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OPEN LETTER

Twinning for the Armenian research infrastructure on cancer research

[version 1; peer review: 2 approved with reservations]

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Abstract

The incidence of cancer is expected to rise globally, with low-and middle-income countries affected disproportionally. One of those countries, Armenia, also faces the challenge of exhibiting one of the lowest research and scientific publication rates within Europe on cancer research. This report presents the experiences of the Twinning for the Armenian Research Infrastructure on Cancer Research (ARICE) program, funded by the European Commission from 2019 – 2024. The project brought together experts from three leading research-intensive, cancer centres: the Medical University of Graz, Austria; the Charles University, Czechia; and the International Agency for Research on Cancer, World Health Organization (IARC/WHO), in partnership with the Yerevan State Medical University. The aim was to enhance the research capacity in Armenia in the field of infrastructure development for clinical genetic research, in particular targeting the collection and use of biological materials, and the data integration for downstream analyses in relation to chronic, non-communicable diseases such as cancer. To this end, training initiatives and educational programmes were developed throughout the duration of the grant and are discussed within their local context.

Plain language summary

This report presents the experiences of the Twinning for the Armenian

Open Peer Review

Approval Status ? ?

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Any reports and responses or comments on the article can be found at the end of the article.

Research Infrastructure on Cancer Research (ARICE) program, funded by the European Commission from 2019 – 2024. The project brought together experts from three leading research-intensive, cancer centres: the Medical University of Graz, Austria; the Charles University, Czechia; and the International Agency for Research on Cancer, World Health Organization (IARC/WHO), in partnership with the Yerevan State Medical University. The aim was to enhance the research capacity in Armenia in the field of infrastructure development for clinical genetic research, in particular targeting the collection and use of biological materials, and the data integration for downstream analyses in relation to chronic, non-communicable diseases such as cancer. To this end, training initiatives and educational programmes were developed throughout the duration of the grant.

Keywords
Armenia, twinning, research infrastructure, cancer research, educational program development



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This article is included in the Cancer collection.

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Introduction

According to the Global Cancer Observatory (Globocan), an increase of 47% new cancer cases worldwide is estimated by the year 2040. Due to demographic changes and an accumulation of cancer risk factors, transitioning countries like Armenia are expected to be affected more severely (+ 64–95% new cases) than already transitioned countries. According to these reports, it is inevitable infrastructure for cancer prevention and research is strengthened so as and to provide the increasing needs of cancer care in these countries[1]. Armenia with its approximately three million population[2] is one of these transitioning countries, affected by increasing numbers of cancer cases, with cancer incidence rising and becoming currently the second leading cause of death nation-wide[3]. Besides aging and population growth, the main cancer risk factors in Armenia include smoking, physical inactivity, obesity, and alcohol use[4]. The latter two are assumed to arise due to the socioeconomic development[5] in transitioning countries and have been particularly prominent in Armenia[6,7].

Additionally, hereditary cancer risk factors have to be taken into account. According to the United States Center for Disease Control (CDC), 5–10% of breast cancer is due to genetic factors, for ovarian cancer the value lies between 10 and 15%[8]. Armenian researchers recently investigated pathogenic gene mutations, responsible for an increased risk for hereditary breast and ovarian cancer (HBOC). Previous small-scale studies in Armenia showed the lack of founder mutations in the investigated panels and indicated that there might exist population-specific mutations, that are responsible for hereditary breast cancers[9]. In Armenia's first large-scale study, investigating population-specific genes, 44 variants were identified responsible for breast cancer[9]. This is significant, as it demonstrates the need for further large-scale, population-specific studies, to further understand the genetic predisposition of the Armenian population to certain cancer types.

Yet, despite the predicted increase in cancer cases and the occurrence of population-specific hereditary cancers, as described above, Armenia is one of the lowest performing countries world-wide, regarding scientific and technical papers[10]. In comparison, in 2020 Austria had a 23-fold higher scientific output than Armenia and Germany, one of the leading academic countries in Europe, showed a publication rate that was 200-times higher[10,11]. This demonstrates the considerable knowledge gap that exists both locally and internationally, as there is very limited research conducted locally, and as such not being visible in the international stage.

On the ground in Armenia, cancer research itself, when undertaken, is insufficient for the population needs and tends to be conducted in silos, rather than as part of a connected healthcare system[12]. The Center of Medical Genetics and Primary Health Care (CMG) at Yerevan State Medical University (YSMU) is one of the few active research units, with hereditary cancers and personalized treatment of cancer the major topics of its research, in addition to the provision of pharmacogenetic testing for cancer patients for all oncological centres of Armenia.

To support the development of cancer research and set the foundations for the subsequent research on cancer treatment and prevention, a consortium was formed, with the participation of the Yerevan State Medical University (YSMU); the International Agency for Research on Cancer, World Health Organization (IARC/WHO); the Medical University of Graz (MUG); and the Charles University (CU). Together they conceptualised the Twinning for the Armenian Research Infrastructure on Cancer (ARICE) programme, funded by the European Commission. The main objective of the ARICE project was to support YSMU in enhancing its research capacity in the field of infrastructure development for clinical genetic research, including foundational aspects such as the standardised collection and use of biological material and associated clinical data. This publication presents the outline and experiences from ARICE as a reflection point from the last months of the project.

Methods

The methodology for establishing a stronger cancer research capacity in Armenia had four pillars: evaluation, co-creation, delivery and assessment. This approach had been implemented previously successfully for educational activities of all three international partners as part of independent projects. Specifically, Charles University was part of the BRoTHER project, standing for "Biobank Research on Telemedical approaches for Human biobanks in a European Region," which was an interactive, inter-regional biobank network of Czech and Bavarian biobanks[13], leading to the creation of the eduBRoTHER training and educational component[14,15]. The Medical University of Graz has been delivering targeted post-graduate education courses for several years including courses with a mix of academic and technical components, e.g., the 'Master of Science in Biobanking'[16]. IARC/WHO has been coordinating the Biobank and Population Cohort Network, with targeted educational material for resource-restricted settings[17], as well as its well-established summer-school[18]. Beyond the direct experience of the international partners, there have been a recent review of educational programmes regarding research infrastructures and biobanks, and these experiences were also considered as part of this work[15,19,20].

Evaluation: The existing training courses of YSMU for cancer research were identified, and the course content was evaluated on three parameters: recency of content and reference material; relevance of content and reference material; and linkage of content and reference material to other educational units. By relevance is meant the degree to which the material is applicable to resource-restricted settings, and its alignment with the current international standards, e.g., ISO standards in medical laboratories, in biobanking, in quality management system, etc. As a result, there was a relevant prioritization for addressing content that was of relative low recency, low alignment to international standards and high potential of being used across one or more areas of cancer research.

Co-creation: A comprehensive educational program was designed over the course of one year to increase the competences of YSMU research staff in fields related to cancer research. The training included components for the transfer of theoretical and practical knowledge. The discipline-specific training was complemented with workshops concerning scientific writing, competitive grant funding application coaching and conference attendance and presentation to improve complementary oral and written skills in scientific presentation.

Delivery: The delivery of the co-created educational material was designed to be both online and in-person, and was delivered over the course of two and a half years, and due to the COVID-19 pandemic, parts of the training that were initially intended to be in-person were either delivered online or in a compressed form in-person when conditions allowed the in-person delivery with appropriate permissions and precautions.

Assessment: The assessment of the impact of these courses was measured in two ways: in terms of scientific output (i.e., number of publications as a result of consortium activities), and in terms of attendee satisfaction in the courses.

Results

Educational program

The following two in-person educational programs were created by the international partners and used as the basis for the training that took place (two × two-day workshops per year for three years):

- Research on cancer biomarkers, including sub-topics Biomarkers in Oncology, Circulating Biomarkers, Precision Medicine and Clinical challenges for cancer research.

- Research on biological samples and data, including handling clinical samples, biobanking best practices (in alignment with international laboratory, ethical and legal standards), pathology methods modelling and training in sequencing, and FAIR data requirements.

Biobanking received particular attention considering the existing knowledge gap and the importance of high-quality and research-ready sample acquisition and storage under appropriate ethical and legal policies with the objective of providing well-documented and annotated samples for research either nationally or internationally.

Regarding the use of associated clinical data for cancer research, it became clear through the development and delivery of the educational material that further development of the existing legal and ethical frameworks is required in Armenia.

The in-person workshops were complemented by frequent online training materials. Specifically, the interaction of ARICE with BCNet was promoted with the cross-posting of information and educational opportunities across the regular newsletters of the two networks (a minimum of three such interactions per year). Furthermore, there were online webinars (2 per year) arranged on the topics identified above, and all these were complemented by the free access to the IARC/WHO online educational platform[21].

As part of the project there were four publications, relating to the general overview of setting up biobanks for cancer research in resource-restricted settings[22,23], the analysis of stakeholders involved in such foundational research activities[24], as well as the overview of the Armenian cancer research field[12]. Finally, the combined activities of ARICE were communicated through dedicated social media platforms: website (https://www.arice.am/) and LinkedIn (https://www.linkedin.com/in/arice-armenia-67035a248/).

Discussion

The ARICE project combined a theoretical and practical learning process, with the acquisition of practical skills supported during the initial implementation under the supervision of international mentors. Knowledge transfer was conducted based on the Dreyfus Model of Skill Acquisition[25]. Teaching and mentoring provided by the expert institutions allowed researchers to develop new skills and witness the close interaction between theoretical knowledge and its implementation in practice. The multidisciplinary approach of the project enabled YSMU researchers from multiple fields to come in contact with the groups from the expert institutions, setting the foundations for potential future collaborations. The involvement of different overlapping expertise by the international experts was made available to a broad range of researchers at YSMU, and allowed for complementarity, in particular when COVID-19 necessitated the adaptation of course design to the new realities in the ground.

One of the major focus areas was biobanking, as it is becoming increasingly important as a key tool for precision medicine[26–28], but neither biobanking nor precision medicine itself have generally been integrated at all in medical curricula in Armenia. However, most medical students will encounter these topics in their future careers as physicians or researchers. As such, the introduction of these new concepts, were very much appreciated by the workshop attendees. Having said that, there exist significant knowledge gaps, for example, in the ethical and legal aspects of biobanking in Armenia, not only for cancer research, but clinical research in general, that still need to be addressed, and the educational content would need to be adapted to reflect new governance and regulatory realities once the latter materialise.

Although research was not planned within ARICE, previously obtained results (i.e., results from previous YSMU research, and previously developed YSMU protocols) were used for hands-on training for educational purposes, and these were welcome by the course participants as provided a familiar starting point upon which new concepts were introduced. As a result, procedure descriptions and protocols were improved making them available for further research projects locally.

Furthermore, the experiences of international exchange -as for many other similar programmes- broadened the horizons of participants and strengthened their scientific communication skills[29].

Conclusions

The ARICE project aimed to support cancer research in Armenia by evaluating, co-creating and implementing educational components for internationally competitive cancer research within Armenia, led by the Yerevan State Medical University and enabling further national and international research cooperation. New scientific developments in the field of cancer prevention, especially in biomarker research and large population-based investigations under-pinned by biobanking were considered as areas of priority following the evaluation of existing resources, and as critical to facilitate success in cancer research. The international collaboration provided an example of a successful such upgrading of existing educational materials, complemented by international experts, exposure to international research networks and access to online educational resources.

Ethics and consent

Ethical approval and consent were not required.

Data availability

No data are associated with this article.

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Open Peer Review

Current Peer Review Status: ? ?

Version 1

Reviewer Report 28 June 2024

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Neela Guha
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In this open letter, the authors clearly state that the objective was to present the experience of a collaborative project aiming to enhance the research capacity in Armenia in the field of infrastructure development for clinical genetic research, as part of the experiences of the Twinning for the Armenian Research Infrastructure on Cancer Research (ARICE) program. The objective is admirable as evidence reviews often identify that there is a paucity of data and solid research that can be used for policy making that originates in lower and middle income countries. Hence a structured approach to capacity building is warranted, and also needed to assess the generalizability of research findings conducted in other areas of the world.
The authors should be commended for the way in which this project was conducted, as they state in the discussion “Teaching and mentoring provided by the expert institutions allowed researchers to develop new skills and witness the close interaction between theoretical knowledge and its implementation in practice.”

Differing views and opinions are not expressed in this letter, but may not be needed as the objective was to present the experience of a collaborative project aiming to enhance the research capacity in Armenia.
This letter is very clearly and logically written. However, this project focuses on clinical genetic research. Were there any efforts to build capacity for etiological research in preventable causes of cancer? This would be a more cost-effective method to tackling the cancer burden in resource limited settings, and is one of the strengths of IARC’s research portfolio. I feel that this could be a huge opportunity that is missed. Recommendations and next steps could be more clearly stated.

Is the rationale for the Open Letter provided in sufficient detail? (Please consider whether existing challenges in the field are outlined clearly and whether the purpose of the letter is explained)
Yes

Does the article adequately reference differing views and opinions?
No

Are all factual statements correct, and are statements and arguments made adequately supported by citations?
Yes

Is the Open Letter written in accessible language? (Please consider whether all subject-specific terms, concepts and abbreviations are explained)
Yes

Where applicable, are recommendations and next steps explained clearly for others to follow? (Please consider whether others in the research community would be able to implement guidelines or recommendations and/or constructively engage in the debate)
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Environmental and occupational epidemiology, cancer epidemiology

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.

Reviewer Report 07 May 2024

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Emad Shash
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1. Clarity and Accessibility:
- **Strengths:** The letter is generally well-organized, with clear sections that delineate the background, objectives, methods, results, and conclusions. The plain language summary is a helpful addition that makes the content more accessible to non-specialists.
- **Weaknesses:** Some sections of the letter could benefit from more detailed explanations to avoid ambiguity. For example, the description of the educational programs and their specific impacts on the local research community could be more detailed.

2. Impact and Relevance:
- **Strengths:** The initiative addresses a critical gap in cancer research infrastructure in Armenia, which is commendable given the rising incidence of cancer in low- and middle-income countries. The international collaboration aspect is likely to enhance the visibility

and applicability of the research conducted.
- **Weaknesses:** The letter could better highlight specific achievements or preliminary outcomes that demonstrate the program's impact beyond the establishment of training programs. Metrics or data on improvements in research output or healthcare outcomes in Armenia would strengthen this section.

3. Methodological Rigor:
- **Strengths:** The program employs a structured approach involving evaluation, co-creation, delivery, and assessment, which is methodologically sound. The involvement of multiple international institutions also adds to the robustness of the training initiatives.
- **Weaknesses:** The letter lacks specific details on how the effectiveness of the training programs was measured. Information on assessment tools, participant feedback, and how adjustments were made based on evaluative data would be beneficial.

4. Scope and Scalability:
- **Strengths:** The focus on building infrastructure in clinical genetic research and biobanking is well-justified given the global trend towards personalized medicine.
- **Weaknesses:** The discussion on scalability is limited. The letter could discuss how the program's successes could be replicated or scaled in other regions with similar challenges.

5. Recommendations for Improvement:
- Include more comprehensive data on the outcomes of the training programs, possibly through case studies or testimonials from participants.
- Enhance the detail on the specific tools and strategies used in the workshops and their direct impact on the participants' research capabilities.
- Address potential scalability by discussing how the program could be adapted for other low-resource settings.
- Provide a clearer linkage between the training programs and observed improvements in cancer research and treatment within Armenia.

6. Additional Elements:
- It might be beneficial to include a section on challenges faced during the implementation of the program and how these were overcome. This could provide valuable insights for similar future initiatives.
- Future directions for the ARICE program could be elaborated upon, especially in terms of next steps post-2024 funding and how the program aims to sustain its impacts.

Overall, while the initiative is undoubtedly impactful and crucial for Armenia's healthcare landscape, the presentation in the letter could be enhanced to more vividly showcase its successes and lessons learned, providing a robust model for similar endeavors globally.

Is the rationale for the Open Letter provided in sufficient detail? (Please consider whether existing challenges in the field are outlined clearly and whether the purpose of the letter is explained)

Yes

Does the article adequately reference differing views and opinions?

Yes

Are all factual statements correct, and are statements and arguments made adequately supported by citations?

Yes

Is the Open Letter written in accessible language? (Please consider whether all subject-specific terms, concepts and abbreviations are explained)
Yes

Where applicable, are recommendations and next steps explained clearly for others to follow? (Please consider whether others in the research community would be able to implement guidelines or recommendations and/or constructively engage in the debate)
Partly

Competing Interests: No competing interests were disclosed.

Reviewer Expertise: Medical Oncology, Breast Cancer, Gynecological Cancers, Genitourinary Cancers, Medical Education, Healthcare Reformation, Healthcare Management & Cancer Research

I confirm that I have read this submission and believe that I have an appropriate level of expertise to confirm that it is of an acceptable scientific standard, however I have significant reservations, as outlined above.