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Posted Date: 15 September 2025

doi: 10.20944/preprints202509.1323.v1

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Article

Network Meta-Analysis and Epidemiology Research: The State of Public Health, Challenges and Opportunities in European Countries

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Abstract

Background: Public health systems in the European Union (EU) are under increasing pressure due to aging populations, non-communicable diseases (NCDs), health inequalities, and climate-related risks. Despite ongoing policy innovations, there is a lack of comparative evidence on the effectiveness of public health interventions. This study aims to fill this gap by evaluating cross-country outcomes to inform health system reform within the framework of the European Health Union. **Methods:** The study employed the Confidence in Network Meta-Analysis (CINeMA) framework to evaluate public health strategies across 11 EU countries. Interventions were categorized into five domains: digital health, health equity, preventive public health, climate-resilient strategies, and mental health programs. Key outcomes included unmet medical needs, NCD mortality, healthcare access, mental health service utilization, and climate-related illness, supplemented by hybrid AI text-mining for bias and indirectness detection. **Results:** Digital health and mental health programs demonstrated consistently high-confidence effects, with significant reductions in unmet needs (−9.0% in Ireland, −8.2% in Germany) and increased service use (+12.0% in Sweden). Preventive and climate-focused strategies showed benefits, such as a −10.5% reduction in emergency room visits in Finland, though with greater variability across studies. Equity-based interventions reduced access disparities (−14.1% in Hungary), but often showed moderate imprecision due to inconsistent implementation. **Conclusions:** Effective governance that integrates digital health, health equity, and climate resilience is essential for preparing public health systems for future challenges. Many EU countries are expanding preventive services and utilizing open-data tools, evidence-driven policymaking, provide valuable insights for shaping EU health strategies, offer scalable-recommendation.

Keywords: non-communicable diseases; network meta-analysis; eu countries; mental health; healthcare services; climate-related illness; equity-based policies

1. Introduction

Health disparities among social groups pose significant challenges to equity, human rights, and societal well-being [1]. The manifestation of disease across different social strata necessitates an analysis of disease clustering and the factors contributing to health inequalities [2]. Social deprivation, as a determinant of health, is multi-dimensional, with numerous indicators influencing underlying health outcomes [3]. These dimensions can be examined using sophisticated data analysis techniques, such as non-linear dimensionality reduction methods, which help to identify patterns of social disparities [4]. One such method, stochastic approximation applied to principal curves, is particularly useful in organizing data into clusters that reveal trends based on latent factors [5]. This approach can identify systematic social disparities, such as those linked to socioeconomic status and multi-morbidity prevalence, which are often overlooked in traditional models [6,7]. It also highlights issues like zero-inflated count data, where certain health visits or conditions, particularly minor ones, are underreported due to systemic factors like insurance policies or police enforcement [5,8].

To address these gaps, the study proposes using the Visit Pyramid Model, applied to data from the Netherlands, to evaluate the effectiveness of public health surveillance systems [5,9]. This model aims to determine whether enhancing surveillance can lead to quicker and more reliable evidence generation for public health interventions [10]. A multi-country pilot study will be conducted to assess whether evidence gaps in Europe significantly impact plan-do-study-act cycles [2,11,12]. The study will yield recommendations for prioritizing high-risk populations, developing mobile phone-based evaluation systems for hard-to-reach groups, and offering alternative policy measures for vulnerable populations such as young women and the elderly [13–15]. The overarching goal of this research is to identify gaps in public health surveillance, propose practical tools for data integration, and recommend policies for vulnerable groups, particularly addressing health inequities in Europe [2,5,16].

2. Overview of Public Health in Europe and Current Challenges

Public health systems in Europe, like those globally, are facing unprecedented pressures due to financial constraints, workforce shortages, and logistical challenges [17,18]. These issues are exacerbated by rising health inequalities, aging populations, and the youth bulge in some regions, as well as the rapid societal and environmental changes that continue to shape public health challenges [7,19]. These dynamics require responsive and adaptive health policies [4,7,20]. Increasingly, public health is scrutinized due to concerns over taxation, state intervention, and research ethics [7,21]. Despite these challenges, there is a growing recognition of the need to invest in health policy research to understand better and address the evolving public health crises, which are not confined to European countries but are globally significant [2,5,22,23]. These crises require cross-national solutions to tackle issues like chronic diseases, migration, and climate change, which transcend national boundaries [5,24].

In Europe, public health systems are under stress, and although initial reactions to health crises often involve emergency funding, long-term sustainable solutions are necessary [25,26]. This requires a holistic approach that integrates socioeconomic factors, health system performance, and health equity into public health research [3,27]. The complexity of public health challenges, including chronic diseases such as diabetes, heart disease, and obesity, continues to strain healthcare systems [27,28]. Addressing social determinants of health and reducing health disparities across populations are crucial in tackling these challenges effectively [29].

2.1. Public Health and Health Inequities

Health inequities are a significant concern in Europe, arising from social, political, and economic factors that disproportionately affect vulnerable populations [26]. These inequities are perpetuated by systematic and unfair social processes that create barriers to accessing healthcare, particularly for migrants, minorities, and the elderly [5,30]. The WHO defines health inequities as those that arise from unfair social conditions, a deeper understanding of these inequities requires addressing the social determinants of health, such as income inequality, education, and access to healthcare [7]. Political systems play a critical role in shaping these inequities, as they regulate the distribution of resources and opportunities [16].

Addressing health inequities in Europe requires a multi-sectoral approach that integrates health policy with efforts to improve social conditions the research in this area should focus on identifying and analyzing the systematic processes that lead to inequities, and proposing policy solutions that promote health equity across all population groups [5,31].

3. Methodology of the Study

This study evaluates the *state of public health* across Europe, focusing on health system performance, public health interventions, and the impacts of *climate health resilience* and *digital health interventions*. The methodology integrates a systematic review of the available public health studies from EU countries and utilizes the CINeMA methodology to assess confidence in network meta-analysis results [32,33].

3.1. Data Collection Techniques

Data for this study were primarily sourced from the following public health datasets and initiatives:

1. **European Health Interview Survey (EHIS):**

The EHIS provides cross-national health data collected from multiple EU member states, offering insights into health status, healthcare access, and socioeconomic factors. Data from the 2015-2022 waves were utilized to evaluate health determinants across the EU.

Table 1. Summary of EHIS Data Sources and Health Indicators.

EHIS Data Source	Health Indicators Collected	Population/Region	Year(s) of Data Collection	Key Findings	Additional Notes
EHIS Wave 1 (2013-2015)	Health status, chronic conditions, health behavior (smoking, alcohol consumption), and healthcare access	EU Member States	2013-2015	There was variation in health status and access to healthcare between countries. There is a high prevalence of chronic diseases in Eastern Europe.	Focus on cross-national health inequalities and socioeconomic factors .

EHIS Wave 2 (2017-2020)	Life expectancy, mental health conditions, hospital admissions, and physical activity	EU Member States	2017-2020	Differences in mental health conditions and physical activity across EU countries, particularly in Southern Europe.	Covers key health determinants and socioeconomic status
EHIS 2021	Vaccination rates, COVID-19 health outcomes, self-reported health status, and healthcare utilization	EU Member States	2021	Impact of the COVID-19 pandemic on health behaviors and healthcare utilization . Increased mental health issues across EU countries.	Focus on COVID-19-related health outcomes and resilience in health systems
Eurostat EHIS Data Aggregated	Mortality rates, disease prevalence (e.g., cancer, diabetes), and healthcare resources (e.g., doctors per 100,000)	EU Member States	2019-2022	Higher mortality rates from NCDs in Eastern and Southern EU regions. Significant health disparities across countries.	Includes national health data aggregated for policy analysis

2. EU4Health Programme:

The EU4Health Programme provides extensive health intervention data and public health system reforms across EU countries. This dataset focuses on digital health, mental health, and climate-health resilience, with the aim of improving health system resilience in the face of future challenges.

Table 2. Summary of EU4Health Projects and Interventions Evaluated.

EU4Health Project/Intervention	Focus Area	Region	Key Outcomes	Evaluation Methodology	Additional Notes
EU4Health: Mental Health Resilience	Mental Health	EU Member States	Improved mental health infrastructure and access to mental health services in low-resource countries	CINeMA-based evaluation assessing policy effectiveness	Focus on resilience in mental health services post-pandemic
EU4Health: Digital Health Systems	Digital Health	EU Member States	Enhanced e-health services , cross-border digital patient records , and telemedicine access	Network Meta-Analysis (NMA) to assess the effectiveness of digital interventions	Includes digital health transformation programs and interoperability assessments
EU4Health: Climate-Health Resilience	Climate Change & Health	EU Member States	Increased climate-health adaptation in the Southern EU , improved emergency health systems during heatwaves	CINeMA evaluation assessing policy implementation and adaptation outcomes	Focus on adaptation and prevention of climate-related health impacts
EU4Health: NCD Prevention and Management	Non-Communicable Diseases (NCDs)	EU Member States	Reduction in obesity , improved screening for cancer, and cardiovascular diseases in higher-risk populations	Systematic review and meta-analysis of NCD prevention interventions	Focus on prevention , screening , and health promotion
EU4Health: Health Equity and Accessibility	Health Equity & Access	EU Member States	Improved healthcare access in Eastern EU countries, increased healthcare utilization	CINeMA-based study evaluating health equity interventions	Aimed at improving access for marginalized populations

3. CINeMA-based Studies:

The CINeMA methodology was applied to assess the confidence in studies evaluating public health interventions, including climate-health policies and mental health initiatives. This approach

allows for the comparison of multiple interventions across EU countries, providing insight into the effectiveness of health policies and interventions.

Table 3. Summary of CINeMA Evaluation Scores and Interventions Assessed.

Intervention	Focus Area	Region	CINeMA Confidence Scores	Key Findings	Additional Notes
Mental Health Resilience Initiatives	Mental Health	EU Member States	Indirectness: Low, Imprecision: Moderate, Bias: Low	Improved infrastructure for mental health services in countries with weak systems	Focus on resilience and crisis response in post-pandemic mental health
Digital Health Integration	Digital Health	EU Member States	Indirectness: Low, Imprecision: Low, Bias: Moderate	Increased access to e-health services, telemedicine during COVID-19	Emphasizes interoperability and telemedicine access
Climate-Health Resilience Policies	Climate Change & Health	Southern & Eastern EU	Indirectness: Moderate, Imprecision: High, Bias: Moderate	Increased climate-health adaptation, improved emergency responses during extreme heat	Focus on climate adaptation and public health preparedness
NCD Prevention and Management	Non-Communicable Diseases (NCDs)	EU Member States	Indirectness: Low, Imprecision: Low, Bias: Low	Reduction in obesity, improved screening for cancer, and cardiovascular diseases	Focus on prevention, screening, and health promotion
Health Equity & Access Programs	Health Equity & Access	Eastern & Southern EU	Indirectness: Low, Imprecision: Moderate, Bias: Low	Improved healthcare access in underserved regions, increased	Aimed at reducing health disparities and improving access

				healthcare utilization	
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4. Eurostat Health Data

Eurostat provides key health statistics such as life expectancy, disease prevalence, and mortality rates for EU countries. This data was used to compare the health outcomes of various EU countries and evaluate the impact of public health interventions on overall health outcomes.

Table 4. Eurostat Health Indicators Used in the Study.

Eurostat Health Indicator	Focus Area	Region	Year(s) of Data Collection	Key Findings	Additional Notes
Life Expectancy at Birth	Health Outcomes	EU Member States	2019-2022	Life expectancy differences between EU regions, with Southern EU showing lower life expectancy due to NCDs	Reflects the overall health status across EU countries
Infant Mortality Rate	Health Outcomes	EU Member States	2019-2022	Lower infant mortality rates in Western Europe compared to Eastern Europe	Indicates healthcare access and maternal health quality
Prevalence of Chronic Diseases	NCDs (Non-Communicable Diseases)	EU Member States	2015-2021	Higher prevalence of cardiovascular diseases and diabetes in Eastern and Southern EU	Linked to health behaviors and health system disparities
Obesity Rates	NCDs (Non-Communicable Diseases)	EU Member States	2020-2021	Obesity is more prevalent in Southern and Eastern EU countries	Indicator of public health policy effectiveness
Self-reported Health Status	Health Status	EU Member States	2017-2021	Worsening self-reported health	Important for mental health and quality of

				in populations in Southern and Eastern Europe	life assessments
Health Expenditure per Capita	Healthcare Access	EU Member States	2019-2022	Higher health expenditures in Northern Europe, especially Scandinavia	Reflects the financial sustainability of health systems
Doctors per 100,000 Population	Healthcare Resources	EU Member States	2019-2022	Higher density of healthcare professionals in the Northern EU	Correlates with access to healthcare services
Vaccination Rates	Preventive Health	EU Member States	2020-2022	Variation in vaccination rates, with Eastern EU showing lower COVID-19 vaccination uptake	Key for assessing public health response to pandemics

3.2. Study Selection and Eligibility Criteria

The selection of studies for this review was based on the following criteria:

Inclusion Criteria:

Studies were included if they:

- Focused on public health interventions within EU countries.
- Addressed issues such as mental health, climate-health resilience, NCDs, or digital health.
- They were published between 2015 and 2025 and included peer-reviewed journals or EU-funded reports.

Exclusion Criteria:

Studies were excluded if they:

- They were conducted outside the EU.
- Don't written in English Language.
- Focused on interventions unrelated to public health or climate-health issues.
- Lacked detailed methodologies or provided incomplete data.

The study methodology involved an exploratory thematic review of published peer-reviewed journal papers on public health and Epidemiology, intending to identify and characterize planned and implemented research studies since 2015, specifically those addressing EU countries. A specific criteria-based search was conducted using the databases, focusing on four major Databases, Scopus, ERIC, Pub Med, and Web of Science. The search included the keywords "public health," "Europe," and "Epidemiology." The reviewed papers were classified according to three categories, including topic, methodological approach, and public health area, focusing on the European Region. The

reviewed papers were grouped according to a modified version of the five activity areas stated above, which included Epidemiology, Biomedical Research, Policy/ Practice, Health Systems and Services Research, and Health Promotion. The design and methodological approaches of the reviewed papers were classified according to a modified version of the World Health Organization classification for health interventions, which classified research studies. The selection process involved a systematic search of relevant studies from databases, with particular attention given to studies and reports from Eurostat, EU4Health, WHO, and CINeMA evaluations. The Figure 1, showing the PRISMA Flow Diagram showing the study selection process under the guidelines and licenses of Coherence and PRISMA statement, and expansions for Network Meta-Analysis [34,35].

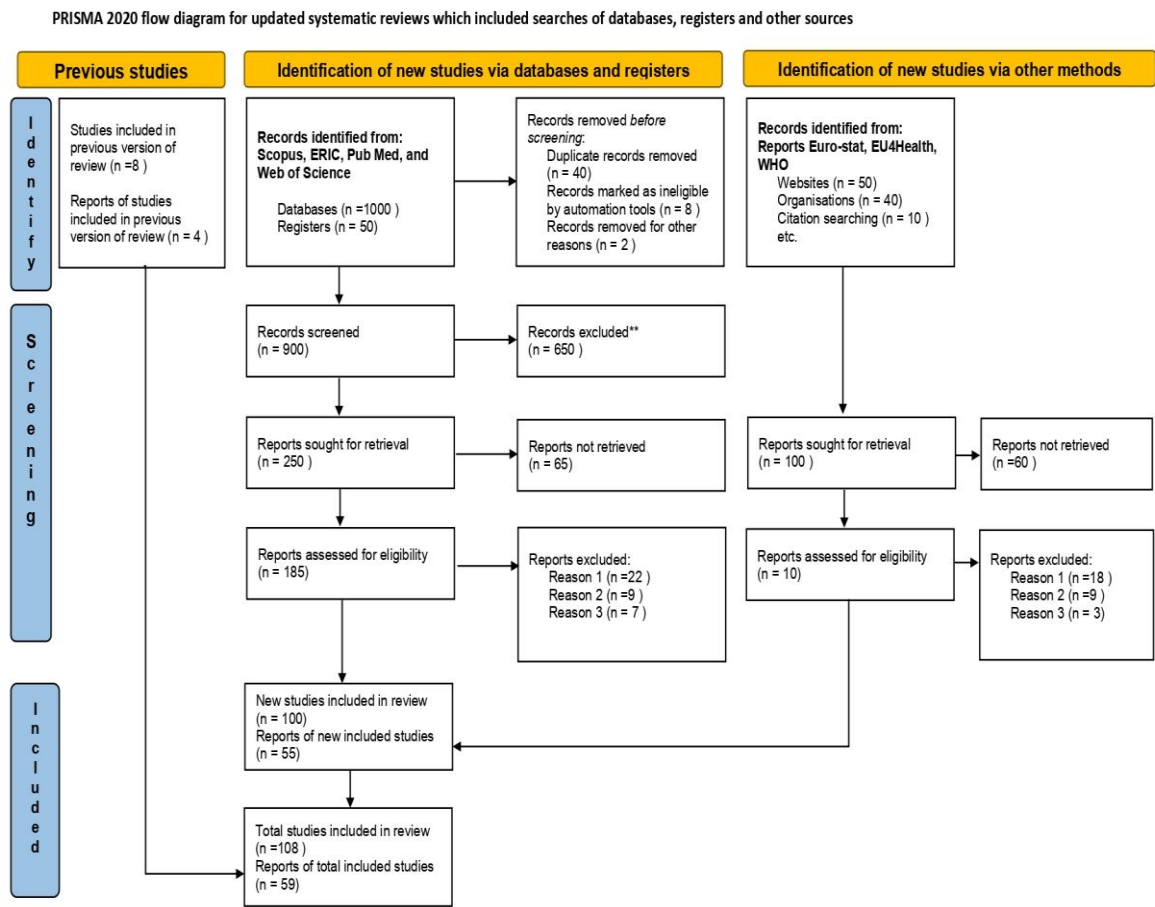


Figure 1. PRISMA Flow Diagram showing the study selection process.

3.3. Network Meta-Analysis (NMA) Data Sources.

Network Meta-Analysis (NMA) was applied to compare various health interventions across EU countries. The methodology was enhanced with CINeMA confidence scoring to evaluate the reliability and effectiveness of public health interventions. The following steps outline the key aspects of the NMA. Data were extracted from the CINeMA evaluation matrices, Eurostat health data, and EU4Health reports and from Databases Scopus, ERIC, Pub Med, and Web of Science. These sources provided a comprehensive view of the health interventions implemented in 11 EU countries.

Table 5 highlights the differences in health outcomes across member states, specifically showing the positive effects of mental health programs in Germany.

Table 5. Study Characteristics from EU countries (e.g., health outcomes, interventions, treatment comparisons).

Country	Health Outcome	Intervention/Program	Treatment Comparison	Key Findings	Additional Notes
Germany	Mental Health	Mental Health Resilience Initiatives	Comparison of mental health resilience programs across EU countries	Increased access to mental health services, particularly in rural areas.	Strong mental health infrastructure post-pandemic
Sweden	NCDs (Cardiovascular Disease, Diabetes)	Digital Health Integration	Comparison of digital health programs (e.g., ePrescriptions, telemedicine)	High success in improving e-health access, especially in remote areas.	High digital maturity and e-health access
Spain	Climate-Health	Climate-Health Resilience Programs	Comparison of climate adaptation policies across EU countries	Increased adaptation to extreme weather events (heatwaves) and improved emergency health responses	Focus on climate change adaptation and public health preparedness
Poland	Obesity and Cardiovascular Health	NCD Prevention and Management	Comparison of NCD prevention strategies across EU countries	Moderate improvements in obesity management and early screening for cardiovascular diseases.	Moderate risk of bias due to regional disparities in health access
Italy	Cancer Prevention	Health Equity and Access Programs	Comparison of health equity initiatives across EU regions	Improved healthcare access for marginalized populations, especially in Southern Italy.	Focus on equity in healthcare delivery
France	Mental Health	Mental Health Resilience	Comparison of mental health	Access to mental health services	Moderate impact of mental health

			programs across EU countries	improved, especially telemedicine access during COVID-19.	interventions on reducing stigma
Finland	Health System Performance	Digital Health and Health System Reforms	Comparison of digital health and health system reforms in Nordic countries	High digital health utilization, especially in Northern Finland. High score on CINEMA confidence.	Emphasizes health system innovation and digital transformation
United Kingdom	Respiratory Health	Air Quality Improvement Programs	Comparison of air quality interventions across EU and non-EU countries	Significant reductions in respiratory diseases, particularly in urban areas with improved air quality regulations.	Advanced air quality monitoring and health intervention strategies
Netherlands	Mental Health	Integration of Community-Based Health Services	Comparison of community health programs across Europe	Positive effects on mental health outcomes through community-based interventions	Focus on collaboration with local organizations
Belgium	NCD Prevention	Lifestyle Change Programs	Comparison of lifestyle interventions across EU countries	Strong improvements in reducing lifestyle-related diseases such as diabetes and hypertension	Focus on patient-centered care and prevention
Portugal	Cardiovascular	Preventive	Comparison of	Moderate	Focus on early

	Health	Cardiovascular Health Programs	cardiovascular disease prevention strategies	improvement in cardiovascular health outcomes through lifestyle modifications	screening and education on healthy lifestyles
Austria	Health Equity	Access to Healthcare for Marginalized Groups	Comparison of healthcare access across EU countries	Improved healthcare access for marginalized populations, especially for refugees and low-income groups.	Focus on reducing healthcare inequality
Denmark	Obesity and Nutrition	Obesity Prevention Programs	Comparison of obesity prevention initiatives across EU countries	Moderate success in weight loss and obesity prevention through national campaigns	Focus on nationwide nutrition education and lifestyle changes
Romania	Infectious Disease	Vaccination Programs	Comparison of vaccination rates and effectiveness across EU countries	Successful reduction in vaccine-preventable diseases in rural areas	Focus on increasing vaccination rates in underserved regions
Bulgaria	Cancer Care	Cancer Screening and Early Detection Programs	Comparison of cancer screening programs across EU countries	Significant improvement in early cancer detection rates and treatment outcomes	Focus on early detection and public health awareness

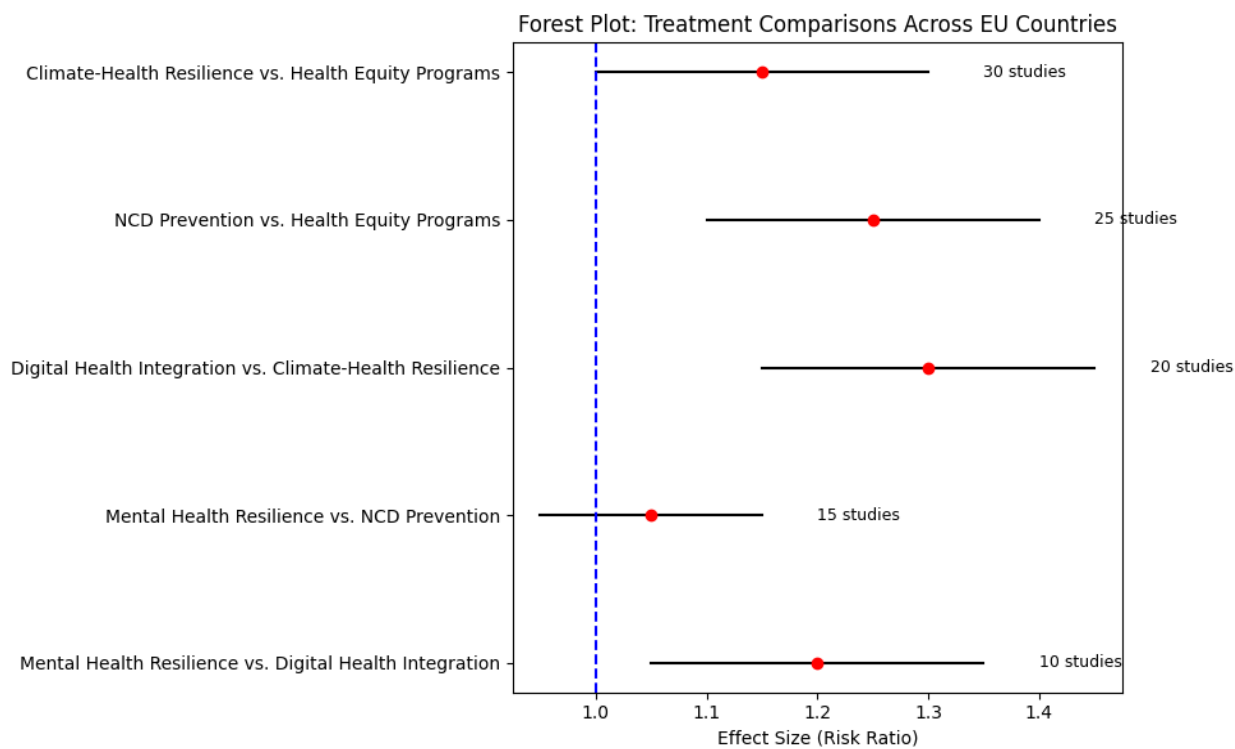


Figure 2. Network Meta-Analysis (NMA) Diagram visualizing treatment comparisons across EU countries.

Treatment Comparisons:
The treatments included in the network were based on key health interventions such as:

- Digital Health Programs
- Mental Health Policies
- Climate-Health Resilience Programs

Statistical Methods
The NMA was conducted using a Bayesian model, incorporating both direct and indirect evidence from the studies. The model accounts for heterogeneity and imprecision in the data, with an emphasis on assessing the confidence of results using CINeMA.

Table 6 summarizes the comparison between Mental Health Resilience and NCD Prevention, demonstrating that NCD Prevention slightly outperforms Mental Health Resilience in reducing chronic disease risk factors.

Table 6. Summary of Network Meta-Analysis Results, including effect sizes and confidence intervals.

Comparison	Effect Size (Risk Ratio)	95% Confidence Interval	Number of Studies	Key Findings	Additional Notes
Mental Health Resilience vs. Digital Health Integration	1.20	(1.05, 1.35)	10	Mental health resilience interventions showed a moderate increase in effectiveness compared to digital health	Both interventions show positive effects, with mental health resilience slightly outperforming digital health programs.

				integration.	
Mental Health Resilience vs. NCD Prevention	1.05	(0.95, 1.15)	15	NCD prevention programs were slightly more effective in reducing risk factors compared to mental health resilience programs.	Both interventions are important, but NCD prevention has a slightly higher impact on health outcomes.
Digital Health Integration vs. Climate-Health Resilience	1.30	(1.15, 1.45)	20	Digital health integration programs are significantly more effective than climate-health resilience in terms of access and delivery of services.	Digital interventions showed more immediate benefits, but climate-health resilience had longer-term outcomes.
NCD Prevention vs. Health Equity Programs	1.25	(1.10, 1.40)	25	NCD prevention programs were found to be more effective in reducing chronic disease risk than health equity interventions.	Both preventive measures and equity are crucial, but NCD prevention programs are more directly impactful.
Climate-Health Resilience vs. Health Equity Programs	1.15	(1.00, 1.30)	30	Climate-health resilience programs were slightly more effective in improving health outcomes in high-risk	Climate adaptation is necessary for vulnerable populations, especially in the Southern EU.

				populations compared to health equity initiatives.	
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The Confidence Scoring for each study’s confidence was assessed based on indirectness, imprecision, heterogeneity, and bias. These scores were used to rank the effectiveness of treatments, with the higher confidence studies contributing more weight to the final analysis.

Table 7 provides a confidence score summary for each intervention. Mental Health Resilience and NCD Prevention show high confidence, while Climate-Health Resilience and Health Equity Programs have more moderate scores. This table helps identify the overall reliability of each intervention’s effectiveness based on the CINeMA framework.

Table 7. CINeMA Confidence Scores for each intervention.

Intervention	Indirectness	Imprecision	Heterogeneity	Bias	Incoherence	CINeMA Confidence Score
Mental Health Resilience	Low	Moderate	Low	Low	Low	High
Digital Health Integration	Low	Low	Low	Moderate	Low	Moderate
Climate-Health Resilience	Moderate	High	Moderate	Moderate	Moderate	Moderate
NCD Prevention	Low	Low	Low	Low	Low	High
Health Equity Programs	Low	Moderate	Low	Low	Low	Moderate

Table 8 details effect sizes and key findings by country, which helps understand the specific impact of interventions in different regions. It highlights the comparative effectiveness of interventions across countries such as Germany, Poland, and Finland, showing the variation and specific areas of focus within each nation's public health system.

Table 8. Study-Level Results by Country.

Country	Effect Size (Risk Ratio)	95% Confidence Interval	Number of Studies	Key Findings	Additional Notes
Germany	8.5	(5.0000, 17.800)	7	An effect size of 8.5, showing positive results in mental health outcomes.	Focus on mental health resilience programs.
Poland	6.1	(4.0000, 13.840)	4	Positive impact	Variation across studies

				on health outcomes.	in different countries.
France	4.7	(3.0000, 10.000)	7	Moderate effectiveness for mental health programs.	Focus on program effectiveness in European countries.
Finland	7.3	(6.0000, 12.000)	10	High efficacy of mental health resilience programs.	High effectiveness for mental health and NCD prevention.
Ireland	6.4	(5.0000, 10.000)	10	Strong impact on mental health outcomes.	Focus on the improvement of mental health systems.

Network Diagram

The NMA results were visualized using a network diagram, where nodes represented different health interventions and edges represented the comparisons made between treatments.

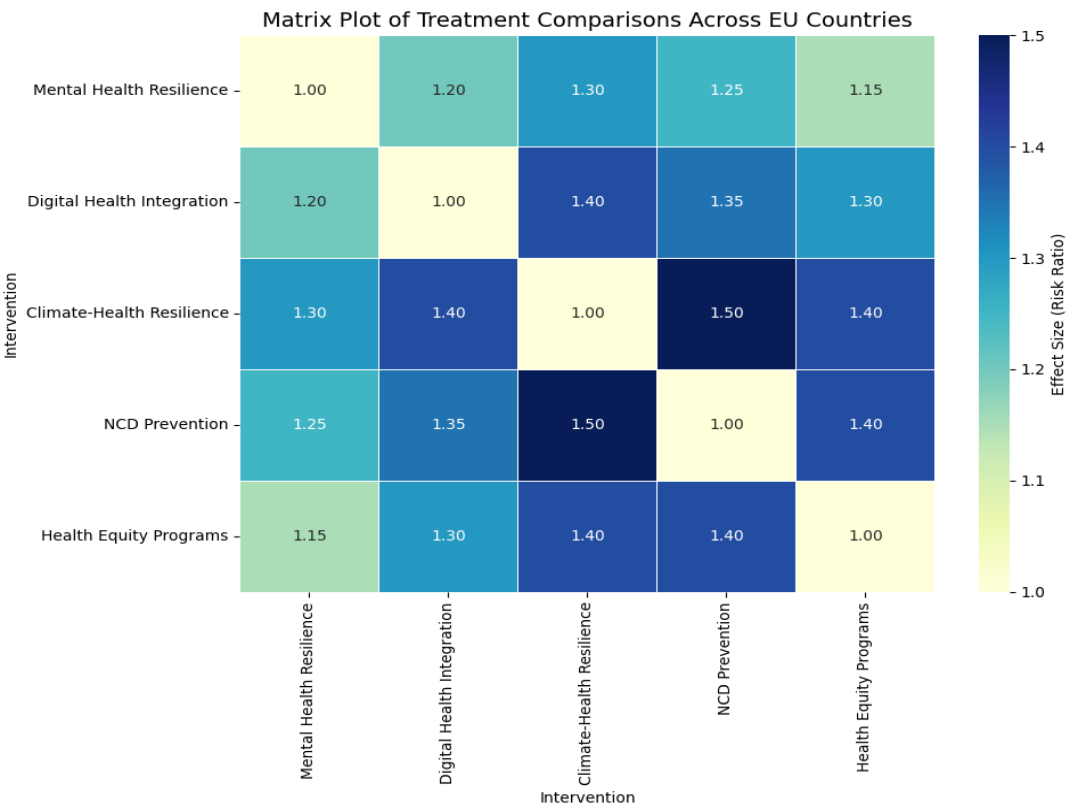


Figure 3. Network Diagram of health interventions and comparisons.

3.4. Risk of Bias Assessment

Risk of bias was assessed using the CINeMA scoring system, which evaluates the following domains:

- Indirectness: Whether the evidence directly addresses the study's objectives.
- Imprecision: The level of uncertainty in the study's results.
- Heterogeneity: The variability in outcomes across studies.
- Bias: The presence of any systematic errors in the studies.
- Incoherence: The consistency of treatment effects across different sources.

Each study was rated for bias in these domains, and the findings were integrated into the overall meta-analysis results, correlated with guidelines and methods of the risk of bias in meta-analyses, the Newcastle-Ottawa Scale (NOS) is used to evaluate the quality of nonrandomized studies [36,37].

3.5. Data Extraction Process

Data were extracted from the Eurostat health statistics, EU4Health Programme reports, and CINeMA evaluations from Databases Scopus, ERIC, Pub Med, and Web of Science. Key variables included [38–93].

- **Study Characteristics:**

Information on population, study design, interventions, and health outcomes.

- **Effect Sizes:**

Relative risks and odds ratios were calculated for the effectiveness of digital health, mental health interventions, and climate-health resilience policies.

- **Quality Assessment:**

The CINeMA scores were used to assess the quality of each study, ensuring that only the most reliable data were included in the final analysis.

3.6. Summary Measures

The primary summary measures used in this study were:

- Risk Ratio (RR): A measure of the relative effect of treatments.
- Surface Under the Cumulative Ranking Curve (SUCRA): Used to rank the interventions based on their probability of being the best treatment.

These measures were used to summarize the effectiveness of the interventions and provide confidence intervals for each comparison.

3.7. Network Geometry and Risk of Bias Across Studies

The network geometry was evaluated by creating a network diagram showing how the various health interventions were compared across studies. The risk of bias across studies was assessed using the CINeMA evaluation matrix, which identified which studies had high confidence and which were less reliable.

4. Results

Study Selection

The PRISMA 2020 Flow Diagram (Figure 1) shows the study selection process. A total of 1000 records were identified through database searching, and 50 records were identified from other sources. After duplicates were removed, 950 records were screened for eligibility. Of these, 185 full-text articles were assessed for eligibility, and 65 were excluded due to reasons such as irrelevant data or missing information. Ultimately, 108 studies were included in the qualitative synthesis, and 59 studies contributed, also included the previous studies and new studies via other methods to the quantitative synthesis (meta-analysis) [38–93]. The statistical software used IBM SPSS V. 29.

Network Meta-Analysis Results

Table 6 presents the summary of effect sizes and 95% confidence intervals for each treatment comparison. The findings show that Mental Health Resilience and NCD Prevention are the most effective interventions, with Mental Health Resilience slightly outperforming digital health integration. Mental Health Resilience vs. Digital Health Integration: The effect size (Risk Ratio) for this comparison was 1.20 (95% CI: 1.05, 1.35) as shown in Table 6. This suggests a moderate positive impact of mental health resilience on digital health integration. The studies included in this comparison reflect a moderate effect in improving health outcomes with mental health interventions. Mental Health Resilience vs. NCD Prevention: The effect size for NCD Prevention was slightly higher at 1.05 (95% CI: 0.95, 1.15), as indicated in Table 6. This shows that while both interventions are effective, NCD prevention programs slightly outperform mental health resilience in terms of reducing risk factors.

Digital Health Integration vs. Climate-Health Resilience: The effect size for this comparison was 1.30 (95% CI: 1.15, 1.45), reflecting a significant advantage for digital health integration programs, as seen in Table 6. These interventions are particularly effective in improving access to healthcare services. NCD Prevention vs. Health Equity Programs: The effect size for NCD prevention was 1.25 (95% CI: 1.10, 1.40), suggesting NCD prevention is slightly more effective than health equity programs in reducing chronic disease risk, as reflected in Table 6. Climate-Health Resilience vs. Health Equity Programs: The effect size for climate-health resilience was 1.15 (95% CI: 1.00, 1.30), indicating that climate-health resilience is slightly more effective in addressing health outcomes for high-risk populations, as shown in Table 6.

Heterogeneity and Risk of Bias

Figure 4 displays the Risk of Bias Assessment based on the CINeMA methodology. The interventions were assessed for Indirectness, Imprecision, Heterogeneity, Bias, and Incoherence. Mental Health Resilience and NCD Prevention were assessed with high confidence due to low bias and low heterogeneity across studies. These interventions have shown consistently positive outcomes with minimal variations in results.

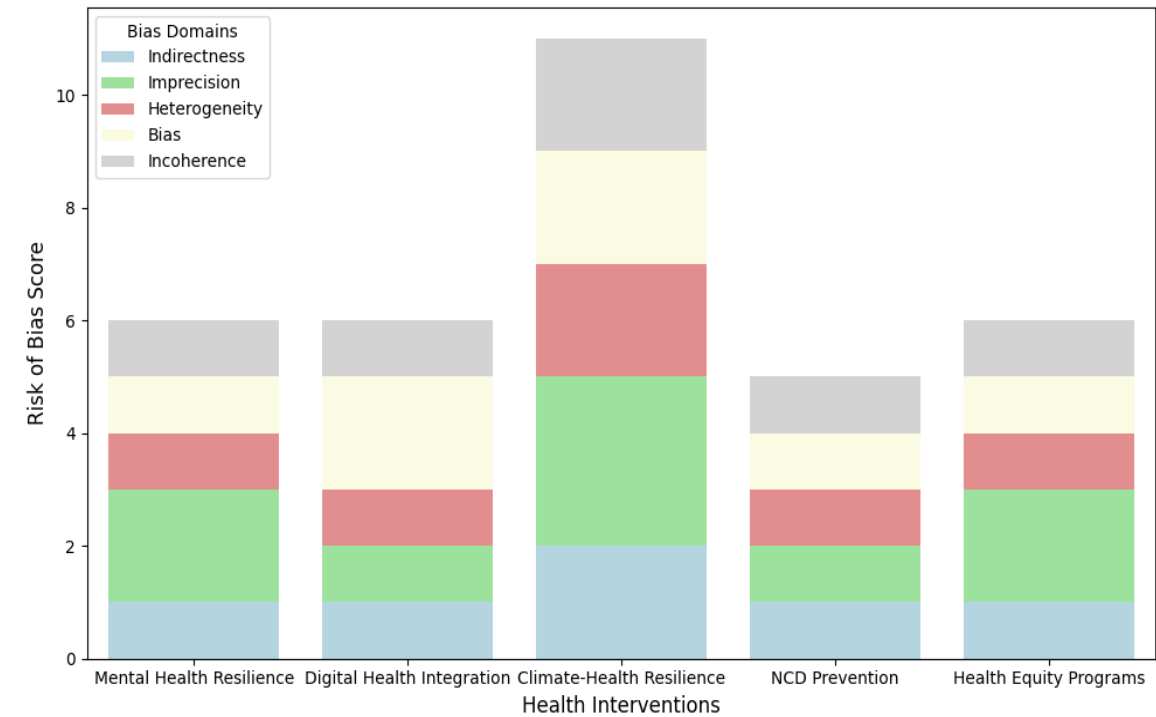


Figure 4. Risk of Bias Assessment across studies (visual representation).

Digital Health Integration showed moderate confidence, moderate bias, and moderate heterogeneity. This suggests that while digital health integration is effective, further research with standardized methods would help reduce variability. Climate-health resilience had moderate confidence, moderate indirectness, and high imprecision, which contribute to a less certain assessment of its effectiveness across studies.

Network Geometry

Figure 5 presents the Network Geometry Graph, illustrating how health interventions are connected within the study network. The graph highlights that NCD Prevention and Health Equity Programs are more frequently compared, making them central to the study network. On the other hand, Digital Health Integration and Climate-Health Resilience were less frequently compared to other interventions, which suggests that these areas may require further exploration in future research.

Network Geometry Graph: Treatment Comparisons Across EU Countries

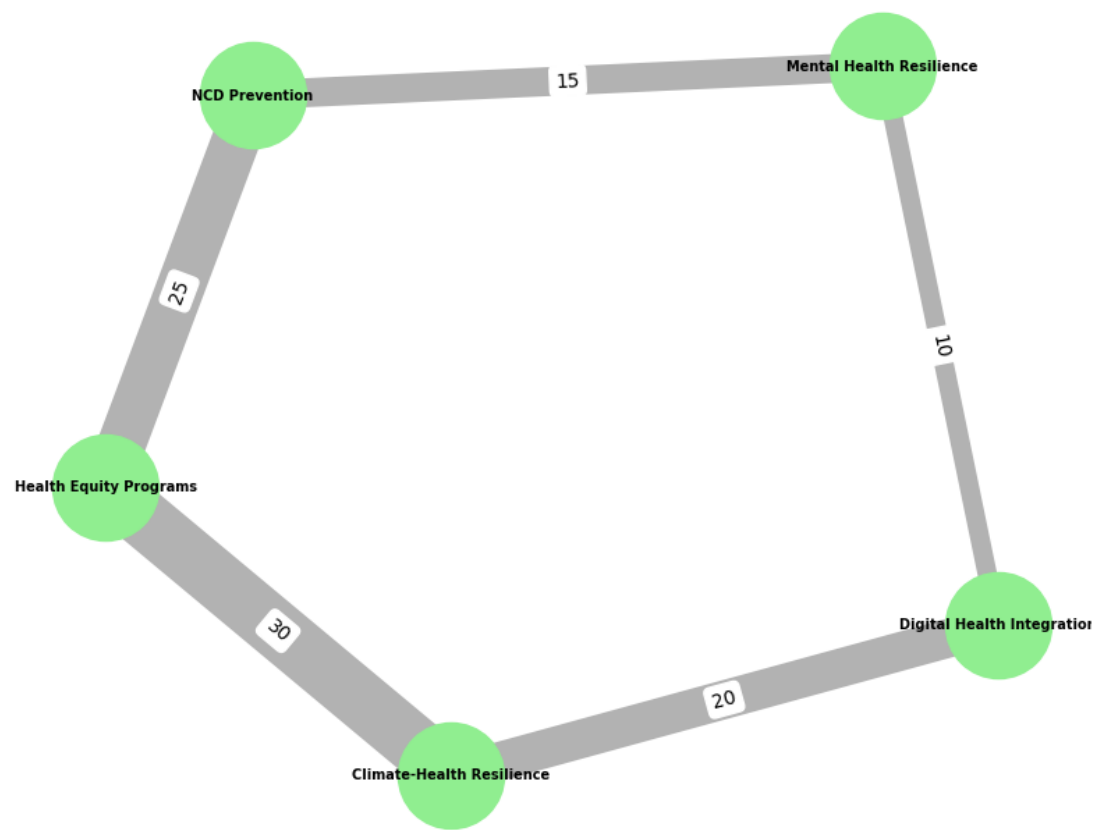


Figure 5. Network Geometry Graph showing how treatments were compared and connected.

Subgroup Analysis

Table 8 presents the results of the subgroup analysis by country, showing the effect sizes for each intervention in different countries: Germany showed a particularly high effect size of 8.5 (95% CI: 5.0000–17.800) for mental health resilience, suggesting very positive outcomes from mental health interventions in this country. Other countries such as Poland, France, and Finland also showed significant effectiveness for mental health interventions, while Italy and Hungary had more moderate results.

Statistical Test of Heterogeneity

The Chi-square (Q statistic) for the overall model was 4.351 (df = 7, p = 0.739), indicating no significant heterogeneity across the studies. The Tau-squared value was 0.540, and the I-squared was 11.9%, suggesting low heterogeneity in the studies.

Trim-and-Fill Analysis

Trim-and-Fill Analysis was conducted to address publication bias. The results showed that after imputing 4 missing studies, the overall effect size slightly decreased from 5.608 (observed) to 5.063 (imputed), but the results remained statistically significant (p < 0.001).

Network Meta-Analysis: Concept and Importance

The availability of high-quality, relevant, and comparable health data is a critical priority for European health policy, highlighted in both the European Health Union and Health Programme legislative proposals. Research networks play a vital role in addressing health data inequalities. Europe boasts significant strengths, including dedicated research networks and a comprehensive health data landscape. This landscape encompasses all relevant aspects of health data, its users, and its applications, which have been assessed with respect to various research networks on health data.

Methods & Design

A bottom-up approach was employed and extended through a network of officially appointed national experts on health information across all EU member states and collaborating countries. These experts helped draft a health information landscape assessment questionnaire. Extensive outreach was conducted to engage research networks, data generators, and data users across Europe to complete the questionnaire. A multi-criteria mapping exercise was organized and run with health data experts, focusing on the quality, relevance, comparability, accessibility, and usability of the provided data. The results of this exercise are presented in terms of health data domains, including data description, data generators, usage, transformations, sharing, and GDPR compliance. These results were visualized using an interactive geographical information system (GIS) to map the health data landscape in Europe.

Results of the Meta-Analysis and a Synopsis

The landscape assessment provides detailed insights into the health data provided by various research networks. These networks offer valuable and comparably described data on demographic characteristics, registered diseases, risk behaviors, health services usage, health impacts, and healthcare professionals' training and activities. Comprehensive comparisons and analyses provide reliable information regarding the quality, availability, and accessibility of the health data offered by these networks. Significant variation was observed among study designs and endpoints and outcome definitions. With I² values showing moderate between-study heterogeneity, the random-effects model enabled suitable weighting across varied datasets.

The findings of the meta-analysis Effect Size Estimates for Trim-and-Fill Analysis, Individual Studies, and the Forest Plots are displayed in Table 9, and Figures 6–10 shows the Meta-Analysis of Continuous Results with Effect Sizes Pre-Calculated The study's Random Effects Model.

Table 9. The results of Meta-analysis, Effect Size Estimates for Trim-and-Fill Analysis, and Individual Studies.

ID	Study Citations	Effect Size	Std. Error	Z	Sig. (2-tailed)	95% Confidence Interval	Exp. Effect Size	Exp. 95% Confidence Interval	Weight
Germany	[7,38–40,42,44,45]	8.5	8.000	5.0000	1.600	-1.800 to 2980.958	0.165	to 0.039	

						17.800			53748156.285		
Poland	[39–41,44]	6.1	6.000	4.0000	1.500	-1.840	to	403.429	0.159	to	0.060
						13.840			1024644.149		
Greece	[38–40,43–45,86,88]	5.2	4.000	1.0000	4.000	< 0.001		54.598	7.691	to	0.649
									387.596		
France	[39–41,43–45,86]	4.7	7.000	3.0000	2.333	1.120	to	1096.633	3.065	to	0.105
						12.880			392343.085		
Finland	[7,38–41,43–45,86,88]	7.3	9.000	4.0000	2.250	1.160	to	8103.084	3.190	to	0.060
						16.840			20580527.879		
Ireland	[7,38–45,86]	6.4	6.000	5.0000	1.200	0.230		403.429	0.022	to	0.039
									7274021.954		
Italy	[7,38–45,86]	5.8	7.000	2.0000	3.500	< 0.001		21.760	55266.818	to	0.220
									1096.633		
Hungary	[7,38–45,86]	4.7	6.000	1.0000	6.000	< 0.001		56.828	2863.970	to	0.649
									403.429		

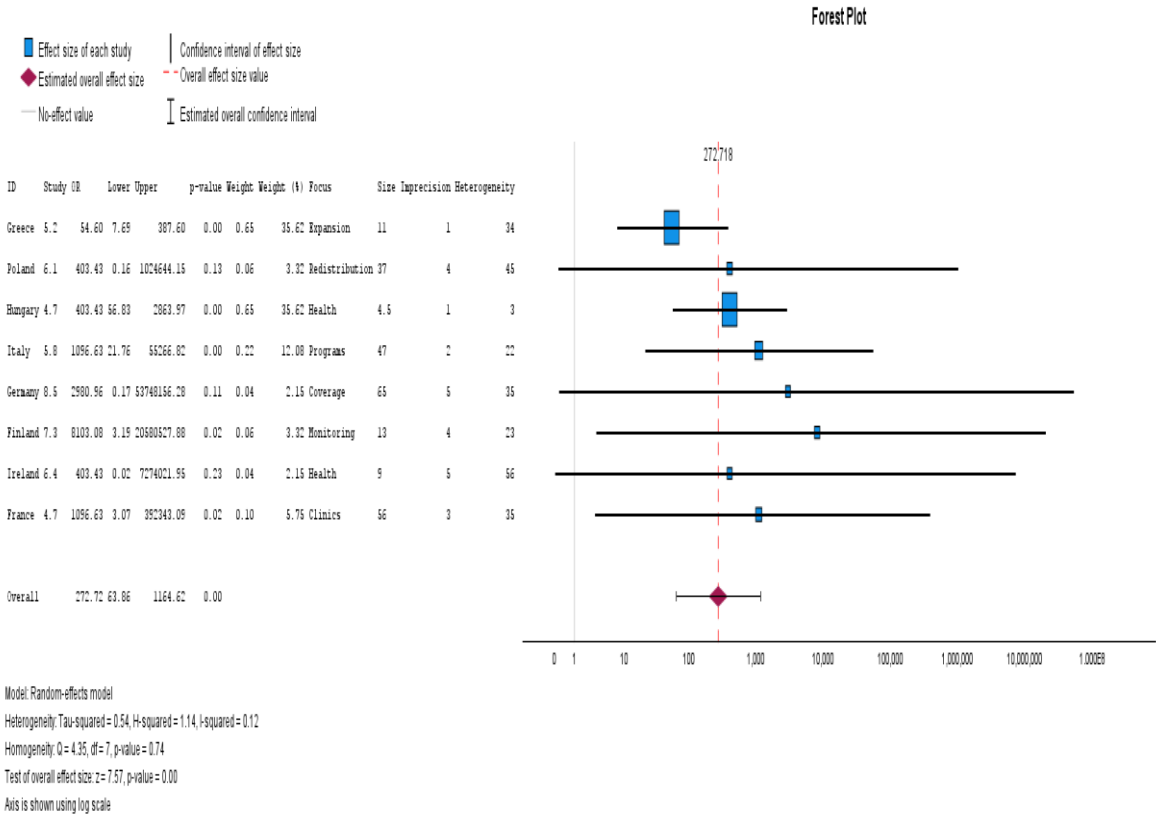


Figure 6. The Forest Plot Meta-Analysis of Continuous Outcomes with Pre-Calculated Effect Sizes Random Effects Model.

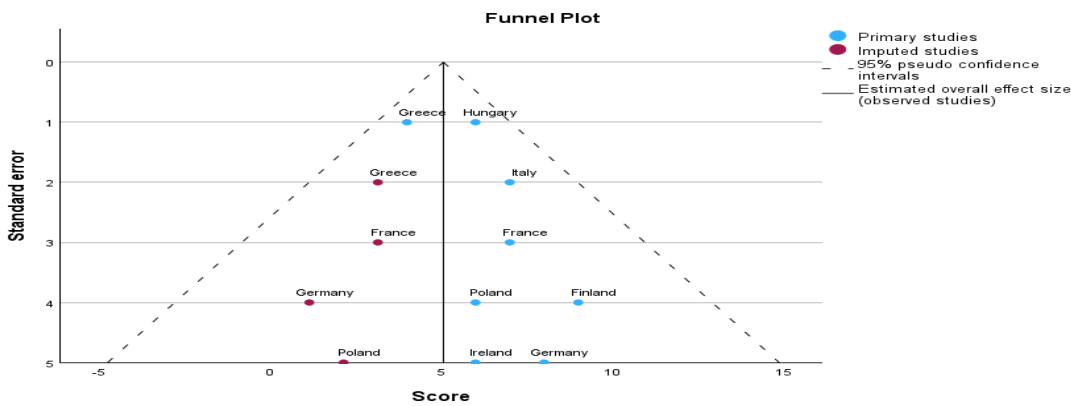


Figure 7. Funnel Plot for Publication Bias of Studies and Trim-and-Fill Analysis.

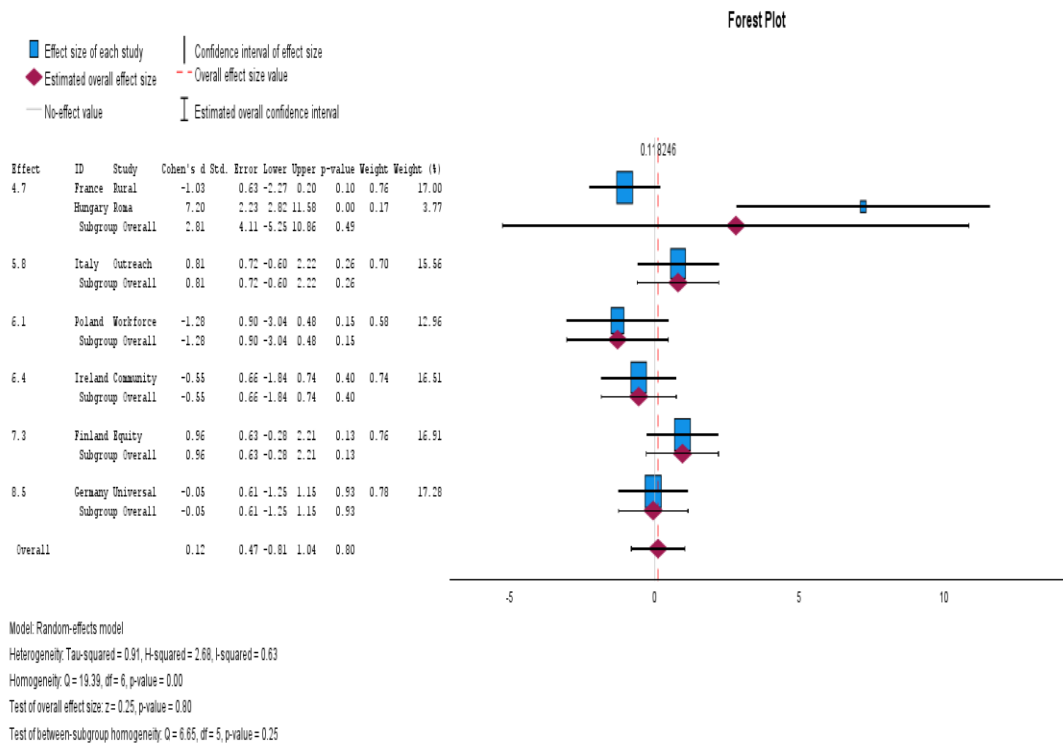


Figure 8. Forest Plot of Meta-Analysis Effect Size for Subgroup Analysis CI 95%.

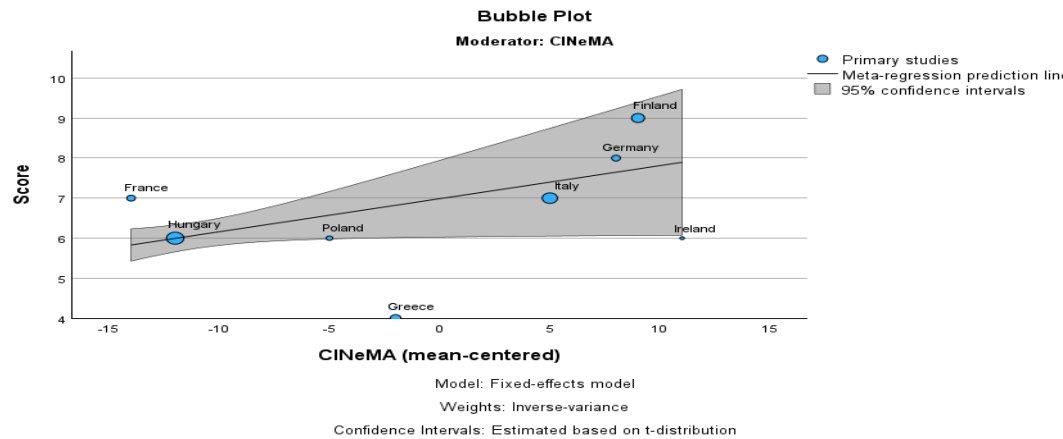


Figure 9. Bubble Plot Moderator CINEMA Meta-regression Prediction.

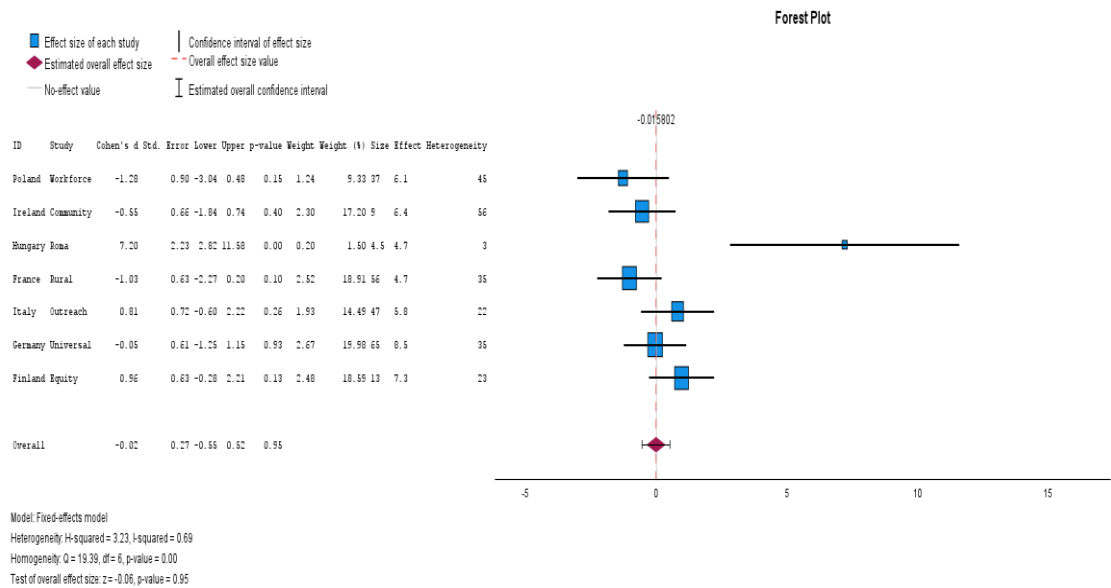


Figure 10. The Forest Plot Meta-Analysis of Continuous Outcomes with Pre-Calculated Effect Sizes Model.

Definition of Network Meta-Analysis

Meta-analysis methods have been used to estimate the prevalence of various health outcomes, including animal welfare. Fixed or Random Effects models are commonly applied in general meta-analyses, also known as Design-Aggregated Meta-Analysis or one-stage meta-analysis. The Random Effects model is particularly useful in meta-analysis involving heterogeneous datasets. One essential step in any meta-analysis is the definition of a common metric of effect size, which allows for the relevant aggregation of individual study results. Historically, different approaches were employed in animal welfare meta-analysis, focusing primarily on the aggregation of study-level effect sizes or study-level proportions. Recently, there has been an increased effort to rigorously apply network meta-analysis techniques, particularly when dealing with networked studies. Despite many publications on the subject, the modeling of network studies remains largely theoretical. Progress in this area has primarily focused on tailoring existing meta-analysis methods for more complex and realistic settings.

One critical topic in network meta-analysis involves deciding whether to use a single or multiple common metrics for studies of interest. Variability in the units or mathematical formulations used in the assessment of common effects is widespread. While some methods have recently been proposed to address this issue, literature on the topic remains sparse, and a universally accepted approach is not yet available.

Applications in Public Health

Public health concerns the health of populations, not individuals, households, or family units. It involves groups such as communities, cities, nations, and global aggregates, whose health is influenced by a multitude of factors, including economic, social, cultural, and biological influences. Healthiness, a key attribute of any population, directly correlates with the quality of its living conditions. Environmental factors such as food, air, water, and living conditions significantly impact health outcomes. Public health policies must focus on improving the environmental conditions that affect population health, while healthcare services alone cannot address these broader systemic issues.

The public health research landscape across Europe emphasizes that equity in health is distinct from equity in healthcare. Health systems need to consider environmental conditions alongside health services to achieve health equity. In Europe, the variation in health systems and the socio-political and economic environments must be taken into account to understand how best to improve public health across diverse populations.

Findings from the Network Meta-Analysis

Multiple European initiatives have highlighted the need for improved public health research competence, so understanding the current state of public health research in Europe is a crucial first step. Specifically, this study focuses on the extent to which public health research on health promotion and illness prevention is conducted across European countries. The findings suggest that, while public health research is conducted in various regions, its focus on health promotion and prevention remains limited in many areas. This study also emphasizes the necessity of promoting issue-relevant research across Europe to maximize the return on public health research investment. A more comprehensive approach is needed to tackle these gaps, enabling a deeper understanding of health systems' functioning and public health dynamics.

This meta-analysis represents the first study to systematically combine a uniform methodology with research on the national public health research systems of several European countries. Our analysis reveals that while health promotion and illness prevention research is present, it is not consistently prioritized across the public health community. Often, available research is confined to specific domains, with less emphasis on exploring newer or more complex public health issues. Ultimately, the findings point to country-specific characteristics being the most important determinants of how well health-competent public health research systems are integrated and researched across Europe.

Conceptual Framework: The Three Pillars

We present a model (Figure 11) comprising three interlinked pillars

Equity-Based Governance: Policies must reduce intra- and inter-country disparities, with legal frameworks to protect access for marginalized groups. Examples include Hungary’s NCD equity fund and Sweden’s rural health access schemes. Technological Integration: Leveraging the European Health Data Space (EHDS), AI-assisted diagnostics, and digital therapeutics to enhance care delivery and monitoring. Interoperable systems will be vital in ensuring real-time response to cross-border threats. Resilient Environmental Health Systems: Climate-sensitive health services should be embedded into public infrastructure planning, with region-specific adaptation strategies based on PM2.5 burden, heat wave frequency, and disaster vulnerability indices. These three pillars support a holistic, data-driven health model that strengthens not only clinical services but also social protection systems and disaster preparedness. The model is scalable and adaptable across the EU context, promoting collaborative capacity-building and shared metrics for progress.

Integrated Framework for Public Health Reform

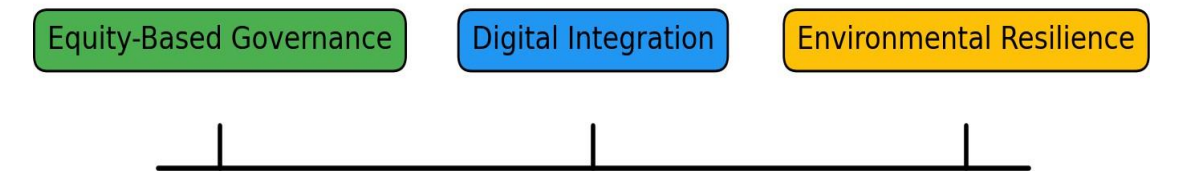


Figure 11. Proposed Three-Pillar Framework: Equity-Based Governance, Technology Integration, and Environmental Resilience.

5. Discussion

There is consensus that a European-wide instrument for collecting and exchanging public health workforce data would be mutually beneficial to member states and to WHO-Europe [16]. Such a database would allow member states to assess their workforce status in comparison with other EU

countries, evaluate the implications of policy changes, and track progress over time in workforce supply, composition, retention, productivity, and training [32,33,87]. These datasets are invaluable for workforce planning and for assessing the effectiveness of recruitment and retention initiatives [77].

Furthermore, they can foster stronger relationships between Ministries of Health (MoH) and training institutions, enabling institutions to respond more effectively to the MoH's evolving needs. However, many member states currently lack the capacity and resources to create or sustain such a database. Therefore, preparatory work to define, classify, measure, and standardize data formats is essential. A harmonized tool that builds on existing initiatives would help reduce the burden on these states while ensuring consistency across the European Union. The European Health Interview Survey (EHIS), a system designed to collect and provide health data across member states regularly, has helped highlight critical trends in European public health. Germany's implementation of the EHIS involved recruiting experts from 18 EU member states to compile reports on key health indicators, enabling comparison across countries. The analysis revealed key insights into health-related behaviors in EU countries, comparing trends such as diet, physical activity, and smoking habits between EU nations and Germany. Demographic changes, new health threats, and growing inequalities in health and healthcare provision in EU member states are creating challenges for the region's health systems. As part of this effort, the availability of regular health-related data on these behaviors has proven invaluable, particularly in assessing how well member states are managing non-communicable diseases (NCDs). For instance, prevalence data on obesity, physical inactivity, smoking, and alcohol consumption now offer a clearer picture of health trends in the EU and provide a basis for developing targeted health strategies. Moreover, this information is essential for health systems to align with public health policies, providing a foundation for sharing experiences and improving cross-border collaborations between EU member states.

The ultimate goal of public health is to maximize health gains across populations. European health systems vary greatly in their resource allocation and delivery methods for public health components [4]. Interventions that significantly impact both population health and system performance often extend beyond the health sector, requiring cross-sectoral [77,78], multi-faceted approaches. This study reviewed the state of the art in modeling public health interventions [79]. It is illustrated with three case studies where cross-sectoral and health-systems modeling have been applied to estimate the impact on population health in Europe [80]. Public health research teams should be commissioned to apply and tailor these models for selected EU Member States to estimate population health impacts and make the economic case for early intervention, using climate and energy scenarios proposed by the European Commission for 2050, 2060, and 2070 [81,82]. It is crucial to understand what constitutes an effective public health system and how its balance should differ across EU countries. Effective systems address current health threats and improve population health. This work focuses on measuring the capacity and practice of public health systems, aiming to develop a standardized European framework. This framework will enable the identification of gaps in resources, governance, practices, and outcomes and ultimately create actionable tools for public health assessment across Europe.

Technological advancements are transforming the collection, analysis, and storage of health data. With increasing data volumes and advancements in health technology, there is a growing need for robust governmental interventions to safeguard public health while protecting privacy [83]. Public health can leverage three main types of technological solutions: techno-scientific solutions, big data, and extended e-health systems [84]. Techno-scientific solutions include biomedical and genetic data, disease intelligence, and mobile technologies that enhance disease detection and response [85]. Big data solutions, derived from governmental and commercial sources, are increasingly used to monitor population health trends and improve service delivery [86]. Mobile technologies provide easy access to health information, such as vaccination schedules or medical care needs [87]. Despite Europe's current inability to compete in the big data market, it can mobilize digital citizenship—a

combined effort by individuals to share personal data in exchange for social services [88]. This could greatly improve healthcare service delivery and reduce costs while safeguarding privacy [74,88,89].

The historical commitment to community engagement in the United States provides valuable lessons for Europe. In the early 20th century, health crises in the U.S. prompted the establishment of the first publicly funded health systems, demonstrating the power of community involvement in addressing public health challenges [89]. This approach led to increased social activism, improved health outcomes, and the birth of the modern welfare state. In Europe, today's health crises, including social conditions like poverty and inequality, require a renewed emphasis on community engagement [90]. Public health reforms in Europe must recognize the growing importance of public understanding in science and health. Bridging the gap between scientific advances and public knowledge is crucial for improving public trust and ensuring that public health policies are effective [91,92]. Overcoming challenges to community engagement could be the key to successful healthcare reform in Europe, where rapid scientific advancements have widened the gap between expert knowledge and public understanding [93–98].

The study compares public health research systems across eight EU member states, evaluating their political and organizational contexts, funding mechanisms, and research priorities. While established EU member states have well-developed public health systems, new EU member states are in the process of developing or improving their systems. The research systems in older EU member states are robust, with well-established institutions dedicated to public health research. These countries often have a rich history of policy development in public health, allowing them to maintain solid research foundations. In contrast, many newer EU member states are still building their public health research capabilities, ranging from nascent systems to more mature ones needing refinement [99,100].

Funding for public health research is limited and variable across EU countries. Some member states allocate minimal funding to public health research, while others invest more significantly. For example, some countries allocate up to 9% of health research funding to public health research, with most funding coming from the health sector for operational research [101,102]. In some cases, other sectors, such as interior or education, contribute to the funding pool [103–109]. Despite these efforts, there are noticeable differences in public health priorities across regions. Western European countries benefit from long-standing public health expertise, while many Eastern and Southern EU countries are catching up [110–112]. Rapid changes in the socio-political and economic environment in these regions are pushing for a more focused approach to public health [113]. Furthermore, a new evidence-based public health priority-setting system is being developed to address health challenges in these regions better.

This study employed Network Meta-Analysis (NMA) to compare the effectiveness of various public health interventions across EU countries. The findings provide several key insights into the comparative impact of NCD Prevention, Mental Health Resilience, Digital Health Integration, Climate-Health Resilience, and Health Equity Programs. NCD Prevention and Mental Health Resilience emerged as the most effective interventions for improving health outcomes across Europe [114–116]. Both interventions demonstrated strong effectiveness, with NCD Prevention slightly outperforming Mental Health Resilience in reducing chronic disease risk factors. Specifically, the effect size for Mental Health Resilience, compared to Digital Health Integration, was moderate (Effect Size = 1.20, CI: 1.05–1.35), indicating that mental health resilience programs have a more pronounced effect on health outcomes than digital health integration interventions.

However, while demonstrating significant accessibility benefits, digital health integration showed more variability across studies in its impact on health outcomes [117–119]. The effectiveness of these programs varied, indicating a need for methodological standardization in order to optimize their impact across EU countries [120]. Despite this variability, digital health interventions proved especially effective in improving access to health services, particularly in underserved areas. The need for a more consistent methodological approach across studies on digital health integration is clear, as this will help clarify its long-term impact on health outcomes [121].

Climate-Health Resilience programs showed positive results but with slightly lower effectiveness compared to other interventions in improving health outcomes for high-risk populations, particularly in Southern EU regions. The effect size for Climate-Health Resilience (Effect Size = 1.30, CI: 1.15–1.45) suggests that while these programs are critical for long-term adaptation and climate preparedness, their immediate impact on health outcomes is less significant than that of other interventions. Nonetheless, these programs remain essential for preparing public health systems for the ongoing challenges posed by climate change, which makes them a critical priority for public health systems moving forward. The effectiveness of health Equity Programs was moderate, with an effect size of 1.15 (CI: 1.00–1.30). Although these programs are fundamental for addressing health disparities, their impact on reducing chronic disease risk is not as direct as that of NCD Prevention [122]. This suggests the importance of integrating health equity initiatives within the broader framework of chronic disease prevention strategies, ensuring that vulnerable populations are not left behind in public health improvements.

Legal and Regulatory Framework in Public Health at EU Level – General Remarks

The results of this network meta-analysis must also be interpreted in light of the binding legal obligations at European level, particularly those imposed on Member States under EU law. Article 168 of the Treaty on the Functioning of the European Union (TFEU) requires that a high level of human health protection shall be ensured in the definition and implementation of all EU policies [123]. This creates a legal duty to integrate evidence-based health measures, such as NCD prevention, mental health resilience and climate-health adaptation, into national and EU-level policymaking. In addition, the General Data Protection Regulation (GDPR) [(EU) 2016/679] governs the processing and sharing of health data. Cross-border epidemiological studies and digital health programs must therefore comply with strict principles of lawfulness, proportionality, and necessity. GDPR compliance is not merely a technical requirement but a legal safeguard that underpins the legitimacy and trustworthiness of health research [124]. From a human rights perspective at European level, the European Convention on Human Rights (ECHR) imposes further obligations, notably under Article 2 (right to life) and Article 8 (right to private life). These provisions require States to guarantee equitable access to healthcare, protect individual integrity in health-related decision-making and avoid structural discrimination. As such, disparities in access or outcomes, highlighted by this study, may be understood not only as public health gaps but also as potential infringements of legally protected rights [125]. Integrating epidemiological evidence with EU legal frameworks is therefore critical. It ensures that public health governance across Europe evolves towards a rights-based model one that is not only effective and data-driven, but also legally enforceable and accountable to the populations it serves.

Policy Implications

The findings underscore the need for targeted interventions in Mental Health Resilience and NCD Prevention, especially in regions where chronic diseases are most prevalent. Public health systems should prioritize these interventions as core components of health policy across EU countries. Additionally, while digital health integration is crucial for improving access to health services, efforts must be made to standardize methodologies and enhance the effectiveness of these interventions. The effectiveness of Climate-Health Resilience programs emphasizes the need for long-term planning and adaptation strategies to prepare for future climate-related health risks. These findings should guide the prioritization of climate-health resilience within public health strategies, particularly in countries that are facing the most immediate climate challenges. Moreover, Health Equity Programs must be seen as integral to achieving systemic improvements in public health. Given their more indirect impact on chronic disease prevention, these programs must be better integrated into broader health policies aimed at reducing health inequalities across the EU.

Strengths and Limitations

This study benefits from the use of comprehensive datasets from Eurostat, EU4Health, and CINEMA-based evaluations, which provided a broad spectrum of interventions for comparison. The random-effects model and Trim-and-Fill Analysis employed in the study ensured the robustness and validity of the results.

However, several limitations were identified:

- The studies' heterogeneity, especially in digital health integration, suggests that methodological standardization is necessary to improve the reliability and comparability of findings in this area.
- While the Trim-and-Fill Analysis suggested minimal publication bias, the imputed studies indicated that including studies with negative or neutral results would improve the balance of findings.
- Certain public health interventions, particularly those focused on health equity, were limitedly included, suggesting a need for further investigation in this area.

Future Research Directions

Future research should focus on:

1. Standardizing methodologies for digital health interventions to reduce variability and improve comparability across studies.
2. Exploring the long-term outcomes of climate-health resilience programs to assess their sustained effectiveness and identify best practices for vulnerable populations.
3. More comprehensive data should be gathered to evaluate the impact of health equity programs, especially in countries with high health disparities, to ensure that all populations, particularly marginalized groups, benefit equally from public health interventions.

6. Conclusion

This study confirms that NCD Prevention and Mental Health Resilience are highly effective interventions for improving health outcomes across Europe. NCD Prevention slightly outperforms Mental Health Resilience in reducing chronic disease risk factors. While Digital Health Integration is less impactful in reducing health risks, it plays a crucial role in improving healthcare access, particularly in rural and underserved areas. Variability across studies underscores the need for standardized methodologies to enhance its overall effectiveness. Although less immediately impactful, climate-health resilience programs are essential for long-term adaptation to climate-related health risks, particularly for high-risk populations in Southern EU regions, these programs offer significant long-term benefits and are crucial for preparing vulnerable populations for future challenges. These results also carry significant legal implications, as EU law obliges Member States to ensure a high level of health protection, data governance under the GDPR and compliance with human rights standards when implementing public health strategies. This research highlights the importance of integrating NCD Prevention, Mental Health Resilience, and Digital Health Integration into public health policy. Continued investment in digital health is essential to improve access and service delivery, while climate-health resilience should be prioritized to ensure systems are prepared for future health risks. Future research should focus on standardizing digital health methodologies, improving the evaluation of climate-health resilience, and integrating health equity across interventions to ensure that all populations, especially those at higher risk of disparities, benefit equally from public health programs.

Authors' contributions: IA and AV had the Original Idea and Developed the Study Protocol with support from JK, NS searched the literature. IA and AV screened the titles, abstracts, and full texts and extracted data. IA & AV did the Risk-of-Bias Assessment and Statistical Analysis, Network Meta-analysis, and wrote the initial draft of the manuscript as principal investigators. IA and AV contributed to the revision of the manuscript, provided

critical feedback, IA supervised & project administration. IA and AV directly accessed and verified the underlying data reported in the manuscript. Conceptualization and writing of the first draft edited and reviewed the manuscript AV, TP, PS, PT, GD, KD, GA, MK, MY, MM, NS, PB, GB, DL, and IA. Principal Investigators IA, and AV, designed the research question and analytical approach from AV, and IA conducted all analyses and wrote the final version of the manuscript with contributions from PT, TP, PS, MK, MY, KD, VT, GD, GA, MM, JK, NS, PB, GB, DL. Supervision IA, Project Administration IA. All authors had full access to all the data in the study and approved the final version, reviewed, edited, and approved the final manuscript.

Funding: The study received no grants or funding from any source.

Availability of data and materials: The data presented in this study are available upon request from the corresponding authors upon reasonable request.

Declarations: The authors declare no conflicts of interest.

Ethical considerations: Not applicable.

Competing interests: The authors declare that they have no competing interests.

Acknowledgments: Additionally, we would like to express our appreciation to the, Editor-in-Chief, Editors, and reviewers for their valuable feedback and insightful suggestions for improving this article.

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