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VACCINE HESITANCY PHENOMENON IN THE REPUBLIC OF MOLDOVA

331.03 SOCIAL MEDICINE AND MANAGEMENT

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CONCEPTUAL FRAMEWORK OF THE RESEARCH

Ph.D. thesis relevance. Vaccines are widely regarded as one of the most significant achievements in modern medicine. Every year, worldwide, vaccinations prevent as many as three million deaths [1]. Due to the successful implementation of immunization programs, the populations in numerous countries enjoy notably higher life expectancy.

However, in recent years, a concerning trend has emerged wherein a significant number of individuals opt not to be vaccinated, despite lacking medical contraindications. This has led to a substantial increase in requests for alternative immunization schedules [2, 3], as well as delays and partial or complete refusal of vaccinations. Multiple studies suggest that even those who have already been vaccinated, such as parents of children, pregnant women, individuals with compromised immune systems, and other targeted vaccination groups, frequently express doubts, anxieties, or fears regarding potential side effects following vaccination, as well as the safety of vaccine ingredients and adjuvants used. These concerns are followed by an underestimation of the risks associated with exposure to diseases that these vaccines aim to prevent [4-10].

Furthermore, the development of modern communication means and the ease of accessing low-quality information often contribute to the spread of vaccine skepticism in the population, including among healthcare professionals, who, in theory, are expected to be the most devoted advocates of such a crucial public health intervention. Other factors, such as a lack of political and social support, anti-vaccine propaganda, conflicting religious and philosophical beliefs, competing health priorities, and challenges resulting from healthcare system reforms in some Eastern European countries, have had a negative impact on the success of the measles elimination program [11]. In 2018, vaccine hesitancy was declared one of the most significant threats to global health, directly connected to two other major threats. The resurgence of vaccine-preventable diseases in several countries underscores the importance of maintaining high population immunity.

Background. In today's context, inadequate vaccination coverage represents an ongoing threat, leading to preventable diseases and deaths, hindering progress towards their elimination. The recent resurgence of vaccine-preventable diseases confirms the need to maintain population immunity at high levels [12-15]. In other words, the success of vaccinations has actually led to a lack of recognition for the significant improvement in public health, substantial reductions in mortality, especially in early childhood, and the lessening of disabling complications caused by many diseases. Lack of awareness has led to confusion to the point where vaccinations are considered as the cause of certain diseases [16]. These concerns are reinforced by alarming data on the current situation in various countries, and the Republic of Moldova is no exception. According to the World Health Organization (WHO) data, in 2017, 19.9 million children worldwide were under-vaccinated. In 11 European countries where vaccinations had previously achieved high success rates, DTP3 coverage has dropped below the 90% threshold, reaching critical levels [17]. Consequently, two of the six WHO regions have experienced diphtheria outbreaks, and one region (AMRO) has lost its "measles-free" status. Furthermore, in 2018, this pathology was declared endemic in all WHO regions. The epidemics in North America and Western Europe underscore the ease with which these diseases can spread, even in countries with mature healthcare systems that report high national vaccination coverage. This highlights the imperative of ensuring extensive coverage at subnational levels, especially among vulnerable populations [18].

One of the main factors contributing to vaccination decline is vaccine hesitancy, a relatively new concept introduced in 2014 by the World Health Organization's Strategic Advisory Group of

Experts on Immunization (WHO SAGE) in response to the global mistrust in vaccines and vaccination. This phenomenon, referred to in English as "*Vaccine Hesitancy*" [19-21], a disagreement with the comprehensive vaccination (which encompasses delayed acceptance or refusal of vaccination, despite the availability of vaccination services), which is a complex and steadily growing issue. Vaccine hesitancy is a behavior specific to the context, with varying degrees of intensity, ranging from undisputed acceptance to complete rejection of vaccinations. It can be driven by factors such as fear of side effects, perception of conflicting opinions regarding the advisability of vaccination (even among healthcare professionals), and an overall skepticism. This skepticism is directly related to the prioritization of personal choice driven by individual beliefs or ideologies [22]. A common, yet mistaken belief is that vaccine hesitancy primarily arises from a lack of specific knowledge on the subject. As a result, most efforts have been aimed at addressing this hypothetical cultural gap with technical concepts and one-sided approaches [23].

Since 2014, the number of countries reporting data on vaccine hesitancy has steadily increased, reaching 83% in 2017, while the number of countries conducting hesitancy assessments has risen to 37%. Only seven countries reported a complete lack of hesitancy, underscoring the fact that this issue has truly become a global challenge [24]. In 2018, the World Health Organization declared vaccine hesitancy as one of the most significant threats to global health, being directly related to both influenza and antimicrobial resistance [25]. This prompted several countries worldwide to adopt, strengthen, or consider mandatory and/or recommended immunization for infants and children.

Similar to other countries, despite the highest priority given to preventable diseases due to vaccination by the National Immunization Program (NIP), the Republic of Moldova is facing significant challenges in ensuring adequate protection for its population. Over the past 15 years, there has been an alarming failing trend to meet the target vaccination rates outlined in the NIP, with a gradual decline in vaccination coverage falling below the critical safety level. According to the annual reports of the National Agency for Public Health (NAPH), immunization coverage for the MMR vaccine in children aged 12 months decreased from 97% in 2006 to 87% in 2017. In 2019, the national average for MMR coverage was was 88%, with a lower level in urban areas (83%) compared to rural areas (90%), some regions having particularly low coverage - the data disaggregated by administrative territories shows a variation between 71% and 97.8 %, with more than half of the regions having coverage below 90%. In 2022, vaccination coverage of children aged 1 year in the territories to the right of the Dniester varied between 68.6% (Rotavirus) and 87.6% (OPV), and in the Eastern territories of the country – between 72, 5% (whooping cough) and 74.3% (MMR), and for the other recommended vaccination (except the BCG vaccine) the 90% threshold was not reached. In the territories of the Transnistrian region, Rotavirus and HPV vaccinations of girls were not carried out.

For several years, these reports have mentioned that the insufficient level of coverage with vaccinations at the national level is determined by the refusal of vaccinations of some population groups under the influence of anti-vaccine propaganda, the low level of knowledge among medical workers regarding contraindications to vaccination and of their insufficient communication skills with parents regarding vaccination counseling. Also, the COVID -19 pandemic and the restrictions imposed in connection with it had a negative influence on routine vaccination coverage, including the adult population [26].

The progressive decrease in immunization coverage rates and the influence of the COVID-19 pandemic has also been observed in other countries of the world. Recent studies report

that the pandemic has brought back to public attention the importance of both the COVID-19 vaccination and routine vaccinations [27-32]. For example, in the period March-May 2020, in the United States routine vaccination rates of children up to one year of age were 18% lower compared to the previous year [33], and the subsequent launch of vaccination against COVID-19 has led to changes in attitudes towards other vaccines. Moreover, subsequent studies showed that the direction of these changes was variable. Opel et al. found that negative attitudes towards pediatric vaccines were much more pronounced before the pandemic than in the immediate post-pandemic period [34], while He et al. concluded that parental vaccine hesitancytancy increased to a small but significant extent during the COVID-19 pandemic [35]. According to some authors, the discrepancies regarding the direction and/or intensity of changes in parents' attitudes could be conditioned by different experiences that people had in relation to the COVID-19 disease and/or vaccination against it, but also by some social and subjective norms, which can contribute to the creation of geographically localized foci of hesitant people [36-39]. Similar results were obtained by Lopes et al., who showed that people who did not accept vaccination against COVID-19 were more likely to believe that the risks of measles, mumps, and rubella (MMR) vaccinations outweighed the benefits [40]. Correlations have also been established between attitudes toward pediatric vaccinations and personal experiences with COVID-19 (such as severity of illness or hospitalization) [41] or community experiences with vaccination against COVID-19.

The presence of these correlations can be explained by the Theory of Planned Behavior, according to which health-related behaviors, such as vaccination, are conditioned by some subjective or social norms that are considered important predictors of parents' beliefs about vaccinating children [42-45].

The phenomenon of vaccine hesitancy in our country is not well understood yet, and the measures taken to maintain high vaccination rates often require extreme solutions, such as introducing mandatory vaccination.

Considering the significant potential of vaccine hesitancy to rapidly undermine the population's immunity, the World Health Organization (WHO) recommends that each country develop strategies to address this behavioral phenomenon. These strategies should include:

-Building trust and actively preventing vaccine hesitancy.

-Continuously assessing vaccine hesitancy and vaccination-related issues both qualitatively and quantitatively at the national level.

-Developing targeted strategies to enhance vaccine acceptance among the population.

-Planning intervention measures for critical situations.

Since 2013, the World Health Organization (WHO) proposed several solutions to aid countries in combatting vaccine hesitancy. One of these solutions is the *Tailoring Immunization Programmes* (TIP) [27], an approach that focusses on evaluating behavioral perspectives and outlines a structured process for gathering information about the obstacles and catalysts related to vaccination. These, in turn, influence the selection and design of appropriate interventions.

This current research aligns with the principles of this approach, sharing a model and theoretical framework based on knowledge drawn from behavioral sciences and adapted to vaccine hesitancy (the COM-B model):

- It assesses the psychological determinants of vaccine hesitancy in relation to past behaviors and future intentions.
- It identifies specific target populations for tailored interventions.
- It provides valuable scientific evidence for designing targeted interventions.

The purpose of the research:

The scientific purpose of this study is to provide a rationale for developing a tool to assess and monitor vaccine hesitancy. This tool will be applied at specific population levels to create evidence-based recommendations for sorting out the issue within the national context.

The research objectives:

1. Analyze contemporary international practices concerning the factors that contribute to vaccine hesitancy and explore evidence-based scientific approaches to address them.
2. Develop and test a diagnostic and monitoring tool for vaccine hesitancy, tailored to the conditions in the Republic of Moldova, using both qualitative and quantitative methods to study this phenomenon.
3. Identify the specific patterns of vaccine hesitancy among medical professionals and healthcare workers with intermediate-level education.
4. Report evidence-based data on vaccine hesitancy and its determinants within a population-level context.
5. Formulate recommendations for designing specific interventions to counteract vaccine hesitancy.

Research Methodology:

The research was conducted in the Republic of Moldova from 2019 to 2023 and represents a comprehensive mixed-method study (qualitative-quantitative approaches). The research design was carried out based on the above-defined objectives.

For the qualitative assessment, group and individual discussions were held with medical specialists in public health and other relevant fields to conduct primary exploratory research and gather the necessary information for the next stage, which was largely related to creating the research instrument. The quantitative part consists of three descriptive, cross-sectional studies (questionnaire-based survey) aimed at describing the existing phenomena and determining the epidemiological relationships.

To achieve the goal and objectives, the following areas were explored:

1) Primary determinants, which are the psychological antecedents of (non)vaccination, for which the 5C measure scale was applied to assess confidence, convenience, constraints, calculation, and collective responsibility.
2) Vaccination pro/con behaviors/attitudes:
    a) Previous typical behaviors of hesitancy (doubts, delays, or refusals);
    b) Self-reported vaccination status for individuals/their children;
    c) Future intentions regarding recommended vaccinations (from outright refusal to acceptance);
    d) Recommendations for routine vaccinations (for healthcare workers).
3) Other barriers/promoters of vaccination:
    a) Institutional trust
    b) Sources of vaccination information used
    c) Beliefs related to vaccination
    d) Contextual barriers (logistical, financial, legal)
    e) Implementation of promotion mechanisms, etc.

The research was conducted in several stages, each of which corresponded to a specific study rationale for the research objectives (see figure 1).

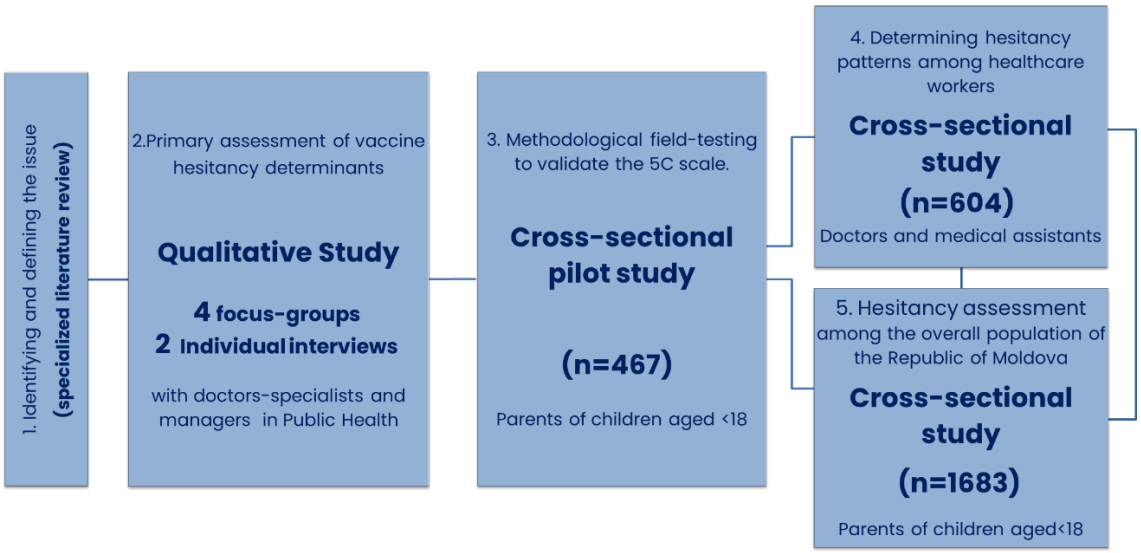

Figure.1. **The Conceptual Stages of Research Implementation**.

Each stage required some general principles to follow, depending on the relevant objective, thus, obtaining the scientific evidence necessary to achieve the final goal:

I. Planning and scheduling the study aligned with the definition of the research's purpose and tasks. During this phase, a comprehensive analysis of international approaches and best practices was conducted, allowing identifying and defining the research problem. In addition, the activities for organizing the study were planned, including the development of the research protocol and programs, as well as the determination of the methods and tools for collecting primary information and processing the obtained data.

II. Accumulating primary information material via data collection techniques, which included both indirect observations (reports, primary and secondary studies, official statistics) and direct interactions (such as focus group discussions, individual interviews, and questionnaire surveys). The collected material underwent quality assessments to confirm its reliability.

III. Processing the accumulated material via quantitative and logical verification, using statistical programs like Microsoft Excel and SPSS 22.0 (SPSS Inc). The analyzed material was organized into tables, diagrams, and graphs.

IV. Finally, an in-depth analysis was conducted on the obtained findings, resulting in the corresponding conclusions and recommendations.

The novelty and scientific originality. In addressing vaccine hesitancy as a behavioral phenomenon, it is crucial to have a deep understanding of its specific characteristics and determinants, obtained through methods that adhere to the consistency and principles of scientific research. The innovative aspect lies in the study and approach to this phenomenon using modern methods and tools, adapted to the current specific conditions.

This research is pioneering in the Republic of Moldova, thus, evaluating the studied phenomenon within the local context using a standardized instrument and adhering to the stages and principles of modern approaches proposed by the Strategic Advisory Group of Experts on Immunization of the World Health Organization (SAGE). This involves assessing the determinants of hesitancy as related to the individuals' past behaviors and future intentions, identifying subgroups within the target population for specific interventions, and designing evidence-based interventions.

The 5C scale for measuring (non)vaccination antecedents extends beyond the qualitative assessments conducted so far and provides a broader theoretical conceptualization of vaccine hesitancy. Unlike other existing assessments, it surpasses the evaluation of trust alone and can serve as a standardized tool for diagnosis, as well as supports the design and evaluation of necessary interventions.

The major applied scientific problem addressed in this Ph.D. thesis involves establishing a scientific and methodological foundation for the continuous and standardized monitoring of the hesitancy determinants. This allows for an enhanced management of modifiable risk factors for vaccine-preventable diseases in the Republic of Moldova, contributing to the improvement of the national surveillance system for these diseases.

The evidence obtained are valuable for identifying sensitive populations and barriers to achieving optimal vaccination coverage, determining evidence-based priority interventions, and monitoring their effectiveness over time.

Theoretical Significance and Practical Value of the Research. The systematic and continuous monitoring of behavioral risk factors through the collection of self-reported data via interviews, as part of a broader system for the surveillance and control of vaccine-preventable diseases, can provide valuable information for the participants involved in response actions. The interested participants include decision-makers at the central and local levels, public health experts, healthcare professionals, communication specialists, community leaders, and influencers, among others.

The results obtained in this research represent scientific evidence that can be useful in shaping policies and strategies for the prevention and control of vaccine-preventable diseases. This helps identify priorities and optimize interventions for primary prevention within this group of diseases. Evaluating the psychosocial determinants of vaccine hesitancy introduces an innovative solution for the Republic of Moldova. It enhances the capacity to identify local inconsistencies and specific subgroups of the population requiring targeted interventions. It allows tocompare data across different regions and tracking trends over time, providing a strong foundation for designing evidence-based interventions and necessary adjustments. Commencing with this research, the periodic application of a standardized diagnostic tool will contribute to obtaining updated information for the identification and prioritization of targeted interventions and for dynamically monitoring the effectiveness of measures taken.

Moreover, the obtained knowledge expands the research horizons and can be applied in the training of public health specialists and healthcare professionals. It can also support the scientific work of educators across the country, serving as a scientific and methodological basis for optimizing the standardized continuous surveillance of behavioral risk factors that contribute to vaccine hesitancy.

Main scientific results submitted for thesis defence:

1. A comprehensive data synthesis of specialized literature was conducted, providing a comprehensive perspective on the global vaccine hesitancy situation. This involved indentifying the modern definitions, the range of manifestations, the prevalence rate, epidemiological patterns, and contributing factors responsible for the development and maintenance of this behavioral phenomenon among the population. Furthermore, the study described the main research milestones at the national, European, and global levels, as well as the methodological approaches proposed by the academic community and international health organizations in public health.

2. The results of the primary qualitative assessment of vaccine hesitancy determinants among the native population revealed that the most prevalent psychosocial factors specific to the Republic of Moldova's population align with the components of the 5C scale.
3. The results of the quantitative assessment of the hesitancy determinants followed by the assessment of the present methodology have identified low levels of confidence (varying degrees of doubt) in the effectiveness and safety of vaccinations and in the motivations behind the political decisions made in this domain, such as, low-risk perception associated with preventable diseases, as well as vaccinations not being considered an essential preventive action; moderate perception of psychological and structural barriers in decision-making and changing the intentions into pro or anti-vaccination behaviors; increased information-seeking behaviors and a propensity to consider the risks and benefits associated with vaccinations; and, low collective responsibility in various aspects, including behaviors described in specialized literature as *"free riding."*
4. The results obtained from validating the 5C scale for measuring the psychological factors related to (non) vaccination have proven the instrument's reliability, construct validity, and concurrent validity when applied to the overall population of the Republic of Moldova. In general, it has been shown that the assessed determinants of the 5C scale are valid predictors of vaccination-related behaviors.
5. The results obtained from exploring the factors contributing to vaccine hesitancy among healthcare workers are crucial in the decision-making process regarding the acceptance of vaccination for the general population.
6. The implementation of monitoring the determinants of vaccine hesitancy via the use of a standardized tool for collecting "information for action" aims to improve the surveillance system for vaccine-preventable diseases.
7. The findings obtained from assessing the prevalence of determinants and characteristic expressions of vaccine hesitancy among parents/guardians of children aged up to 18 in the Republic of Moldova.

Implementation of Scientific Results. The research results have been applied in the management processes within the General Directorate of Medical and Social Assistance of the Chișinău Municipal Council, within the managerial processes at the University Primary Medical Care Clinic of the "Nicolae Testemițanu" State University of Medicine and Pharmacy, as well as in the scientific and educational processes at the School of Public Health Management of the "Nicolae Testemițanu" State University of Medicine and Pharmacy and the National Public Health Agency.

The thesis was discussed and approved during a meeting at the School of Public Health Management (minutes number 7 dated 21.04.2020), by the Research Ethics Committee (favorable opinion number 6 dated 14.10.2021), at the scientific seminar for the 331 PUBLIC HEALTH specialty, including 331.03 Social Medicine and Management, and the 331.04 Healthy Lifestyle Module on 10.11.2021, as well as during the Consortium Scientific Council meeting (minutes number 1/4.14 dated 02.12.2021).

Publications on the thesis topic

A total of 11 scientific works has been published, comprising 6 articles and 5 theses on the topic o the present Ph.D. thesis. Among these, there are 2 national and 9 international publications, whereas 3 of them have an impact factor. Additionally, 3 implementation acts and 1 innovator certificate have been obtained.

Thesis volume and structure: The results of the research were presented on 115 pages of basic text and it contains introduction, five chapters, conclusions and recommendations. The paper contains 12 tables, 44 figures and five appendices.

Keywords: immunizations, vaccine hesitancy, surveillance, the 5C scale, psychosocial determinants, confidence, complacency, constraints, calculation, and collective responsibility.

Ph.D. THESIS CONTENT

1. INTERNATIONAL AND NATIONAL PRACTICES REGARDING VACCINE HESITANCY PHENOMENON

This chapter describes the modern approaches and international best practices regarding vaccine hesitancy, as well as providing an overview of the issue's global relevance and its specific implications across the Republic of Moldova. To identify effective solutions for our research, it has been determined that vaccine hesitancy is a highly intricate and ever-changing phenomenon, influenced by various contextual factors. Notably, this present research will, for the first time in the Republic of Moldova, aim to quantitatively assess the situation in the country. The 5C scale offers a more extensive framework for measurement and provides a broader theoretical understanding of vaccine hesitancy and acceptance. Unlike other existing measures, the 5C scale goes beyond simply assessing trust in vaccine effectiveness, safety, or the healthcare system providing them. It can be employed as a diagnostic tool to facilitate the design and evaluation of necessary interventions. To develop evidence-based, long-term strategies, it is essential to periodically, systematically, and consistently evaluate the psychological factors influencing vaccination decisions. The data obtained through this process can shape health policies and the development of targeted campaigns for specific target groups.

2. MATERIALS AND METHODS

The comprehensive, staged research include four studies, which collectively served as the foundation for achieving the set-up research purpose. The design of these studies adheres to the requirements of scientific methodology commonly employed in population health research (see Figure 1). As a result, following an examination of contemporary international practices (secondary study), the following steps were undertaken:

1. Qualitative Study involved focus groups with specialized physicians and individual interviews with public health managers. The findings from this study were employed for the initial assessment of the determinants of vaccine hesitancy among the local population, as well as in assessing the applicability of the original questionnaire elements and considering the need for the addition of new elements.
2. Observational Descriptive Cross-Sectional Pilot Study, conducted to:
   - Field-testing the chosen methodology and data gathering for reviweing the questionnaire and organizing the study for the next stage.
   - Validating the research instrument involved the following steps:
     a) Developing (translating and adapting to the national context) the components of the diagnostic instrument (standardized questionnaire).
     b) Conducting qualitative pre-testing, which included 5 individual interviews to adjust the research instrument.

c) The actual validation of the questionnaire was carried out on a diverse convenience sample of 467 parents or guardians of children up to the age of 18. This validation aimed to assess the questionnaire's reliability, construct validity, and concurrent validity, tailored to the specific requirements of the study.

3. A descriptive cross-sectional observational study was conducted on a non-probabilistic sample of 604 healthcare workers to determine the vaccine hesitancy patterns among them.
4. A descriptive cross-sectional observational study was conducted on a representative sample of the population, consisting of 1683 participants, to assess the prevalence, characteristics, and determinants of vaccine hesitancy among parents or guardians of children up to 18 years.

During the qualitative study, the following activities were conducted: three focus group sessions, each consisting of 10-11 medical specialists from various fields, one focus group session involving 5 public health specialists, and two individual interviews with healthcare specialist-managers. The discussions were audio recorded and later transcribed into an electronic format (Microsoft Word document) to facilitate manual analysis, allowing us to identify and select the discussed thopics and subtopics. After reviewing the transcriptions using a coding system, the study identified the specific findings and made up the conclusions for each of the topics under discussion.

In quantitative studies, both manual and computer-assisted methods (using Microsoft Excel and IBM SPSS version 23) were employed for the statistical data analysis. The processing and statistical analysis of the research data were carried out in accordance with the requirements of the scientific research methodology, considering the specific design characteristics used apart.

The key conceptual points of the statistical analysis were as follows:

- Data verification, performed at the time of creating the electronic database.
- Data transformation through encoding, grouping, creating categories, and classification by levels, and others.
- Use of descriptive statistics for numeric, nominal, and ordinal measurement scales, including the subsequent as well as the multifactorial analysis of the phenomenon under study via developing the scores and an overall assessment framework.

This test provided a calculation for a 95% confidence interval of the rates of interest and the p-value (the probability that the null hypothesis, H0, is true). To compare groups with more than 2 categories, the chi-square test was used, and the p-value was calculated. When the condition $p \leq 0.05$ was met, it indicated the statistical significance of the differences observed in the responses provided by the participants. Subsequently, to assess the strength of the relationships between nominal variables, the Cramer's V index was calculated. Depending on the degree of freedom (df) associated with it, this allowed categorization into associations with minor, moderate, or major effects.

The differences between rates obtained from nominal variables were estimated via the inferential analysis using the *z-test* for two proportions within a sample. This test provided a 95% confidence interval for the rates of interest and the *p-value* (the probability that the null hypothesis, H_0, is true). To compare groups with more than 2 categories, the χ*-square* test was used to calculate the *p*-value. Unless $p \leq 0.05$, the study revealed a statistical significance of the differences provided by the respondents. Subsequently, to determine the strength of the relationships between the nominal variables, the *Cramer's V index* was calculated. This allowed categorizing the associations into minor, moderate, or major effects based on the corresponding degrees of freedom (*df*).

Extrapolation of the obtained results was carried out after the use of inferential statistics, which included the estimates based on the confidence intervals (CI), calculated for a confidence level of 95% using the Wald method (provided: normal distribution, large samples, dichotomous variable) and Wilson (provided: asymmetric distribution, small samples). In addition, the association between exposure (determinants studied) and outcome (past behavior or future intentions) was assessed by calculating the Prevalence Odds Ratio (POR) and Prevalence Ratio (PR), allowing formulating the hypotheses for further research.

Regression models were also built to identify possible predictors of the corresponding outcome (Y). Relevant items (subscales) were used as predictors to estimate specific behaviors towards each vaccination in the corresponding regression model, based on age, gender, geographic region, education level, etc. At each stage, variables were removed based on the resulting p-values, models were optimized by stepwise component selection to set a limit on the total number of variables included in the final model, using Akaike Information Criteria (AIC) and calculating Odds Ratios and 95% Confidence Intervals (CI_{95}). Nagelkerke's pseudo-R^2 coefficient of determination was used to evaluate the goodness-of-fit analysis, and variance inflation factors (VIFs) were calculated to test for multicollinearity, interpreting VIF values <5 as being non- multicollinearity issues.

The chosen type of design allowed us to define the current situation *(snapshot),* with the goal of describing the existing phenomena, establishing epidemiological connections, and identifying research directions and future hypotheses. The preparatory stage included the development, validation and pre-testing of a diagnostic tool (questionnaire) adapted to the local context so that it could be applied across the Republic of Moldova. The methodology for developing the survey instrument is based on a protocol for adapting the 5C scale to assess the psychological antecedents of (non)vaccination, developed by a group of European researchers (Center for Empirical Research in Economics and Behavioral Sciences of the University of Erfurt, Germany) supported by the WHO Strategic Advisory Group of Experts on Immunization.

3. IDENTIFYING VACCINE HESITANCY PECULIARITIES WITHIN A NATIONAL CONTEXT AND VALIDATING THE 5C SCALE TO ASSESS PSYCHOSOCIAL DETERMINANTS OF HESITANCY

Based on the results obtained, the most common psychosocial factors characteristic of the population in the Republic of Moldova aligns with the elements of the 5C scale. While there are other aspects that could be evaluated by introducing new elements within this tool, it's important to note that the vaccination argument is a highly intricate one, and there are numerous reasons influencing people's decisions to accept or hesitate regarding vaccination. Currently, there is no ideal instrument for measuring each individual reason. These reasons may be specific to certain population subgroups or particular vaccines, requiring more comprehensive studies that focus on these aspects, tailoring research to the ever-evolving situation using a general scale. Developing or adapting new elements to the specific context requires careful consideration and a balance between the costs and efforts involved in achieving this goal. At this moment, it has been determined that, for an initial field application, the original general scale does not require significant structural modifications.

During the reliability testing, the translated and contextually adapted 5C scale exhibited a strong internal consistency, with the Cronbach's α values for each construct (sub-scale) corresponding to the recommendations found in the relevant literature. By accepting the working

hypotheses, statistically significant relationships ($p \leq 0.05$) were observed among all elements of the 5C scale and their corresponding psychological components. These correlations corresponded with our expectations.

Furthermore, the regression analysis demonstrated that the 5C sub-scales serve as valid predictors of vaccination behavior for multiple vaccinations, and the variance proportion was relatively high. Overall, the 5C scale validated within this research can effectively predict vaccination acceptance within the population, ensuring data comparability with findings from subsequent studies, including international ones, being conducted according to the described methodology.

The *Confidence* level on the effectiveness and safety of vaccinations, as well as on the motivation behind policy decisions in this area, is low, with three-quarters of the population expressing doubts of varying intensity on these issues. Doubt among highly educated people, and especially among health professionals, is a problem because their opinion represents a point of reference for other categories of the population. High levels of *Complacency* with preventable diseases and lack of consideration of vaccinations as a preventive measure are also problematic, indicating barriers to communicating the benefits of vaccination to common people, including the most disadvantaged groups and nursing staff, who appear to be more affected according to the results of our study. The barriers in decision-making and translating intention into behavior (*Constrains*) are a minor but not insignificant issue, considering the varying intensity of these problems in different population groups. High levels of *Calculation* suggest communication problems. It is highly likely that while combining these issues with the low level of confidence among healthcare workers plays a significant role in reinforcing motivations for non-vaccination among the general population. The phenomenon of *free riding*, as well as other aspects related to *collective responsibility*, are quite common in society and require educational interventions.

Correlations with great effects in explaining the variance among the 5 antecedents and vaccination intentions indicate that altering any of the examined determinants, whether intentionally or unintentionally, influences the increase or decrease in vaccination intentions. This, in turn, leads to a behavioral change, specifically resulting in vaccine hesitancy.

The 5C scale has been shown to be an adaptable instrument used for diagnosing vaccine hesitancy in various population groups and settings.

4. DETERMINING THE VACCINE HESITANCY PATTERNS AMONG HEALTHCARE WORKERS

4.1. Previous behaviors typical of vaccine hesitancy

Regarding the vaccination of children, 30.8% (CI_{95} 28.6%-33.0%) of respondents indicated one or more hesitant behaviors. In particular, when asked whether they were against or in doubt about routine vaccinations of their own children in the past, health workers gave a positive answer in 16.7% (CI_{95} 14.0%-19.9%) of cases. About one in four respondents (26.7%, CI_{95} 23.3%-30.3%) declared that at least once they postponed these vaccinations for some reason, and 7.0% (CI_{95} 5.2%-9.3 %) of the respondents - that they refused them (table 1).

Table 1. **Distribution of typical past hesitant behaviours in the population under study**

Past behaviours	Yes		CI_{95}		χ^2 (Pearson)	p
	n	%				
Opposed to or unsure about vaccinating their child	101	16,7	14,0	19,9	0,1457	0,7026
Opposed to or uncertain about being vaccinated	106	17,7	14,7	20,8		
Postponed the child's vaccination	161	26,7	23,3	30,3	7,7956	0,0052
Postponed their own vaccination	120	19,9	16,9	23,2		
Refused to vaccinate their child	42	7,0	5,2	9,3	58,3192	<0,0001
Refused to get vaccinated	136	22,5	19,4	26,0		df=1

Regarding vaccinations for themselves, at least one of these behaviors was determined in 30.5% (CI_{95} 28.3%-32.7%) of healthcare workers, while 17.5% (CI_{95} 14.7%-20.8%) of them stated that they were against or in doubt about the vaccinations recommended for adults, about one in five healthcare workers (19.9%, CI_{95} 16.9%-23.2%) – that at least once they postponed these vaccinations, and 22.5% (CI_{95} 19.4%-6.0%) of the interviewees – that they refused them for various reasons.

According to the results presented in table 1, respondents were equally against or doubtful about accepting recommended vaccines either for children or for themselves. Against this background, it was determined that with regard to vaccinations for children, hesitant health workers more often preferred to postpone them than to refuse them, in contrast to their own vaccinations, where the differences are less pronounced.

The results obtained show that the respondents were against or in doubt to the same extent regarding the acceptance of recommended vaccines either for children or for themselves. Against this background, it was determined that, regarding vaccinations for children, hesitant health workers more frequently preferred to postpone them than to refuse them, in contrast to their own vaccinations, where the differences revealed in the responses are less pronounced.

4.2. Behavioral determinants of vaccine hesitancytancy (the 5C scale)

The data obtained indicate a low level of *Confidence* – most doubts were expressed for the trust in the authorities that make decisions about vaccinations, followed by those about the safety of vaccines, while the effectiveness of vaccinations seems to be a less doubted argument. Thus, only half of the respondents (47.4%, CI_{95} 43.4%-51.3%) are confident that vaccinations are safe and that decisions in the field taken by the authorities are well-reasoned (40.7%, CI_{95} 36.8%-44.7%), while 60.4% of respondents (CI_{95} 56.5%-64.3%) believe that vaccines are effective (figure 2).

The lack of doubts under these aspects was determined to be less pronounced among people from the southern part of the country (categorically agree– 36% of respondents), people younger than 25 years old (33%, respectively), from rural areas (38%, respectively), without higher education (38%, respectively), and among the workers of medical institutions – to the average medical staff (41%, respectively) and to medical workers from public institutions (46%, respectively).

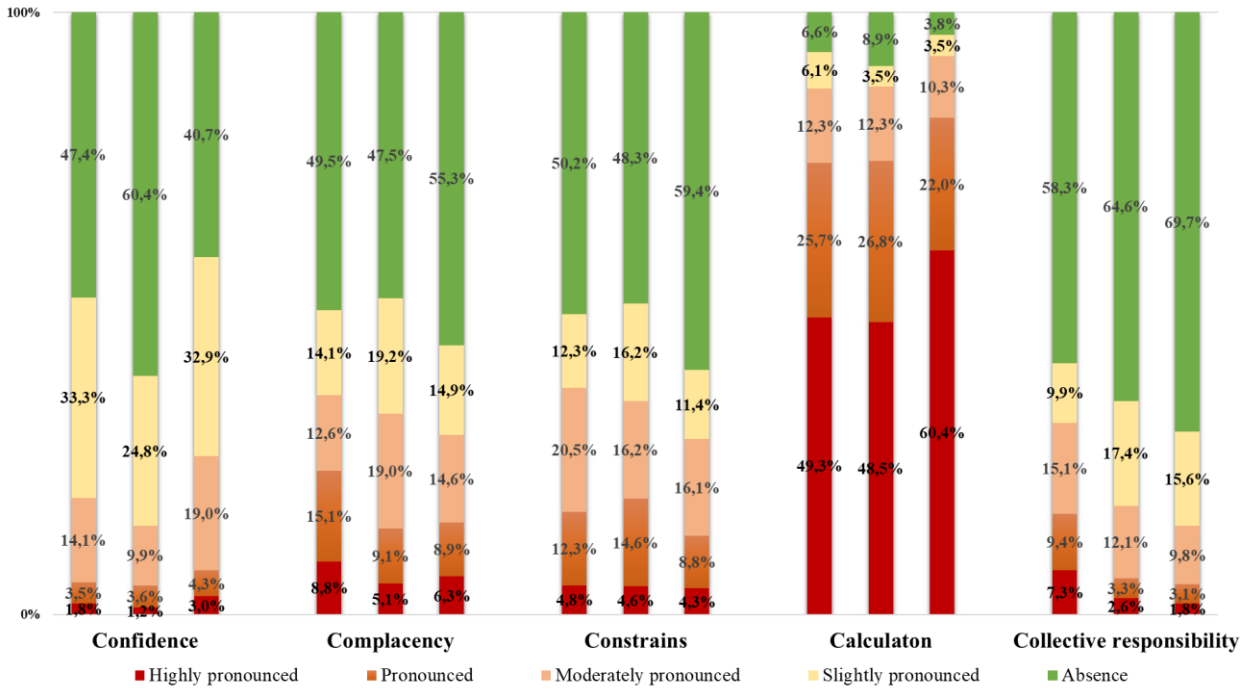

Figure 2. **The degree of manifestation of the behavioral determinants of vaccine hesitancytancy seen through the lens of Scale 5C elements (healthcare workers)**

For the *Complacency* subscale, which refers to the inadequate perception of the risks entailed by vaccine-preventable diseases and not considering vaccinations as an indispensable preventive action, only about half of the respondents (49.5%, CI_{95} 45.5%-53.5%) they are convinced of the need for vaccinations, regardless of the fact that vaccine-preventable diseases are not so common anymore. Likewise, only 47.5% (CI_{95} 43.5%-51.5%) of respondents are convinced that the immune system is not strong enough to protect children by avoiding vaccination, and for 55.3% (CI_{95} 51.3%-59.2%) the severity of these diseases leaves no doubt about the need for vaccination as a preventive measure of protection. This antecedent was more pronounced in people younger than 25 years old (58% of cases), in people without higher education (56% of cases), without divergence between the rural population (51%) and the urban population (49% of cases), the average medical staff being again the most affected group among medical institution workers (42.0% of cases).

Psychological and/or structural barriers in making the pro-vaccination decision and transforming the intention into actual behavior (the *Constraints* subscale items), such as daily stress, difficulties in obtaining vaccinations or relating to medical workers, represent a problem of variable intensity for respondents. It was determined that daily stress is not a barrier to obtaining a vaccination for 50.2% (CI_{95} 46.2%-54.1%) of respondents and that only for 48.3% (CI_{95} 44.4%-52, 3%) of the respondents it is not necessary to make a lot of efforts to get the child vaccinated. Less pronounced was the perception of discomfort in the presence of a medical worker as a barrier to vaccinate their child – categorical disagreement with this statement was indicated by 59.4% (CI_{95} 55.5%-63.3%) of the participants in study. This type of barriers was more common in people under 25 years of age (71% of cases), from rural areas (55% of cases), in people without higher education (59% of cases), medical assistants (58% of cases), and in medical workers from public institutions (51% of cases, respectively).

The level of manifestation of the items of the *Calculation* subscale, which refers to the deliberate confrontation of the risk of disease with the possible risks of vaccination, was determined by measuring the need for individuals to understand the argument well before making the decision about vaccination, with careful assessment of the risks and the benefits and practical utility at the individual level of the proposed vaccinations. Thus, it was determined that only 6.6% (CI_{95} 4.7%-8.7%) of respondents do not perform their own risk-benefit analysis before accepting a vaccination and that only 8.9% (CI_{95} 6.8 %-11.3%) of the respondents do not need a careful evaluation of the usefulness of vaccination for the child. Even more pronounced was the need to get to the bottom of things before accepting a recommended vaccination – this was determined by a major importance for 60.4% (CI_{95} 56.5%-64.3%) of respondents and vice versa – not a problem for only 3.8% (CI_{95} 2.4%-5.4%) of participants. This antecedent was more pronounced in people younger than 25 years of age (67% of cases), with no significant differences between doctors and assistants.

For the *Collective responsibility* subscale, around 41.7% (CI_{95} 39.4%-44.1%) of the respondents believe, to varying degrees, that they might not vaccinate when everyone around them is already vaccinated, thus taking advantage of the immunity effect collective without contributing to its creation and maintenance (*free riding* phenomenon). About a third of respondents (30.3%, CI_{95} 28.1%-32.5%) expressed doubts of varying intensity about the fact that vaccinations are a collective preventive action, and for 35.4% (CI_{95} 33.2% -37.7%) of the interviewees it is not important that by accepting the vaccination they will also protect those who cannot be vaccinated. Lower levels of *Collective responsibility* were obtained in people from rural (vs. urban) localities, in people without higher education, but also among representatives of the professional category of medical assistants from public (43% of cases) and private (29% of cases).

4.3. Intentions for future vaccinations recommended in the NIP

For the future intentions regarding their own vaccinations, for their children and the recommendation of vaccinations for patients, it was determined that only 54.5% (CI_{95} 52.1%-56.9%) of the respondents, at least in the near future, would accept undoubtedly a vaccination for himself, and 52.2% (CI_{95} 49.8%-54.6%) – for their children. Regarding the recommendation of vaccinations to patients, pro-vaccination intentions were determined in 61.4% (CI_{95} 59.1%-63.7%) of the participants who stated that they would recommend all vaccines to patients without a doubt (figure 3).

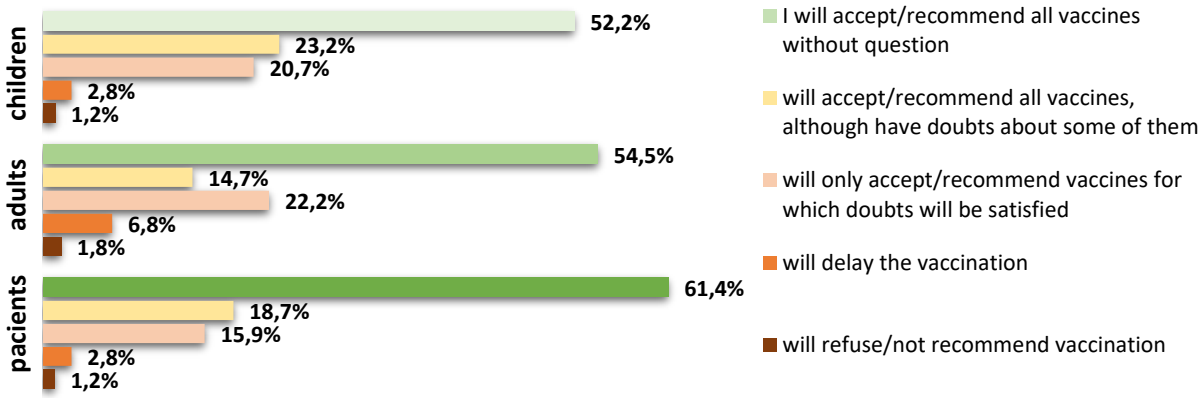

Figure 3. **Distribution of future intentions to accept vaccinations for their children, for themselves, or to recommend vaccinations for patients**

Among the barriers and motivations for hesitating to vaccinate were mentioned medical contraindications, adverse reactions to vaccination, fear of the vaccine, lack of the vaccine they would like to vaccinate with, lack of confidence in the quality of the vaccine, unavailability at the required time (e.g., the flu vaccine) and the influence media resources.

The results obtained in the study confirm that vaccine hesitancytancy among medical personnel is a widespread phenomenon, which undermines the efforts of immunization programs and represents a real threat to public health that needs to be addressed.

5. ASSESSING VACCINE HESITANCY AMONG PARENTS OF CHILDREN AGED ≤18 YEARS (POPULATIONAL STUDY)

5.1. Previous behaviors typical of vaccine hesitancy

The interviewees were asked to indicate whether they had experienced any doubts, delays, or refusals of vaccinations as part of the immunization program, both for their children and for themselves in the past. In the context of vaccinating their children, at least one of these past behaviors was reported in 52.7% of the questionnaires (CI_{95} 50.3% and 55.1%). Specifically, when asked if they had been against or had doubts about routine child vaccinations in the past, parents responded positively in 40.0% (CI_{95} 37.6%-42.4%) of cases. Approximately two out of three respondents (69.8%, CI_{95} 67.7%-72.0%) stated that they had postponed these vaccinations for some reasons at least once, and approximately one in five respondents (21.4%, CI_{95} 19.5%-23.4%) stated that they had refused them. As for their own vaccinations, at least one of these behaviors was identified in 57.5% (CI_{95} 55.1%-59.8%) of parents, while 40.3% (CI_{95} 38.0%-42.7%) of parents stated that they had been against or had doubts about recommended adult vaccinations. About one in three parents (29.3%, CI_{95} 27.2%-31.5%) admitted to postponing these vaccinations at least once, while 46.3% of parents (CI_{95} 44.0% and 48.7%) revealed that they had refused them for various reasons.

Differences observed in parents' responses to corresponding similar questions were tested for statistical significance, and the results of the analysis are presented in table 1:

Table 2. **Distribution of typical past hesitant behaviours in the population under study**.

Past behaviours	Yes		CI_{95}		χ^2 *(Pearson)*	*p*
	n	%				
Opposed to or unsure about vaccinating their child	674	40,0	37,7	42,4	0,0308	0,8605
Opposed to or uncertain about being vaccinated	679	40,3	38,0	42,7		
Postponed the child's vaccination	1175	69,8	67,6	72,0	552,7759	<0,0001
Postponed their own vaccination	493	29,3	27,2	31,5		
Refused to vaccinate their child	360	21,4	19,5	23,4	233,9821	<0,0001
Refused to get vaccinated	780	46,3	44,0	48,7		

df = 1

Based on the obtained results, the respondents were equally against or doubtful when it comes to accepting recommended vaccines, whether for children or for themselves. Therefore, it was found that, in the case of children's vaccinations, parents tend to lean more towards postponement, in contrast to their own vaccinations, where typical behavior tends more towards refusal. However, it's important to note that interpreting these results should consider the context in which the data was collected. The respondents' answers were likely influenced by attitudes toward COVID-19 vaccinations, which were generally unpopular among the general population at that time. In most instances, hesitancy, delays, or refusal of vaccinations were influenced by factors such as distrust in the safety of vaccines. This distrust was evident in 51.1% of responses (CI_{95} 47.9%-54.2%) regarding adult vaccinations and in 35.2% of responses (CI_{95} 32.1%-38.4%) concerning children's vaccinations.

The second most significant factor is the lack of trust in the vaccine's safety, as indicated by 38.2% of responses (CI_{95} 35.2%-41.3%) for adult vaccinations and 22.7% of responses (CI_{95} 20.0%-25.5%) for child vaccinations. The situation differs for the third and fourth rankings: while, for adult vaccinations, some people believe that the disease isn't severe enough to necessitate vaccination (15.5% of responses, CI_{95} 13.4%-17.9%) and that other preventive measures are more effective (12.3% of responses, CI_{95} 10.4%-14.5%), for child vaccinations, reasons include unpleasant past experiences with post-vaccination side effects (14.9% of responses, CI_{95} 12.7%-17.4%) and concerns about the complete immunization process (13.0% of responses, CI_{95} 10.9%-15.3%).

5.2. Perceived barriers to accept PNI-recommended vaccinations.

To deepen the information obtained regarding past vaccinations, the interviewees were proposed to answer to a series of questions about their attitudes and practices related to vaccination. As a result, 77.0% (CI_{95} 74.9%-79.0%) of the total study participants acknowledged that they have ever heard or seen negative information about vaccination, and 51.3% (CI_{95} 48.9%-53.7%) indicated that they know someone who has had an adverse reaction to a vaccine. About 2 out of 5 respondents (38.6%, CI_{95} 36.3%-41.0%) stated that they generally trust the information they come across about vaccinations, regardless of whether it's pro or anti-vaccination. Meanwhile, when they need specific knowledge about vaccinations, the majority of interviewees pointed to various sources of information. Family doctors topped the list of preferences, with 78.6% of participants (CI_{95} 76.5%-80.4%) considering them a source of information, followed by pediatricians (26.6% of participants, CI_{95} 36.3%-41.0%), and nurses (26.6% of participants, CI_{95} 36.3%-41.0%).

A significant quote of individuals who self-document from other sources account for 15.3% of participants (CI_{95} 13.7%-17.1%) admitted to obtaining information from online social networks, 11.9% of participants (CI_{95} 10.5%-13.6%) from the Internet websites, and 6.9% of participants (CI_{95} 5.8%-8.2%) from mass media sources (television, newspapers, radio, etc.). Relatives or friends were mentioned as a source of information by 9.3% of participants (CI_{95} 8.0%-10.8%), while religious leaders were mentioned in isolated cases. Pharmacists and alternative medicine specialists (acupuncture, homeopathy, etc.) are less popular; they were indicated by 4.5% (CI_{95} 3.6%-5.6%) and 2.2% (CI_{95} 1.6%-3 .0%) of participants, respectively.

In this context, the majority of respondents (79.3%, CI_{95} 77.3%-81.1%) stated that they openly discuss their concerns about vaccinations with their family doctor. However, in some cases (19.7% of participants, CI_{95} 17.9%-21.7%), they felt pressured by their doctor to make a decision

regarding vaccination, and in others (3.7% of participants, CI_{95} 2.9%-4.8%), they were discouraged from getting a vaccine they wanted for their child. Additionally, 25.5% of the total number of respondents (CI_{95} 23.5%-27.6%) reported that at least once they had the impression that health services did not provide them with the best vaccine available on the market. Another 13.0% (CI_{95} 23.5%-27.6%) believed that private vaccinations were superior to the free ones offered by the health center. They supported this opinion partly by citing concerns related to the quality, origin, and safety of the vaccines used and partly by pointing out perceived differences in the organization of the vaccination process, such as the expertise of the staff, the ability to choose the desired vaccine, etc.

On the other hand, 25.3% of the study participants (CI_{95} 37.3%-42.0%) were convinced that vaccines are administered to children at too young age, while 24.7% (CI_{95} 22.7%-26.8%) and 10.4% of the participants (CI_{95} of 9.0%-11.9%), respectively, preferred to respond with *"I don't know"* or omitted their response. Consequently, only 39.6% of the participants (CI_{95} 37.3%-42.0%) displayed a clear pro-vaccination attitude. A similar situation was related to the number of vaccinations administered during childhood: 29.0% of the study participants (CI_{95} 26.9%-31.2%) believed that children receive too many vaccines, while 27.5% (CI_{95} 25.4%-29.7%) and 10.8% of the participants (CI_{95} 9.4%-12.4%), respectively, opted to respond with "I don't know" or omitted their response to this question. In this case, the quote of participants with a pro-vaccination attitude accounted for 32.7% (CI_{95} 30.5%-35.0%).

5.3. Behavioral determinants of vaccine hesitancy (the 5C scale)

The psychological determinants that can influence pro-vaccination or anti-vaccination behaviors (*Confidence*, *Complacency*, *Constraints*, *Calculation*, and *Collective responsibility*) were assessed using the Likert scale. The degree of agreement with that statement being expressed from "strongly disagree" to "strongly agree".

The *Confidence* subscale refers to several aspects of trust viz. trust in the effectiveness and safety of vaccines, trust in the medical system that provides vaccination, including the professionalism and quality of the medical personnel administering the vaccine, and trust in those responsible for vaccine policies and vaccination. Among the total number of respondents, approximately 53.1% (CI_{95} 50.7%-55.4%) expressed strong disagreement, moderate disagreement, or a neutral opinion (score 1-3) regarding the statement "*I am convinced that vaccines are safe*." The average total score for this variable was 3.39 points (SD=1.05, median=3, IQR=1).

Upon examining the data, it was determined that a relatively lower level of trust in the safety of vaccines is prevalent among individuals who: a) do not have higher education – *PR*=1.23 (CI_{95} 1.015-1.502); b) had typical past hesitancy behaviors regarding being vaccined - *PR*=1.97 (CI_{95} 1.605-2.417) and getting their children vaccine – *PR*=1.69 (CI_{95} 1.383-2.059); c) have not been vaccinated – *PR*=1.48 (CI_{95} 1.215-1.796) and have not vaccinated their children according to the National Immunization Program (PNI) provisions – *PR*=1.30 (CI_{95} 1.015-1.674); d) are likely to hesitate in accepting recommended vaccinations in future, for both adults – *PR*=2.00 (CI_{95} 1.628-2.462) and their children – *PR*=1.89 (CI_{95} 1.537-2.328), respectively. The differences detected in the responses provided by other categories of study participants were not statistically significant.

Regarding the second element of the Confidence subscale, where the corresponding questionnaire statement is *"Vaccination is an effective method of protection against certain diseases,"* it was found that 35.9% of respondents expressed a hesitant attitude (CI_{95} 33.6% to

38.2%), the overall mean score being 3.69 points (SD=1.03, median=4, IQR=1). At the same time, relatively lower levels of confidence were recorded among people who: a) don't have a higher education degree – *PR*=1.47 (CI_{95} 1.195-1.819); b) had previously expressed doubts, delayed, or refused their own vaccinations – *PR*=1.97 (CI_{95} 1.605-2.417) and for their children – *PR*=1.57 (CI_{95} 1.287-2.908); c) had not been vaccinated themselves – *PR*=1.74 (CI_{95} 1.413-2.135) and did not vaccinate their children as scheduled – *PR*=1.55 (CI_{95} 1.213-1.975); d) exhibited future hesitancy in accepting recommended vaccinations for both adults – *PR*=2.55 (CI_{95} 2.028-3.214) and for children – *PR*=2.48 (CI_{95} 1.007-3.065), respectively. No other statistically significant differences were reported.

For the last element of the subscale, which relates to trust in authorities making decisions regarding vaccinations, "negative" attitudes were reported by 52.7% (CI_{95} 50.3%-55.1%) of respondents, resulting in an average score of 3.42 points (SD=1.09, median=3, IQR=1). Less trust in immunization policy decision-makers was observed among individuals who: a) expressed past doubts, delays or refusal on vaccinations – *PR*=1.67 (CI_{95} 1.364-2.033) and for their children – *PR*=1.57 (CI_{95} 1.287-2.908); b) had not been vaccinated – *PR*=1.74 (CI_{95} 1.413-2.135) and did not vaccinate their children according to the schedule – *PR*=1.55 (CI_{95} 1.213-1.975); c) exhibited future hesitant attitudes about vaccinations recommended for adults – *PR*=2.55 (CI_{95} 2.028-3.214). As regarding other variables, including intentions for future child vaccinations, the differences found were not statistically significant.

Responses with a negative or uncertain connotation (scores ranging from 3 to 10 points) regarding the overall *Confidence* subscale were identified in 47.2% (CI_{95} 44.8%-49.6%) of responses. The average total score on the subscale was 3.50 points (SD=0.90, median=3.67, IQR=1). The data cross-referencing confirmed the differences in each specific element, with the following Prevalence Ratio (PR) values and their corresponding confidence intervals: parents without higher education versus parents with higher education (PR=1.31, CI_{95} 1.074-1.594); parents, who in the past showed behaviors typical for hesitancy versus parents who did not show them regarding their own vaccinations (PR=2.06, CI_{95} 1.676-2.529) and regarding children's vaccinations (PR=1.85, CI_{95} 1.517-2.263); parents with their own vaccination status - unvaccinated versus vaccinated according to recommendations (PR=1.62, CI_{95} 1.327-1.967) or of children - unvaccinated versus vaccinated (PR=1.36, CI_{95} 1.063-1.738); parents, who regarding future vaccinations will hesitate versus not hesitate for themselves (PR=2.17, CI_{95} 1.759-2.679) or for their children (PR=2.08, CI_{95} 1.691-2.552). Additionally, the analysis of aggregated data showed the statistical significance of the differences between parents working in medical institutions and parents of other professional categories, being as following: *PR*=1.35 (CI_{95} 1.009-1.795).

As regarding the *Complacency* subscale, which determines people's erroneous perception of the risk of the disease and not considering vaccinations as indispensable, of the total number of respondents, 60.3% (CI_{95} 58.0%-62.6%) are convinced of the necessity of vaccinations, regardless of the fact that those diseases are rare. The average score was 2.73 points (SD=1.17, median=3, IQR=2). Increased levels of this element were determined in female versus male parents (PR=1.61 CI_{95} 1.211-2.143); parents, who in the past hesitated about their own vaccinations (PR=1.38, CI_{95} 1.132-1.683) and children's vaccinations (PR=1.31, CI_{95} 1.073-1.594); parents, who in the past did not vaccinate themselves according to PNI recommendations (PR=1.25, CI_{95} 1.004-1.555); For other variables, including child vaccination status and future vaccination intentions, the obtained differences were not significant.

For the belief that the immune system is so strong as to be able to protect children by avoiding vaccination (the second element of the *Complacency* subscale) it was determined that a pro-hesitating attitude was shown by 55.2% (CI_{95} 52.8%-57.6%) of the respondents, the average score being 2.64 points (SD=1.16, median=3, IQR=1).

The more affected categories were female interviewees (PR=1.36 CI_{95} 1.023-1.795); respondents who did not vaccinate themselves (PR=1.32 CI_{95} 1.052-1.654,) and did not vaccinate their children (PR=1.39, CI_{95} 1.065-1.811) according to the schedule; interviewees who believe they will hesitate in future vaccinations for themselves (PR=1.45, CI_{95} 1.142-1.834) and children's vaccinations (PR=1.49, CI_{95} 1.189-1.864). No significant statistical significance was proved for other repored differences.

According to the last element of the *Complacency* subscale, hesitant behaviours were identified in 56.4% (CI_{95} 54.0%-58.7%) of respondents, the average score being of 2.63 (SD=1.15, median=3, IQR=1). Statistically significant differences were identified only in the respondents who doubted about their vaccinations – *PR*=1.22 (CI_{95} 1.004-1.485) and about their children being vaccinated – *PR*=1.24 (CI_{95} 1.020-1.505).

Overall, the categorical, moderate or neutral responses on the elements of the *Complacency* subscale were identified in 57.3% (CI_{95} 54.9%-59.6%) of cases, the general mean score being 2.67 (SD=0, 99, median=2.67, IQR=1.33). The comparative analysis of aggregated data revealed significant statistical differences only in: a) parents who do not comply with recommendations, compared with parents who comply with PNI recommendations and got vaccinated on time – PR=1.47 (CI_{95} 1.142-1.882); b) parents who do not intend to vaccinate, compared with parents who intend to vaccinate their children in future – PR=1.47 (CI_{95} 1.154-1.884).

For the *Constraints* subscale, which refers to the psychological and/or structural barriers in making the pro-vaccination decision and transforming the intention into an effective behavior, it was determined that daily stress represents a barrier for around 50.1% (CI_{95} 47.7%-52 .5%) of respondents. The average score obtained was 2.45 points (SD=1.19, median=3, IQR=2). Through the comparative analysis of the aggregated data, statistically significant differences were determined only regarding: parents without higher education versus with higher education (PR=1.31, CI_{95} 1.074-1.594); parents, who in the past showed behaviors typical for vaccine hesitancy versus parents who did not show them regarding their own vaccinations (PR=1.37, CI_{95} 1.125-1.664) and regarding children's vaccinations (PR=1.26 CI_{95} 1.037 -1.525); parents who stated that they were unvaccinated versus vaccinated according to recommendations (PR=1.42, CI_{95} 1.115-1.807).

The need to make a lot of effort to get the child vaccinated was considered important by 45.8% (CI95 43.8%-48.2%) of the respondents, the average score being 2.41 points (SD=1.23, median=2, IQR=2). Through the comparative analysis of the aggregated data, statistically significant differences were determined only in terms of: parents, who in the past exhibited typical behaviors for hesitancy versus parents who did not exhibit them regarding their own vaccinations (PR=1.31, CI95 1.073 -1.589) or children (PR=1.34 CI_{95} 1.105-1.629).

Discomfort in the presence of a medical worker as a barrier to vaccinate their child was indicated by 36.4% (CI_{95} 34.1%-38.7%) of the respondents, obtaining an average score of 2.04 points (SD=1.14, median=2, IQR=2). This type of barriers was more frequent in parents without higher education versus parents with higher education (PR=1.31, CI_{95} 1.074-1.594); parents, who in the past showed behaviors typical for hesitancy versus parents who did not show them regarding

their own vaccinations (PR=1.46, CI_{95} 1.187-1.793) or regarding children's vaccinations (PR=1.34, CI_{95} 1.099-1.644); unvaccinated versus vaccinated parents according to PNI recommendations (PR=1.49, CI_{95} 1.042-2.118); parents, who in the future will hesitate to vaccinate for themselves (PR=1.33, CI_{95} 1.039-1.709) or for their children (PR=1.28, CI_{95} 1.007-1.618). In total, pro-hesitating attitudes for the elements of the *Constraints* subscale were revealed in 17.5% (CI_{95} 15.7%-19.4%) of the answers, the total average score on the subscale being 2.30 points (SD=0.98, median=2.33, IQR=1.67). Comparative analysis of the aggregated data determined statistically significant differences only in the responses provided by parents not intending versus parents intending to vaccinate their children in the future (PR=1.38, CI_{95} 1.022-1.864).

Regarding the *Calculation* subscale, which refers to the extent to which people intentionally seek information and then perform their own risk-benefit analysis to decide whether or not to vaccinate, it was determined that about 89.8% (CI_{95} 88, 3%-91.2%) of respondents before accepting a vaccination weigh the likely benefits and risks well to make the best decision, the mean score being 4.09 points (SD=1.11, median=4, IQR=1). About 89.8% (CI_{95} 88.3%-91.2%) of the respondents think very carefully about each vaccination if it makes sense for their child, the average score being 4.09 points (SD=1.12). The importance of understanding the vaccination argument before acceptance was considered crucial for 93.1% (CI_{95} 91.8%-94.2%) of respondents, obtaining a mean score of 4.29 points (SD=1.02, median=5, IQR=1). In total, regarding the elements of the *Calculation* subscale, pro-hesitating attitudes were revealed in 90.9% (CI_{95} 89.5%-92.2%) of the answers, the average total score on the subscale being 4.16 points (SD=0 .94, median=4.33, IQR=1.33). It should be noted that in the comparative analysis of the aggregated data on the entire subscale according to the socio-demographic variables, no statistically significant differences were determined. suggesting that this antecedent is of major magnitude and universal distribution among the study population.

The *Collective responsibility* subscale refers to the willingness of individuals to protect others by vaccinating themselves, as part of a joint effort to achieve a satisfactory level of herd immunity. With regard to this subscale, the interviewees were asked to express their agreement with the statements: "*When everyone around is vaccinated, my child does not need to be vaccinated immediately*", "*I vaccinated my child because in this way I will also protect other people with a weak immune system*" and "*Vaccination is a collective action to prevent the spread of diseases*". As can be seen, the items of the subscale have an opposite semantic connotation, which means that people with behavioral tendencies towards hesitancy will provide answers with higher scores (from three to five points) for the first statement, and for the second and third – answers with lower scores (from one to three points).

The agreement or neutral opinion towards the first statement was expressed by 56.8% (CI_{95} 54.4%-59.2%) of the total number of respondents, the average score being 2.66 points (SD=1.31, median=3, IQR=3). The comparative analysis revealed increased levels of this element of the subscale in parents without higher education versus parents with higher education (PR=1.47, CI_{95} 1.166-1.855); parents, who in the past have shown typical behaviors for hesitancy regarding their own vaccinations (PR=1.36, CI_{95} 1.117-1.656) or regarding children's vaccinations (PR=1.41, CI_{95} 1.157-1.715); unvaccinated parents (PR=1.38, CI_{95} 1.109-1.729) and who did not vaccinate their children according to PNI recommendations (PR=1.51, CI_{95} 1.168-1.958); parents, who will hesitate about future vaccinations for themselves (PR=1.42, CI_{95} 1.130-2.795) or for their children (PR=1.47, CI_{95} 1.178-1.829)

Refusal to vaccinate the child in order to protect people who cannot be vaccinated was identified in 40.8% (CI_{95} 38.5%-43.2%) of the respondents, the average score being 3.68 points (SD=1.19, median=4, IQR=2). The comparative analysis revealed increased levels of this element of the subscale in the following categories of respondents: parents, who in the past showed typical behaviors for hesitating about their own vaccinations (PR=1.64, CI_{95} 1.335-2.006) or about vaccinations children (PR=1.89, CI_{95} 1.544-2.319); vaccinated parents (PR=1.44, CI_{95} 1.178-1.749) or who vaccinated their children according to PNI recommendations (PR=1.48, CI_{95} 1.163-1.891); parents, who regarding future vaccinations will hesitate for themselves (PR=2.49, CI_{95} 2.996-3.108) or for their children (PR=2.13, CI_{95} 1.739-2.619).

For the last element of the subscale (consideration of vaccination as a collective action to prevent the spread of diseases), pro-hesitancy manifestations were determined in 64.1% (CI_{95} 61.7%-66.3%) of the respondents, obtaining an average score of 3.85 points (SD=1.15, median=4, IQR=2). The comparative analysis revealed increased levels of this element of the subscale in the following categories of respondents: parents, who in the past showed typical behaviors for hesitating about their own vaccinations (PR=1.83, CI_{95} 1.483-2.269) or about vaccinations children (PR=1.87, CI_{95} 1.520-2.307); unvaccinated parents (PR=1.69, CI_{95} 1.377-2.078) or who did not vaccinate their children according to PNI recommendations (PR=1.76, CI_{95} 1.375-2.246); parents, who regarding future vaccinations will hesitate for themselves (PR=3.00, CI_{95} 2.362-3.108) or for their children (PR=2.64, CI_{95} 2.131-3.267).

When calculating the final score for the Collective Responsibility subscale and the overall score of the 5C scale, in order to correct the direction of the semantic meaning of the statements, the original scores were subjected to a recoding procedure (if applicable), thus obtaining the following result: the higher the assigned score small, the more pronounced the degree of hesitancy.

Thus, in total, attitudes of hesitancy regarding the elements of the *Collective responsibility* subscale were revealed in 44.5% (CI_{95} 42.2%-46.9%) of the answers, the average total score on the subscale being 3.40 points (SD=0.73, median=3.67, IQR=0.67).

When comparing the aggregated data, the following categories of study participants were determined, who provided lower scores, the differences revealed being statistically significant: parents, who in the past hesitated about their own vaccinations (PR=1.38, CI_{95} 1.132 -1.683) and children's vaccinations (PR=1.53, CI_{95} 1.254-1.867); parents, who in the past did not vaccinate themselves (PR=1.27, CI_{95} 1.046-1.542) and did not vaccinate their children according to PNI recommendations (PR=1.29, CI_{95} 1.010-1.649); parents who do not intend to vaccinate in the future (PR=1.733, CI_{95} 1.413-2.120) and to vaccinate their children (PR=2.09, CI_{95} 1.701-2.557).

Regarding the overall score, the 5C *ad integrum* scale revealed typical attitudes towards vaccine hesitancy in 56.8% (CI_{95} 54.4%-59.2%) of the responses, the total mean score on the scale being 3.20 points (SD=0.45, median=3.2, IQR=0.47). In this case, statistically significant differences were found only for the answers provided by parents who believe that they will hesitate about future vaccinations for themselves (PR=1.35, CI_{95} 1.007-1.813) and for children's vaccinations (PR=1.43, CI_{95} 1.044-1.957).

The process of semantic realignment, combined with the recoding of the obtained scores, allowed us to create a comprehensive overview of the frequency of various psychological determinants related to (non)vaccination within the study. These determinants were measured using the 5C scale, as illustrated in figure 4. As observed in the graphical representation, the intensity of vaccine hesitancytancy, as seen through the elements of the 5C scale, varies for each individual element. The "green" zone on the graph signifies a lack of hesitancy and is most

pronounced in the *Constraints* subscale. This subscale, as previously mentioned, encompasses various factors related to the availability, accessibility, and appeal of immunization services. The "yellow" zone could be considered as a state of mild hesitancy (or transition) because the corresponding response option (*moderately agree*) on the Likert scale used theoretically allows for the presence of doubts regarding the discussed argument. This concept aligns with the definition of vaccine hesitancy proposed by SAGE in 2014. However, after a review of recent publications with similar studies, it was decided that, this category should be classified as a type of non-hesitant behavior. In any case, it was determined that this zone is more pronounced for the *Confidence* subscale. This subscale encompasses aspects of trust in the safety and effectiveness of vaccinations, as well as trust in the public authorities and institutions that promote and provide them.

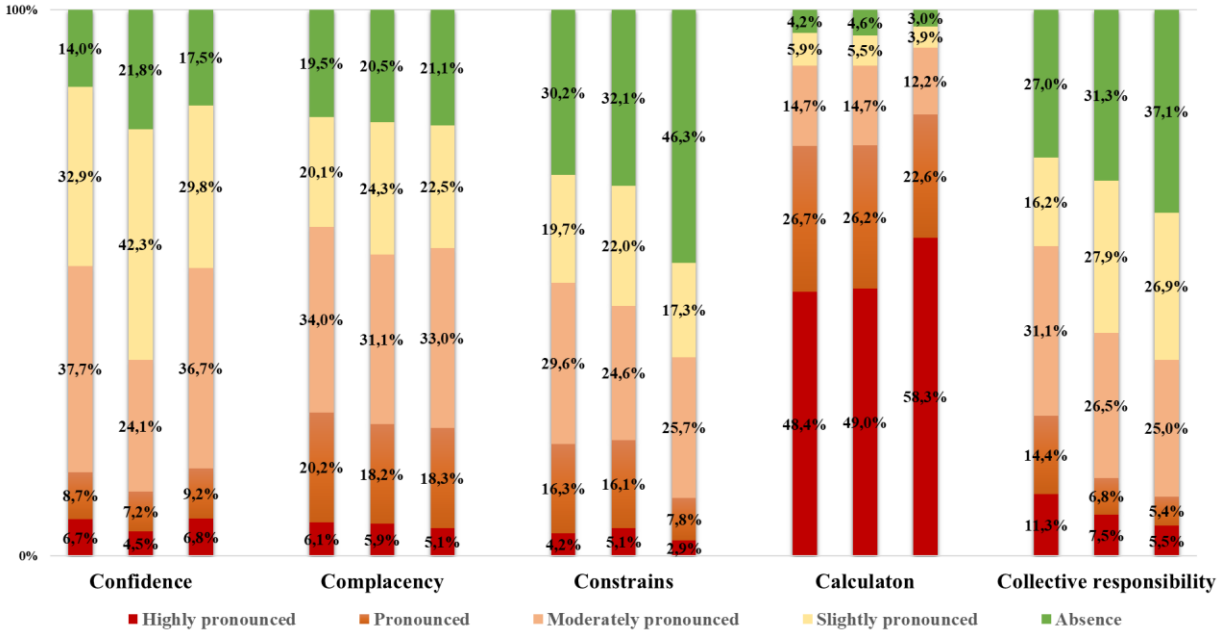

Figure 2. **The extent of vaccine hesitancytancy assessed through the perspective of the 5C Scale components (recoded).**

There are three distinct zones of red color, each with a different level of intensity, and their meanings align closely with the concept of hesitancy. The "pale pink" zone represents complete indecision or a "neutral opinion" regarding the arguments presented in the questionnaire. It is expressed with roughly the same intensity for both the *Confidence* and *Complacency* subscales, and with slightly lower intensity for the *Constraints* and *Collective responsibility* subscales. The "red" zone, signifying "*moderate disagreement*," reflects a state of moderate hesitancy up to a strong refusal regarding vaccinations, which is further exemplified by the "crimson" zone. Both of these zones are more pronounced, especially the "crimson" one, in the Calculation subscale, which involves the deliberate pursuit of information and a risk-benefit analysis before deciding on vaccinations.

In other words, it has been found that the most significant psychological factors affecting (non)vaccination are as follows: first, *Calculation* (the assessment of disease risk compared to vaccination risks), followed by *Complacency* (a perception that the risks associated with vaccine-preventable diseases are low), and *Confidence* (a lack of trust in various forms). To a lesser extent (approximately equally pronounced), factors like *Collective responsibility* (unwillingness to

contribute collectively to achieve herd immunity) and *Constraints* (limited availability, accessibility, and appeal of immunization services) were reported.

Consequently, the results of this analysis can already be valuable in identifying primary approaches for targeted interventions aimed at reducing vaccine hesitancy in the population.

5.4. Intentions for future vaccinations recommended by the NIP

The final set of questions aimed to assess the participants' future intentions regarding the recommended vaccinations in the National Immunization Program (NIP), both for the participating parents and their children. Participants were asked the following questions: *"Imagine you've been invited to the doctor for a vaccination according to the immunization schedule. How would you make your decision?*" and *"If you were to have another child, would you want them to receive the recommended vaccinations?"*

Approximately one in four parents expressed a clear willingness to either unquestionably accept vaccinations for themselves (23.7%, CI_{95} 21.7%-25.8%) or for their children (27.7%, CI_{95} 25.6%-29.9%). Conversely, 7.7% (CI_{95} 6.5%-9.0%) and 4.6% (CI_{95} 3.7%-5.7%) have firmly declared their refusal for both types of vaccinations. The most common opinion for both categories was that parents would only accept vaccinations if their doubts about them were satisfied, or that they would accept only certain vaccines. The other responses are unevenly distributed, suggesting that parents are more inclined to vaccinate their children than to vaccinate themselves (figure 5). In support of this hypothesis, the average score was 3.38 points (SD=1.17, median=3, IQR=1) for intentions in adults and 3.69 points (SD=1.08, median=4, IQR=2) for children.

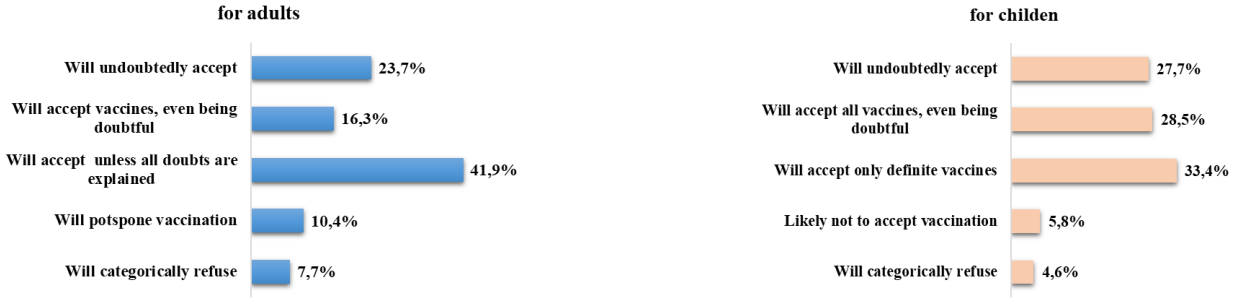

Figure 5. **Distribution of participants'future intentions regarding their own and/or their children 's vaccination**

Furthermore, to investigate the observed differences, the χ^2 test was employed for independent samples, which revealed highly significant statistical diferences ($p < 0.0001$, χ^2=112.6682, df=4) in the participants' opinions. The obtained Cramer's V index value of 0.1829 implies a moderate association between these variables ($0.15 \leq$ Cramer's V ≤ 0.25, df=4).

Finally, it was established that the picture determined for past behaviors, for the degree of expression of psychological determinants and for intentions for the future differs from that determined in the study carried out on healthcare workers, pro-hesitating behaviors being generally more expressed (which appears as something normal, or better said – explainable), but essentially, the same behavioral pattern can be seen in both models.

CONCLUSIONS

1. The study results have revealed that vaccine hesitancy is a highly complex, specific, and time-variable phenomenon that is increasing worldwide. The frequent and rapid ability to change and the significant potential of vaccine hesitancy in compromising the population's immune layer, requiring periodic assessments of the predominant determinants and evidence-based strategies tailored to specific contexts.
2. The study has found that the 5C scale for assessing vaccine hesitancy extends beyond the range of elements captured by other existing instruments. It is easily adaptable and applicable in various contexts for diagnosing and monitoring the current situation, offering evidence-based data for designing necessary interventions and assessing the impact of those undertaken. The developed tool facilitates the continuous collection, analysis, interpretation, and dissemination of data to the interested parties involved in maintaining high vaccination coverage rates.
3. This study has revealed that healthcare professionals exhibit high levels of skepticism paired with low confidence in vaccine safety, as well as in the authorities responsible for vaccination decision-making. This could potentially play a significant role in vaccine hesitancy among the general population. Elevated levels of skepticism signify the presence of communication issues, meaning that individuals actively seek information from reliable sources.
4. The primary factors contributing to vaccine hesitancy among the general population included intentional information-seeking about vaccinations, followed by individual risk-benefit analysis. Inadequate perception of disease risks, low confidence in vaccinations, and low collective responsibility were also significant contributors. It is a concern that these factors impact healthcare workers, particularly those with moderate levels of education, as their opinions often serve as a reference point and may significantly impact vaccine hesitancy among other population groups.
5. The study revealed that parents exhibited doubts or resistance when it came to accepting recommended vaccinations for both their children and themselves. However, they more tend to delay their children's vaccinations compared to their own, where typical behaviors tended more toward refusal. Concerning future intentions, parents were more willing to vaccinate their children than themselves. Hesitant behaviors were more commonly driven by distrust in the safety and efficacy of vaccines, as well as considering the particular diseases as not severe ones, and that other measures were more effective. Unpleasant experiences related to past vaccinations also influenced these behaviors.
6. The research findings provide valuable, evidence-based data that can be employed to monitor the occurrences of the studied phenomenon at a national level and to periodically evaluate the effectiveness of vaccine hesitancy management in the Republic of Moldova.

RECOMMENDATIONS

I. At Central Public Administration Level:

1. Including vaccine hesitancy into the Government of the Republic of Moldova's list of strategic public health priorities, while ensuring effective national intersectoral collaboration and international communication to strengthen the capacity to counter this global challenge.
2. Enhancing the literacy within public health, especially regarding vaccine hesitancy, for all decision-makers at central and local levels.
3. Implementing curricular adjustments at all educational levels aimed at including topics related to vaccine-preventable diseases and their preventive measures, their impact on public health, increasing literacy, and intensifying efforts to combat infodemics.
4. Combatting the infodemic by promoting accurate evidence-based information and debunking myths related to immunization, vaccine-preventable diseases, and associated adverse reactions.
5. Developing targeted awareness campaigns using modern technologies to inform the population about the risks of vaccine-preventable diseases and their prevention measures. Additionally, developing and applying skills to obtain information from reliable sources regarding the risks of vaccine-preventable diseases and post-vaccination adverse events. Proactive communication, providing data dissemination from reliable and official sources to counter vaccine-related myths.
6. Supporting and promoting research on vaccine hesitancy and its impact on public health is essential for gathering evidence-based data required to develop context-specific strategies and interventions.

II. At the level of health authorities:

7. Developing and implementing a Surveillance System for vaccine hesitancy factors using the 5C scale as a diagnostic and monitoring tool, reporting the outcomes to international field-related bodies.
8. Developing and including a response plan wihin the National Immunization Program to address changes in the patterns of vaccine hesitancy determinants among various population groups, as an integral component of the program's best practices.
9. Revising the curriculum to enhance professional programs within undergraduate, university, postgraduate, and continuous education of healthcare professionals regarding the issue of vaccine hesitancy. This involves the development of training courses and improvement programs for medical personnel on vaccine hesitancy as a behavioral phenomenon.
10. Proper motivation of medical personnel is crucial as the primary source of information for the population on public health issues. This includes promoting immunization policies, debunking myths that influence vaccine acceptance, and implementing activities to promote vaccinations and counteract vaccine hesitancy.
11. Active participation in public health awareness and literacy campaigns, particularly concerning vaccine hesitancy, in collaboration with central and local public authorities, media outlets, etc., aiming at promoting clear and precise messages regarding vaccinations.

BIBLIOGRAPHY

1. World Health Organization. 10 facts on immunization; 2019. Disponibil la: https://www.who.int/features/factfiles/immunization/en/
2. Dempsey AF, Schaffer S, Singer D, Butchart A, Davis M, Freed GL. Alternative vaccination schedule preferences among parents of young children. Pediatrics. 2011;128(5):848–856pmid:21969290
3. Robison SG, Groom H, Young C. Frequency of alternative immunization schedule use in a metropolitan area. Pediatrics. 2012;130(1):32–38pmid:22711719.
4. Gust DA, Darling N, Kennedy A, Schwartz B. Parents with doubts about vaccines: which vaccines and reasons why. Pediatrics. 2008;122(4):718–725pmid:18829793.
5. Dube E, Laberge C, Guay M, Bramadat P, Roy R, Bettinger J. Vaccine hesitancy: an overview. Hum Vaccin Immunother. 2013;9(8):1763-73.
6. Papagiannis D, Rachiotis G, Symvoulakis EK, Daponte A, Grivea IN, Syrogiannopoulos GA, et al. Vaccination against human papillomavirus among 865 female students from the health professions in central Greece: A questionnaire-based cross-sectional study. Journal of Multidisciplinary Healthcare. 2013;6:435-9.
7. Navarro-Illana P, Diez-Domingo J, Navarro-Illana E, Tuells J, Aleman S, Puig-Barbera J. Knowledge and attitudes of Spanish adolescent girls towards human papillomavirus infection: where to intervene to improve vaccination coverage. BMC Public Health. 2014;14(490).
8. Lehmann BA, Ruiter RAC, Wicker S, van Dam D, Kok G. 'I don't see an added value for myself': a qualitative study exploring the social cognitive variables associated with influenza vaccination of Belgian, Dutch and German healthcare personnel. BMC Public Health. 2014;14.
9. Wicker S, Rabenau HF, Betz W, Lauer HC. Attitudes of dental healthcare workers towards the influenza vaccination. International Journal of Hygiene and Environmental Health. 2012;215(4):482-6.
10. Brandt C, Rabenau HF, Bornmann S, Gottschalk R, Wicker S. The impact of the 2009 influenza A(H1N1) pandemic on attitudes of healthcare workers toward seasonal influenza vaccination 2010/11. Eurosurveillance. 2011;16(17). Maltezou HC, Maragos A, Katerelos P, Paisi A, Karageorgou K, Papadimitriou T, et al. Influenza vaccination acceptance among healthcare workers: a nationwide survey. Vaccine. 2008;26(11):1408-10.
11. Meeting of the Strategic Advisory Group of Experts on Immunization. November 2008 – conclusions and recommendations. Wkly Epidemiol Rec 2009;84(1–2):1–16.
12. Parent du Châtelet I, Antona D, Freymuth F, Muscat M, Halftermeyer-Zhou F, Maine C, et al. Spotlight on measles 2010: update on the ongoing measles outbreak in France, 2008-2010. Euro Surveill 2010; 15:15; PMID:20843472.
13. De Serres G, Markowski F, Toth E, Landry M, Auger D, Mercier M, et al. Largest measles epidemic in North America in a decade--Quebec, Canada, 2011: contribution of susceptibility, serendipity, and superspreading events. J Infect Dis 2013; 207:990-8; PMID:23264672; Disponibil la: http://dx.doi.org/10.1093/infdis/jis923.
14. Oostvogel PM, van Wijngaarden JK, van der Avoort HGAM, Mulders MN, Conyn-van Spaendonck MAE, Rümke HC, et al. Poliomyelitis outbreak in an unvaccinated community in The Netherlands, 1992-93. Lancet 1994; 344:665-70; PMID:7915354. Disponibil la: http://dx.doi.org/10.1016/S0140-6736(94)92091-5.

15. Centers for Disease Control and Prevention (CDC). Notes from the field: Pertussis—California, January–June 2010. Morbidity and Mortality Weekly Report2010; 59:817.
16. http://www.epicentro.iss.it/temi/vaccinazioni/CommentoFranco2014.asp.
17. https://www.epicentro.iss.it/vaccini/dati_Mondo.
18. 2018 Assessment report of the Global Vaccine Action Plan. Strategic Advisory Group of Experts on Immunization. Geneva: World Health Organization; 2018 (WHO/IVB/18.11). Licence: CC BY-NC-SA 3.0 IGO).
19. Addressing Vaccine Hesitancy. WHO 2016. www.who.int/immunization/ programmes_ systems/vaccine_hesitancy/en/.
20. Vaccine hesitancy: A growing challenge for immunization programmes. WHO 2015. www.who.int/mediacentre/news/releases/2015/vaccine-hesitancy/en/.
21. Current practices in immunisation policymaking in European countries. European Centre for Disease Prevention and Control (ECDC). http://ecdc.europa.eu/en/ publications/Publications/Current-practices-on-immunisation-policymaking-processes-Mar-2015.pdf.
22. MacDonald NE, SAGE Working Group on Vaccine Hesitancy. Vaccine hesitancy: Definition, scope and determinants. Vaccine 2015;33(34):4161-4164.
23. http://www.asset-scienceinsociety.eu/news/features/numbers-and-evidence-better-health-communication.
24. 2018 Assessment report of the Global Vaccine Action Plan. Strategic Advisory Group of Experts on Immunization. Geneva: World Health Organization; 2018 (WHO/IVB/18.11). Licence: CC BY-NC-SA 3.0 IGO.
25. Ten Health Issues WHO Will Tackle This Year. https://www.who.int/news-room/spotlight /ten-threats-to-global-health-in-2019.
26. Agenția Națională pentru Sănătate Publică (ANSP). Supravegherea de stat a sănătății publice în Republica Moldova: (Raport național, 2022). Disponibil la: https://ansp.md/rapoarte/ [accesat la 01.12.2023]
27. Santoli, J. M., Lindley, M. C., DeSilva, M. B., Kharbanda, E. O., Daley, M. F., Galloway, L., et al. (2020). Effects of the COVID-19 pandemic on routine pediatric vaccine ordering and administration—United States, 2020. MMWR, 69(19), 591–593.
28. Bramer, C. A., Kimmins, L. M., Swanson, R., Kuo, J., Vranesich, P., Jacques-Carroll, L. A., et al. (2020). Decline in child vaccination coverage during the COVID-19 pandemic—Michigan Care Improvement Registry, May 2016–May 2020. MMWR, 69(20), 630–631.
29. The Lancet Child & Adolescent Health. (2019). Vaccine hesitancy: A generation at risk. Lancet Child & Adolescent Health [Internet]., 3(5), 281. https://doi.org/10.1016/S2352-4642(19)30092-6.
30. Santibanez, T. A., Nguyen, K. H., Greby, S. M., Fisher, A., Scanlon, P., Bhatt, A., et al. (2020). Parental vaccine hesitancy and childhood influenza vaccination. Pediatrics, https://doi.org/10.1542/peds.2020-007609
31. Goldman, R. D., McGregor, S., Marneni, S. R., Katsuta, T., Griffiths, M. A., Hall, J. E., et al. (2021). Willingness to vaccinate children against influenza after the coronavirus disease 2019 pandemic. Journal of Pediatrics, 228, 87-93.e2.
32. Pullan, S., & Dey, M. (2021). Vaccine hesitancy and anti-vaccination in the time of COVID-19: A Google Trends analysis. Vaccine, 10, 20. https://doi.org/10.1016/j.vaccine. 2021.03.019

33. DeSilva M.B., Haapala J., Vazquez-Benitez G., Daley M.F., Nordin J.D., Klein N.P., et al. Association of the COVID-19 pandemic with routine childhood vaccination rates and proportion up to date with vaccinations Across 8 US health systems in the vaccine safety datalink. JAMA Pediatrics, 176 (1) (2022), pp. 68-77, 10.1001/jamapediatrics.2021.4251.
34. Opel D.J., Furniss A., Zhou C., Rice J.D., Spielvogle H., Spina C., et al.. Parent attitudes towards childhood vaccines after the onset of SARS-CoV-2 in the United States. Academic Pediatrics (2022), 10.1016/j.acap.2022.06.014.
35. He K., Mack W.J., Neely M., Lewis L., Anand V. Parental perspectives on immunizations: Impact of the COVID-19 pandemic on childhood vaccine hesitancy. J Commun Health, 47 (2022), pp. 39-52, 10.1007/s10900-021-01017-9.
36. Hegde S.T., Wagner A.L., Clarke P.J., Potter R.C., Swanson R.G., Boulton M.L. Neighbourhood influence on the fourth dose of diphtheria-tetanus-pertussis vaccination. Public Health, 167 (2019), pp. 41-49, 10.1016/j.puhe.2018.11.009.
37. Masters N.B., Eisenberg M.C., Delamater P.L., Kay M., Boulton M.L., Zelner J. Fine-scale spatial clustering of measles nonvaccination that increases outbreak potential is obscured by aggregated reporting data. Proceedings of the National Academy of Sciences, 117 (2020), pp. 28506-28514, 10.1073/pnas.2011529117.
38. Lieu T.A., Ray G.T., Klein N.P., Chung C., Kulldorff M.. Geographic clusters in underimmunization and vaccine refusal. Pediatrics, 135 (2015), pp. 280-289, 10.1542/peds.2014-2715.
39. Gromis A, Liu K-Y. Spatial clustering of vaccine exemptions on the risk of a measles outbreak. Pediatrics 2021;149:e2021050971. https://doi.org/10.1542/peds.2021-050971.
40. Lopes L, Schumacher S, Presiado M, 2022. KFF COVID-19 Vaccine Monitor: December 2022. KFF 2022. https://www.kff.org/coronavirus-covid-19/poll-finding/kff-covid-19-vaccine-monitor-december-2022/.
41. Tenforde M.W., Self W.H., Adams K., Gaglani M., Ginde A.A., McNeal T. et al. Association between mRNA vaccination and COVID-19 hospitalization and disease severity. Journal of the American Medical Association (JAMA), 326 (2021), pp. 2043-2054, 10.1001/jama.2021.19499.
42. Xiao X., Wong R.M.. Vaccine hesitancy and perceived behavioral control: A meta-analysis. Vaccine, 38 (2020), pp. 5131-5138, 10.1016/j.vaccine.2020.04.076.
43. Li J.-Y., Wen T.J., McKeever R., Kim J.K.. Uncertainty and negative emotions in parental decision-making on childhood vaccinations: extending the theory of planned behavior to the context of conflicting health information. Journal of Health Communication, 26 (2021), pp. 215-224, 10.1080/10810730.2021.1913677.
44. Sturm L.A., Mays R.M., Zimet G.D.. Parental beliefs and decision making about child and adolescent immunization: from polio to sexually transmitted infections. J Develop Behav Pediatr, 26 (2005), p. 441.
45. Chu H., Liu S.. Integrating health behavior theories to predict American's intention to receive a COVID-19 vaccine. Patient Education and Counseling, 104 (2021), pp. 1878-1886, 10.1016/j.pec.2021.02.031
46. Tailoring Immunization Programmes (TIP). Copenhagen: WHO Regional Office for Europe; 2019. Licence: CC BY-NC-SA 3.0 IGO.

PUBLICATIONS AND PARTICIPATION IN SCIENTIFIC FORUMS

Valentin Mîța, carried out within the Ph.D. thesis in medical sciences
On the topic *"Vaccine Hesitancy Phenomenon in the Republic of Moldova"*
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SCIENTIFIC PAPERS

- **Articles in scientific journals abroad:**

✓ **Articles in ISI, SCOPUS and other international databases.**

1. Amadori F., Terracciano E., Gennaio I., **Mita V.**, Gargano D., Zaratti L., Franco E., Arigliani R. Opinions and attitudes of Italian healthcare workers towards recommended but not compulsory Rotavirus vaccination. In: *Human Vaccines & Immunotherapeutics.* 2020; Jul 2;1-6. ISSN: 2164-5515. doi: 10.1080/21645515.2020.1776546.
2. **Mita V.**, Arigliani M., Zaratti L., Arigliani R., Franco E. Italian Physicians' Opinions on Rotavirus Vaccine Implementation. In: *Pathogens.* 2017; Nov 3;6(4). ISSN: 2076-0817. doi: 10.3390/pathogens6040056.
3. Gervasi G., Capanna A., **Mita V.**, Zaratti L., Franco E. Nosocomial rotavirus infection: An up-to-date evaluation of European studies. In: *Human Vaccines & Immunotherapeutics*. 2016; May 16:1-6. ISSN: 2164-5515. doi: 10.1080/21645515.2016.1183858.
4. **Mita V.**, Capanna A., Gervasi G., Zaratti L., Franco E. Universal vaccination for Rotavirus infection control. In: *Igiene e sanita pubblica*. 2015; Jul-Aug;71(4):447-54. PMID: 26519750.
5. Dugo V., Zaratti L., **Mita V.**, Franco E. Update of recommendations for the prevention of Hepatitis A in Italy. In: *Igiene e sanita pubblica*. 2014 Jul-Aug;70(4):431-41. PMID: 25353273.

- **Articles in accredited national scientific journals:**

✓ **Articles published in B-category journals.**

6. Cornei A., **Mita V.**, Lozan O. Conlucrarea serviciului de supraveghere de stat a sănătății publice cu asistența medicală primară la nivel teritorial. In: *One Health & Risk Management*. ISSN (Online): 2587-3466 (in press).
7. Timotin A., Paladi A., **Mita V**., Chihai V., Lozan O. Digital social listening in COVID-19 pandemic for informed interventions in the Republic of Moldova: integrated data. In: *One Health & Risk Management*. ISSN (Online): 2587-3466 (in press).

- **Summaries/abstracts/theses presented at national and international scientific conferences:**

8. **Mîța V**. Fenomenul de ezitare la vaccinare în Republica Moldova. În: Managementul sănătății publice: realizări, provocări și perspective. În: *Materialele Conferinței științifice dedicate aniversării a 75 de ani de la fondarea USMF" Nicolae Testemițanu".* Chișinău; 2020, pp. 23-24.
9. Terraciano E., **Mita V**., Regina I., Arigliani R., Zaratti L., Franco E. Gastroenteriti da Rotavirus: quale futuro? In: *Atti congressuali 51° Congresso Nazionale della Società Italiana di Igiene, Medicina Preventiva e Sanità Pubblica*. Garda; 2018, p. 228.

10. **Mita V**., Arigliani M., Arigliani R., Franco E. Cosa pensano i medici italiani della vaccinazione anti-rotavirus? In: *Atti congressuali 49° Congresso Nazionale della Società Italiana di Igiene, Medicina Preventiva e Sanità Pubblica.* Napoli; 2016, p. 658.
11. **Mita V**., Gervasi G., Capanna A., Zaratti L., Franco E. Ruolo dell'infezione da rotavirus nelle ospedalizzazioni e nelle infezioni nosocomiali. In: *Atti congressuali 48° Congresso Nazionale della Società Italiana di Igiene, Medicina Preventiva e Sanità Pubblica.* Milano; 2015, p. 44.
12. Dugo V., Zaratti L., **Mita V**., Franco E. Attuali rischi per l'epatite A in Italia e indicazioni per la prevenzione. In: *Atti congressuali 47° Congresso Nazionale della Società Italiana di Igiene, Medicina Preventiva e Sanità Pubblica*. Riccione; 2014, pp. 165-166.

- **Presentations within scientific forums:**

✓ **international**.

13. Terraciano E., **Mita V**., Regina I., Arigliani R., Zaratti L., Franco E. Gastroenteriti da Rotavirus: quale futuro? *51° Congresso Nazionale della Società Italiana di Igiene, Medicina Preventiva e Sanità Pubblica*. Garda; 2018.
14. **Mita V**., Gervasi G., Capanna A., Zaratti L., Franco E. Ruolo dell'infezione da rotavirus nelle ospedalizzazioni e nelle infezioni nosocomiali. *48° Congresso Nazionale della Società Italiana di Igiene, Medicina Preventiva e Sanità Pubblica.* Milano; 2015.

✓ **national**

15. **Mîța V**. Fenomenul de ezitare la vaccinare în Republica Moldova. În: Managementul sănătății publice: realizări, provocări și perspective. *Conferința științifică a USMF" Nicolae Testemițanu",* 29 septembrie - 01 octombrie 2020.

- **Posters within scientific forums:**

✓ **international**

16. **Mita V**., Arigliani M., Arigliani R., Franco E. Cosa pensano i medici italiani della vaccinazione anti-rotavirus? 49° Congresso Nazionale della Società Italiana di Igiene, Medicina Preventiva e Sanità Pubblica. Napoli 2016.
17. Dugo V., Zaratti L., **Mita V**., Franco E. Attuali rischi per l'epatite A in Italia e indicazioni per la prevenzione. *47° Congresso Nazionale della Società Italiana di Igiene, Medicina Preventiva e Sanità Pubblica*. Riccione 2014.

- **Patents, Registration Certificates, and Materials for Invention Exhibitions:**

18. Lozan O., Paladi A., Timotin A., Bîrcă L., Țurcan L., **Mîța V.** Aplicarea chestionarului standardizat de evaluare a determinanților psihosociali ai ezitării la vaccinare în rândul populației Republicii Moldova. Certificat de Inovator Nr. 6013, 2023.03.04.

ADNOTARE

Valentin Mîța „Fenomenul de ezitare la vaccinare în Republica Moldova”,
Teză de doctor în științe medicale, Chișinău, 2023.

Structura tezei: introducere, cinci capitole, concluzii generale și recomandări practice, bibliografia cu 122 surse, 115 pagini de text de bază, 12 tabele, 44 de figuri, 5 anexe. La subiectul cercetării au fost publicate 11 lucrări științifice, inclusiv 6 articole și 5 teze, 2 publicații naționale și 9 internaționale, 3 cu factor de impact, au fost obținute 3 acte de implementare, 1 certificat de inovator.

Cuvinte-cheie: vaccinare, imunizări, ezitare la vaccinare, scala 5C, determinanți psihosociali, antecedente psihologice, convingere, confort, constrângeri, calcul, responsabilitate colectivă.

Scopul: Argumentarea științifică a dezvoltării instrumentului de evaluare și de monitorizare a ezitării la vaccinare și aplicarea lui la nivel specific și populațional pentru elaborarea unui set de recomandări bazate pe dovezi cu privire la contracararea fenomenului studiat în context național.

Obiectivele cercetării: analiza practicilor internaționale contemporane privind factorii determinanți ai ezitării la vaccinare și abordarea acestora prin metode științifice bazate pe dovezi; dezvoltarea și testarea instrumentului de diagnostic și monitorizare a ezitării la vaccinare adaptat la condițiile Republicii Moldova prin explorarea calitativă și cantitativă a fenomenului studiat; identificarea particularităților ezitării la vaccinare în rândul medicilor și lucrătorilor medicali cu studii medii; repurtarea datelor bazate pe dovezi privind fenomenul de ezitare și factorii săi determinanți în context populațional; elaborarea recomandărilor pentru proiectarea intervențiilor specifice cu privire la contracararea fenomenului de ezitare la vaccinare.

Noutatea și originalitatea științifică: în premieră a fost realizat un studiu complex bazat pe dovezi ale bunelor practici internaționale folosind un instrument standardizat de evaluare a factorilor determinanți ai ezitării la vaccinare. Elementul de inovație constă în studierea și abordarea fenomenului cu ajutorul unor metode și instrumente moderne, adaptându-le la condițiile actuale concrete.

Semnificația teoretică și valoarea aplicativă a lucrării: fundamentarea științifică și metodologică de obținere a informațiilor actualizate, necesare pentru determinarea și prioritizarea intervențiilor țintite de contracarare a fenomenului studiat și pentru monitorizarea în dinamică a eficacității măsurilor întreprinse pentru fortificarea managementului factorilor de risc modificabili pentru bolile prevenibile prin vaccinare în Republica Moldova. De asemenea, cunoștințele obținute lărgesc orizontul de cercetare în acest domeniu la nivel mondial și vor putea fi aplicate în procesul de instruire a specialiștilor în sănătate publică și a cadrelor medicale, precum și în activitatea științifică din țară.

Implementarea rezultatelor: rezultatele cercetării au fost implementate în procesul managerial în cadrul Direcției Generale de Asistență Medicală și Socială a Consiliului municipal Chișinău în cadrul IMSP Clinica Universitară de Asistență Medicală Primară a USMF „Nicolae Testemițanu”, în procesul științifico-didactic în cadrul Școlii de Management în Sănătate Publică a USMF „Nicolae Testemițanu” și a Agenției Naționale pentru Sănătate Publică.

ANNOTATION

Valentin Mita "Vaccine hesitancy phenomenon in the Republic of Moldova", Ph.D. thesis in medical sciences, Chisinau, 2023

Structure of the thesis: introduction, five chapters, general conclusions and practical recommendations, bibliography of 122 titles, 115 pages of basic text, 12 tables, 44 figures, 5 appendices. On the subject of research, 11 scientific papers were published, including 6 articles and 5 theses, 2 national and 9 international publications, 3 with an impact factor; 3 implementation documents and 1 innovator certificate were obtained.

Keywords: vaccination, immunizations, vaccine hesitancy, 5C scale, psychosocial determinants, confidence, complacency, constraints, calculation, collective responsibility.

Aim of the study: The scientific argumentation of the development of the evaluation and monitoring tool for vaccine hesitancy and its application at a specific and population level for the development of a set of evidence-based recommendations on countering the phenomenon in a national context.

Study's objectives: analyzing contemporary international practices concerning the determinants of vaccine hesitancy and explore evidence-based scientific approaches to address them; development and testing of a diagnostic tool for vaccine hesitancy determinants tailored to the conditions in the Republic of Moldova through the qualitative and quantitative exploration of the studied phenomenon; determining the specific vaccine hesitancy patterns among healthcare workers; assessing vaccine hesitancy among parents of children aged ≤18 years; obtaining evidence-based data on vaccine hesitancy and its determinants within a population-level context; developing recommendations for designing specific interventions to counteract vaccine hesitancy.

Scientific novelty and originality: for the first time, a comprehensive scientific study based on evidence of good international practice was carried out using a standardized tool to assess factors determining vaccine hesitancy. The innovative aspect lies in the study and approach to this phenomenon using modern methods and tools, adapted to the current specific conditions of the Republic of Moldova.

Theoretical relevance and applicative value: The scientific and methodological argumentation for obtaining updated information, necessary for the determination and prioritization of targeted interventions to counteract the studied phenomenon and for the dynamic monitoring of the effectiveness of the measures undertaken to strengthen the management of modifiable risk factors for vaccine-preventable diseases in the Republic of Moldova.

Implementation of Scientific Results: The research results have been implemented in the management processes within the General Directorate of Medical and Social Assistance of the Chisinau Municipal Council, and within the University Primary Medical Care Clinic of the "Nicolae Testemițanu" State University of Medicine and Pharmacy, as well as in the scientific and educational processes at the School of Public Health Management of the "Nicolae Testemițanu" State University of Medicine and Pharmacy and the National Public Health Agency.

АННОТАЦИЯ

Валентин Мыца

«Феномен нерешительности в отношении вакцинации в Республике Молдова», Диссертация на соискание учёной степени кандидата медицинских наук, Кишинев, 2023.

Структура диссертации: введение, 5 глав, общие выводы и практические рекомендации, библиография из 122 источников, 115 страниц основного текста, 12 таблиц, 44 рисунка, 6 приложений. По теме исследования опубликовано 11 научных работ, в том числе 6 статей и 5 тезисов, 2 национальных и 9 международных публикаций, 3 с импакт-фактором, 3 акта внедрения, получено 1 свидетельство инноватора.

Ключевые слова: вакцинация, иммунизация, неуверенность в отношении вакцинации, шкала 5С, психосоциальные детерминанты, психологические предпосылки, убеждение, комфорт, ограничения, расчет, коллективная ответственность.

Цель работы: Научное обоснование разработки инструмента для оценки и мониторинга нерешительности в отношении вакцинации и его применения на конкретном и популяционном уровне для разработки комплекса рекомендаций, основанных на фактических данных, относительно мер противодействия изучаемому явлению в национальном контексте.

Задачи исследования: анализ современной международной практики в отношении факторов, определяющих нерешительность вакцинации, и устранение их с помощью научно обоснованных методов; разработка и тестирование инструмента диагностики и мониторинга нежелания вакцинироваться, адаптированного к условиям Республики Молдова, путем качественного и количественного исследования изучаемого явления; выявление особенностей неуверенности в вакцинации среди врачей и медицинских работников со средним образованием; представление научно обоснованных данных о явлении нерешительности и его детерминантах в популяционном контексте; разработка рекомендаций по предпринятию конкретных мер в противодействии явлению нерешительности в отношении вакцинации.

Научная новизна и оригинальность: Впервые было проведено комплексное исследование, основанное на доказательствах передовой практики, с использованием стандартизированного инструмента для оценки факторов, определяющих нерешительность вакцинации. Элемент инновации состоит в изучении и подходе к явлению с помощью современных методов и инструментов, адаптации их к конкретным текущим условиям.

Теоретическая значимость и прикладная ценность работы: научно-методическое обоснование получения информации, необходимой для выявления и приоритизации целевых вмешательств по противодействию изучаемому явлению и для динамического мониторинга эффективности мер, предпринимаемых для усиления управления модифицируемыми факторами риска вакциноуправляемых заболеваний в Республике Молдова.

Внедрение научных результатов: результаты исследования были внедрены в управленческий процесс в Главном управлении медико-социальной помощи Муниципального совета Кишинэу, в Университетской клинике первичной медицинской помощи ГУМФ «Николае Тестемицану», в научно-дидактическом процессе в Школе Управления общественным здравоохранением ГУМФ «Николае Тестемицану» и Национального агентства общественного здравоохранения.

MÎȚA VALENTIN

FENOMENUL DE EZITARE LA VACCINARE ÎN REPUBLICA MOLDOVA

331.03 SOCIAL MEDICINE AND MANAGEMENT

Summary of Doctoral Thesis in Medical Sciences

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