Monitoring of prostate cancer screening in the European Union: development of key performance indicators through the PRAISE-U project

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Summary

Background Monitoring and evaluation of prostate cancer (PCa) screening is key to ensure that the programme achieves the desired objectives. Utilizing a set of prioritized, feasible and harmonized key performance indicators (KPIs) is crucial for this purpose. We describe the methodology used to identify the PCa screening KPIs and the outcome of this process within the scope of the EU-funded PRostate cancer Awareness and Initiative for Screening in the EU (PRAISE-U) project. Feasibility of implementing these KPIs will be evaluated in the five pilots set up at multiple sites in the EU (Spain-2 sites, Poland, Ireland, Lithuania).

Methods The indicators were developed following a structured methodology involving the following steps: (i) Development of a specific conceptual framework for PCa screening is adapted from the existing risk-based algorithms and modified to guide the selection and mapping of indicators (from identification of population eligible for screening to the decision for treatment or follow-up), (ii) Scoping review of literature (coverage from 1971 to June 2023) to identify existing performance indicators for PCa screening to adapt to the new framework with redefining the indicators, where necessary, (iii) Survey among experts (October–November 2023) to select the indicators fulfilling pre-determined criteria such as accuracy of definition and calculation, importance, and feasibility, and (iv) Deliberations among experts to list the finalized set of indicators, held in December 2023.

Findings A total of 63 KPIs were selected for review using the step-wise methodology as described earlier. Following the review, survey, and deliberations, 21 KPIs were finalized to be piloted in the PRAISE-U project. The resulting 21 KPIs cover the different phases of the screening programme, including invitation, screening test, risk stratification, diagnosis, and also on treatment, harms, and impact. Each KPI has been defined with agreed numerator and denominator.

Interpretation Continuous monitoring of PCa screening programmes using the KPIs will serve as a powerful tool for optimizing service delivery, programme improvement, comparison per screening site, and ultimately contributing to a better benefit to harm ratio. The KPIs will be implemented in five pilot sites identified to be included in the PRAISE-U project aiming to identify an evidence-based scalable model for risk adapted PCa screening for Europe.

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The PRAISE-U consortium is listed in the Appendix II.

Keywords: Prostate cancer; Screening; Key performance indicators; Programme evaluation

Research in context

Evidence before this study

We conducted a scoping review of literature to identify key performance indicators (KPIs) for prostate cancer (PCa) screening. Firstly, we searched four major databases, MEDLINE (1946–June 2023), Embase (1971–June 2023), Web of Science Core Collection (1975–June 2023), and Google Scholar for relevant records. The specific search strategy or criteria used for the search is outlined in Appendix I. Secondly, a review of grey literature was conducted to identify performance indicators recommended and/or reported by PCa screening programmes at the national or regional level within the European Union (EU). The experts in the PRAISE-U consortium were contacted to suggest any national/international recommendations or trial protocols available online that might have included KPIs. Finally, performance indicators developed by the CanScreen-ECIS project, which formulated KPIs for breast, cervical and colorectal cancers, were reviewed for relevance to PCa. Our multi-stage search strategy yielded a total of 63 KPIs, which after removing the duplicates or those considered as non-relevant were included in the review. This comprehensive review of literature identified the need for prioritized, feasible and harmonized KPIs which is crucial for standardization and benchmarking of PCa screening across the EU.

Added value of this study

Our systematic stepwise methodology led to the development of robust KPIs with definitions and calculation that are feasible and important to monitor prostate cancer screening programmes. The resulting 21 KPIs will be crucial to ensure process and outcome of screening programme effectiveness, including invitation, screening and risk assessment, further risk assessment, diagnosis, treatment and follow up. This study identified a number of additional indicators that are important and unique to PCa screening, such as those diagnosed with prostate cancer who undergo active surveillance and the tumour grade distribution of PCa.

Implications of all the available evidence

The KPIs will serve as a tool for standardized programme evaluation in a unified manner across countries while ensuring the feasibility across diverse health care delivery settings. Pilot testing and evaluation of KPIs are needed to ensure generalizability and to optimize service delivery. Evaluation of KPIs can further inform the development of the European Quality Assurance Scheme for Prostate Cancer Services.

Introduction

Prostate cancer (PCa) is the second most common cancer among men globally and the most commonly diagnosed cancer among men in the European Union (EU).[1] The incidence varied between 104.1/100,000 in Bulgaria and 265.3/100,000 in Lithuania in 2022.[2] With mortality rates ranging between 25.7/100,000 in Italy and 80.4/100,000 in Estonia, PCa was the third highest cause of cancer specific mortality, after lung and colorectal cancer in the EU. The considerable variation in mortality rates between the EU countries suggests inequalities in access to early detection and subsequent care. In 2022, Council of the EU recommended member states to evaluate the feasibility and effectiveness of organised PCa screening using magnetic resonance imaging (MRI) to make biopsy decisions.[3]

Population-based, quality-assured screening programmes are instrumental in achieving the desired outcomes of screening in terms of mortality reduction with a positive benefit to harm ratio.[4–6] The PRAISE-U project (co-funded by EU4health programme of the European Commission) aims to implement and evaluate a risk stratified PCa screening programme in five pilot sites with health systems at different levels of organization: Spain (Galicia), Spain (Manresa), Lithuania (Vilnius), Poland (Wroclaw), and Ireland (Dublin)[7] (Fig. 1). In addition to risk stratification using prostate specific antigen (PSA) test results and the Rotterdam Prostate Cancer Risk Calculator (RPCRC) risk calculator 3 & 4, the pilots will utilize MRI to refine patient selection for biopsy. This protocol is designed to address various aspects of delivery of PCa screening within an organized framework. Details of the pilots are described elsewhere.[7,8]

Just like other screening programmes, monitoring and evaluation of PCa screening are key to ensure that the programmes are effective in achieving the desired objectives of saving lives from the cancer and reduce metastatic disease.[9] Utilizing a set of key performance indicators (KPIs) is crucial for this purpose. Also, KPIs helps to compare the PCa screening programme performance across regions and countries. The pilots designed by the PRAISE-U consortium are a good opportunity to evaluate the KPIs in real healthcare settings before they can be considered for a pan-European scaled up programme. In this paper, we aim to describe the

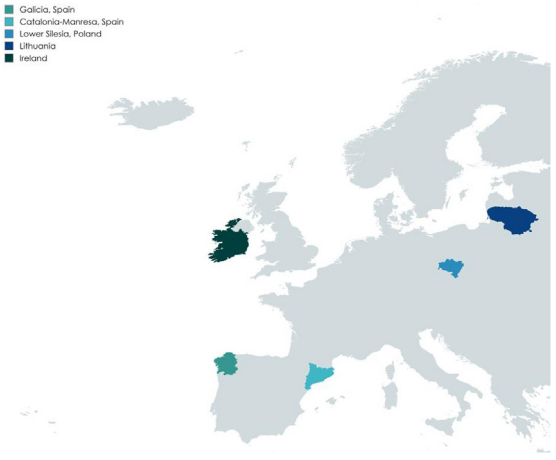

Fig. 1: PRAISE-U pilot sites.

methodology used to identify the PCa screening KPIs and outcome of the process. The KPIs identified can be classified into three categories: (i) indicators to monitor performance of the screening programme that reflect the provision and quality of care across the screening processes; (ii) indicators to evaluate outcome of the screening programme in detecting PCa; and iii) indicators to assess impact of screening such as incidence and mortality due to PCa.

Methods

We developed the indicators following a structured methodology that involved the following steps: (i) Development of a specific conceptual framework for PCa screening based on the European Association of Urology (EAU) clinical algorithm to guide the selection and mapping of indicators (from identification of population eligible for screening to the decision for treatment or follow-up), (ii) Scoping review of literature to identify existing performance indicators for PCa screening, (iii) Survey among experts to select indicators fulfilling a few pre-determined criteria such as accuracy of definition and calculation, importance, and feasibility, and (iv) Deliberations in a meeting of experts to finalize the indicators. More details of the steps are described in the subsequent sections.

Development of conceptual framework for PCa screening

The conceptual framework for screening was adapted from the existing risk-based algorithms of randomized clinical trials and modified to guide the selection and mapping of KPIs.[10] The care pathway was divided into different phases across the screening continuum: (i) invitation of eligible men, (ii) screening with PSA and first level risk stratification for further management, (iii) further risk assessment with risk calculator, MRI and second level risk stratification, and (iv) diagnosis, treatment, and follow-up. Steps in each phase were clearly defined. Cut-off values, re-screening intervals, and risk stratification criteria were finalized based on expert consultation within the PRAISE-U consortium and existing literature.[10–12] The risk stratification methods vary according to pilot sites ranging from the use of risk calculators and PSA density (PSA level divided by prostate volume, ng/ml^2) (Fig. 2). The indicators were distributed across different phases of the screening continuum as described in the framework (Fig. 2).

Scoping review of literature to identify key performance indicators for PCa screening

Three streams of search strategy were employed to identify the KPIs (Fig. 3). First search strategy involved querying multiple databases and search platforms for relevant records. The databases included Medline ALL via Ovid (coverage from 1946 to June 2023), Embase through Embase.com (coverage from 1971 to June 2023), and Web of Science Core Collection via Web of Knowledge (coverage from 1975 to June 2023) published in English language. Additionally, a search was conducted on Google Scholar. The specific search strategy is outlined in Appendix I. Two reviewers (DS & BS) screened the study titles and abstracts for potential eligibility, according to the inclusion criteria of relevance to PCa screening and potential indicators.

As a second step, a review of grey literature was carried out to identify performance indicators recommended and/or reported by PCa screening programmes from national and regional authorities within EU. The experts in the PRAISE-U consortium were contacted to suggest any national/international recommendations or trial protocols available online (in English or local language) that might have included KPIs.

Finally, performance indicators developed by the CanScreen-ECIS project funded by EU4Health programme (Grant Agreement No 101056947) that formulated KPIs for breast, cervical and colorectal cancers were screened for relevance to PCa. The CanScreen-ECIS project selected the indicators through a systematic review of literature followed by a Delphi process among international experts in cancer screening.[13] Eighteen indicators that were considered relevant for PCa screening were selected.

Indicators from all three streams were reviewed by an internal panel of cancer experts at IARC and definitions were reviewed. Indicators that were considered irrelevant and redundant were removed. Irrelevance was defined as those without valid clinical and empirical rationale, whereas redundance was assumed if the indicators were semantically close to one another or calculated in a similar way. Where necessary, indicators were modified to adapt to the new framework of PCa screening.[10] This exercise led to the selection of 22 KPIs which was then reviewed by the PRAISE-U consortium and finalized before development of the survey.

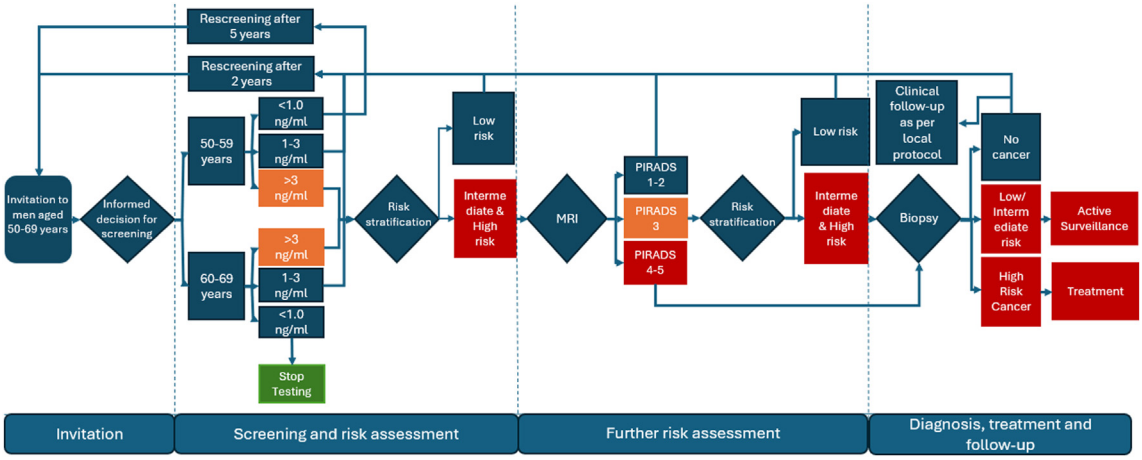

Fig. 2: Conceptual framework developed for PCa Screening (high risk cancer = intermediate to high risk).

Survey for opinion from European experts

A survey tool was designed using the RedCap electronic data capture software tool to capture agreement of the experts on the following aspects:

1. Agree with selection of the indicators as relevant for PCa screening;
2. Agree with definition of the indicators and the manner they were calculated (numerator and denominator);
3. Agree on feasibility of using the indicators in real programmatic setting;
4. Agree that these KPIs are important to monitor PCa screening.

For this survey, an expert was defined as an individual who had experience and/or influence in (i) cancer screening (including PCa screening) in Europe and/or (ii) PCa management and/or (iii) patient experience on the disease. The relevant experts were identified using

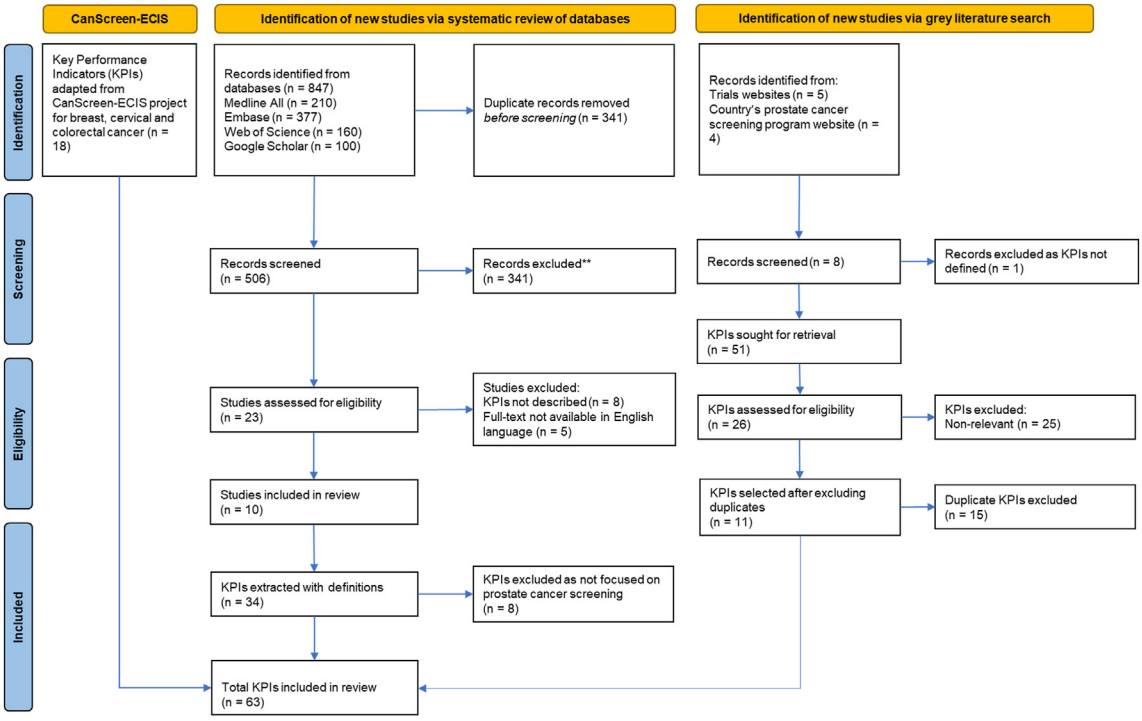

Fig. 3: Identification process of key performance indicators.

personal and professional networks of the PRAISE-U consortium members and invited to participate in the survey. Experts who were contacted were informed about the purpose of the exercise and the confidentiality measures in place. They were also informed that their responses would be confidential. Those who declined to participate and did not respond to the invitation were not contacted further. A positive response to the invitation was considered as consent to participate in the survey. The survey responses were pseudonymized. All feedback and contributions were treated with the utmost confidentiality.

The recruited experts comprised of representatives from the following groups: (i) patient/patient groups affected by PCa, (ii) healthcare providers who were directly or indirectly involved with the PCa screening programme, and (iii) public policy makers, programme managers and academics in (PCa) cancer screening.

Definitions and method of calculation of the KPIs were described in the survey and the experts were asked for agreement with a binary (yes/no) answer for definitions and calculation. If they did not agree to the definition and calculation, experts were asked to suggest alternative definitions and calculation (free text option was provided for all KPIs). In addition, experts were asked to rate the feasibility and importance of the KPIs based on a 5-point Likert Scale ranging from 1 to 5. Experts were given an option for expressing their comments on any aspects of selection of the indicators as free text in the survey form. It was pre-decided that an arbitrary cut-off of 75% for definition and calculation and Likert Scale values of 4 (agree) and 5 (strongly agree) for feasibility and importance would be used to decide on agreement.

Deliberations on KPIs selected through the survey

An expert meeting was held online in December 2023 hosted by the International Agency for Research on Cancer (IARC/WHO) and the PRAISE-U Consortium to discuss the outcomes of the survey. A further engagement session with pilot sites on feasibility and relevance was held during a PRAISE-U consortium meeting. The final list of KPIs was based on consensus of all the participating experts.

Role of the funding source

The funders of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report.

Results

The scoping review resulted in a total of 847 records. After removing duplicates, the number of unique records was 506. After title/abstract screening 23 articles were assessed for eligibility and 10 were included for full text review. Two reviewers (DS & BS) then independently confirmed the eligibility of the literature and extracted the indicators based on full text assessment. A total of thirty-four (34) indicators were extracted with definitions from this literature search.

From the review of grey literature, 28 KPIs were extracted from screening recommendations and clinical audit data on quality indicators from three countries (Lithuania, Sweden, Scotland) and 23 KPIs were extracted from different trial websites. Eleven indicators were selected from grey literature search after removing duplicates for further review.

From the three streams, 63 KPIs were identified and were reviewed by an internal panel of cancer experts at IARC. 22 indicators were finalized for review by the PRAISE-U expert group for their agreement and a rating exercise (Table 1). Each indicator was defined with a numerator and denominator and was adapted when necessary to the PCa screening framework. For the sake of harmonization, the definitions mirrored the indicators for other cancer sites included in CanScreen-ECIS project as much as possible.

Survey outcome

A total of 31 experts (of the 40 invited) expressed an interest in participating in the survey. Of those, 23 completed the survey (completion proportion = 74%). The survey completion proportion was evenly distributed in most of the areas of expertise. The background

Selected performance indicators	Phase
KPI 1 Invitation coverage	Invitation
KPI 2 Participation rate	
KPI 3 Examination coverage	Screening and risk assessment
KPI 4 Retention rate	
KPI 5 Test result	
KPI 6 Positive predictive value screening test	
KPI 7 False positive rate	
KPI 8 Opportunistic testing	
KPI 9 Compliance with risk assessment	
KPI 10 Complications of screening test	
KPI 11 Interval between screening steps	
KPI 12 Episode sensitivity	
KPI 13 Compliance with further assessment	Further risk assessment
KPI 14 Complications of further Assessment	
KPI 15 Radiologist's assessment of MRI	
KPI 16 Compliance with biopsy	Diagnosis, treatment, and follow up
KPI 17 Detection rate	
KPI 18 Compliance with treatment	
KPI 19 Crude incidence rate	
KPI 20 Cause-Specific mortality rate	
KPI 21 Interval cancer rate	
KPI 22 Active surveillance	

Table 1: **Key performance indicators for PCa screening selected through systematic review process.**

of the experts invited and accepted to participate in the survey is illustrated in Fig. 4.

The agreement of the experts on definitions and calculations of the indicators and their rating of feasibility, and importance of the indicators are summarized in Table 2.

More than 75% of the experts agreed on definitions of 14 KPIs and on the calculation of 11 KPIs. Over 75% of the experts agreed or strongly agreed on the feasibility and the importance of 13 KPIs. Seven KPIs were accepted by at least 75% experts as appropriately defined and calculated, as well as feasible and important.

Deliberations on KPIs for PCa screening

During the expert meeting, 7 KPIs (KPI 1: Invitation Coverage, KPI 2: Participation rate, KPI 3: Examination coverage, KPI 5: Test result, KPI 16: Compliance with biopsy, KPI 17: Detection rate, KPI 20: Cause-specific mortality) which were accepted by at least 75% experts as appropriately defined and calculated, important and feasible to be estimated in PCa screening programmes received unanimous acceptance, warranting no additional deliberation. In addition, the editorial error on definition and calculation of KPI 19: Crude Incidence Rate in the survey was acknowledged and full consensus was obtained for this indicator as well.

Rest of the KPIs were discussed at the online meeting, and consensus was obtained for all except KPI 12: Episode Sensitivity. Experts agreed to remove this indicator from the framework. In the feedback on the set of indicators, experts noted additional areas to potentially include. An additional KPI on Pathology was proposed as following; KPI International Society of Urological Pathology (ISUP) Tumour Grade Distribution of the screened population. This KPI received unanimous agreement among the experts.

Following a further engagement with pilot sites on feasibility and relevance during the PRAISE-U consortium meeting held in February 2024, the group reached a consensus to combine KPI 10 (Complication of screening test) and KPI 14 (Complications of further assessment) into a single indicator 'Complications in screening procedure'.

Final set of KPIs

Following the review, survey, and deliberations, 21 KPIs were finalized to be piloted in the PRAISE-U project (Table 3).

Discussion

Using a systematic process of database search and concensus of leading experts in PCa screening and management, we described the process and outcomes of developing 21 KPIs for monitoring PCa screening programmes in the EU which will be tested in the five PRAISE-U pilot sites. The resulting 21 KPIs cover the different phases of the screening programme, including invitation, screening test, risk stratification, diagnosis, and also on treatment, harms, and impact. The current KPIs compare favourably to existing frameworks for monitoring other cancers in the EU as well as those

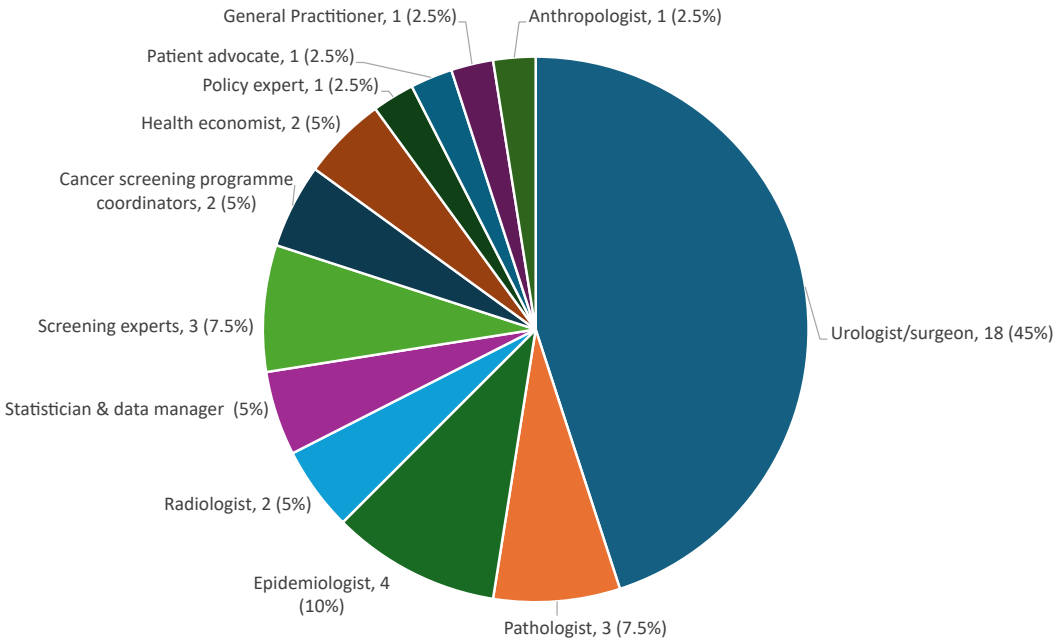

Fig. 4: Background of experts invited and accepted to participate in the survey.

No.	Description	Definition	Calculation	Feasibility	Importance
		n (%) agreed		n (%) strongly agreed/agreed	
KPI 1	Invitation coverage	23 (100%)	22 (96%)	20 (87%)	22 (96%)
KPI 2	Participation rate	21 (91%)	21 (91%)	23 (100%)	21 (91%)
KPI 3	Examination coverage	18 (78%)	21 (91%)	21 (91%)	19 (83%)
KPI 4	Retention rate	20 (87%)	15 (65%)	14 (61%)	18 (78%)
KPI 5	Test result	22 (96%)	18 (78%)	22 (96%)	21 (91%)
KPI 6	PPV of screening test	16 (70%)	16 (70%)	20 (87%)	22 (96%)
KPI 7	False positive rate	17 (74%)	18 (78%)	22 (96%)	22 (96%)
KPI 8	Opportunistic testing	18 (78%)	17 (74%)	9 (39%)	17 (74%)
KPI 9	Compliance with risk assessment	18 (78%)	20 (87%)	18 (78%)	17 (74%)
KPI 10	Complications in screening procedure	18 (78%)	18 (78%)	13 (57%)	16 (70%)
KPI 11	Interval between screening steps	18 (78%)	N/A	18 (78%)	18 (78%)
KPI 12	Episode sensitivity	16 (70%)	15 (65%)	11 (48%)	16 (70%)
KPI 13	Compliance with further assessment	16 (70%)	16 (70%)	21 (91%)	21 (91%)
KPI 14	Complications of further assessment	17 (74%)	16 (70%)	14 (61%)	17 (74%)
KPI 15	Radiologist 's assessment of MRI	18 (78%)	17 (74%)	17 (74%)	18 (78%)
KPI 16	Compliance with biopsy	20 (87%)	20 (87%)	21 (91%)	22 (96%)
KPI 17	Detection rate	18 (78%)	19 (83%)	22 (96%)	21 (91%)
KPI 18	Compliance with treatment	16 (70%)	21 (91%)	16 (70%)	15 (65%)
KPI 19	Crude Incidence rate	10 (43%)	14 (61%)	19 (83%)	19 (83%)
KPI 20	Cause -specific mortality	22 (96%)	18 (78%)	18 (78%)	20 (87%)
KPI 21	Interval cancer rate	19 (83%)	11 (48%)	14 (61%)	20 (87%)
KPI 22	Active surveillance	17 (74%)	16 (70%)	17 (74%)	15 (65%)

Color indication in the table: dark green: agreement of 75% or more; light green: agreement of 60-74%; yellow: agreement of 50-69%; red: agreement of less than 50%.

Table 2: **Agreement of experts on definition and calculation of key performance indicators and their feasibility and importance in the context of PCa screening in the EU.**

developed by the CanScreen-ECIS for breast, cervical and colorectal cancer screening, which additionally proposed to monitor the programmes by various measures of inequity.[13] However, our process identified a number of additional indicators that may be important to consider and are unique to PCa screening, such as the proportion of patients who undergo active surveillance and the tumour grade distribution of PCa detected through screening.

The strength of this process is our stepwise methodology that includes a comprehensive review of literature, multiple sources of identifying of KPIs including national screening programs and ongoing EU projects, as well as an expert consultation, which is consistent with previous research on selecting monitoring and evaluation indicators.[13–17] The indicators and definitions were agreed by a group of experts with broad knowledge in the relevant areas through a rating and ranking exercise that also facilitated in eliminating indicators deemed not useful for PCa screening. Structured feedback was obtained from these experts. To limit social desirability bias, we highlighted that the indicators needed constructive feedback for revision as well as anonymized the responses. While seven of the indicators scored highly (more than 75% agreement) against all predetermined criteria, there were certain scores that ranged widely and text responses

No.	Description	Definition
KPI 1	Invitation coverage	The proportion of eligible individuals from the target population personally invited for screening within a given timeframe. • Numerator (N): Number of individuals invited to be screened. • Denominator (D): Target population.
KPI 2	Participation rate	The proportion of invited individuals who have undergone a screening test within a given timeframe following an active invitation. • Numerator (N): Number of invited individuals screened in a given timeframe. • Denominator (D): The number of individuals invited in a given timeframe.
KPI 3	Examination coverage	The proportion of eligible individuals from the target population who had the recommended screening test within a given timeframe. • Numerator (N): Number of individuals in the target population who had the recommended test within a given time frame. • Denominator (D): Target population (entire population) for that same timeframe.
KPI 4	Retention rate	The proportion of eligible individuals re-screened after a negative screening within a specified interval. • Numerator (N): Number of individuals returning to agreed screening algorithm. • Denominator (D): The number of individuals eligible for subsequent screening adjusted for losses due to death or cancer diagnosis.
KPI 5	Test result	The results of the screening test. • Numerator (N): Number of men with PSA result of "<1 ng/ml", "1–3 ng/ml" or ">3 ng/ml". • Denominator (D): Total number of individuals having screening tests performed within the programme.
KPI 6	PPV of screening test to detect any prostate cancer (6.1) and clinically significant prostate cancers (6.2)	KPI 6.1–The proportion of individuals who have histopathologically confirmed PCa to all those who had positive test results (with PSA result of >3 ng/ml) *(including healthy subjects who were incorrectly diagnosed to have prostate cancer)* • Numerator (N): Number of individuals who returned a positive screening test (with PSA result of >3 ng/ml) that underwent workup and diagnostic procedures and were diagnosed with PCa on histopathology in a given timeframe. • Denominator (D): Number of individuals who underwent workup and diagnostic procedures to follow up a positive screening test (with PSA result of >3 ng/ml) within a given timeframe and had available diagnostic information. KPI 6.2–The proportion of individuals who have histopathologically confirmed clinically significant PCa to all those who had positive test results (with PSA result of >3 ng/ml) *(including healthy subjects who were incorrectly diagnosed as clinically significant PCa)*. • Numerator (N): Number of individuals who returned a positive screening test (with PSA result of >3 ng/ml) that underwent workup and diagnostic procedures and were diagnosed with a clinically significant PCa on histopathology in a given timeframe. • Denominator (D): Number of individuals who underwent workup and diagnostic procedures to follow up a positive screening test (with PSA result of >3 ng/ml) within a given timeframe and had available diagnostic information.
KPI 7	False positive rate to detect any PCa (7.1) and clinically significant PCa (7.2)	7.1 The proportion of screened individuals who received a positive screening result in which **no cancer** was detected after workup and diagnostic procedures. • Numerator (N): Number of screened individuals who received a positive screening result (>3 ng/ml) in which no target cancer was detected after workup and diagnostic procedures. • Denominator (D): Number of men with positive screening test result (PSA >3 ng/ml). 7.2 The proportion of screened individuals who received a positive screening result in which **no clinically significant cancer** was detected after workup and diagnostic procedures. • Numerator (N): Number of screened individuals who received a positive screening result (>3 ng/ml) in which **no clinically significant cancer** was detected after workup and diagnostic procedures. • Denominator (D): Number of men with positive screening test result (PSA >3 ng/ml).
KPI 8	Opportunistic testing	The proportion of individuals screened outside the population-based screening programme. • Numerator (N): Number of individuals undergoing screening test outside the population-based screening programme within a specified time frame. • Denominator (D): Target population within the same time frame.

(Table 3 continues on next page)

No.	Description	Definition
(Continued from previous page)		
KPI 9	Compliance with risk assessment	The proportion of individuals from the screened population undergoing risk assessment (as per protocol of the programme). • Numerator (N): Number of individuals who undergo a risk assessment (as per protocol of the programme) from the screen population. • Denominator (D): Number of individuals referred for risk assessment from the screened population.
KPI 10	Complications in screening procedure	The proportion of individuals reporting at least one complication incurred during the screening procedure. • Numerator (N): The number of individuals reporting at least one complication related to screening (any complication requiring additional visit to a health professional and/or hospitalization) within 2 weeks of the procedure. • Denominator (D): The number of individuals screened within the programme.
KPI 11	Interval between screening steps	Time from PSA test sample collection to histopathological confirmation of a malignant diagnosis (further disaggregated by different procedures) to treatment initiation: 1. Time from PSA test result to undergoing MRI (for those requiring MRI). 2. Time from MRI to histopathology result. 3. Time from histopathological confirmation of malignancy to onset of treatment (including active surveillance).
KPI 12	Compliance with further assessment	The proportion of individuals referred for diagnostic work up based on elevated PSA and risk assessment (as per protocol of the programme) attending all workup and diagnostic procedures assigned. • Numerator (N): Number of individuals who attended diagnostic workup after a positive screening test and risk assessment (as per protocol of the programme). • Denominator (D): Number of individuals referred for diagnostic workup procedures after a positive screening test and risk assessment (as per protocol of the programme).
KPI 13	Radiologist's assessment of MRI	Radiologist assessment of MRI. • Numerator (N): Number of MRIs assessed as PIRADS score of 1–2,3,4–5 in men with PSA <10 ng/ml. • Denominator (D): Number of MRIs assessed in men with PSA <10 ng/ml.
KPI 14	Compliance with biopsy	Proportion of eligible men who underwent biopsy. • Numerator (N): Number of men who underwent biopsy. • Denominator (D): Number of men who were eligible for biopsy.
KPI 15	Detection rate of PCa	The proportion of individuals with a screen positive test who underwent further assessment with histopathologically proven cancer detected [expressed per 1000 individuals screened]. • Numerator (N): Number of individuals diagnosed with prostate cancer. • Denominator (D): Number of individuals screened within the programme.
KPI 16	Tumour grade distribution	Proportion of prostate cancers detected after positive screening test reported as ISUP grade (group) 1, 2, 3 and 4–5. • Numerator: Number of biopsy diagnosed prostate cancers reported as ISUP grade 1, 2, 3 and 4–5 in the screened population. • Denominator: Number of screened men who were diagnosed with prostate cancer.
KPI 17	Compliance with treatment	The proportion of individuals with cancer diagnosed within the screening programme referred for treatment who initiated treatment (including active surveillance, when applicable). • Numerator (N): Number of individuals with cancer diagnosed within the screening programme referred for treatment who initiated treatment (including active surveillance, when applicable). • Denominator (D): The number of individuals with cancer diagnosed within the screening programme referred for treatment.
KPI 18	Crude Incidence rate	The number of new cases of PCa arising in a specified population (expressed per 100,000) within a time frame of 12-months. • Numerator (N): Number of new cases of prostate cancer in a given timeframe. • Denominator (D): Entire population.
KPI 19	Cause-specific mortality	The mortality from prostate cancer (primary cause of death only) per 100,000 target population within a time frame of 12-months. • Numerator (N): Number of prostate cancer deaths in a 12-month period. • Denominator (D): Entire population.

(Table 3 continues on next page)

No.	Description	Definition
(Continued from previous page)		
KPI 20	Interval cancer rate	The proportion of individuals with a negative screening test or a positive screening test but negative further assessment results who were diagnosed with prostate cancer prior to the next screening round. • Numerator (N): Number of men who returned either i) negative screening test or, ii) negative further assessment (stratified as low risk) or, iii) negative biopsy results who were diagnosed with prostate cancer prior to their next screen. • Denominator (D): Number of men who returned either i) negative screening test or, ii) negative further assessment or, iii) negative biopsy results.
KPI 21	Active surveillance	The proportion of patients recommended AS due to low/low-intermediate risk PCa who accepted and initiated AS. • Numerator (N): Number of patients initiating AS within a specified time frame after being recommended AS due to low/low-intermediate risk PCa. • Denominator (D): Number of patients recommended AS due to low/low-intermediate risk PCa within a specified timeframe.

Table 3: **Final key performance indicators for prostate cancer screening effectiveness.**

on feedback included constructive critique of the indicators (Table 2).

Our work on developing KPIs for PCa screening in the EU holds significance for several reasons. Firstly, the KPIs were developed to ensure both process and outcomes of programme effectiveness. By monitoring KPIs that directly measure impact of programme effectiveness, such as "crude incidence rate" and "cause-specific mortality," programmes can assess their success in achieving their core objectives. For process indicators, well-defined KPIs allow programme managers to systematically track performance across various stages of the screening pathway. This enables early identification of areas where a programme might be excelling or falling short. For example, "compliance with biopsy" reveals if a programme is encountering difficulties in translating positive screening tests into biopsies for confirmatory diagnosis. In the conceptual framework, we have identified men with different risks who can be recommended for active surveillance or treatment group (Fig. 2) based on the EAU position on PCa screening and Prostate cancer Research International: Active Surveillance (PRIAS) guidelines[10,18] which will be also be captured by the KPIs.

The ethical aspects of collecting information on key performance indicators has been approved by the respective ethics committees at each of the pilot sites involved in the PRAISE-U project.

Standardization and benchmarking of PCa screening across the EU in an early stage as programmes are piloted are critical due to the potential for informing future programme development and optimization strategies.[19,20] For example, a high interval cancer rate could reveal a high number of cases missed by the given screening strategy and can prompt investigations into optimizing screening protocol including risk stratification methods or screening intervals.

It is also important to acknowledge the variations between regional healthcare systems in the EU.[21] These harmonized indicators will serve as a tool for standardized programme evaluation despite this variation. Collection of information in a unified manner across countries to estimate the values of the KPIs will be crucial. Pilot testing in multiple countries through the PRAISE-U project will play a crucial role in refining the KPIs and ensuring their feasibility within diverse settings. The findings from this exercise can further inform the development of the European Quality Assurance Scheme for Prostate Cancer Services, similar to existing schemes for breast cancer[22] and those under development for colorectal and cervical cancers.[23]

Some limitations need to be considered. Firstly, the feasibility and the relevance of some KPIs may vary depending on the specific context of the screening programme. Further piloting and evaluation of the KPIs are needed to ensure their generalizability beyond the PRAISE-U pilot sites. It is therefore imperative to acknowledge that the specific KPIs employed might need contextualization based on a programme's unique strategy, target population, recall and referral mechanisms. Given the availability of easy access to PSA testing outside the screening program, there is a risk of a high non-response rate or selective participation, particularly among men from lower socio-economic backgrounds. This could lead to selection bias within the screening program. Next, the KPIs focus on screening programme effectiveness and do not include KPIs for cost-effectiveness. A recent systematic review indicated risk-stratified prostate cancer screening programme has the potential to be cost-effective. The current study collects data that will allow measurement of cost-effectiveness as part of its monitoring and evaluation framework. Finally, there is a possibility of missing KPIs published in non-English language in peer-

reviewed journals. However, our comprehensive search of grey literature, including in non-English sources, web searches of existing trials, existing organized testing or opportunistic screening programmes, and any mention of recommendations for PCa screening minimized the likelihood of missing relevant KPIs.

In conclusion, the development of robust KPIs for PCa screening programmes serves as a powerful tool for programme evaluation and improvement. By systematically monitoring performance across various aspects of the screening pathway in the five pilot sites, these indicators empower programmes to ensure effectiveness, optimize service delivery, and ultimately contribute to better patient outcomes within the PRAISE-U project, but may also be applied in future screening initiatives.

Contributors

DS, AC, and PB conceptualized and designed the study. DS and AC accessed and verified the data and did the formal analysis. DS and AC wrote the report. DS, AC, ACL, IMM, and PB contributed to data interpretation. All authors critically reviewed the manuscript for important intellectual content and drafting of the manuscript. All authors had full access to all the data in the study and had final responsibility for the decision to submit for publication.

Data sharing statement

The data that support the findings of this study are available on request.

Declaration of interests

None declared.

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Appendix A. Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.eclinm.2024.103022.

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