LUCIA
LUng Cancer-related risk factors and their Impact Assessment

# LUCIA Understanding Lung Cancer related risk factors and their Impact

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## Acronyms & Abbreviations

| Term | Description |
|---|---|
| AI | Artificial Intelligence |
| CDx | Companion Diagnostic devices |
| DMP | Data Management Plan |
| GA | Grant Agreement |
| EHR | Electronic Health Records |
| EU | European Union |
| FAIR | Findable, Accessible, Interoperable, Re-usable |
| GDPR | General Data Protection Regulation |
| M | Month |
| R&I | Research and Innovation |

## Executive summary

This report summarizes the Policy brief formulating recommendations based on the research and innovation strand of the 'Understanding' annual cluster meeting-Y2. The goal of this deliverable is to provide an annual policy brief with recommendations on Research & Innovation (R&I) on the macro scale, i.e., from the perspective of the 'Understanding' (Risk Factors and Determinants) Cluster. This policy brief formulates recommendations to foster collaboration, focusing on data/material management, technological advancements, risk factor analysis, and policy implementation, based on the research and innovation strand of the 'Understanding' annual cluster meeting in the second year. This deliverable raises common barriers and potential recommendations as well as practical recommendations for the near future.

# 1 Policy brief formulating recommendations

The second 'Understanding' (Risk Factors and Determinants) annual cluster meeting (M24) was organized by the DISCERN project and held in Lyon, France, on 15 October 2024. The meeting discussed key areas for scientific collaboration within the cluster. This policy brief formulates recommendations to foster collaboration, focusing on data/material management, technological advancements, risk factor analysis, and policy implementation, based on the research and innovation strand of the 'Understanding' (Risk Factors and Determinants) annual cluster meeting.

## 1.1 Sharing and Agreeing on Common Practices for Data/Material Management:

The cluster produced the common deliverable on the data management plan (DMP) for the first year. Within this deliverable, topics such as Accessibility and repository; Interoperability; Reusability, etc., were included.

The **'Understanding' Cancer** cluster works to integrate retrospective data from European registries, biobanks, and cohort studies with prospective data to fill in gaps. This includes clinical, epidemiological, demographic, and environmental information. This integration aims to enhance our understanding of cancer through three main collaboration points:

1. **Data Re-use and Generation**: Emphasis is placed on maximizing the use of existing data while creating new insights.
2. **FAIR Data Management**: Implementation of cluster data management follows FAIR principles—ensuring that data is Findable, Accessible, Interoperable, and Reusable.
3. **Establishment of a Data Management Board**: Addressing the main challenge of data heterogeneity across projects.

**Common Barriers**

One of the significant problems regarding data is the heterogeneity among data management protocols in different healthcare institutions and across countries.

**Recommendations**

- Using standardized protocols for data and material management, ensuring consistency.
- The creation of a centralized repository for sharing datasets, which will facilitate collaboration.
- Adoption of common nomenclature and data exchange protocols to improve interoperability.
- Promotion of harmonization of GDPR compliance and the use of one-time consent, streamlining the data protection process.

**Practical Actions**

To tackle these challenges and implement the recommendations effectively, we propose the following actions:

1. **Meetings/Workshops**: Organize meetings and workshops to discuss the legal and ethical basis and framework for reusing data and biological samples across institutions, focusing on risk factors and relevant clinical information for future research.
2. **Data Source Links**: Create links across different data sources while identifying methodologies and tools for joint exploitation.
3. **Common Protocols**: Implement common data management protocols for progressively mandatory implementation, significantly enhancing data quality.

Common data models and software, along with regulations for mandatory data storage (particularly for patients with specific diseases), would ensure data homogenization, facilitating more consistent data sets and thus knowledge extraction.

4. **Centralized Databases**: Generate European centralized databases that consolidate data from multiple studies, ensuring robust sample sizes. These databases, accessible only with authorization and ensuring patient anonymity, will provide more comprehensive data sets for studies.

5. **Clinical Guidelines**: Edit clinical guidelines related to risk factor information from the project in the cluster, ensuring findings translate into actionable recommendations for healthcare providers. Exploring common standardized guidelines for EU-based clinical trials to address ethical concerns, timelines, and approvals across countries in European-funded projects.

## 1.2 Collaborations in Technology, Tools, Knowledge, and Best Practices for Data Exploitation and Computational (AI) Modelling:

Information technology plays a pivotal role in advancing cancer research, particularly in prevention, diagnosis, treatment, and improving the quality of life for patients. The vast amounts of data generated from digital diagnostics, such as radiological imaging, digital pathology, and omics technologies, offer detailed insights into cancer phenotypes. These insights are crucial for understanding the biological mechanisms behind cancer onset and progression by leveraging both research data and real-world evidence. Advanced computational techniques, particularly AI, are employed for integrating diverse data types and identifying patterns, which are crucial for discovering new diagnostic and prognostic biomarkers essential for developing innovative strategies in cancer care. AI facilitates the identification of biomarkers, enabling the development of new diagnostic and prognostic

tools vital for early detection and personalized treatment plans. At the population level, electronic health records (EHRs) provide valuable datasets for identifying common risk factors and predicting future cancer risks. By linking EHRs with lifestyle data, researchers can enhance public health policies and enable personalized cancer screening methods. Integrating lifestyle data with clinical information allows for a more comprehensive understanding of cancer risks, leading to improved public health strategies and personalized care.

**Common Barriers and Proposed Strategies**

As we advance our cancer research initiatives, several significant barriers, particularly related to data protection and access, must be addressed. To overcome these challenges, we propose two key strategies:

- **Federated Learning:** This approach allows us to train models on distributed data sources without directly accessing sensitive data. By training on local datasets, we maintain data privacy while still extracting meaningful patterns that can inform our research.
- **Synthetic Data Generation:** Creating artificial datasets can help us overcome data limitations, enabling robust model training and validation without compromising real patient data.

With these strategies we also encounter difficulties related to the explainability, trustworthiness, and validation of the models we develop. Therefore, it's essential to address these challenges to build confidence among stakeholders and ensure our findings can be reliably applied in clinical settings.

**Recommendations**

1. **Standardized Information and Knowledge Models**

   Establishing standardized models will facilitate the integration and exploitation of data across various sources, ensuring consistency and reliability.
2. **Methodologies, Technologies, and Tools**
3. **Data Integration and Feature Extraction**

   Develop robust methodologies and tools for data integration, feature extraction, and classification.
4. **Statistical and AI Models**

   Introduce new statistical and AI models for personalized prediction of cancer risk, enhancing early detection and treatment strategies.
5. **New Technologies and Tools for Data Analytics**

   Promote the development of advanced tools for data analytics, hypothesis generation, and discovery. These tools will enable more effective data utilization and innovative research approaches.

## 1.3 Sharing and Cross-Comparison of Risk Factors and Molecular Features:

Developing standardized information models is essential for improving data interoperability across various platforms and institutions, ensuring seamless integration and utilization of data. Robust methodologies for integrating different data sources are critical for comprehensive data analysis, and collaborative efforts in this area will enhance the quality and consistency of research findings. The collaborative development of predictive models using AI will drive innovation in cancer diagnosis and treatment, providing accurate predictions and personalized recommendations to improve patient outcomes.

## 1.4 Cross-Comparison and Integration of Risk Stratification/Early Diagnosis Tools

As mentioned in the previous report, introducing new technologies to study risk factors in projects is challenging, particularly because they involve clinical studies with tools still in the research stage and not yet CE-marked. This creates hurdles in obtaining ethical approval, further complicated by varying regulations across different countries involved in the study.

**Recommendations:**

1. Facilitate collaborative efforts to cross-compare and integrate risk stratification and early diagnosis tools. Develop frameworks for standardized assessment and validation of these tools to enhance their clinical applicability.
2. To streamline the process of obtaining ethical approvals across different countries for technology-supported clinical studies, produce a common outline format for the European Commission to support submissions to EU ethical agencies. This format should be part of the initial Grant Agreement (GA) for each project, aiding and expediting the process, especially when multiple countries are involved.

The next steps will be discussed in the working group meetings starting next year and necessary actions implemented thereafter.

## 1.5 Sharing of Best Practices on Implementation of Healthcare Policies

Effective policy implementation is crucial for delivering high-quality services, improving patient outcomes, and optimizing resource utilization. However, the complexity of healthcare systems and diverse socioeconomic and cultural contexts pose challenges in translating policies into actionable strategies.

**Common barriers to sharing best practices include:**

1. **Language Barriers:** Non-fluency in English among patients and healthcare professionals can hinder knowledge transfer. The absence of translators may introduce biases.
2. **Lack of Consensus:** There is no agreement on the optimal risk prediction model, and uncertainties about their robustness have prevented the implementation of pre-screening strategies in many EU countries.
3. **Data Validation:** To share best practices in target population management, databases should collect accurate and relevant data.

**Suggested actions:**

1. Develop a knowledge-sharing platform for healthcare policymakers and enhance collaborative projects.
2. Hold meetings at the end of the project.
3. Present findings to EU stakeholders and other projects.

### 1.6 Harmonizing Regulatory Procedures for Medicinal Products and Companion Diagnostic Devices in the EU

The European Union faces a policy issue concerning the development of medicinal products and Companion Diagnostic devices (CDx). Unlike the integrated regulatory approach in the United States, these procedures remain largely independent in the EU. This separation can lead to gaps in evidence and validation, hindering the effective use of CDx with their corresponding medicinal products.

**Recommendations:**

To address this issue, the EU should consider harmonizing the regulatory procedures for medicinal products and CDx development. This can be achieved by:

1. **Integrating Regulatory Frameworks**: Establish a unified regulatory framework that synchronizes the development and approval processes for medicinal products and their companion diagnostics, similar to the FDA model in the US.
2. **Streamlining Evidence and Validation Processes**: Create joint guidelines for evidence generation and validation of CDx in conjunction with medicinal products to ensure comprehensive and simultaneous approval.
3. **Enhancing Collaboration**: Foster greater collaboration between regulatory bodies, pharmaceutical companies, and diagnostic developers to facilitate a cohesive development pathway.

Implementing these measures will bridge the current gaps in evidence and validation, enhancing the efficacy and safety of biomarker-driven therapies in the EU.

# 2 Conclusions

Strong collaboration and strategic planning are key to advancing cancer research. This policy brief outlines recommendations which, when followed, can accelerate progress toward a comprehensive understanding of cancer. In addition, this work can enable strategies for early detection, treatment and prevention of cancer.

In this report, the main limitations and barriers to this collaborative research have been highlighted and recommendations to overcome these have been provided. This has been informed by the experience gained in the first and second years of the "Understanding (Risk Factors & Determinants)" cluster projects. These findings lay a foundation for future initiatives in the work and mission of the cluster. Key recommendations include:

1. **Data/Material Management:** Adopt standardized protocols, create a centralized data repository, and harmonize GDPR compliance to ensure data interoperability and reusability.
2. **Technological Advancements:** Leverage AI and federated learning to enhance data analysis while maintaining privacy. Develop standardized models and advanced tools for personalized cancer prediction and treatment.
3. **Risk Factor Analysis:** Standardize information models and methodologies to improve data integration and predictive model development, enhancing early diagnosis and treatment.
4. **Policy Implementation:** Overcome language barriers, establish consensus on risk models, and ensure data validation to improve healthcare policies. Create platforms for knowledge sharing and engage with EU stakeholders to promote best practices.

The cluster will continue to work towards implementing these recommendations, fostering collaboration, enhancing research quality, and translating findings into actionable healthcare strategies.

# 3 References

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[2] LUCIA factsheet in CORDIS webpage

[3] ELMUMY factsheet in CORDIS webpage

[4] DISCERN factsheet in CORDIS webpage

[5] MELCAYA factsheet in CORDIS webpage