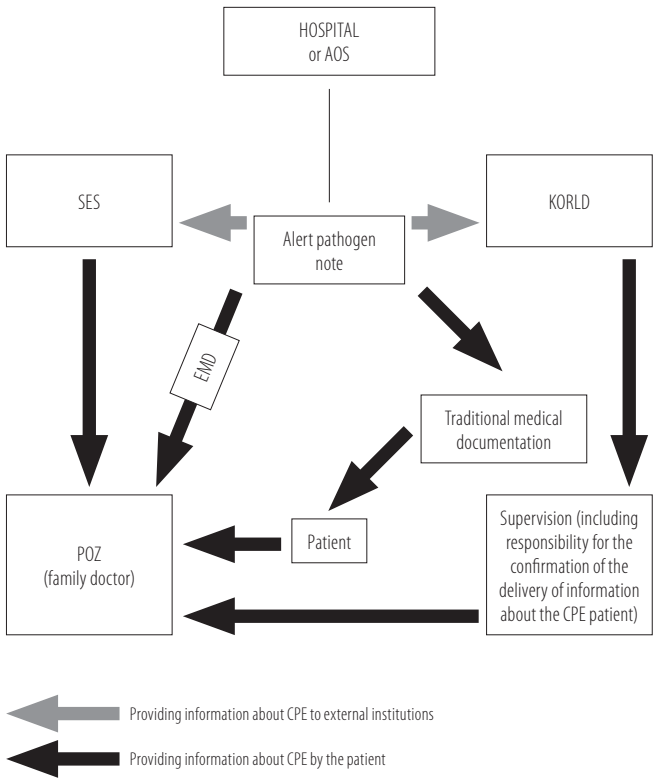
- contact isolation until the end of hospitalisation;
- screening tests of patients hospitalised at the same ward >48 h (every week for a month, if there are no new cases – end of testing), screening patients at high risk of colonisation (hospitalised long-term and subjected to antibiotic therapy) once a week for the next 2 months;
- creating an alert pathogen note;
- notifying the SES on a form for notification of a positive result of a test for the presence of biological pathogens (form ZLB-1);
- verification of the principles of isolation by the Hospital Associated Infections Control Team and a monthly report to SES.

The guidelines contain recommendation for entering information about the CPE diagnosis in the discharge chart, but they do not refer to the non-hospital care system.



CPE – carbapenemase producing *Enterobacteriaceae,* KORLD – National Reference Centre for Antimicrobial Susceptibility of Micro-organisms (Krajowy Ośrodek Referencyjny ds. Lekowrażliwości Drobnoustrojów), POZ – primary health care (podstawowa opieka zdrowotna), SES – National Sanitary and Epidemiological Station.

Figure 1. Flow of information in Polish healthcare system



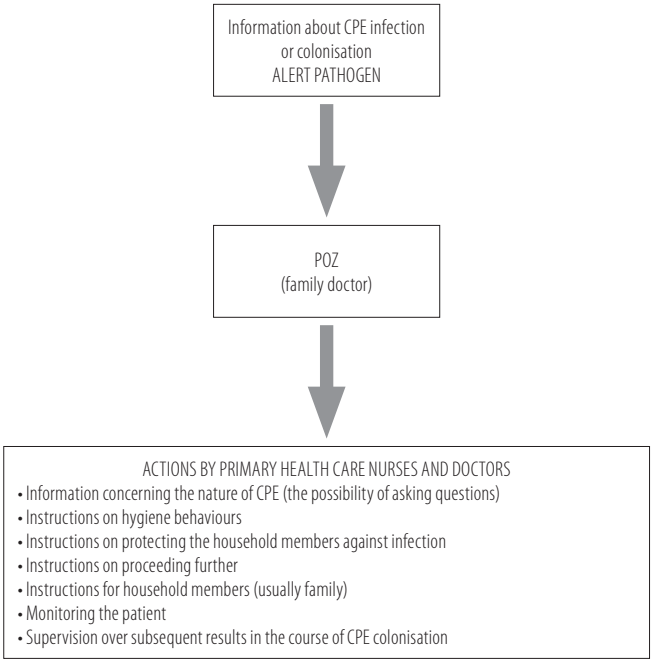
AOS – ambulatory specialist care (ambulatoryjna opieka specjalistyczna), CPE – carbapenemase producing *Enterobacteriaceae,* EMD – electronic medical documentation, KORLD – National Reference Centre for Antimicrobial Susceptibility of Microorganisms (Krajowy Ośrodek Referencyjny ds. Lekowrażliwości Drobnoustrojów), POZ – primary health care (podstawowa opieka zdrowotna), SES – National Sanitary and Epidemiological Station.

Figure 2. Proposed flow of information about an infection of the patient with an alert pathogen: CPE

In 2018 in Switzerland, based on the results of a multi-centre survey study conducted in public and private health care facilities, it turned out that the current recommendations for screening tests for patients at high risk of MDRO are known and performed in 96% of hospitals, and despite that fact only 44% of patients at high risk of MDRO are detected [25]. This indicates inadequate screening procedures compared to the current epidemiological situation.

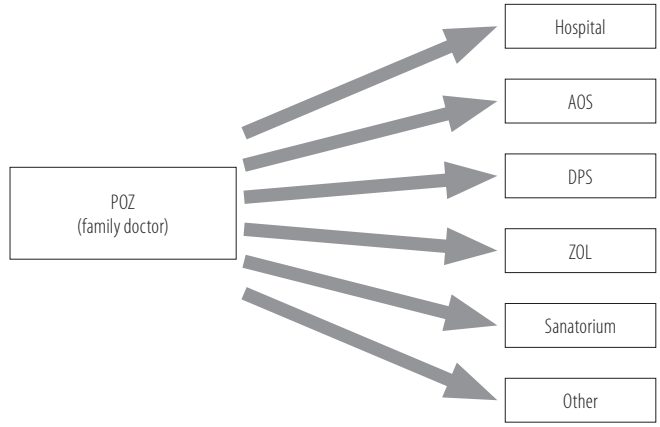
Actions concerning CPE and other alert pathogens in Poland only cover the long-term treatment facilities and the hospital sector of health care. The sector of primary health care is ignored, the potential of this part of the health care system is not being used, and this is the system that is most accessible to patients. Its employees reach a much wider group of patients than the employees of hospitals, the care provided by primary health care facilities is not related to situations of sudden risk to health and life, it is care which is provided over a long time in a continuous manner. The primary health care employees are engaged in preventive medicine in the group of their patients. Since the global epidemic situation is constantly changing, and there is an increasing number of reports of infections outside of hospitals, it seems that it may be worthwhile to think about combating the spread of CPE as team work based on close cooperation and exchange of information between all the levels of the health care system. The current flow of information in the Polish health care system for a CPE patient is illustrated by Figure 1.

The facility where CPE is detected (in Polish conditions it is a hospital, primary health care clinics are not able to perform a microbiological test for CPE) is required to create an alert pathogen note and to notify SES and KORLD. The notification about every detected case of CPE should be entered in the hospital discharge report. None of the aforementioned institutions nor the patient are required to notify the primary care physician about the CPE detection.



CPE – carbapenemase producing *Enterobacteriaceae*,
POZ – primary health care (podstawowa opieka zdrowotna).

Figure 3. Potential actions resulting from obtaining information about infection or colonisation by CPE



AOS – ambulatory specialist care (ambulatoryjna opieka specjalistyczna),
DPS – nursing home (dom pomocy społecznej), POZ – primary health care (podstawowa opieka zdrowotna), ZOL – health care centre (zakład opiekuńczo-leczniczy).

Figure 4. Proposed flow of information about an increased risk of colonisation of the patient with an alert pathogen: carbapenemase producing *Enterobacteriacae* (CPE)

In the primary care clinics, it is possible to work towards breaking the CPE transmission chain. Patients with CPE and contact persons should be educated, and active efforts should be made to look for people with CPE carrier status risk factors. Activities intended to establish risk groups and CPE carriers are intended to improve the quality of provided services.

The figure demonstrates that without financial expenditure on research, using knowledge and good organization, the primary health care facilities may also be included in this aspect of medical procedure. When establishing procedures, supervising and controlling, algorithms are created, which, if operating well in one facility, may be used in other primary health care facilities. These actions are called, as permanent, repeatable and providing positive effects, and also used in similar conditions by other facilities to be "good practices". A condition for the effectiveness of these actions is the ease of their introduction and of their use, as well as effective flow of information.

In order to improve communication between individual levels of the health care system the already functioning communication channels may be used. The most important task is introducing standardised information about a case of CPE to the discharge report, which is transmitted by electronic means to the primary health care facility. The next item is the visualisation of the problem using the EWUŚ system – electronic verification of entitlements of beneficiaries, the use of the Gabinet.gov.pl portal [26]. In this model information is provided to the primary health care system directly from the hospital, but also from SES and KORLD. The proposed model of the flow of information is presented on Figure 2.

The primary health care facility in current solutions of the health care system is not capable of collecting a swab for CPE. This does not mean that it may not be used to combat the spread of CPE. The potential of this sector of health care has to be used. Primary health care may contribute to effective combating of the spread of CPE:

- by providing support and knowledge about CPE to patients with diagnosed CPE carrier status and to their families,
- by maintaining reliable documentation, data can be collected about the CPE carrier status risk factors, which may be provided by the primary health care in the situation the patient is required to undertake treatment in another facility of the health care system, which will facilitate the performance of tests for the detection of CPE colonisation.

CONCLUSIONS

As a result of the conducted analysis the following conclusions were arrived at:

- There are no models of good practice for patients with positive CPE results implemented in multiple European Union member states.
- The established model of good practice coveringprocedures for patients with a positive result for CPE

and for patients from CPE colonisation risk groups in primary health care facilities requires implementation and further improvement.

- The established model of notifying a primary health care facility about a patient colonised by CPE by selected institutions (hospital, Ambulatory Specialist Care [ambulatoryjna opieka specjalistyczna – AOS], District Sanitary and Epidemiological Station [Powiatowa Stacja Sanitarno-Epidemiologiczna – PSSE], KORLD) (Figure 3) requires changes to legal regulations with implementing acts in order to enable its implementation in clinical practice.
- The proposed early warning model (Figure 4) in case of a patient from a group of increased risk of CPE colonisation at the level of the primary health care facility may in the future limit the spread of CPE in other health care facilities.
- The established procedure for patients with CPE colonisation for a primary health care facility (Figure 3) is prepared for implementation and further assessment, which would enable the improvement of good practice.

Author contributions

Research concept: Małgorzata Timler, Dariusz Timler, Michał Marczak, Remigiusz Kozłowski

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Interpretation of results: Dariusz Timler, Małgorzata Timler

References: Dariusz Timler, Wojciech Timler

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