Assessment report: MT770 ProKnow cloud-based system for radiotherapy data archiving, communication and management

EAG team: Rosalyn Parker, Kim Keltie, Rachel O'Leary, Emma Belilios, Andrew Sims, Sonia Garcia Gonzalez-Moral, Fiona Beyer, Gurdeep S Sagoo, Sedighe Hosseinijebeli, Luke Vale

Project lead(s): Rosalyn Parker

Information specialist: Sonia Garcia Gonzalez-Moral, Fiona Beyer

Clinical evidence reviewer: Rosalyn Parker, Kim Keltie, Rachel O'Leary, Andrew Sims

Economic evidence reviewer: Gurdeep S Sagoo, Sedighe Hosseinijebeli, Luke Vale

Communications Lead: Emma Belilios

EAG sign-off: Andrew Sims

Version number	Brief description of changes	Author/reviewer (e.g. J Smith)	Date (DD/MM/YY)	Date sent to NICE (if applicable)
0.01	Copying content from draft previously started by E Belilios, and adding to technology and clinical sections Adding content to report	R O'Leary R Parker	14/10/2022 26/10/2022	
0.02	Adding responses from Company, QA	K Keltie	01/11/2022	
0.03	Continuing QA Adding content to clinical evidence sections	K Keltie R Parker	09/11/2022 09/11/2022	
0.04	Continuing QA Adding content to clinical evidence sections	K Keltie R Parker	15/11/2022 15/11/2022	
0.05	Adding literature search write up	S Garcia Gonzalez-Moral	23/11/2022	

Version number	Brief description of changes	Author/reviewer (e.g. J Smith)	Date (DD/MM/YY)	Date sent to NICE (if applicable)
	Continuing QA Adding to summaries Economic evidence summary Literature search oversight Adding to economic section	K Keltie R Parker S Hosseinijebeli F Beyer G Sagoo	23/11/2022 24/11/2022 24/11/2022 25/11/2022 28/11/2022	
0.6	Review	K Keltie R Parker L Vale	01/12/2022	
0.7	Adding to economic section	S Hosseinijebeli, G Sagoo	01/12/2022	
1.0	Version for NICE	K Keltie R Parker		01/12/2022
1.01	Adding expert comments Addressing reviewer comments	E Belilios K Keltie	02/12/2022 05/12/2022	
1.02	Review Addressing reviewer comments Adding expert comments Adding to economic section Review of economic literature search write up	AJ Sims K Keltie R Parker G Sagoo S Garcia Gonzalez-Moral	05/12/2022 07/12/2022 13/12/2022 14/12/2022 15/12/2022	

Version number	Brief description of changes	Author/reviewer (e.g. J Smith)	Date (DD/MM/YY)	Date sent to NICE (if applicable)
1.03	Review	R Parker, K Keltie	16/12/2022	
1.04	Clean up Review	K Keltie, R Parker AJ Sims, L Vale	16/12/2022 19/12/2022	
1.05	Addressing reviewer comments	K Keltie, R Parker, G Sagoo	19/12/2022	
1.06	Removing comments Adding response from RCR	K Keltie, R Parker	20/12/2022	
2.00	Clean version for NICE	K Keltie	20/12/2022	20/12/2022
2.01	Adding response from RTDS	K Keltie	20/12/2022	
2.02	Formatting and pre-submission checks	E Belilios	21/12/2022	
2.03	Merging changes	R Parker	22/12/2022	
2.04	Final review	K Keltie	23/12/2022	
3.00	Final version	K Keltie, R Parker	23/12/2022	23/12/2022
4.00	Updated redaction	K Keltie	05/01/2023	05/01/2023

NATIONAL INSTITUTE FOR HEALTH AND CARE EXCELLENCE

Early Value Assessment

MT770 ProKnow cloud-based system for radiotherapy data archiving, communication and management

External Assessment Group report

Produced by: Newcastle External Assessment Group (EAG)

Authors: Rosalyn Parker, Evaluation Healthcare Scientist, NuTH
Kim Keltie, Lead Healthcare Scientist, NuTH
Rachel O'Leary, Clinical Scientist, NuTH
Emma Belilios, Project Coordinator, NuTH
Sonia Garcia Gonzalez-Moral, Research Associate, Newcastle University
Fiona Beyer, Senior Research Associate, Newcastle University
Gurdeep S Sagoo, Senior Lecturer (Health Economics), Newcastle University
Sedighe Hosseinijebeli, Research Associate (Health Economics), Newcastle University
Luke Vale, Professor of Health Economics, Newcastle University
Andrew Sims, Head of Department, NMPCE, NuTH

Correspondence to: Andrew Sims
Northern Medical Physics and Clinical Engineering,
NMPCE (Medical Physics, NCCC Level 2)
Freeman Hospital
Freeman Road,

High Heaton,
Newcastle upon Tyne
NE7 7DN
nuth.nmpce.hta@nhs.net

Date completed: 23 December 2022

Contains confidential information: Yes

Number of attached appendices: 4

Purpose of the assessment report

The purpose of this External Assessment Group (EAG) report is to review the evidence currently available for included technologies and advise what further evidence should be collected to help inform decisions on whether the technologies should be widely adopted in the NHS. The report may also include additional analysis of the submitted evidence or new clinical or economic evidence. NICE has commissioned this work and provided the template for the report. The report forms part of the papers considered by the Medical Technologies Advisory Committee when it is making decisions about the early value assessment.

Declared interests of the authors

Description of any declared interests with related companies, and the matter under consideration. See NICE's Policy on managing interests for board members and employees.

None.

Acknowledgements
Tasia Aghadiuno, Clinical Oncology ST5, Velindre University NHS Trust

Alex Beardmore, Clinical Specialist Radiographer, Newcastle upon Tyne Hospitals NHS Foundation Trust

Ian Boon, Consultant Clinical Oncologist, University Hospital Southampton NHS Foundation Trust

John Byrne, Deputy Head of Radiotherapy Physics, Newcastle upon Tyne Hospitals NHS Foundation Trust

Stephen Tozer-Loft, Head of Radiotherapy Physics, Sheffield Teaching Hospitals NHS Foundation Trust

Samantha Warren, Consultant Clinical Scientist, Newcastle upon Tyne Hospitals NHS Foundation Trust

Amanda Webster, Therapy Radiographer, University College London Hospitals NHS Foundation Trust

Nicky Whilde, Chair of ProKnow Steering Group

Responsibility for report

The views expressed in this report are those of the authors and not those of NICE. Any errors are the responsibility of the authors.

Contents

Abbreviations

Term	Definition
AI	Artificial intelligence
CADTH	Canadian Agency for Drugs and Technologies in Health
COSD	Cancer Outcomes and Services Dataset
CT	Computed tomography
DES	Discrete event simulation
DICOM	Digital Imaging and Communications in Medicine
Dmax	Maximum point dose
EAG	External Assessment Group
EBRT	External beam radiotherapy
EMR	Electronic medical record
GTV	Gross tumour volume
Gy	Gray
HES	Hospital Episode Statistics
IQR	Interquartile range
IMRT	Intensity modulated radiotherapy
IPEM	Institute of Physics and Engineering in Medicine
Linac	Linear accelarator
MAUDE	Manufacturer and User Facility Device Experience
MDT	Multi-disciplinary Team
MHRA	Medicines & Healthcare products Regulatory Agency
MRI	Magnetic resonance imaging
NDRS	National Disease Registration Service
NHSE	National Health Service England
NICE	National Institute for Health and Care Excellence
NR	Not reported
OAR	Organs at risk
OR	Operations research
PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analyses
PSA	Prostate specific antigen
PSSRU	Personal Social Services Research Unit
PTV	Planning target volume
QA	Quality assurance
RCR	Royal College of Radiologists
RTDS	National Radiotherapy Dataset
RTTT	Ready-to-treat to treatment time
SaMD	Software as a medical device
SABR	Stereotactic ablative radiotherapy
SACT	Systemic Anti-Cancer Therapy
SBRT	Stereotactic body radiotherapy
SD	Standard deviation
TROG	Tasman Radiation Oncology Group
VMAT	Volumetric modulated arc therapy
vs	Versus

Executive summary

Quality and relevance of clinical evidence

ProKnow (Elekta) is a cloud-based software as a medical device (SaMD) that can be used to support radiotherapy treatment planning across all cancers suitable for external beam radiotherapy, and facilitates collaborative working, including peer review of radiotherapy treatment plans.

The EAG included 12 publications in the clinical evidence (6 of which were conference abstracts), 4 explicitly reported the inclusion of UK centres. Only 5 of the 9 outcomes within the NICE Final Scope had relevant published evidence with limitations across all. It is feasible to collect prospective and comparative evidence, but such evidence is so far lacking. Randomised evidence is unlikely to be forthcoming because of the widespread commissioning of ProKnow across the NHS in England. ProKnow may facilitate peer review of treatment plans, however there are no benchmark data currently available from the NHS.

Quality and relevance of economic evidence

No economic studies specific to ProKnow were identified from the literature. The EAG identified 3 discrete event simulation studies, which examined the impact of clinical resource on the average waiting time for patients to receive their radiotherapy treatment; this modelling approach may be applicable in future economic evaluations of ProKnow. Seventeen additional studies reported the proportion of radiotherapy treatment plans requiring changes following peer review, ranging between 2% and 74%; which highlights variation in standard care and the need for prospective data collection.

Evidence gap analysis

In April 2022, as part of the Radiotherapy Transformation Programme, NHS England commissioned a 3-year funded pilot of ProKnow across 49 specialist cancer centres, which could yield data to fill some of the evidence gaps. To inform future economic modelling, future data collection should focus on quantifying the number of radiotherapy treatment plans and the proportion that undergo peer review, and resource use data such as staff time and band needed for peer review, the

proportion of treatment plans requiring change and the magnitude of that change, and uploading time. Future analysis could also focus on the use of ProKnow reducing variation in practise (demonstrating or monitoring staff competency, improved quality of treatment plans through ProKnow scorecards, or surrogate markers such as dose to organs at risk), and improving knowledge sharing among healthcare professionals involved in treatment planning through evaluating the impact of these outcomes on patient outcomes through data linkage to national routine databases.

1. Decision problem

The EAG has provided minor clarifications to the decision problem specified in the Final Scope (NICE MT770 Final Scope, 2022), Table 1.

Table 1: Scope of the decision problem

Decision problem	Scope	EAG comment
Population	People having image-guided planned radiotherapy with 3D dose distribution	The EAG note that this may include patients receiving brachytherapy. The EAG recognise that for evidence relating to the use of ProKnow to facilitate quality assurance of radiotherapy treatment the population would be the services delivering radiotherapy. For evidence relating to the use of ProKnow as a training tool, the population reflected in the scope would be the radiotherapy professionals involved with treatment planning.
Intervention	ProKnow (includes ProKnow DS, ProKnow PS, and ProKnow CA)	No variation.
Comparator(s)	Standard care	The EAG recognise there is variation in standard care across the NHS, with most centres implementing local protocols for planning peer review. The EAG will consider local standard care protocols, including where planning peer review is not used, as comparators.
Outcomes	The outcome measures to consider include: • Impact on radiotherapy treatment planning quality assurance, including surrogate, qualitative, and quantitative measures such as: - Structural changes to radiotherapy treatment plans - Dose prescription changes - Dose volume distributions - Scorecards • Usability/user experience • Ease of retrieving and archiving patient data	No variation. ProKnow is compatible with all types of external beam radiotherapy treatment planning software systems that are used across the NHS. To clarify, the EAG have therefore considered the impact of the use of ProKnow on treatment planning time and time to treatment only.

Decision problem	Scope		EAG comment
	• Radiotherapy treatment planning time (including difference in time to start of treatment) • Number of internal and external peer reviews performed • Impact on staffing and treatment planning resources • Impact of the system on clinical oncology training (including training of all healthcare professionals contributing to radiotherapy treatment planning) • Ability for data linkage to national registries (including change in the number of treatment plans added to national registries) • Reduction in inequality of access		
Economic analysis	A health economic decision model will be developed comprising a cost-comparison analysis. The time horizon should be long enough to reflect all important differences in costs or outcomes between the technologies being compared. Costs will be considered from an NHS and Personal Social Services perspective. Sensitivity and scenario analysis should be undertaken to address the relative effect of parameter or structural uncertainty on cost-comparison estimates.		No variation. The EAG recognise that evidence may be limited and therefore restrict the feasibility of conducting analyses and the robustness of economic conclusions drawn.
Other considerations	49 specialist cancer centres in the NHS currently have access to ProKnow. It is being used as part of the Radiotherapy Transformation Programme, aiming to improve the quality and reducing the variability of radiotherapy service delivery across England.		The EAG will consider the directive from NHS England regarding the recommended use of ProKnow across the NHS as part of this programme.
Special considerations, specifically related to equality	Are there any people with a protected characteristic for whom this device has a particularly disadvantageous impact or for whom this device will have a disproportionate impact on daily living, compared with people without that protected characteristic?	No	No variation.
	Are there any changes that need to be considered in the scope to eliminate unlawful discrimination and to promote equality?	No	
	Is there anything specific that needs to be done now to	No	

Decision problem	Scope		EAG comment
	ensure the Medical Technologies Advisory Committee will have relevant information to consider equality issues when developing guidance?		
Any other special considerations	Not applicable.		No variation.
Related NICE recommendations	None.		No variation.
Related National Policy	The NHS Long Term Plan, 2019. NHS Long Term Plan Royal College of Radiologists (2017) Radiotherapy target volume definition and peer review		The EAG note that the Royal College of Radiologists updated the 2017 guidance in October 2022: Radiotherapy target volume definition and peer review second edition.

2. Overview of the technology

ProKnow (Elekta) is a cloud-based software as a medical device (SaMD) that can be used to support radiotherapy treatment planning. ProKnow can be used to view treatment plan information, visualise images and the structures they contain, and inspect dosimetric data, such as dose volume histograms and dose distributions, and custom plan quality metrics can be extracted, such as local radiotherapy control, survivorship, and side effects. An advantage of ProKnow is that it allows teams to work together to mark the areas of interest (for example, the target volume for treatment, and organs at risk) on images, in a process known as 'contouring'. This can be done from anywhere, without the need for a dedicated workstation, and therefore allows collaboration and peer review of treatment plans between centres using ProKnow. The functions of the software can be used for retrospective and prospective cases and can be used on single patient datasets or on collections of datasets. ProKnow works with any type of radiotherapy equipment and uses the Digital Imaging and Communications in Medicine (DICOM) standard, so it can be used across existing NHS systems.

ProKnow comprises 3 separate modules, each with its own functionalities:

- ProKnow DS is the database system that is used for importing and analysing patient data.
- ProKnow CA is a contouring accuracy tool that allows users to practice, study, and improve anatomical contours.
- ProKnow PS is a platform for creating and comparing radiotherapy treatment plans.

Initial online training is provided by the Company and is expected to take radiotherapy treatment planners no more than 4 hours to complete. Further short (1 to 2 hour) sessions are run regularly on Microsoft Teams, and all training is included within the cost of the technology (Appendix D1). The Company also confirmed that ProKnow is provided as a Software as a Service and therefore all maintenance and upgrades are included.

The Company has confirmed that ProKnow was commercialised in February 2020, and CE marked since April 2020 as a class I medical device for radiotherapy data archiving, communication, and management (Appendix D1). As a web-based cloud-based system, ProKnow has undergone many version and release updates prior to its commercialisation date. The Company note that the software iterations have focused on permissions, DICOM upload capabilities, and plan comparison (Appendix D1).

3. Clinical context

Radiotherapy uses radiation to kill cells, such as cancer cells. In 2019, there were 113,851 courses of radiotherapy delivered in the NHS in England (Powell et al. 2022). Estimations of the proportions of patients diagnosed with cancer who are treated with radiotherapy vary;

- Cancer Research UK reported 27% between 2013 and 2014,
- Public Health England reported 31% between 2013 and 2016, and
- Radiotherapy UK reports that over 50% of cancer patients need radiotherapy as part of their treatment.

The EAG notes that these proportions may include brachytherapy and radionuclide therapy, which are not planned with the same software as external beam radiotherapy. Nevertheless, the numbers of patients where ProKnow could be used is likely to be sizable.

Treatment planning includes clinical oncologists, radiographers, dosimetrists, and medical physicists, with the qualified clinical oncologist taking overall responsibility for planning and final sign off. Peer review is an important step in treatment planning, to make sure the proposed plan will deliver safe and effective treatment, and to identify issues that could affect quality of care. The peer review process is also intended to allow standardisation, reduce variation in practise, and improve knowledge sharing among healthcare professionals involved in treatment planning. In most NHS centres, the treatment planning team uses local protocols for peer review. Updated guidance from the Royal College of Radiologists (RCR) on radiotherapy target volume definition and

peer review (2022), states that departments should have agreed radiotherapy protocols for each tumour subsite. These protocols should include target volume guidelines, be agreed by the departments working together, and should be standardised across, and ratified by, operational delivery networks (aligned with the regional Cancer Alliances), or equivalent bodies in the devolved nations. As well as across the local operational delivery network, protocols should also be standardised nationally or internationally, if possible. Recommendations for peer review include that each department should have an agreed process, and that it should be used prospectively when the defined target volume contours rely heavily on individual judgement or do not conform to the departmental protocol (Recommendation 6). For other cases, the RCR guidance recommends retrospective review of a proportion of defined contours for quality assurance (for example, 10%). The guidance also highlights examples of peer review methods used in UK NHS practise including in person, using a Microsoft Access database, over videoconferencing, and using a contouring platform (unspecified). Six Clinical Experts noted that currently peer review can take place in person, and using videoconferencing, 1 Expert noted the use of radiotherapy treatment planning software. Another Expert also noted the use of telephone when conducting peer review, although the EAG note that this method may not allow synchronous visualisation of the treatment plan (Appendix D2b). The updated peer review guidance from the RCR (2022) recommends that sufficient protected time for peer review should be available to radiotherapy professionals to prevent delays to treatment start and 1 Clinical Expert noted that peer review should not delay treatment start (Appendix D2a).

Spencer et al. (2021) identified a significant reduction in overall radiotherapy activity as a result of the COVID-19 pandemic, which was partly suppressed by a concurrent reduction in new cancer diagnoses. Concerns relating to resumption of radiotherapy services and managing the backlog of cancer diagnoses and treatments has been highlighted in a flash survey of 277 radiotherapy professionals in October 2021, conducted by the Institute of Physics and Engineering in Medicine and Action Radiotherapy. Respondents reported that the following could support the recovery and delivery of

radiotherapy services: the introduction of artificial intelligence (AI) contouring for the NHS, reducing the time taken for quality assurance, increasing cross-network working, and the use of ProKnow 'for better connectivity and peer review'.

Special considerations, including issues related to equality

The ProKnow DS instructions for use do not list any contraindications, however, do list known limitations: 'ProKnow DS currently supports exporting structures that are closed and located on a single plane'. The EAG notes that non-axial computed tomography (CT) slices are used with brachytherapy, a procedure more commonly used with gynaecological cancers. The Company have confirmed intention for ProKnow to support non-axial structures, however, they do not have an anticipated timescale for this enhancement (Appendix D1).

4. Clinical evidence selection

4.1. *Evidence search strategy and study selection*

The search strategy was devised from the original NICE scoping searches with additional candidate search terms identified from hand searching manufacturer's websites, browsing database thesauri (for example, Medline MeSH and Embase EMTREE), and existing literature identified during the initial scoping searches.

The final clinical effectiveness search strategy consisted of free-text search terms for product name combined with the Boolean operator OR to maximise sensitivity. For the economic search strategy, radiotherapy search terms were combined with the manufacturer's name using Boolean AND to focus the topic on scope. No time or language limits were applied in the search. Search strategies were developed for MEDLINE and then translated, adapted and run independently for each individual database (Embase, Cochrane Library CENTRAL, International HTA Database, National Institute for Health and Care Research). Additional searches included grey literature sources to identify unpublished or pre-print papers (Google Scholar and Google Advanced Search, EngRxiv, MedRxiv, FDA Devices Database); relevant journals and

professional associations (Journal of Applied Clinical Medical Physics and Journal of Medical Physics Research and Practice, and American Association of Physicists in Medicines), and completed and ongoing clinical trials (ScanMedicine, Clinicaltrials.gov, EudraCT, and Australian and New Zealand trial registry database). No time or language limits were used (Appendix A1).

Clinical effectiveness searches retrieved a total of 202 records of which 151 remained after de-duplication. The title and abstract of each were sifted by a single reviewer (RP) based on intervention only (Appendix A2).

4.2. *Included and excluded studies*

A total of 33 full papers were retrieved and reviewed by a single reviewer (RP), of which 24 were subsequently excluded (Appendix B), 18 of which did not fully align with the NICE Final Scope (2022), however have been summarised within this report, highlighting additional uses of ProKnow (Appendix B). An additional 3 papers were identified through hand literature searching. A total of 12 publications were included (Table 2).

Table 2: Studies selected by the EAG as the evidence base (N=12)

Anatomical location of cancer	Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Gynaecology	Bertero et al. (2021)† Argentina **Sponsor or Funding Source:** NR	**Study design**: Service evaluation/audit (quantifying plan variance) **Intervention**: Anonymised plans uploaded to ProKnow (Elekta) optimised using scorecards to evaluate dosimetric and volumetric data ☑ **Comparator**: original radiotherapy treatment plans ☑	**Patients**: Patients with whole pelvic radiotherapy plans for gynaecological cancer with a prescription dose of 46 Gy in fractions of 2 Gy per day planned in TPS Monaco (Elekta) with Volumetric Arc Therapy technique (n=NR).☑ **ProKnow users**: NR.☑☒ **Setting**: single centre.☑ **Study period:** patients treated between June 2018 and June 2020 included.	Use of scorecards (dose delivered to organs at risk, planning target volume [PTV] dose coverage), number of monitor units (as a surrogate marker of complexity of the plan).☑☒	Non-UK setting. Number of patients, plans, and staff members involved not explicitly reported.
Lung	Byrne et al. (2021)† UK **Sponsor or Funding Source:** NR	**Study design:** Service evaluation/audit (quantifying plan variance) **Evaluation**: Review of retrospective patient treatment plans dataset against 20 scorecards developed using SABR Consortium Guidelines uploaded to ProKnow ☑	**Patients**: Patients undergoing stereotactic ablative radiotherapy (SABR) treatments for primary lung tumours (n=NR).☑ **ProKnow users**: NR **Setting**: single centre.☑ **Study period:** NR	Use of scorecards (dose delivered to organs at risk, PTV dose coverage) for radiotherapy treatment planning quality assurance compared against SABR consortium guidelines, ease of use.☑	Evidence shows the feasibility of creating scorecards and comparison of a patient dataset within ProKnow with national guidelines.

Anatomical location of cancer	Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Head and neck	Chamberlain et al. (2021) Switzerland* **Sponsor or Funding Source:** Open Access funding provided by Universität Zürich.	**Study design:** Service evaluation/audit (quantifying plan variance) **Evaluation**: Review of a treatment plan approaches used among MRIdian System (ViewRay) users with intensity modulated radiotherapy (IMRT), system uploaded to ProKnow and users had one month to create a treatment plan.☑	**Patients:** Single case, patient with a squamous cell carcinoma of the posterior oropharyngeal wall. Pre-contoured MRI and CT images were provided to participants with planning constraints relating to dose-volume histogram parameters and delivery time.☑ **ProKnow users**: 14 planners with mean (SD) and median [range] planning experience of 9.2 (6.9) and 7.0 [2.0 to 20.0] years respectively. Median (range) of ViewRay planning experience was 1 (0-2) years. All users from high-volume centres (not explicitly defined).☑ **Setting**: 14 centres, locations not specified.☑ **Study period:** NR	Use of scorecards (conformity of prescription doses, sparing of organs at risk, PTV dose coverage), number of beams used, number of segments, beam-on time, total delivery time, between-centre comparison of scorecards.☑	Evidence shows the use of ProKnow as a platform to share a treatment planning case study between multiple centres, but does not quantify ease of use.

Anatomical location of cancer	Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Brain	Hardcastle et al. (2019)† 28 countries (NR) **Sponsor or Funding Source:** NR	**Study design:** Service evaluation/audit (quantifying plan variance) **Evaluation**: Anonymised patient planning CT scan with tumour and organs at risk contours shared through ProKnow. Dosimetric scoring matrix provided to planners.☑	**Patients:** Single stereotactic radiosurgery patient case with 5 brain metastases of volumes between 0.07 and 2.82 cm^3 located throughout the brain including adjacent to the brainstem.☑ **ProKnow users:** A total of 160 plans were submitted; top 50 scoring plans used for analysis. Treatment devices included VMAT (n=101), GammaKnife (n=20), CyberKnife (n=16), and IMRT (n=7).☑☒ **Setting**: 28 participating countries, no. of centres not explicitly specified.☑ **Study period:** NR	Between-planner treatment plan quality evaluation including stereostatic radiotherapy delivery time, and dose coverage.☑	Authors acknowledged lack of data collection of planning time, QA time, QA results; where large variations between treatment techniques may exist.

Anatomical location of cancer	Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Vertebral	Hardcastle et al. (2020) 26 countries including Australia, New Zealand, US **Sponsor or Funding Source:** ProKnow LLC provided services and technology and hosted this planning challenge at no cost. Co-author is a founder of ProKnow.	**Study design**: Service evaluation/audit (quantifying plan variance) **Evaluation**: Anonymised patient radiotherapy treatment plans uploaded to ProKnow optimised using score matrix to evaluate dosimetric and volumetric data. Local quality assurance methods submitted for 39 plans; Arc-Check (41%), Octavius (15%), Delta4 (13%), EPID (10%), MatriXX (8%), MapCheck (8%), Mobius3D (3%), and Film (2%).☑	**Patients**: A single patient with challenging anatomy; thoracic vertebral lesion with adjacent oesophagus and spinal cord, and target volume wrapping partially around the spinal canal. **ProKnow users:** A total of 149 plans were submitted, using a range of techniques (VMAT technique 82%, sliding window IMRT 9%, TomoTherapy 4%, CyberKnife 3%, step-and-shoot IMRT 2%, and proton or ion beam 1%). Staff (planners) had approximately 3 months to submit a plan, with no limit on the number of submission iterations, the latest submission was included in data analysis.☑ **Setting**: 26 participating countries, all countries not specified however, majority submitted from Australia (31%), USA (21%), and New Zealand (8%). **Study period:** NR	Ability to meet treatment plan protocol constraints (compliance with treatment plan guidance) based on dose delivered to organs and PTV dose coverage, number of monitor units and number of beams (as a surrogate marker of complexity of the plan).☑☒	Dataset and scoring matrix available on ProKnow website. Non-deliverable plans were removed from analysis. QA results were submitted for 39 plans.

Anatomical location of cancer	Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Parotid gland	Irabor et al. (2019) US, Nigeria, Tanzania, Cameroon, Rwanda **Sponsor or Funding Source:** Support from the Africa Oxford Cancer Foundation	**Study design:** Service evaluation/audit (competency and training) **Evaluation**: 2-hour real-time video teaching and demonstration of contouring using ProKnow followed by 1-week access to ProKnow CA and PS modules for all participating treatment planners. ☑	**Patients:** single case of left parotid gland on axial CT images.☑☒ **ProKnow users:** 19 planners from Nigeria (n=11), Tanzania (n=3), Cameroon (n=2), US (n=2), and Rwanda (n=1). Planner roles were resident radiation oncologists (n=10), medical physicists (n=4), consultant or attendee radiation oncologists (n=4), and therapeutic radiographer (n=1).☑ **Setting**: 19 participants from 4 countries, number of centres not explicitly reported.☑ **Study period:** NR	Self-reported competence (for anatomic structure identification, contouring ability, treatment plan evaluation, tissue delineation, port-film evaluation, cone-beam CT evaluation, dose-volume histogram evaluation), acceptability of ProKnow system for training and image-guided radiotherapy planning.☑	Study published prior to ProKnow commercialisation, see Section 5.2. Remote contouring training evaluation captured.

Anatomical location of cancer	Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Mediastinum, spine	Johnson et al. (2022)† US **Sponsor or Funding Source:** Educational grant provided by Elekta	**Study design:** Service evaluation/audit (competency and training) **Evaluation:** all users registered with ProKnow portal to allow access and interaction with the case data (including images, contours, dose, registrations and plan documentation).☑	**Patients**: 2 case studies with embedded errors (one Mosaiq/RayStation and 3DCRT treatment of mediastinum, one Aria/Eclipse and spine SBRT treatment).☑ **ProKnow users**: Over 100 attendees at the national workshop, of which 53 provided feedback. Experience levels of attendees were residents (13%), <10 years (30%), 10-20 years (29%), >20 years (9%).☑ **Setting:** Single workshop held on online teleconferencing platform (split into 4 breakout rooms).☑ **Study period:** Workshop held between 25 and 29 July 2021 at American Association of Physicists in Medicine Annual Meeting.	Case study error detection rates, user feedback on efficacy of ProKnow dataset as a training tool.☑☒	

Anatomical location of cancer	Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Cervical	Li et al. (2020)† 8 countries (not explicitly defined) **Sponsor or Funding Source:** NR	**Study design:** Service evaluation/audit (quantifying plan variance) **Evaluation**: Anonymised treatment plans and contouring (using each institution's planning software) were uploaded to and analysed with ProKnow DS. ☑	**Patients:** Single anonymised case study (given in English, Spanish, and Portuguese) of locally advanced cervical cancer.☑ **ProKnow users**: Review conducted by radiation oncologists, residents, medical physicists, and dosimetrists. Each centre asked to plan pelvic external beam radiotherapy using either IMRT or VMAT according to local practices. ☑ **Setting**: 12 centres across 8 countries. **Study period:** NR	Plan comparison of dose coverage including organs at risk, maximum point dose, volume of delineated gross tumour and organs at risk, contour volume, number of arcs. ☑☒	

Anatomical location of cancer	Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
N/R	McLaren et al. (2021)† Australia **Sponsor or Funding Source:** NR	**Study design:** Service evaluation/audit (competency and training) **Evaluation:** radiotherapy planning training involving the use of ProKnow.☑	**Patients**: Patient characteristics (including type of cancer and number of patients) not reported.☑ **ProKnow users**: Radiation therapy students (n=NR).☑☒ **Setting**: single centre (University setting). **Study period:** Not explicitly reported. ProKnow introduced in March 2019.☑☒	Formal and informal student feedback. Academic staff observations relating to quality of student planning submissions.☑☒	Limited reporting with no specific outcome measures. Comparator and participant characteristics not explicitly reported. Unclear whether ProKnow replaces alternative tool or is in addition to existing training methods. Study period includes time prior to ProKnow commercialisation, see Section 5.2.

Anatomical location of cancer	Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Lung	Moghanaki et al. (2020) More than 14 countries (US, China, Australia, Japan, Canada, Russia, India, UK, Germany, Italy, New Zealand, Israel, Spain, Switzerland, Others; supplementary table E1); 2.6% (6/227) treatment plans submitted from UK. **Sponsor or Funding Source:** None	**Study design:** Service evaluation/audit (quantifying plan variance) **Evaluation**: Anonymised treatment plans and contouring (using each institution's planning software) were uploaded to and analysed with ProKnow.☑	**Patient dataset**: Two parts: 1) single anonymised patient case with left-sided suprahilar stage I non-small cell lung cancer used to evaluate the quality of a lung SBRT treatment plan, 2) single anonymised patient case with right-sided suprahilar stage 1 non-small cell lung cancer used for contouring accuracy (trachea, proximal bronchial tree, large vessels, and oesophagus) evaluation.☑ **ProKnow users:** 227 treatment plans submitted from medical physicists (n=118), dosimetrists (n=56), therapists (n=16), physicians (n=10), students (n=5), or other (n=22). Treatment plans submitted from 7 different treatment planning systems and 7 different delivery methods.☑ **Setting**: Multiple participating countries, number of centres not explicitly reported. **Study period:** not explicitly defined, however initial findings presented at the Radiosurgery Society Annual Scientific Meeting on 4 November 2017.☑☒	Plan comparison of dose coverage including PTV and organs at risk, maximum point dose, contour volume, contour accuracy, score card, adherence to contouring instructions.☑	Scoring was completed using PlanIQ (Sun Nuclear), which was licenced for use in ProKnow for the study. Recruitment period likely pre-dates ProKnow commercialisation, see Section 5.2. Number of submitted contour sets differed depending on location; oesophagus (n=49), trachea (n=33), proximal bronchial tree (n=25), great vessels (n=22).

Anatomical location of cancer	Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
Breast	Roumeliotis et al. (2022) Canada **Sponsor or Funding Source:** None	**Study design:** Service evaluation/audit (competency and training) **Evaluation:** Evaluation of training programmes comparing learner treatment planning quality with qualified professional benchmarking (participants).☑	**Patient dataset:** single anonymised case with contoured CT images for a patient with synchronous bilateral breast cancer; 55 years old, post-mastectomy with the same tumour characteristics for both breasts (supplementary appendix E1). Learners had access to bilateral breast training datasets (n=NR).☑ **ProKnow users:** 34 experienced participants (medical physicists, n=23; dosimetrists, n=11) completed treatment plans on 3 different techniques (VMAT, TomoTherapy, proton treatment). 6 learners participated in the study. Participants instructed to develop a plan with a prescription dose of 50 Gy in 25 fractions and given dosimetric constraints for guidance. ☑ **Setting:** Learners came from 3 Commission on Accreditation of Medical Physics Education Programs accredited residency programs. Participants were international, but no additional detail was reported. **Study Period:** NR. Anonymised dataset uploaded to ProKnow and made available for 30 days. An independent	Treatment planning competency evaluation, inter-and intramodality comparison, learner feedback.☑☒	ProKnow not used for training, rather to assess the competency of the learners against qualified professionals.

Anatomical location of cancer	Study name and location	Design and intervention(s)	Participants and setting	Outcomes	EAG comments
			expert assessed the learner. Each participant was given an additional week to refine the treatment plan for submission to the study.		
Prostate	Taylor and Richmond (2020) UK **Sponsor or Funding Source:** NR	**Study design**: Service evaluation/audit (quantifying plan variance) **Evaluation**: anonymised prostate radiotherapy treatment plans retrieved and uploaded through ProKnow.☑	**Patients**: single patient with histologically confirmed adenocarcinoma of the prostate, T1b–T3a, N0, M0 disease, a PSA of <30 ng ml−1 with moderate or high risk of seminal vesicle involvement. ☑ **ProKnow users**: Total of 102 radiotherapy staff able to download and submit data, with no restriction on the number of plans that could be submitted per centre. ☑ **Setting**: multi-centre (48 radiotherapy departments; 44 NHS hospitals and 4 private radiotherapy centres. **Study period:** data was available between 02 July to 11 August 2019.	Dosimetric and volumetric radiotherapy treatment plan data, participant questionnaires relating to treatment planning approaches used. ☑☒	Shows the feasibility of sharing a single dataset across multiple UK services, qualitative data on use and usability not explicitly reported. Study reported intra-departmental variation where multiple plans were submitted.

Key: †available as conference abstract or poster only; *assumed from author affiliations; ☑ aspect of study in scope; ☒ aspect of study not in scope; ☑☒ aspect of study partially in scope, or elements of this are not in scope
Abbreviations: CT, computed tomography; Gy, gray; IMRT, intensity modulated radiotherapy; MRI, magnetic resonance imaging; N/A, not applicable; NR, not reported; PSA, prostate specific antigen; PTV, planning target volumes; QA, quality assurance; SABR, stereotactic ablative radiotherapy; SBRT, stereotactic body radiotherapy; SD, standard deviation; VMAT, volumetric modulated arc therapy

5. Clinical evidence review

5.1. *Overview of methodologies of all included studies*

A total of 12 publications were included. The EAG note that all included publications related to the use of ProKnow to facilitate the evaluation of variance in radiotherapy treatment planning, or as a tool to deliver radiotherapy training exercises. Ethical approval was not needed for any of the included evidence and there remains an evidence gap of research relating to the use of ProKnow, for example, no randomised evidence relating to ProKnow was identified and no publication used a patient cohort or dataset for prospective treatment planning or quality assurance. The evidence included within the report are:

- 8 service evaluations or audits of plan quality variance:
    - 5 quantified variation in plan quality between centres or treatment planners using scorecards
        - Bertero et al. (2021), 1 centre for all patients seen between June 2018 and June 2020 [number of planners and patients not reported];
        - Chamberlain et al. (2021), 14 centres for 1 patient;
        - Hardcastle et al. (2019), across 160 treatment plans submitted from 28 countries;
        - Hardcastle et al. (2020), across 149 treatment plans submitted from 26 countries for 1 patient;
        - Moghanaki et al. (2020), across 227 treatment plans and between 22 and 49 contours submitted from multiple countries for 2 patients;
    - 2 quantified the variation in plan quality:

- Li et al. (2020), across 38 plans submitted from 8 countries for 1 patient;
- Taylor and Richmond (2020), across 102 treatment plans submitted from 48 UK centres for 1 patient;

- 1 quantified departmental treatment plan variance with published guidelines [number of planners and patients not reported] (Byrne et al. 2021);

- 4 service evaluations or audits assessed the use of ProKnow during training
  - at a virtual training workshop (N=2), Irabor et al. (2019); Johnson et al. 2022;
  - in a university setting (N=1), McLaren et al. 2021;
  - in an accredited residency programme (N=1), Roumeliotis et al. 2022).

5.2. *Critical appraisal of studies*

Of the included evidence, 6 were reported in full peer reviewed publications (Chamberlain et al. 2021; Hardcastle et al. 2020; Irabor et al. 2019; Moghanaki et al. 2020; Roumeliotis et al. 2022; Taylor and Richmond 2020), 6 were available as a conference abstract, presentation, or poster only (Bertero et al. 2021, Byrne et al. 2021; Hardcastle et al. 2019; Johnson et al. 2022; Li et al. 2020; McLaren et al. 2021). No evidence was identified that evaluated the use of ProKnow and its impact on patient outcomes, or compared the use of ProKnow with standard practise. As the included evidence was formed from service evaluations and audits, and none of the evidence was directly relevant to the decision problem, no formal critical appraisal checklists were applied by the EAG.

The specific modules of ProKnow under evaluation were not well reported within the available evidence. None of the included publications reported the version of ProKnow used and those studies reporting study dates overlap

release updates for ProKnow DS. Four publications were published or included recruitment periods prior to ProKnow commercialisation in February 2020 (Hardcastle et al. 2019; McLaren et al. 2021; Moghanaki et al. 2020; Taylor and Richmond 2020); the EAG have considered all evidence, however acknowledge that these studies may relate to a prototype or pre-commercialised version. The Company highlighted ProKnow DS Release Notes [accessed 18 November 2022] and summaries of version updates dating back to version 0.8.0 on 07 September 2018. The EAG note that evaluation period dates for included evidence were rarely reported, Table 2. As the overall features and functions of ProKnow have remained consistent pre- and post-commercialisation, the EAG consider the evidence to be generalisable across the commercially available version of ProKnow and the EAG have considered all evidence relating to ProKnow before and after commercialisation.

The reporting of the number of patients and number of radiotherapy professionals reviewing treatment plans was poorly reported, such that the EAG cannot robustly estimate the numbers using ProKnow from the available evidence. Of the 12 included publications:

- the largest sample patient dataset size that was uploaded to ProKnow was 2 (Johnson et al. 2022; Moghanaki et al. 2020);
- the number of plans submitted for single or multiple patient datasets ranged from 14 (Chamberlain et al. 2021) to 227 (Moghanaki et al. 2020);
- the number of centres accessing the same dataset in ProKnow ranged from single centres (Bertero et al. 2021; Byrne et al. 2021; McLaren et al. 2021) to 48 centres (Taylor and Richmond 2020);
- studies that included multiple countries ranged from 5 (Irabor et al. 2019) to 28 (Hardcastle et al. 2019) countries (Table 3).

The EAG consider the sharing of single cases to be appropriate when evaluating variance in individual radiotherapy treatment planning, however

recognise that the use of ProKnow to support quality assurance across the NHS would need significantly larger data sets.

Evidence gap: There is an evidence gap relating to the sharing of larger patient data sets, representing a heterogeneous case mix of cancer location, stage and complexity, using ProKnow within or between organisations.

Two publications were conducted exclusively in a UK or NHS population (Byrne et al. 2021; Taylor and Richmond 2020). The remaining publications were set in the following locations:

- Argentina [N=1] (Bertero et al. 2021),
- Australia [N=1] (McLaren et al. 2021),
- Canada [N=1] (Roumeliotis et al. 2022),
- US [N=1] (Johnson et al. 2022),
- Multiple countries [N=5] (Hardcastle et al. 2019; Hardcastle et al. 2020; Irabor et al. 2019; Li et al. 2020; Moghanaki et al. 2020),
- Not explicitly reported [N=1] (Chamberlain et al. 2021).

The anatomical location of cancers included in the evidence were:

- brain (Hardcastle et al. 2019),
- breast (Roumeliotis et al. 2022),
- gynecological (Bertero et al. 2021; Li et al. 2020),
- head and neck (Chamberlain et al. 2021),
- lung (Byrne et al. 2021; Moghanaki et al. 2020),
- mediastinum (Johnson et al. 2022),
- parotid gland (Irabor et al. 2019),

- prostate (Taylor and Richmond 2020),
- vertebral (Hardcastle et al. 2020; Johnson et al. 2022),
- unspecified (McLaren et al. 2021).

Funding for the included publications was not reported in 6, and 2 received no funding. The Company provided an educational grant for the training evaluation by Johnson et al. (2022) and technology and services were provided for Hardcastle et al. (2020). Chamberlain et al. (2021) and Irabor et al. (2019) received external funding from university or charitable awards.

5.3. *Results from the evidence base*

Each of the 12 included publications reported on the outcomes listed in the NICE Final Scope (2022), Table 3. Of the 9 outcomes of interest 5 had no relevant published evidence.

Table 3: Cross-tabulation of included studies against outcomes (N=12)

Study (Author, Year, Location)	Study design	Comparator	No. of centres	No. of staff reviewing	No. of patients/data sets	Outcomes								
						Impact on radiotherapy treatment planning quality assurance	Usability or user experience	Ease of retrieving and archiving patient data	Radiotherapy treatment planning time	Number of internal and external peer reviews performed	Impact on staffing and treatment planning resources	Impact of the system on clinical oncology training	Ability for data linkage to national registries	Reduction in inequality of access
Bertero et al. (2021)† Argentina	Retrospective comparative cohort	Original plans	1	NR	NR	✓	✓	✓ *						
Byrne et al. (2021)† UK	Service evaluation	SABR consortium guidelines (scorecard)	1	NR	NR	✓	✓	✓ *						
Chamberlain et al. (2021) NR	Service evaluation	Between centre (scorecard)	14	14 (1 from each centre)	1	✓		✓ *						
Hardcastle et al. (2019)† 28 countries	Service evaluation	Between centre (scorecard)	NR	NR (160 plans submitted)	1	✓		✓ *						
Hardcastle et al. (2020) 26 countries including Australia, New Zealand, US	Service evaluation	Between centre (scorecard and local quality assurance plans in a subset)	NR	NR (149 plans submitted)	1	✓		✓ *						
Irabor et al. (2019) 5 countries (US, Nigeria, Tanzania, Cameroon, Rwanda)	Evaluation of training	N/A	NR	19	1		✓	✓ *				✓		
Johnson et al. (2022)† US	Evaluation of training	N/A	NR	53	2			✓ *				✓		
Li et al. (2020)† 8 countries (Latin America)	Service evaluation	N/A	12	38	1	✓		✓ *						
McLaren et al. (2021)† Australia	Evaluation of training	N/A	1	NR	NR			✓ *				✓		
Moghanaki et al. (2020) More than 14 countries (NR)	Service evaluation	N/A	NR	227 plans submitted	2 (1 for planning, 1 for contouring)	✓		✓ *						
Roumeliotis et al. (2022) Canada	Evaluation of training	Plans submitted by experienced participants	NR	40 (6 learners, 34 experienced participants)	1	✓		✓ *				✓		
Taylor and Richmond (2020) UK	Service evaluation	Values obtained from CHHIP trial protocol	48 (44 NHS, 4 private)	102	1	✓		✓ *						

Key: *ProKnow used for retrieving and archiving data, qualitative data relating to ease not reported; †available as an abstract only
Abbreviations: N/A, not applicable; NR, not reported; US, United States of America

5.3.1. Impact on radiotherapy treatment planning quality assurance

Of the 9 publications reporting on the use of ProKnow for quality assurance of treatment planning, no publication reported the use or impact of ProKnow to prospectively review and amend patient treatment plans. Variation in treatment planning or revalidation of retrospective patient treatment plans were evaluated using scorecards in 6 publications and defined dose metrics in 3 publications. Scorecards are tools within ProKnow that provide visual and numerical feedback on the quality of a radiotherapy treatment plan based on custom metrics determined by the user, including dose, dose volume histograms, or structure-specific traits. Scorecards can be used to compare plans on individual or multiple patient datasets to optimise treatment plans, audit compliance against standards, or compare plans with peers across local and national networks. The terms 'scorecard', 'score matrix', and 'score system' were used across the included evidence; the EAG has used the term scorecard within this report for consistency.

Scorecards

Six publications reported on the use of scorecards within ProKnow to quantify the quality of radiotherapy treatment plans in reference to metrics based on sample population or clinical guidance, where available.

One study reported the use of ProKnow scorecards for evaluation of Stereotactic ablative radiotherapy (SABR) treatment plans (Byrne et al. 2021). SABR is a highly targeted form of radiotherapy, which targets a tumour with radiation beams from different angles at the same time. In March 2020, NHS England (NHSE) released a Clinical Commissioning Policy for SABR for patients with metachronous extracranial ogliometastatic cancer. The UK Government, NHSE, and NHS Improvement noted the planned expansion of SABR for lung cancer patients. In 2019, the SABR UK Consortium updated guidance for clinical implementation of SABR across lung, liver, hepatocellular, prostate, spinal, and adrenal metastases or cancer locations. The guidance provides an introduction to quality assurance approaches, review of SABR literature, an overview of patient selection criteria for different clinical sites, and examples of radiotherapy dose, fractionation schedules, and

planning guidelines. Byrne et al. (2021) developed 20 scorecards based on these SABR Consortium Guidelines stratified by 5 planning target volume (PTV) volume groups and 4 prescription options, to evaluate compliance of radiotherapy treatment plans for primary lung tumours. The authors concluded that the ProKnow DS enabled comparisons of compliance between patients, patient groups, departments, networks and nationally.

Bertero et al. (2021) reported the use of scorecards in ProKnow to enable the evaluation and optimisation of radiotherapy treatment plans for a retrospective cohort of patients with gynecological cancer. Scorecards were developed using evaluation metrics including medium and maximum doses for organs at risk (bladder and rectum), homogeneity, and conformality index (an independent quantitative assessment tool for radiotherapy treatment plans). Median of each evaluated metric was selected for statistical analysis and used to define optimisation parameters. Authors reported that radiotherapy doses to organs at risk were reduced through treatment plan optimisation without significant variation in the planned target volume (PTV) or plan complexity. Authors concluded that the use of scorecards in ProKnow offered a useful tool for statistical analysis of the population enabling continuous improvement in treatment planning. However, they did not make comparisons with existing methods of evaluating treatment plans nor did they assess the robustness of the strategies used to develop the scorecards.

An abstract (Hardcastle et al. 2019) and a full publication (Hardcastle et al. 2020) used ProKnow as a platform to conduct a treatment planning challenge for 2 individual patient cases across 28 and 26 countries respectively. The impact of ProKnow was not specifically evaluated, although the EAG note that ProKnow was used to share and retrieve all data relating to the planning challenge (the patient cases and the submitted treatment plans) and scores were available to planners, so the EAG assumes that the ProKnow scorecards were used, although not explicitly stated. Hardcastle et al. (2019) conducted a stereotactic radiotherapy treatment planning challenge for an individual patient case with 5 brain metastases. A total of 160 plans were submitted and scored from 28 countries, with the top scoring 50 plans used

for analysis. Authors noted a large range in treatment delivery time between radiotherapy systems used (VMAT, CyberKnife, GammaKnife, IMRT). Authors acknowledged the time taken for treatment planning or quality assurance was not captured and may vary between treatment techniques. Hardcastle et al. (2020) conducted a treatment planning challenge, comparing 149 treatment plans, submitted across 26 countries, for an individual patient case with thoracic vertebral metastases. A scorecard which considered prescription doses and organ at risk tolerances, was used to evaluate submitted treatment plans. Plan complexity was measured via the number of monitoring units and the number of beams. Participants had 3 months to submit a plan and the number of iterations of the submission was not restricted with each submission generating a score visible to the participant. A total of 39 of 149 plans (26%) submitted quality assurance results from a range of software tools (Arc-Check 41%, Octavius 15%, Delta4 13%, EPID 10%, MatriXX 8%, MapCheck 8%, Mobius3D 3%, and Film 2%). The authors concluded that most treatment plans (144 of 149, 96.6%) plans met protocol constraints outlined from the scorecards. However, they reported that there was large variation in coverage of target volume, and that high-quality plans were not dependent on any technical aspects of planning but on planner skill (number and experience of planners not explicitly reported).

Chamberlain et al. (2021) used scoring to evaluate the quality of treatment plans using MRIdian (ViewRay) planning software for a single patient case with oropharyngeal cancer across 14 centres. The single case study was shared, accessed, and analysed using ProKnow. None of the centres had unacceptable performance on any of the metrics. Planning experience was moderately correlated with improved planning results for some specific organs at risk (spinal cord, glottis).

Moghanaki et al. (2020) used scorecards to evaluate quality of treatment plans for a single clinical case using their institution’s planning software and scores were generated through PlanIQ (Sun Nuclear), which was licensed for use in ProKnow for the study. Scores were generated for each submission and planners could re-plan and resubmit multiple times to improve scores

during the study period. The EAG would consider this use as a training exercise, which shows how ProKnow scorecards could be implemented in the NHS. Scores were generated based on metrics including the target coverage, conformality values, and organs at risk avoidance. Most plans were submitted by medical physicists (n=118), followed by dosimetrists or therapists (n=72), physicians (n=10), students (n=5), or other (unspecified, n=22). A second individual clinical case was used to evaluate organ at risk contouring variation. The number of contour plans submitted varied depending on the 4 anatomical locations: esophagus (n=49), trachea (n=33), proximal bronchial tree (n=25), and large vessels (n=22). The authors concluded that there was wide variability in treatment planning and frequent contouring errors that were independent of delivery modality, treatment planning system, planner role, or on-beam time. The findings support the benefit of quality assurance and peer review comparisons and that more readily available accessible quality evaluation software, such as ProKnow, may support this aspect of clinical practise.

Scorecards could be developed or used outside of ProKnow as standalone or transferable audit tools; however, the availability within a widely used system would likely increase use and standardisation, and could streamline the audit process, releasing associated resources, including staff time (Appendix D2a). The flash survey of radiotherapy professionals conducted by the Institute of Physics and Engineering in Medicine and Action Radiotherapy in 2021 highlighted a lack of planning slots, staffing issues, and time being taken for quality assurance had slowed the planned SABR expansion. The use of scorecards, developed from national guidelines in a universally accessible system such as ProKnow, may offer treatment planners an additional quality assurance tool, which may facilitate the wider adoption of complex treatment modalities such as SABR. However, 6 Clinical Experts considered that scorecards would be unlikely to or would not replace peer review (Appendix D2c).

Retrospective quality assurance of treatment plans

Three studies did not explicitly report the use of scorecards but reported use of ProKnow to quantify variability in quality of retrospective treatment plans for patient cases previously treated with radiotherapy (Taylor and Richmond 2020; Li et al. 2020; Roumeliotis et al. 2022).

Taylor and Richmond (2020) reported variability in PTV and dose to organ at risk (OAR) between 102 plan submissions made from 48 UK radiotherapy departments; the number of treatment planners was not reported. Similarly, the abstract by Li et al. (2020) reported use of ProKnow DS, to document the range of dose covering 95% of the PTV, maximum point dose (Dmax), gross tumour volume (GTV) and volume of the bladder covered by 40 Gy across 39 plans submitted for a case of locally advanced cervical cancer from 8 Latin American countries.

Roumeliotis et al. (2022) compared dosimetry data in ProKnow for treatment plans submitted from 6 learners with plans submitted from 23 qualified medical physicists and 11 dosimetrists for a single case study with synchronous bilateral breast cancer. All participants (learners and qualified planners) submitted acceptable treatment plans using VMAT treatment modality against pre-defined dosimetric targets.

An additional 4 service evaluations or audits identified by the EAG quantified variability in specific aspects of radiotherapy treatment planning, such as delineation or contouring, without considering quality of the overall treatment plans (Bisgaard et al. 2022; Sritharan et al. 2022; Lin et al. 2022; Wahid et al. 2022). The EAG recognise that variation in contouring and delineation would likely result in variation in treatment plans, however as the treatment plan quality has not been considered within these 2 conference abstracts and 2 full publications on pre-print servers, the EAG consider these publications to fall outside the NICE Final Scope however have been summarised in Section 5.3.10. The EAG recognise that ProKnow CA may support with improving contouring accuracy and could potentially reduce inter-observer variation.

5.3.2. Usability or user experience

Three publications reported on general usability of ProKnow as secondary outcomes (Irabor et al. 2019; Byrne et al. 2021; Bertero et al. 2021).

An evaluation of training by Irabor et al. (2019) used a questionnaire to evaluate the acceptability of ProKnow as an image-guided radiotherapy planning and training tool in sub-Saharan Africa. All respondents agreed or strongly agreed that ProKnow was easy to use, helpful for professional development, and would recommend the web-based contouring tool.

Byrne et al. (2021) developed 20 scorecards to evaluate compliance of radiotherapy treatment plans with SABR consortium guidelines for primary lung tumours. The authors concluded that the use of scorecards within ProKnow was intuitive and supported the ability to complete audit activities at local and national levels with ease.

Bertero et al. (2021) also developed and used scorecards to evaluate and optimise treatment plans for patients with gynecological cancer. The authors reported that there was no difference in the number of monitor units (used as a surrogate marker for the complexity of the plan) when using ProKnow, however the number of plans submitted was not explicitly reported. The authors concluded that the use of scorecards in ProKnow offered a useful tool for optimising workflow and streamlining the evaluation and comparison of plans for clinical decision-making.

5.3.3. Ease of retrieving and archiving patient data

No publication reported qualitative outcomes specifically relating to the ease of retrieving or archiving patient data. Furthermore, reports of data loss, transfer, or accessibility issues were not reported. However, all included publications reported the use of ProKnow for the sharing of patient datasets across either multiple users, multiple centres, or multiple countries, thus demonstrating the versatility of the software across systems.

ProKnow as a data-sharing platform

Taylor and Richmond (2020) shared a single patient dataset with 102 radiotherapy staff from 44 NHS hospitals and 4 private radiotherapy centres. Information relating to accessibility were not reported. The authors note that 176 individual expressions of interest to take part in the planning study were received, of these 102 plans were submitted. However, the number of treatment planners and reasons for non-submission were not reported and it is unclear whether the patient data was shared with those who did not submit an eventual plan. Data was made available to all participants after the evaluation to enable participant self-assessment and benchmarking against that of their peers, although the use, uptake, or outcomes related to this was not reported.

Hardcastle et al. (2019) shared and compared the 50 top scoring stereotactic radiotherapy treatment plans, from 160 plans that were submitted from 28 countries. The plans all related to a single patient with 5 brain metastases using ProKnow. Qualitative data relating to the ease of use or user experience were not reported.

Hardcastle et al. (2020) compared plan variance across a total of 149 stereotactic body radiotherapy (SBRT) treatment plans submitted from 26 countries (most plan submissions were from Australia 31%, US 21%, and New Zealand 8%; remaining countries not explicitly defined) for a single patient with thoracic vertebral metastases. Qualitative data relating to ease of use or user experience was not reported.

Byrne et al. (2021) reported the comparison of a patient dataset (number of patients not reported) against 20 scorecards developed using SABR consortium guidelines for primary lung tumours to evaluate compliance of radiotherapy treatment plans in a single centre. The number of individuals or centres retrieving and archiving data was not reported, although authors note that the scorecards could be used for local and national networks.

Bertero et al. (2021) included all patients with whole pelvic radiotherapy treatment plans for gynaecological malignancies using TPS Monaco (Elekta) with volumetric arc therapy (VMAT) technique, with a prescription dose of 46

Gy in fractions of 2 Gy per day, treated between June 2018 and June 2020; however, the numbers of patients or reviewing staff were not explicitly reported.

Moghanaki et al. (2020) shared 2 clinical lung cancer cases, 1 for treatment planning and 1 for contouring, across 14 countries and 7 different treatment planning systems (Eclipse 43%, Monaco 38%, Pinnacle 9%, CyberKnife 4%, RayStation 4%, Tomothrapy 1%, Astroid 0.5%). The number of ProKnow users was also not reported, however 227 treatment plans were submitted and between 22 and 49 contours were received, depending on the anatomical location (trachea, oesophagus, proximal bronchial tree, large vessels).

Li et al. (2020) shared a single clinical case with 12 centres from 8 countries with 40 contours and plans received, 38 of which were available for analysis.

Chamberlain et al. (2021) shared a single clinical case with 14 participants (each from a different centre) using ProKnow.

ProKnow as a training platform

ProKnow was used as a platform for training in 4 publications (Irabor et al. 2019; Johnson et al. 2022; McLaren et al. 2021; Roumeliotis et al. 2022). Irabor et al. (2019) shared a single patient case with 19 planners from 5 countries. Johnson et al. (2022) shared 2 clinical cases with 53 planners. McLaren et al. (2021) used ProKnow as a training tool in a university setting and did not define the number of ProKnow users or the size of the dataset. Roumeliotis et al. (2022) shared a single synchronous bilateral breast cancer dataset with 34 worldwide experienced participants and 6 learners who had access to a bilateral breast training dataset, with the size not defined. The number of institutions involved was not reported.

5.3.4. Radiotherapy treatment planning time

No publication directly reported the impact or use of ProKnow on radiotherapy treatment planning time, including time to treatment start.

Only 1 treatment planning evaluation reported on the radiotherapy treatment planning time as an outcome. Taylor and Richmond (2020) investigated variation in clinical practise across radiotherapy services based on radiotherapy treatment plans submitted for a single patient diagnosed with prostate cancer. Estimated planning times ranged from less than an hour to more than 7 hours, with just over 75% of plans taking less than 2 hours. Possible reasons for large variance in treatment planning time was not reported. The EAG note that multiple treatment planning software were used; 46% Eclipse (Varian Medical Systems Incorporated), 33% Pinnacle (Koninklijke Philips), 12% Raystation (Raysearch Laboratories), 6% Monaco (Elekta AB), and 3% TomoTherapy (Accuray Incorporated). Plans were submitted retrospectively following patient treatment and reviewed independently by the study team without any specified peer review; it is unclear how this may have influenced the time taken to complete planning.

Five Clinical Experts advised that radiotherapy treatment planning time can vary significantly depending on the anatomical cancer location, severity, prognosis, and complexity with planning time estimates ranging from 15 minutes to over 2 weeks, with 1 Expert suggesting a minimum of 1 hour (Appendix D2b). One Clinical Expert noted that this would depend on whether the treatment planning time is taken from imaging to treatment start or the time taken to plan the radiotherapy treatment. Additionally, 6 Clinical Experts noted that the time taken for peer review of radiotherapy treatment plans may range from 15 to 45 minutes, depending on the complexity of the plan, patient characteristics, and expertise of the peer reviewer(s) with 1 Clinical Expert noting that complex cases could take much longer (Appendix D2b).

5.3.5. Number of internal and external peer reviews performed

No publication reported the impact of ProKnow on the number of internal and external peer reviews performed.

5.3.6. Impact on staffing and treatment planning resources

No publication reported the impact of ProKnow on the impact of staffing and treatment planning resources.

5.3.7. Impact of the system on clinical oncology training

The EAG note that ProKnow PS and ProKnow CA are modules predominantly focused on the training of staff involved in radiotherapy treatment planning. Four publications reported experience of ProKnow during training (Irabor et al. 2019; Johnson et al. 2022; McLaren et al. 2021; Roumeliotis et al. 2022).

Irabor et al. (2019) conducted a 2-hour online virtual training session with 19 radiotherapy treatment planners from US, Nigeria, Tanzania, Cameroon, and Rwanda followed by 1 week of ProKnow PS and CA module access. Planners self-reported competence, relating to anatomic structure identification, contouring ability, tissue delineation, and evaluation of treatment plan, cone-beam CT, and port-film, before and after training and ProKnow access. Improvements in all competency areas were noted; the percentage improvement in the mean self-reported competency scores ranged from 14.3% (dose-volume histogram evaluation) to 32.8% (plan evaluation). Authors noted that only a few respondents felt confident or strongly confident prior to training and the use of ProKnow and this was improved following the intervention.

The conference abstract by Johnson et al. (2022) reported the use of ProKnow as part of a workshop-based exercise for over 100 participants to review 2 clinical cases with embedded errors. Participants had 20 minutes with each case study with error detection rates ranging from 21% to 92%. Authors did not report error detection rates against experience levels, which although experience varied between residents (assumed by the EAG to be equivalent to UK trainee doctors) to those with over 20 years' experience. User feedback from 53 participants was positive, with 96% agreeing and 75% of respondents strongly agreeing that the datasets were an effective training tool and that they planned to utilise the datasets for training at their institution.

The conference abstract by McLaren et al. (2021) reported the use ProKnow as a teaching tool for radiation therapy students in an Australian University setting. Authors noted positive formal and informal student feedback and academic staff observed an initial improvement in quality of student planning

submissions; however, the number and type of cases reviewed and number of students were not reported.

Roumeliotis et al. (2022) assessed the competency of 6 learners against qualified medical physicists (n=23) or dosimetrists (n=11). Learners were offered access to a bilateral breast training dataset (sample size not reported) and all participants submitted a treatment plan for a single synchronous bilateral breast cancer case. All participants submitted acceptable VMAT treatment plans relative to pre-defined dosimetric targets with no significant differences in mean dose to the heart (D_{mean}) or organs at risk ($D_{0.03cc}$). The volume of the lung receiving at least 20 Gy (V_{20Gy}) was poorer in the learner cohort compared with the qualified cohort (p=0.01). The use of ProKnow was not evaluated independently from the overall training, which was delivered in the existing framework of Commission on Accreditation of Medical Physics Education Programs accredited residency programmes.

5.3.8. Ability for data linkage to national registries

No publication reported on the ability of ProKnow to link to national registries. The EAG identified 1 study abstract, that did not meet eligibility for inclusion (Becksfort et al. 2021). This study designed a custom database, capable of handling current and historical CT and dose data for a paediatric population in a single centre, with the input and linkage from ProKnow DS. Although this does not consider data linkage to national registries, the study authors highlighted the possible data linkage to custom databases.

The Company has confirmed that ProKnow has the potential to collect patient identifiers, including date of birth, NHS number, gender, and postcode (Appendix D1), which are important to enable data linkage to other databases. Therefore, long-term patient benefits may be realised through data linkage of extracts from ProKnow data to administrative databases, such as:

- Cancer Outcomes and Services Dataset (COSD), which is the national standard for reporting cancer in the NHS in England and is collected and managed by the National Disease Registration Service (NDRS) at NHS Digital. This collects information such as: age, sex, stage of

disease, route of diagnosis, menopausal status, date of surgery, previous malignancies, grade and size of tumour, histological subtype, record of multi-disciplinary team (MDT) meetings, cancer care plan intent, planned cancer treatment type, adult comorbidity evaluation, recurrence, and mortality outcomes.

- Systemic Anti-Cancer Therapy (SACT) collected and managed by the National Disease Registration Service (NDRS) at NHS Digital, and a mandated dataset as part of the Health and Social Care Information Standards. This collects information on the use of systemic anti-cancer therapies across all NHS trusts in England (such as chemotherapy regimen and start date).

- Radiotherapy Dataset (RTDS) collected and managed by the National Disease Registration Service (NDRS) at NHS Digital. This collects radiotherapy data from NHS acute trusts in England including: treatment modality, prescription, route and method of administration, treatment intent, dose, fractions, use of radiopharmaceuticals.

- Diagnostic Imaging Dataset (DID) collected and managed by the National Disease Registration Service (NDRS) at NHS Digital. This includes chest xrays in the diagnosis of lung caner, non-obstetric ultrasound in the diagnosis of ovarian and other abdomino-pelvic cancers, magnetic resonance imaging (MRI) in the diagnosis of brain cancer, computed tomography (CT) scans in the diagnosis of many cancers.

- Hospital Episode Statistics (HES) collected and managed by NHS Digital. This includes all admissions (including day-cases), Accident & Emergency attendances, outpatient appointments, and adult critical care episodes at NHS hospitals in England as well as mortality registration.

5.3.9. Reduction in inequality of access

No publication reported the impact of ProKnow on improving equality of access to radiotherapy treatment.

5.3.10. Additional evidence identified by the EAG not captured within NICE Final Scope

The EAG identified 18 publications that used ProKnow, however did not include any outcomes or relevant population captured within the NICE Final Scope (2022) and have been excluded from the main clinical evidence (Appendix B). A protocol outlining an evaluation for treatment planning and contouring using ProKnow with no results were reported in an abstract by Shepherd et al. (2022) has been summarised in Section 9.4. An abstract by Becksfort et al. (2021), highlighting the use of ProKnow as a data source to build a custom database, has been previously considered in Section 5.3.8. The remaining 16 publications have been summarised in this section to highlight additional uses of ProKnow.

Use of ProKnow to develop independent datasets or quantify clinical practise variability

A publication by Jordan et al. (2022) used ProKnow software for contouring up to 29 structures from computed tomography (CT) images in the thorax, abdomen, and pelvis in a dataset of 359 paediatric patients undergoing routine imaging (that is, the population was not undergoing radiotherapy treatment). The aim was to develop a dataset of expert contours to enable the evaluation and development of organ autosegmentation algorithms for paediatric variations, which may be beneficial in radiation therapy, diagnostic tasks, surgical planning, and organ dose estimations.

The use of ProKnow to evaluate delineation variability or generate consensus regions of interest contours was reported in 2 conference abstracts (Bisgaard et al. 2022; Sritharan et al. 2022) and 2 full publications available on pre-print servers (Lin et al. 2022; Wahid et al. 2022). Bisgaard et al. (2022) shared 4 clinical case studies, each with a different anatomical cancer location (prostate, adrenal gland, pelvic, pancreatic), with oncologists (number not

reported) across 9 centres to quantify delineation-related variation. Variation in delineation was seen across all 4 anatomical locations and between-centre variation in apparent diffusion coefficient followed the same trend. Sritharan et al. (2022) reported use of ProKnow CA to evaluate inter-observer variability in prostate bed clinical target volume delineation on MRI. A total of 48 contours for 3 patients, submitted by 17 oncologists from across 11 institutions in 7 countries, were analysed and compared. The authors concluded that this could be used to develop a consensus guideline for contouring the prostate bed clinical target volume on MRI.

The pre-print publications by Lin et al. (2022) and Wahid et al. (2022) report data or outcomes from the same trial (Contouring Collaborative for Consensus in Radiation Oncology, C3RO). The evaluation invited participants to contour 5 clinical cases (breast, sarcoma, head and neck, gynecology, and gastrointestinal) with an aim to characterise the variability in segmentation performance and generate, evaluate, and compare aggregated segmentations. The evaluation used ProKnow to share and contour the clinical cases with 221 participants (radiation oncologists, n=169; resident physicians, n=40; radiation therapists, n=7; medical physicists, n=1; or other, n=4). The number of individual institutions was not reported. Inter-observer (within and between 'experts' and 'non-experts') variation was seen for all cases. The impact of the variability on treatment planning, quality assurance, or patient outcomes was not reported.

Use of ProKnow to evaluate AI-based treatment planning

The EAG identified 7 publications that used ProKnow to evaluate the performance of AI-based treatment planning; this included 3 peer reviewed publications (Shen et al. 2020; Shen et al. 2021b; Sprouts et al. 2022b), 1 PhD thesis (Sprouts 2022a), and 3 abstracts (Gao et al. 2022; Shen et al. 2021a; Sprouts et al. 2021). The EAG noted significant overlap in co-authorship, and the same US institution across all 7 publications, therefore there is a high risk of duplication of results. An additional abstract by Zheng et al. (2018) used ProKnow to evaluate the effect of dose calculation algorithms

(Ansiotropic Analytical Algorithm, Acuros XB, Pencil Beam Convolution) on lung SBRT optimisation, and plan quality scoring using ProKnow.

The flash survey conducted by the Institute of Physics and Engineering in Medicine and Action Radiotherapy of 277 radiotherapy professionals in October 2021 highlighted the possible use of AI technologies within radiotherapy as a useful tool to support quality assurance and reduce planning time for radiotherapy treatment.

Comparison of treatment planning software

Comparison of aspects of radiotherapy treatment planning (dose volume histograms, scorecards) between systems, including ProKnow were reported in 1 full paper (Pepin et al. 2022) and 2 conference abstracts (Penoncello et al. 2022; Schmidt et al. 2021).

Pepin et al. (2022) compared dose volume histogram calculators for 5 systems (Eclipse, MIM Maestro, Mobius3D, ProKnow and RayStation). Authors noted dose volume histogram calculation methodology differences between the systems, which led to differences in the summary metrics and dose volume histogram curves for two structures; cochlea (head and neck radiotherapy treatment) and the penile bulb (prostate treatment). The range of the median [IQR] dose volume histogram precisions across the 5 systems and all structures was 0.93% [0.01% to 2.86%] to 3.22% [1.95% to 5.86%] and 1.05% [0.70% to 1.79%] for ProKnow.

Penoncello et al. (2022) compared dose volume histogram construction differences between 4 commercial treatment planning systems (Eclipse, Pinnacle, RayStation, Elements) and 4 dose reporting systems (MIM, Mobius, ProKnow and Velocity). Dose files from 10 clinically treated plans with a hypo-fractionation or stereotactic radiotherapy prescription were created and anonymised in Eclipse and exported into the other 7 systems. Median value differences for all dose volume histogram points across the 8 systems were within 1%. Structure volumes relative to Eclipse were larger with median and mean values *up to* 3.0% and 10.5% respectively, however did not specify structure volume values for ProKnow exclusively.

Schmidt et al. (2021) compared Eclipse Plan Scorecard (Varian Medical) for 8 patients with ProKnow plan scores. The percentage difference across the 8 plans ranged from -3.16% to 2.42%, with a mean difference of -0.15%. Authors noted minor discrepancies in the plan scores resulting from sampling differences between the dose volume histograms because of the extraction and file type used between systems. Authors did not report the impact of using ProKnow scorecards on the quality or quality assurance of treatment plans.

6. Adverse events

On 18 October 2022, the EAG searched for Medicines and Healthcare products Regulatory Agency (MHRA) field safety notices, using the term 'ProKnow', and found no results. The EAG also searched for 'Elekta' and found some results relating to radiotherapy equipment or treatment planning software, but notes that these do not relate to ProKnow and are therefore out of scope for this report.

On 18 October 2022, the EAG searched the Manufacturer and User Facility Device Experience (MAUDE) database, using the brand name 'ProKnow', and separately the brand name 'ProKnow' and manufacturer name 'Elekta', and found no results for dates between 01 April 2020 and 30 September 2022. The EAG also searched for manufacturer name 'Elekta' alone and found 122 results. These were checked manually, and none related to ProKnow, and are therefore out of scope for this report.

No publications reported adverse events specifically relating to the use of ProKnow. The EAG note that adverse events relating to patient care would not be expected for the evidence included, that is, evaluation of training or plan variance independent of prospective patient treatment. The EAG note that adverse events may relate to confidentiality breaches or issues relating to the accessibility or retrieval of data, which were additionally not reported across the included publications. The ProKnow most recent release note (version 1.31.1, dated 10 June 2022, accessed 18 November 2022) highlight a recent bug fix to correct 'a security defect that could expose a patient's

medical record number and name to unauthorised users in the organisation'; the Company clarified the security defect related to a specific workflow management tool and did not affect any users within the NHS and has since been resolved (Appendix D1). There is an evidence gap relating to adverse events relating to data or patient care in large case datasets, such as those that could be used across the NHS, which could be addressed as part of the NHSE commissioned pilot of ProKnow.

7. Evidence synthesis

The EAG has not conducted meta-analysis, because most of the publications are quality assurance service evaluation or audit, there is heterogeneity in terms of population (different anatomical cancer locations, different treatment outcomes for example: curative, palliative), and poor quality of reported evidence (7 conference abstracts).

Furthermore, there is likely heterogeneity associated with the population of interest and the various functions of ProKnow. Professionals may use the functionalities in different ways such as for treatment planning, contouring training or exercises, retrospective or prospective planning review, or use of scorecards based on different parameters or standards.

The EAG identified a meta-analysis by Ohri et al. (2013) that reported that radiotherapy treatment protocol deviations were associated with an increased risk of treatment failure and overall mortality, across 8 cooperative group trials (none using ProKnow). Five anatomical cancer locations (lung, brain, bone, pancreatic, and head and neck) and both adult and paediatric studies were included in this meta-analysis. The EAG recognise that clinical trials often have strict eligibility criteria, quality assurance and radiotherapy treatment plan protocols, therefore results of this meta-analysis may not be representative of all patients receiving radiotherapy treatment across the UK NHS. However, the EAG consider that future analysis may be possible if sufficient robust data is available (see Section 9.5), with consistently defined minor and major treatment plan deviations which could be explored by

subgroups (such as, anatomical location and type of cancer, or treatment type and intent).

8. Economic evidence

8.1. *Published economic evidence*

Economic evaluation literature searches were expanded to include additional search terms that described the product functional specifications, these were searched as free-text, keyword, and controlled vocabulary terms. The final search strategy was developed in MEDLINE (Ovid MEDLINE(R) and In-Process, In-Data-Review & Other Non-Indexed) and then translated, adapted and run independently for each individual database (Embase Ovid, RePEC IDEAS and CEA Registry).

In the first round of literature searches conducted alongside the effectiveness searches, no relevant literature was found on the operational cost of implementing ProKnow or the cost-effectiveness of using ProKnow (that is, no full or partial economic evaluations identified). Therefore, additional literature searches were performed with the aim of identifying any published economic evaluations of Elekta ProKnow. To maximise the sensitivity of these searches the broad Canadian Agency for Drugs and Technologies in Health search filter (CADTH, 2022) was appended to the MEDLINE and Embase searches in order to identify cost and economic studies in databases that are not specific to health economics (Appendix C1).

A total of 295 records were identified; 280 remained after deduplication. After a single reviewer (SH) sifted through the results of the searches, no studies were identified on either the operational costs or the cost-effectiveness of using ProKnow or any form of economic evaluation of ProKnow. Within these 280 records, the largest body of evidence (44 studies) was focused on dose calculation simulation in the radiotherapy planning process, which the EAG believe are not relevant to the costs of implementing and using ProKnow.

Evidence gap: There are no full or partial economic evaluations directly or indirectly comparing the use of ProKnow versus standard care for radiotherapy treatment planning.

Through hand searching, reference checking, and targeted searches, the EAG identified 3 discrete event simulation (DES) studies, which modelled waiting times in radiotherapy treatment and 1 cost-minimisation analysis. Although they do not include the use of ProKnow, they illustrate a way to evaluate the decision problem. As these studies are not specific to ProKnow, no formal critical appraisal checklists were applied by the EAG.

The 3 DES studies examined different scenarios by changing the number of clinical resources available to inform the optimum resource allocation to reduce the average waiting time for patients to receive their treatment (Table 4). However, it is currently unknown whether the use of ProKnow will impact either the ready-to-treat to treatment time (RTTT) or the overall treatment planning time per patient (which is defined as the time from confirmation of diagnosis to time of treatment start).

Table 4: Summary of discrete event simulation studies

Author (year) Country	Title	Aim of the study	Key findings
Babashov et al. (2017) Canada	Reducing patient waiting times for radiation therapy and improving the treatment planning process: a discrete-event simulation model (radiation treatment planning)	To analyse the radiotherapy planning process at a regional cancer program to determine bottlenecks and to quantify the effect of specific resource levels with the goal of reducing waiting times.	Increasing the number of dosimetrists by 1 reduced the mean RTTT from 10.83 to 10.12 days (with 84.9% of patients were treated within 14 calendar days target), adding 1 more oncologist decreased the mean RTTT from 10.83 to 10.55 days (such that 82% of patients were treated within 14 days).
Vieira et al. (2019) The Netherlands	Improving workflow control in radiotherapy using discrete-event simulation	To assess the impact of using different push and pull strategies and alternative interventions on timeliness in radiotherapy.	Balancing the consultation slots had the greatest impact on the performance by reducing waiting times from 7.8 to 6.2 days and reduced the number of patients breaching their wait time targets by 74%.
Kapamara et al. (2007) UK	A simulation of a radiotherapy treatment system: a case study of a local cancer centre	To better understand the radiotherapy treatment process, identify the complexities and bottlenecks from the interactions between patients and human or machine resources using discrete event simulation.	An extension of shift hours for both human and machine resources to the time window, 9am to 8pm, reduced the average time patients took to complete their first treatment dose from 33.14 to 32.55 days. This do not impact the intermittent crowding of patients for doctors but lowered average waiting time (for palliative, radical and all patients combined).
Abbreviations: RTTT, ready-to-treat to treatment time.			

The cost-minimisation analysis by Norum et al. (2005) evaluated the use of videoconferencing technology for radiotherapy treatment planning in the departments of radiotherapy at 2 hospital in Norway. Remote simulation procedures were carried out for 5 patients. A cost-minimisation analysis was performed considering that there was no significant effect on health outcome relating to the travel itself. Only costs that differed between the treatment arms were included, such as costs relating to transportation, equipment

investments, implementation (installation, IT firewalls), maintenance, training and personnel-related costs at the host and satellite institution. The main benefit of tele-radiotherapy from this study, was the cost of patient transportation avoided (with patients frequently transported between centres by air ambulance). This approach would require the economic evaluation to take a different perspective, but highlights a potential patient benefit which could be realised when implementing ProKnow in the NHS.

One Clinical Expert considered the greatest benefit of ProKnow (or by extension, a similar unspecified tool) was the possibility that it increased the accessibility of peer review (AppendixD2a). Peer review provides quality assurance of treatment plans and can reduce the risk of errors. The RCR guidance for radiotherapy target volume definition and peer review (2022) recommends that all radiotherapy departments 'should adopt a standardised peer review meeting structure' and the peer reviews are 'recorded against nationally agreed minimum dataset requirements'. The guidance also recommends that prospective peer review of contours should be conducted for cases where considerable individual clinical judgement is needed. Where major changes are recommended, further peer review of final contours should also occur. The EAG has not identified any evidence evaluating the cost-effectiveness of peer review of radiotherapy treatment plans.

One Clinical Expert confirmed that conduct of peer review increases resource use including staff time but advised that the lack of peer review of treatment plans would not delay the start of treatment (Appendix D2a). Five Clinical Experts considered that ProKnow has the potential to increase the proportion of radiotherapy treatment plans that undergo peer review, including increasing the proportion of those conducted externally, particularly for smaller centres (Appendix D2c). One Clinical Expert noted that if local planning software is used for peer review, the additional time to transfer data may not enable additional peer review and could interrupt the workflow. The published economic evidence identified considers that timings of the overall pathway may be dominated by availability of dosimetrists (to create the treatment plans) and availability of linear accelerator (linac) machines (to start

treatment). Three Clinical Experts noted that the number of peer reviews currently conducted is restricted by availability of clinical oncologists to review and approve treatment plans (Appendix D2a,c). While implementation of ProKnow is likely to increase access to treatment plans among dosimetrists or oncologists (increasing the quality of the treatment plan), it is unclear whether its implementation in the NHS would enable faster treatment. Better understanding of the current pathway, staffing, machine capacity and rate limiting steps between diagnosis and initiation of treatment in the NHS, may inform future DES modelling to evaluate the impact of interventions which introduce efficiencies, such as ProKnow (discussed further in Section 8.2.5).

8.2. *Conceptual modelling*

Given the absence of any economic evaluations of ProKnow, the EAG met with 1 Clinical Expert to determine the potential impact of ProKnow in treatment planning and from there specify what the value proposition would look like, with a view to validating this with the remaining Clinical Experts. At the initial meeting, the Clinical Expert highlighted that ProKnow does not conduct anything different or in addition to standard of care (Appendix D2a). ProKnow, however, is a tool that can facilitate peer review and so enable centres to follow national guidance. Given its potential to act as a facilitator, the use of ProKnow could potentially increase the proportion of treatment plans undergoing peer review. This would incur an additional cost because of the increase in staff time needed to undertake the peer review activity that was previously not done, but this activity could potentially lead to improved patient outcomes. Broadly, the EAG consider that the value proposition of ProKnow in the NHS could be:

- Greater adherence to national guidance, local peer review protocols, and higher quality radiotherapy treatment plans because of the increased proportion of treatment plans undergoing peer review (either internally or externally). **Challenge:** The Clinical Experts advised that peer review is not conducted for all cases at every centre. Conduct of internal or external peer review will vary by case (for example, anatomical location and type of cancer, complexity, centre availability

of oncologists) and locally agreed protocols (Appendix D2c). Two Clinical Experts also noted that internal peer review may not be performed using ProKnow, for example using local treatment planning software or in person, neither requiring an upload to an independent system (Appendix D2c). A snapshot audit by the RCR is due to be undertaken in early 2023, which will help quantify current peer review practise in radiology compliance with RCR standards for cancer multidisciplinary team meetings rather than peer review within radiotherapy treatment planning (Appendix D5). The uptake of ProKnow may facilitate an increase in peer review over time and may capture which staff members conduct peer review, which could be audited in a similar way. The EAG did not identify any evidence which evaluated the cost-effectiveness of peer review; however, acknowledge that their literature search was focused on ProKnow.

- Increased ease in archiving or retrieving patient data for further analysis, leading to a reduction in staff resources needed for future bespoke audits (for example monitoring peer review practise). **Challenge:** The use of ProKnow could lead to efficiency gains, releasing staff resources to support other parts of the radiotherapy treatment pathway, or treatment of additional patients. There is no evidence at present which shows this benefit of ProKnow when used in the NHS.

- Faster peer review. Five Clinical Experts noted that the use of ProKnow could enable external review to be as efficient as internal peer review (Appendix D2c). The RCR guidance (2022) offers examples of peer review timings using a range of methods (not using ProKnow):

    - *In-person*: weekly 30-minute meetings involving 2 head and neck oncologists with active contouring with cases taking between 10 and 20 minutes to review.

    - *In-person with recording using Microsoft Access Database:* independent treatment planning for lung cancer patients by

oncology trainees with weekly 90-minute meeting involving at least 2 oncologists, a specialist radiographer, and oncology trainees. Major and minor changes may be recommended with all plans with recommended modifications scheduled for further review the following week. The number of cases reviewed or *per case* review time was not reported.

- *Video conference software (Microsoft Teams):* weekly 60-minute meetings involving 6 head and neck oncologists across 3 services with active contouring of clinical cases. Trainees, radiographers, and physicists are also invited to join the meetings. The number of cases reviewed or *per case* review time was not reported.

- *Contouring or treatment planning software (undefined):* contoured cases are submitted with a request for on-demand peer review by contouring clinicians and experienced head and neck specialist radiographers. In a pilot evaluation of this on-demand approach, 62 cases were reviewed with a mean review time of 17 minutes *per case.* A mean (median) of 27.9 (18.8) staff hours was saved using the on-demand approach when compared with a weekly meeting approach. The proportion of cases requiring significant changes was 11% and were mostly considered to be complex cases.

Challenge: There is currently no direct evidence evaluating the time taken to peer review in current NHS practise with and without ProKnow. Six Clinical Experts considered 15 to 45 minutes for peer review to be conducted using ProKnow (Appendix D2b). For other methods of conducting peer review, 1 Expert felt the same range would be appropriate, 2 Experts noted it could take longer (up to 8 hours) if sending data externally, and 1 Expert, who uses planning software to facilitate peer review, noted that the use of ProKnow could increase the time taken due to the uploading and retrieval of data (Appendix D2b).

- Faster time to treatment initiation. **Challenge:** Three Clinical Experts advised that peer review is not the rate-limiting step (Appendix D2a-b). Faster peer review may not reduce time to treatment as this may be limited by dosimetrist, oncologist, and linac availability confirming the published evidence in Section 8.1. This could however be examined using a DES populated with data either from primary sources (for example, using observational study or survey data) or from routinely collected real world data sources (such as, local operational systems or electronic health records) in an NHS setting.

- Reduction in adverse events or subsequent litigation costs associated with errors in treatment planning. Hayakawa et al. (2019) highlighted the significant deterioration of health-related quality of life with increasing radiotherapy doses delivered to organs at risk in 53 patients with head and neck cancer. The RCR 2022 guidance highlights the importance of quality assurance and use of peer review to reduce risks of treatment planning errors resulting in direct patient harm. Four Clinical Experts highlighted that the observation of potential errors is driven by the peer review process (Appendix D2b). If ProKnow increases the proportion of treatment plans undergoing peer review then this patient benefit is plausible. Furthermore, a recent study by Hill et al. (2022) suggests that the public value the use of low-cost interventions that could prevent medical error regardless of the potential for harm as a result of that error. **Challenge:** Adverse events are rare, may occur long-term and would be difficult to attribute to the method of treatment planning peer review. Surrogate markers (such as dose to organs at risk) or outcomes could be identified and validated, if treatment plan data (and any corresponding treatment plan changes) from ProKnow was linked to national registries, which capture longer-term patient outcomes including survival.

- Better quality treatment plans because of increase in rate of peer review and addressing recommended changes to treatment plans. A recent systematic review of peer review in radiotherapy (Lewis et

al. 2021) reported that 6 of the 17 included studies used 'major change', 'minor change', or 'no change' nomenclature. Furthermore, authors also reported that in 9 of 17 studies included, the recommended changes were to contours, volumes, or plans and were made in real time which did not require additional re-planning time. The EAG has identified an additional 17 studies where the proportion of radiotherapy treatment plans requiring a change following peer review ranged between 2% and 74% (see Section 8.2.1). **Challenge:** Unwarranted variation is not easily attributable to particular factors, for example, it is difficult to determine whether there is greater centre-to-centre variation for a particular anatomical location or type of cancer, or for virtual versus in-person peer review. Two Clinical Experts advised that there is no universal definition of major and minor changes, and 6 Clinical Experts advised that the recommendation for major or minor changes in treatment plans is not captured routinely across all centres, however they may be documented locally (Appendix D2c). Furthermore, 4 Clinical Experts noted that ProKnow has the potential to improve quality through the training facilities, the involvement with peer review, or through the reduction in inter-observer variability (Appendix D2c).

- Change in treatment modality, doses, or fractionation (driven by use of standardised scoring systems and analysis of multiple datasets). Improved understanding of treatment could lead to changes in thresholds in national guidance, such as the UK SABR Consortium Guidance. **Challenge**: This is speculative and only achievable through consistent and comprehensive use of a tool or database being used across the NHS. Associations between scorecards and long-term outcomes may enable a greater understanding of the impact of different treatment modalities, doses or fractionation, on safety and treatment outcomes; as suggested by 1 Clinical Expert (Appendix D2a).

The lack of data directly relevant to the use of ProKnow and the uncertainty around whether ProKnow would lead to any of the benefits identified by the Clinical Experts precludes the development of any plausible decision analytic model. The EAG considered different model approaches, acknowledging that peer review could occur at several or multiple stages, be defined as internal or external, or requiring major, minor, or no changes to the treatment plans. The EAG consulted with 6 Clinical Experts who noted that modelling these variables may overcomplicate the pathway and the assumptions required to support the model would not be appropriate (for example, 4 Clinical Experts noted the proportion of peer reviews conducted externally versus internally varies by local centre arrangements and resources and may not be conducted using ProKnow, Appendix D2c). The EAG have therefore presented a highly simplified conceptual model (represented by the treatment planning pathway, Figure 1) of the radiotherapy treatment pathway from diagnosis (determined by clinical need for radiotherapy as a treatment option) through to treatment delivery. The stages within the model include where the patient and clinical team decide to proceed with radiotherapy as treatment modality, undertaking images for the planning of radiotherapy, production of the treatment plan (which simplistically includes target definition and dosimetry calculation), peer review of the treatment plan, plan verification, and finishes with the planned treatment being delivered. The EAG have used a combined target definition and dosimetry calculation step for illustrative purposes. As the main value of ProKnow focuses on its facilitation and support of the peer review process within the pathway, the EAG have considered the associated costs and resources within this aspect of radiotherapy treatment planning.

The overall time horizon of the treatment planning pathway for an individual patient will vary (for example, by anatomical location or type of cancer, complexity, treatment intent, and treatment modality) but is expected to number in days to weeks as confirmed by 6 Clinical Experts (Appendix D2b). Therefore, no discounting of costs and effects over this time horizon would need to be applied. Costs should be taken from the perspective of the NHS. The addition of a personal social services perspective, as per the NICE reference case, would not be needed unless long-term impacts on patient's

health and subsequent treatments might occur. In this case, consideration of discounting would be needed.

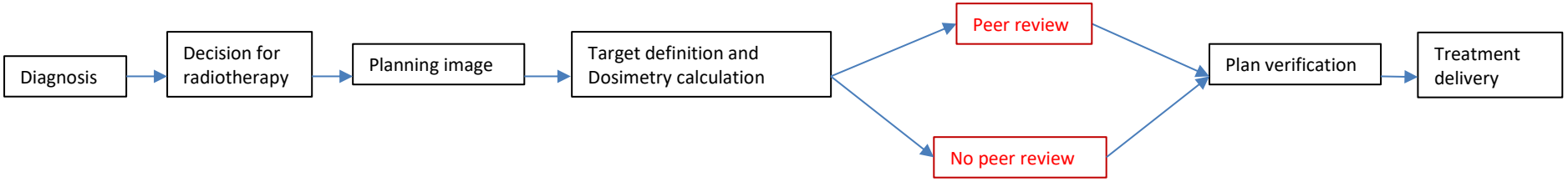
As previously described, there is an evidence gap in using ProKnow for peer review, including against other methods of peer review. There is also an evidence gap about the impact of using ProKnow on the resulting change in treatment plan, the extent of that change, and the impact of the change in the treatment plan (both financial and health-related) on the individual patient when compared with current NHS standard of care. The model does not consider the clinical impact of changes in treatment plans and focuses on the cost with the following key assumptions:

- Peer review is defined, as stated by Lewis et al. (2021) referring to RCR Guidance 2017, as '*a formal review by another expert of the delineated contours used to produce a radiotherapy plan. Reviewing target volumes also implies a review of dose and fractionation'.*

- ProKnow currently only has a direct impact on facilitating the peer review process and not treatment decision making either within the peer review process or out with.

- Using ProKnow to conduct peer review has the same clinical impact as conducting peer review by other means (for example, MDTs via video conference, telephone, or in-person).

Figure 1 Treatment planning pathway with peer review stages in red



8.2.1. Comparator: current practise (peer review process)

An early cost comparison should focus on the difference in costs of using ProKnow as a facilitator of peer review when compared with current peer review practise. Peer review itself in radiotherapy is an essential step in clinical quality assurance of radiotherapy treatment planning to avoid planning-related errors that can affect patient safety and treatment outcomes. However, there is significant variation across peer review practise in the NHS. The RCR guidance (2022) recommends that 'prospective peer review of contours should occur in cases where considerable individual judgement is required' and provides examples of who should be peer reviewed (for example protocol-specified and individualised volumes requiring peer review) and how peer review should be conducted (including in-person, online, and via contouring software). However, to date there have been no formal guidelines set out to standardise the process (Lewis et al. 2021). Five Clinical Experts have confirmed that currently peer review can take place using a range of methods (Appendix D2b). If this variation in current practise was quantified, then a potential benefit of ProKnow may be to reduce this variation. The RCR is due to undertake an audit in early 2023 focusing on the analysis of current methods used to deliver radiology peer review and peer feedback in addition to assess compliance with the RCR standards for radiology events and learning meetings (REALM) (Appendix D5). The RCR confirmed the intention for anonymised results from this planned audit to be made available in a peer reviewed journal when available (Appendix D5). The EAG note that this audit is unlikely to provide additional evidence relating to radiotherapy treatment planning peer review, however highlights the potential and possible limitations of audit data because of inconsistencies in the methods of data collection (Appendix D5), which could potentially be alleviated if data was captured consistently and comprehensively through a tool, such as ProKnow.

Evidence gap: While the RCR guidance offers examples of UK-based radiology peer review in cancer multidisciplinary meetings, there is currently a lack of audit data and standardised practise in radiotherapy treatment planning within the NHS and the use of peer review against which ProKnow

can be directly compared. Data should be collected prior to the implementation of ProKnow to define what current standard practise looks like to quantify the variation and uncertainty, which would allow for a later consistent and meaningful comparison following implementation of ProKnow. Data collection should include the total number of treatment plans created (pan-cancer and per cancer), total number of treatment plans requiring peer review (pan-cancer and per cancer), actual number of peer reviews conducted (pan-cancer and per cancer), peer review outcomes (can be reported as proportion of changes required using prospective definition of major, minor and no change), and how the peer reviews were done (in person, virtual). This would facilitate either a before-and-after study or an interrupted time series assessment (that would control for temporal trends that a before-and-after study cannot).

The EAG identified 17 studies, which reported changes to radiotherapy treatment plans following peer review practises, through hand-searching, Table 5. The EAG acknowledges that these studies may reflect peer review at different timepoints in the treatment planning pathway, that there is heterogeneity across these studies in terms of type and complexity of cancer, treatment intent and modality, and lack of standardisation in defining ‘minor’ and ‘major’ changes to treatment plans. However, the studies identified by the EAG highlight the variation in proportion requiring change (between 2% and 74%), and magnitude of change (major changes between 1% and 15%) required following peer review. Due to this variation, the EAG would recommend that information regarding the magnitude and type of change to treatment plans following peer review is prospectively defined and captured in the UK NHS prior to implementation of ProKnow, and reviewed regularly (for example, within annual audits to provide feedback to centres).

Table 5: Summary of studies measuring the rate of discordance of peer reviewers

Author (year); Country	Design and method	Proportion of plans undergoing changes			Key findings
		Any changes	Major change	Minor change	
Albert et al. (2018) US	Retrospective analysis of peer reviewed cases	23.3%	8.2%	NR	The total dose was changed in 16.4% of cases presented and dose per fractionation was changed in 6.8% of cases.
Amarasena et al. (2017) Australia	Retrospective analysis of peer reviewed cases	40.9%	14.8%	21%	Additional 3.8% had major changes and 2.4% had minor changes recommended but not implemented due to lack of consensus. Within the major changes recommended, the most common were changes to the GTV (primary 28/126, 22%, or nodes 21/126, 16.6%), and changes to the high-dose PTV (72/126, 57.1%). There were only 5 (3.4%) changes to the total dose or fractionation.
Ballo et al. (2014)* US	Prospective analysis of peer reviewed cases	12.2%	2.6%	NR	Changes included dose change (28.3%) and target change (69.1%). When examined by year of treatment, the number of changes recommended decreased over time (between 2007-2010). The number of changes recommended varied by disease site and physician. Head and neck, gynaecologic and gastrointestinal malignancies accounted for the majority of changes made.
Brammer et al. (2014) UK	Prospective analysis of peer reviewed cases (following introduction of weekly departmental meetings for radiotherapy QA)	NR	*Jan 2012:* 10% *Sept 2013:* 4.2%	*Jan 2012:* 6.3% *Sept 2013:* 4.2%	Major changes defined as any alterations that required a change in the delivery of radiotherapy, including: alteration in CTV delineation, change in dose fractionation, treatment cancellation. Minor changes defined as those that did not require a physical alteration of the treatment plan, that is, alterations in documentation or labelling. Difference in major changes between time points was not statistically significant (p=0.17).
Brunskill et al. (2017) Australia, Canada, Spain, Singapore, UK, US	Systematic review and meta-analysis (N=8 studies, 6 reporting magnitude of change)	10.8%	1.8%	7.3%	The most common changes were related to target volume delineation (45.2% of changed plans), dose prescription or written directives (24.4%), and non-target volume delineation or normal tissue sparing (7.5%).

Gwynne et al. (2016) UK	Analysis of peer reviewed prospective (n=39) and retrospective (n=44) cases	10.8%	NR	NR	9 cases required resubmission for approval after recommended modifications, 6 prospectively and 3 retrospectively. No delays to treatment start were observed.
Joye et al. (2014) Belgium	Central review of cases (N=20 centres)	74%	NR	NR	Of the 74% cases requiring modification, 51% fully accepted, 3% partly accepted, 13% the suggested modification was rejected, and in 8% no feedback was given on acceptance of the modification.
Kotecha et al. (2021) US	Prospective analysis of peer reviewed cases	21%	NR	NR	5.8% (29/500) required more than 1 modification. A total of 149 modifications were made including changes to patient positioning and immobilisation, treatment site and care path, simulation co-ordination activities, treatment technique and planning instructions.
Lefresne et al. (2012)* Canada	Prospective analysis of peer reviewed cases	7%	1%	6%	Plans categorised as 'adequate and do not require modification', 'plans are satisfactory to continue treatment but receive suggestions for potential changes that should be incorporated into similar plans in the future', or 'plans are unsatisfactory and require correction before next fraction of radiation therapy is delivered'.
Lymberiou et al. (2015)* Canada	Prospective analysis of peer reviewed cases	4.4%	2.3%	2.1%	Major modifications included change required prior to start of treatment. Minor modifications included suggestions to be considered in future similar plans.
Mackenzie et al. (2016) Canada	Prospective analysis of peer reviewed cases	22%	9%	NR	Plans categorised as 'satisfactory with no suggested changes', 'issues to consider for future patients', or 'unsatisfactory plan with a change recommended before the first or next fraction'.
Martin-Garcia et al. (2020) Spain	Prospective analysis of peer reviewed cases	20.9%	6%	11.5%	3.4% of plans were rejected with indication of new presentation.
McClelland et al. (2021) US	Retrospective analysis of in-person peer reviews (2017/18) compared to virtual peer reviews (2021)	*In person:* 8.0% *Virtual*: 2.6%	*In person:* 4.0% *Virtual:* 1.0%	*In person:* 4.0% Virtual: 1.5%	The number of any deviations per month was 7.3 for in-person (3.7 minor, 3.7 major) versus 5.0 (3.0 minor, 2.0 major) for virtual plans; there was no trend over time for number of deviations per month. There were significant differences in palliative intent (36% versus 22%; p=0.002), but not in total time between simulation and the start of treatment (9.2 versus 10.0 days; p=0.10) for in-person and virtual respectively.

Qureshi et al. (2019) Pakistan	Retrospective analysis of peer reviewed cases	22.4%	8.6%	12.9%	The frequency of change recommendations was greater in radical radiation plans than in palliative plans (92.3% versus 7.7%).
Rooney et al. (2015)* UK	Prospective analysis of peer reviewed cases	27%	NR	NR	All patients were planned with curative intent at the outset and after peer review 3% of plans were changed to either induction chemotherapy or to palliative-intent radiotherapy due to the size of the treated volume and the normal tissue dose constraints not being achieved. In total, 6% of patients had plan adjustment after review of dose volume histograms and treated volumes. CPR led to a change in 17% of treated volumes.
Rouette et al. (2017) Canada	Prospective analysis of peer reviewed cases (N=14 centres)	3.3%	1.3%	1.6%	Major changes were defined as requiring repeat planning or having a major effect on planning or clinical outcomes, or both. 0.4% of peer reviewed treatment plan had documented change but magnitude of change was not reported.
Thompson et al. (2018) Canada	Prospective analysis of peer reviewed cases	2.1%	1.6%	0.5%	9.8% (139/1,413) plans required more involved discussion
Key: *also included within systematic review and meta-analysis by Brunskill et al. (2017) Abbreviations: GTV, gross tumour volume; PTV, planned target volume; NR, not reported					

Regarding features of peer review, the systematic review by Lewis et al. (2021) included 17 studies investigating the existing structures and processes in radiotherapy peer review; 3 of the included studies were conducted in a UK setting. The results of Lewis et al. (2021) identified significant variation in peer review tasks between centres and a general lack of consensus. Key parameters of peer review were identified across the included studies, Table 6. These parameters could be collected within a future study to determine costs associated with current peer review of radiotherapy treatment plans in the NHS and could be used to inform a DES model to evaluate the impact of ProKnow on time, cost, capacity, effectiveness and thereafter cost-effectiveness.

Table 6: Key parameters of peer review process (adapted from Table 1 of Lewis et al. 2021)

Parameter	Findings from 17 studies included in the systematic review by Lewis et al. 2021
Meeting length or frequency	• 8 studies with weekly meetings • 5 studies reported 2-3 meetings per week • 2 studies daily meetings • 1 study with fortnightly meetings • And 1 study reported on demand meetings. For those study reporting the length, it was 1 hour
Meeting format	• 5 studies reported that meetings happened between 2 or more centres and 12 studies mentioned a single centre. • For meetings between multiple centres, desktop sharing or video-tele conference technologies were used • For those 12 studies in a single centre, meetings were conducted face to face and in one case in the presence of patients
Prospective or retrospective	• 13 studies were prospective • 3 studies both prospective and retrospective peer review were conducted • Not defined in 1 study
Cases discussed	• In 8 studies, all tumour sites were discussed, considering non-palliative and complex cases. • In 5 studies, all head and neck cases were discussed. • In the remaining 4 studies, the criteria were quite varied based on the tumour site or complexity of cases
Attendees	• In all 17 studies a physician attended meetings. • In 13 studies, a medical physicist was present • In 9 studies a dosimetrist was present • In 7 studies a radiation therapist attended meetings.

	• Other specialists such as physician assistant, nurse or radiologists were also present in few studies
Review type	• In all 17 studies volumes were reviewed • In 9 studies plans were also reviewed
Standard or protocol used to determine treatment plans which required peer review	• 7 studies reported using an institutional guideline or trial protocol • 4 studies used consensus decision • 6 studies did not report this item
Feedback mechanisms	• In 8 studies recommended changes were included in the electronic medical report • 4 studies used face to face discussion as well • The remaining studies used different methods such as cases re-discussed in another meetings, changes in volume/contours in real time, feedback by email or changes made according to group consensus
Peer review Outcome	• 6 studies used Major/Minor changes as a grading system • 2 studies used ABC rating* • 5 studies used bespoke approaches • 1 study used approved/not approved • And 1 study used change/no change
Key: *ABC rating: A, adequate; B, potential changes for future suggested; treatment can proceed; C, unsatisfactory, requires change before next treatment.	

8.2.2. Intervention

As defined in the decision problem, the intervention here is using ProKnow in radiotherapy treatment planning, including treatment quality assurance.

8.2.3. Cost Parameter

The EAG has summarised unit costs which could be included in a future economic evaluation, Table 7. The total cost of purchasing ProKnow in its base form, which is for a single linac and includes 1TB of data storage with unlimited users (as well as additional fees per linac added and per 1TB data storage per year) was provided by the Company (Appendix D1). The annual cost of using ProKnow was divided by the number of patients treated using a single linac in a single year, this could be assumed be 500 patients per year as a starting point based on 3 Clinical Experts estimating a range of 500 to 800 patients (Appendix D2c). One Clinical Expert noted that data capturing the number of annual new patient treatments started per linac is not routinely collected and so may be difficult to capture from existing sources although another Expert highlighted that this may be captured within RTDS, Institute of Physics and Engineering in Medicing (IPEM), or other sources (such as audit

data) (Appendix D2c). The cost of training, maintenance, and upgrades is included within the cost of the technology (Appendix D1).

Based on the studies reviewed by EAG on the peer review process it is expected that the same parameters (Table 6) should be recorded following the implementation of ProKnow to quantify staff role, time, and costs associated. As for the staff costing, the cost of an oncologist is calculated per minute based on the Unit costs of Health and Social Care publication (PSSRU, 2021) reference costs. To calculate the cost of a peer review activity, the EAG assumed that each plan was reviewed together by 2 consultant oncologists (1 involved in the development of the initial plan and a peer to review) in real-time in person, the duration of which was advised by Clinical Experts as between 15 and 45 minutes (Appendix D2b). This duration will vary by case but will incorporate the time to present per case, contour definition, treatment target coverage, and assessment of risk to critical structures.

Table 7: Key cost parameters for the cost comparison – unit costs

Parameter	Value	Source	Assumptions
Annual cost of purchasing ProKnow	[redacted]	Company	This is out with the NHS England commission. This is the base package for 1 linac and includes 1TB of data storage and includes unlimited users and is per year
Annual cost per additional linac	[redacted]	Company	This is out with the NHS England commission. Base package includes 1 linac.
Annual cost per additional 1TB of data storage	[redacted]	Company	This is out with the NHS England commission. Base package include 1TB of data storage.
Consultant oncologist (cost per minute)	£2.05	PSSRU, 2021 (p141 table 14)	This is a cost per minute of a consultant medical (assumed to be similar to consultant oncologist) using the non-London based weight, working 1,841 hours per year.
Peer review activity (15 minutes)	£61.50	EAG / Clinical Expert opinion	This involves 2 consultant oncologists for 15 minutes each
Peer review activity (30 minutes)	£123.00	EAG / Clinical Expert opinion	This involves 2 consultant oncologists for 30 minutes each
Peer review activity (45 minutes)	£184.50	EAG / Clinical Expert opinion	This involves 2 consultant oncologists for 45 minutes each
Abbreviations: PSSRU, Personal Social Services Research Unit			

8.2.4. Potential Outcomes

The EAG note that the impact of peer review using ProKnow versus standard practises of peer review in the NHS on patient outcomes is unclear, would need a large study, and may be difficult to attribute directly to ProKnow.

The EAG acknowledges that use of ProKnow to facilitate additional peer review, as highlighted by 6 Clinical Experts, could lead to improved treatment plans (for example, changes to plans resulting in reduction in dose to organs at risk) as a surrogate for improved patient benefits. A literature review by Fairchild et al. (2013) and meta-analysis by Ohri et al. (2013) investigated the association between quality assurance of radiotherapy treatment plans and patient outcomes, including overall survival and disease control, across multiple cooperative group trials. Trials from North America, Europe, and Australia were considered with hematologic, head and neck, lung, breast, pancreas, brain, and bone anatomical cancer locations in paediatric and adult populations represented. The EAG noted some overlap between the included trials within the 2 reviews. Fairchild et al. (2013) reported 5 of 8 (56%) trials suggested compliance with radiotherapy treatment planning quality assurance significantly increased overall survival and 7 of 14 (50%) studies reported significantly better disease control with quality assurance of treatment plans. Ohri et al. (2013) used a random-effects model to determine that quality assurance of radiotherapy treatment plans were associated with statistically significant improvement in overall survival and disease control across 8 studies. The EAG note that clinical trial designs frequently have stringent radiotherapy treatment plan protocols to perform quality assurance against that may be lacking within a general population, however accept the plausibility that quality assurance measures, such as peer review, could lead to better plan quality.

Two Clinical Experts suggested that in the short-term ProKnow may lead to an increase in the proportion of radiotherapy treatment plans requiring a major change or re-plan, however that as competency increases ProKnow may be used to show a reduction in major changes following peer review if such data

were routinely collected (Appendix D2c). Definitions of what constitutes a major change to treatment plan should be agreed and prospectively collected to inform future economic modelling. The EAG note that Appendix 6 of the RCR guidance (2022) provides suggested definitions of major and minor changes to radiotherapy treatment plans. The EAG also consider that ProKnow CA and PS modules, which support training, could be used to monitor treatment planning competency or quality improvements over time.

Future explorative data analysis could be considered if data linkage between all patients having external beam radiotherapy (captured in RTDS) and administrative datasets (such as HES) was performed to determine whether peer review or scores from ProKnow scorecards were predictive of outcome.

The cost-minimisation analysis by Norum et al. (2005), while not specific to use of ProKnow, did consider that access to remote treatment planning may lead to a reduction in referrals to specialist centres, and subsequently a reduction in patient travel. This patient benefit should be considered as an outcome measure in future prospective studies.

8.2.5. Potential Future Model Structure

Discrete event simulation

DES modelling is a valuable tool for investigating system capacity and throughput. The use of DES models when evaluating health care includes applications of interventions in hospitals, outpatient clinics, emergency departments and pharmacies. DES can help decision-makers to carry out a 'what if?' analysis to determine good policies for scheduling patients, optimising resources, reducing waiting times of patients in clinics, and improving workflows. DES models have also been used to investigate patient scheduling challenges, waiting time bottlenecks, overall system throughput and system configuration in emergency rooms, optimal intensive care unit size as well as staffing levels and bed requirements in various healthcare settings (Babashov et al. 2017). However, such studies depend on robust modelling of the distributions of waiting times between steps, which should be informed by real world data.

In radiotherapy, minimising the time between referral and start of treatment (waiting time) is important to potentially mitigate tumour growth and avoid psychological distress in cancer patients (Vieira et al. 2019). Simulation modelling has been applied in the field of radiation therapy to explore target waiting times through varying capacities and to analyse the number of linear accelerators to achieve shorter waiting times (Babashov et al. 2017).

Three studies identified by EAG (Babashov et al. 2017; Vieira et al. 2019; Kapamara et al. 2014) formulated certain human and physical resources into a DES model to measure the effect of changes in the resources in the outputs such as ready-to-treat to treatment (RTTT) waiting time. As previously described in Section 8.1, EAG has reviewed the implication of the DES technique in evaluating radiotherapy treatment process and believes that this method could be used to evaluate system capacities in different settings using various treatment planning systems including ProKnow. This complex modelling would need the following additional data:

- Number of physical resources (for example, number of linear accelerators);
- Number of staff (for example, dosimetrists, oncologists, radiographers);
- Patient or cancer characteristics (for example, age, gender, anatomical cancer location, stage);
- Treatment characteristics (for example, palliative or curative, treatment modality, dose, fractionation).

Evidence gap: Any future DES would need detailed data regarding the inputs described above so that system capacity and costs can be accurately captured and included for any estimation of cost-effectiveness for using ProKnow.

8.3. *Approach to cost analysis*

There currently remains some uncertainty regarding the impact on peer review of using ProKnow. Therefore, in the absence of any relevant published

economic studies, the EAG has conducted a simple cost-minimisation analysis to determine the cost of implementing ProKnow, which will likely need to be offset either through cost savings elsewhere in the pathway or through improved patient benefit. A cost-minimisation analysis (similar to that applied by Norum et al. 2005) was developed in Microsoft Excel focusing on the difference in costs for peer review between ProKnow and standard care from the perspective of the NHS. Given the significant amount of uncertainty these analyses are only intended to provide an indicative reflection on cost based on assumptions for standard care and the impact of ProKnow on peer review.

8.4. *Results from the economic modelling*

In order to determine a per-patient cost of implementing ProKnow, the EAG has assumed that each centre has a minimum of 2 linacs (range suggested by Clinical Experts was 2 to 15 linacs per centre, Appendix D2b), with 500 individual patients (classed as new treatment starts) treated on each linac each year. Distributing the cost of ProKnow (with 1 additional linac and additional 1TB storage) at a total annual fixed cost of [redacted] over 1,000 patients is the equivalent to [redacted] per patient per year. For those individuals who previously needed and received peer review for clinical reasons, that will remain unchanged with the addition of ProKnow. There is the possibility that there may have been some individuals whose treatment plans could or should have been peer reviewed but were not, and ProKnow may facilitate this to now happen. For every additional peer review that takes place using ProKnow, which would not have previously done so, a peer review lasting 30 minutes with 2 clinical oncologists would cost a further £123. Scenario analysis exploring the cost implication of increased patient throughput and 1% increase in plans undergoing peer review using ProKnow are presented in Table 8. Intuitively, the more patients a linac can treat in a year, the more the cost of ProKnow is distributed and the lower the cost per patient cost. A conceptual 1% increase in the proportion of plans undergoing peer review lasting 15, 30, and 45 minutes would cost an additional £0.62, £1.23, and £1.85 per patient respectively (irrespective of patient throughput) based on staff time of 2 oncologists conducting this review.

Table 8: Scenario analysis for cost of using ProKnow per year

Scenario	Cost of technology per year	Cost per patient per year			
		500 patients*	1000 patients* (EAG basecase)	1500 patients*	2000 patients*
ProKnow base package plus additional linac and additional 1TB storage, no change in peer review activity	[redacted]	[redacted]	[redacted]	[redacted]	[redacted]
Using ProKnow (as above) with an additional 1% undergoing peer review (each 15 minutes).	[redacted]	[redacted] (additional £0.62)	[redacted] (additional £0.62)	[redacted] (additional £0.62)	[redacted] (additional £0.62)
Using ProKnow (as above) with an additional 1% undergoing peer review (each 30 minutes).	[redacted]	[redacted] (additional £1.23)	[redacted] (additional £1.23)	[redacted] (additional £1.23)	[redacted] (additional £1.23)
Using ProKnow (as above) with an additional 1% undergoing peer review (each 45 minutes).	[redacted]	[redacted] (additional £1.85)	[redacted] (additional £1.85)	[redacted] (additional £1.85)	[redacted] (additional £1.85)

*assuming 2 linacs per centre
Abbreviations: N/A, not applicable.

The cost of reversing a decision to adopt ProKnow if following the generation of further evidence suggests that the technology is not likely to be either cost effective or cost saving is likely to be relatively minimal when compared to the cost of a new linac. This is because the pricing model is based on an annual software license that could be stopped with no other equipment costs or currently envisaged changes to the treatment planning pathway, which would need to be reversed or 'written-off'. Furthermore, discussion with a Clinical Expert around the value proposition highlighted that ProKnow does not conduct anything different or in addition to standard of care (Appendix D2a), which would support this minimal cost to reserve the adoption of ProKnow.

Value of information analysis

A value of information analysis for the early economic evaluation model has not been conducted. A value of information estimate is specific to the model and the parameters used within a model. Here an early economic model has been conducted focusing only on costs and though technically a value of information could be estimated it would not be informative because the model as presented does not capture the full nature of the decision problem. For example, the model is currently a simplified cost analysis. Therefore, any value of information analysis would exclude impacts on patient health.

9. Interpretation of the evidence

9.1. *Interpretation of the clinical evidence*

Currently, there is a lack of prospective and comparative evidence for ProKnow. This means that it is not possible to show the impact of ProKnow on treatment planning outcomes, quality assurance, or hospital resource use. The evidence highlights the versatility of ProKnow to enable the sharing of data, including radiotherapy treatment plans and tools to enable quality assurance and review either through peer-to-peer review or scoring metrics. ProKnow offers a standardised platform for services to share data enabling accessibility across multiple professionals or multiple centres to facilitate peer review in line with RCR guidance. Future uses of ProKnow may include evaluation of AI technologies for treatment planning and contouring, or data linkage to national routine datasets to determine impact on patient outcomes.

9.2. *Interpretation of the economic evidence*

No full or partial economic evaluations of ProKnow were identified by the EAG. It is feasible that ProKnow may facilitate an increase in peer reviews and provide a platform to document quality assurance of radiotherapy treatment plans, which may lead to patient benefit (reduced travel, better outcomes). However, increased peer review (by any means, not specific to ProKnow) is likely to increase staff time and costs associated, which should be considered in addition to the initial capital purchase costs of ProKnow. Improvement in treatment plan quality attributed to ProKnow is likely to be difficult to quantify and attribute costs to. The EAG identified DES modelling as the most relevant modelling approach to investigate the impact of

introducing ProKnow into the process of radiotherapy treatment planning, which would allow the quantification of broader staff and machine resourcing. A more complex 'whole system' DES, or multiple separate DES models could be built to incorporate the treatment of all cancers within a radiotherapy centre, including the complexity of individual cancer anatomical locations or types, treatment modalities, and workforce issues specific to the different specialties involved in radiotherapy treatment. However, a better understanding of current practise, and quantification of rate limiting steps and uncertainty regarding the radiotherapy treatment plan process would be needed before this could be constructed.

9.3. *Integration into the NHS*

As part of the Radiotherapy Transformation Programme, aiming to improve the quality and reduce variability of radiotherapy service delivery, NHSE commissioned a pilot of ProKnow (including all 3 modules) in March 2022, across 49 specialist cancer centres with funding provided until March 2025 (Appendix D3). The Clinical Experts confirmed that NHSE did not specify any data collection requirements as part of the commission (Appendix D2b). NHSE advised that they plan to audit the data uploaded to ProKnow using plan quality metrics and produce anonymised reports demonstrating the range of compliance. The number of Trusts submitting data will be monitored and the reports will be received by a clinical leadership group (Appendix D3). The EAG note that data routinely collected within RTDS includes treatment modality, prescription, route and method of administration, treatment intent (curative, palliative), use of radiopharmaceuticals, and dose metrics. The EAG consulted with the RTDS who advised that neither peer review nor specific use of ProKnow is captured explicitly within the proposed update (version 6) of the RTDS. This update is still under consultation and has not yet been implemented across the NHS (Appendix D4). RTDS have proposed capturing the conduct of peer review in an 'other' free text data item (associated with data field RLP9); however the EAG is uncertain to the completeness or quality of the contents of this particular data field.

None of the Clinical Experts, from 4 different NHS Trusts, noted practical difficulties in implementing ProKnow at their centre. All 5 Clinical Experts who responded to the EAG were able to submit data to ProKnow as of 18 November 2022 (Appendix D2b). One Clinical Expert noted that the uploading and retrieval of radiotherapy treatment plans using ProKnow could introduce safety concerns if the naming convention is changed during this process (Appendix D2b). One Clinical Expert noted that some treatment planning software does not allow an easy connection to ProKnow without an external manufacturer's input or software upgrade (Appendix D2b). Recommendation 12 of the RCR radiotherapy target volume definition and peer review guidance notes that 'hospitals and Cancer Alliances should facilitate peer review between departments by investing in appropriate IT infrastructure and information governance'. NHSE informed the EAG that as of 28 November 2022 all commissioned centres have local administrators for ProKnow in place, however there are some issues (not specified) with information governance leads impacting the full implementation of ProKnow (Appendix D3).

9.4. *Ongoing clinical trials*

A total of 34 clinical trial registrations were identified by the EAG during literature searching; all described 'Elekta', but none included the use of ProKnow. The Company confirmed there are no ongoing or completed clinical trials relating to ProKnow (Appendix D1). The Company highlighted an Australian cancer research organisation, Tasman Radiation Oncology Group (TROG), as a ProKnow user. The EAG did not identify any study using ProKnow from a search of the open trials (recruiting, in follow-up), upcoming, and past trials did not listed on the TROG website (accessed 08 December 2022).

A conference abstract by Shepherd et al. (2022) outlined an evaluation of dosimetric review using ProKnow on the quantity and frequency of re-plans and patient time to treatment in a single Australian centre. Between February and September 2021, 55 patients had plan metric and time comparisons available for analysis. Currently, no results have been reported and there are

no details of a corresponding author so preventing the EAG seeking further data. The EAG consider that this study may be able to provide information relating to radiotherapy treatment planning time and resources, however note that no planned end date for analysis has been reported. The EAG notes that this service evaluation may lack applicability to the UK NHS.

An abstract by Henson et al. (2020) outlined an ongoing pilot evaluation of the impact of an online training programme, delivered by educators based in the US, to develop plan evaluation and contouring skills for staff managing head and neck cancer cases in the Philippines using ProKnow. No further publications or results were reported from this work and no study dates were provided. The EAG contacted the lead author on 28 October 2022; no response was received as of 23 December 2022. The EAG notes that this evaluation of training may lack applicability to the UK NHS.

9.5. *Evidence gap analysis*

The evidence identified and summarised by the EAG comprises service evaluation or audits not requiring ethical approval; there is a lack of published research, including real world evidence, relevant to the decision problem. Prospective and comparative evidence is feasible but lacking. There is large variation in peer review practise across the NHS, including the proportion of treatment plans undergoing peer review, who conducts peer review, and the tools to support how peer review is conducted in the NHS. Additional work is needed to quantify this variation and uncertainty associated with the costs of delivering standard of care in radiotherapy treatment planning. As ProKnow has been widely commissioned across the NHS in England, further randomised evidence using ProKnow may be unfeasible, however real world data collection should be considered (NICE Real World Evidence Framework, 2022) to attempt to quantity the heterogeneity of current practise in the NHS. Real world data could be used to map out the current standard of care patient pathway in the NHS, with its associated costs, real world data could also be used to evaluate the impact of ProKnow on this pathway. The EAG has identified that there is a lack of existing routine data collection that captures

relevant outcomes, which limits the applicability of retrospectively collected data. However, prospective data collection is feasible.

Population gaps:

None of the available evidence evaluates the impact of ProKnow on prospective radiotherapy treatment and patient outcomes. Of the included evidence, 9 anatomical cancer locations were considered, but these were represented mainly by 1 or 2 clinical case studies, and so may not be representative of the type or complexity of cancer cases seen within UK NHS standard care. There remains some anatomical locations where evidence relating to the impact of using ProKnow is lacking. Three Clinical Experts note that some complex cancers may need more in-depth peer review and take longer to plan treatments and ranges in peer review between cases can vary greatly (Appendix D2b). One Clinical Expert noted that local radiotherapy software would be used for peer review, with most reviews taking place internally, they also noted that the peer review workflow could be interrupted using ProKnow through the uploading and downloading of plans for revision, which may introduce variation or safety concerns if the naming convention is altered in the process (Appendix D2b). The use of ProKnow, in support of peer review and treatment plan quality assurance, may result in certain cancers experiencing greater benefits, may support wider adoption of more complex treatment modalities, and may improve outcomes at smaller centres through ProKnow facilitating access to oncologists across the UK. However, evidence to support this is wholly lacking.

Intervention gaps:

All 12 included studies outlined in Table 2 and 18 studies included in Appendix B involved the use of ProKnow. There is some evidence to show wider use of ProKnow for evaluation of other methodologies to quality assure treatment plans, such as AI technologies. This may be beneficial in future as these technologies could improve standardisation and training across radiotherapy services.

There are no published economic evaluations of ProKnow. In addition, there is currently no direct evidence on how ProKnow affects peer review or the patient pathway.

Comparator gaps:

The Clinical Experts highlighted that ProKnow may be used to facilitate peer review, particularly with external colleagues (Appendix D2a-c). Data relating to the number of peer reviews performed (internal and external), time taken to perform peer review, method of peer review (ProKnow, in-person, on demand, other), compliance with local peer review protocols (number of peer reviews conducted where deemed appropriate), could be collected to quantify current practise, including the use of ProKnow to facilitate this aspect of treatment planning including improved accessibility, service delivery streamlining, or increased quality assurance.

During the scoping meeting, NHSE noted that data fields relating to the conducting of peer review have been added to the most recent version (version 6) of the national Radiotherapy Dataset (RTDS). However, it is unclear to 6 Clinical Experts contributing to this report, where or how this would be recorded in RTDS (Appendix D2b). NHS Digital have advised the EAG that version 6 of RTDS is currently under consultation but does not contain any specific data item to capture specific use of ProKnow, and that no data items currently capture conduct of peer review (Appendix D4). NHS Digital also advised that free-text fields are available in RTDS which could capture some of the key outcomes relating to the use of ProKnow and the number of peer reviews conducted, however guidance to users is currently lacking. Therefore, the EAG would recommend that clear instructions should be provided to specialist services delivering external beam radiation to accurately document the peer review process within routine data collection within RTDS. This would enable centres to demonstrate improved adherence to national guidelines regarding peer review of radiotherapy treatment plans without ProKnow, and after implementation of ProKnow, which may continue to improve over time.

Outcome gaps:

Currently, there is no evidence for 5 of the outcomes within the NICE Final Scope (2022) (radiotherapy treatment planning time, number of internal and external peer reviews performed, impact on staffing and treatment planning resources, ability for data linkage to national registries, reduction in inequality of access). However, due to the different functions of the ProKnow modules and variety of outcomes of interest, such as impact on radiotherapy treatment planning using ProKnow DS or impact on radiotherapy training using ProKnow CA, the EAG consider that a single study design is unlikely to measure all the outcomes of interest, as defined in the NICE Final Scope (2022). The recommended study design (pragmatic in the NHS and utilising real world evidence where possible) to fill the evidence gap therefore varies by outcome of interest, Table 9.

There is no evidence demonstrating the impact of ProKnow on prospective patient treatment planning, quality assurance, or the patient pathway. There are no published economic evaluations of ProKnow. There is limited robust evidence relating to usability or user experience of ProKnow. There is evidence highlighting the ability to share data using ProKnow with a wide range of professionals, between centres, and also between countries, however there is no published qualitative evidence relating to the ease of use of ProKnow. There is no evidence demonstrating the impact of ProKnow on clinical oncology training in the UK.

Table 9: Evidence gap analysis

Outcomes	Summary of Existing Evidence (detailed PICO found in Table 2 Section 4.2)	Ongoing Clinical Trials (detailed PICO in Section 9.4)	Real World Evidence	Models and Economic outcomes
Impact on radiotherapy treatment planning quality assurance, Including surrogate, qualitative, and quantitative measures such as:	There remains a lack of evidence within a prospective patient cohort, including the number of changes to treatment plans, changes in treatment plan scores, number of plan revisions based on ProKnow feedback, and patient outcomes ☑☒	Shepherd et al. (2022): single centre study in Australia (n=55), reporting plan dose metrics and planning time. Lacks applicability to the UK NHS☑☒	None ☒	None ☒
Usability or user experience	There is limited (qualitative or non-qualitative) evidence reporting on the usability or user experience of ProKnow ☑☒	None ☒	None ☒	None ☒
Ease of retrieving and archiving patient data	No study reported qualitative outcomes specifically related to ease of retrieving or archiving patient data ☒	None ☒	None ☒	None ☒
Radiotherapy treatment planning time	No study investigated the impact of using ProKnow on radiotherapy treatment planning time ☒	Shepherd et al. (2022): single centre study in Australia (n=55), reporting plan dose metrics and planning time. Lacks applicability to the UK NHS ☑☒	None ☒	None ☒
Number of internal and external peer reviews performed	None ☒	None ☒	RTDS (Appendix D4) may provide an indication of the number of peer reviews conducted using either ProKnow or other methods if this detailed information is reported within an existing free-text data field. To ensure data quality and completeness, further instruction should be provided to specialist NHS radiotherapy treatment centres advising them of how and where this should be entered into RTDS ☑☒	None ☒
Impact on staffing and treatment planning resources	None ☒	**Shepherd et al. (2022)**:single centre study in Australia (n=55), reporting plan dose metrics and planning time. Lacks applicability to the UK NHS ☑☒	None ☒	None ☒
Impact of the system on clinical oncology training	No comparative evidence or validated competency assessment ☑☒	**Henson et al. (2020);**pilot evaluation of online training programme (n=7 academic centres offering radiation oncology residencies in the Philippines). May not be representative of NHS practise or standards of UK-based training ☐☐	None ☒	None ☒
Ability for data linkage to national registries	None ☒	None ☒	It is unclear how comprehensively peer review conduct (how frequently and how it is conducted) is captured in RTDS (**Appendix D4**) ☑☒	None ☒
Reduction in inequality of access	None ☒	None ☒	None ☒	None ☒
Key: ☑ evidence available; ☒ evidence unavailable; ☑☒ limited evidence available				

Only 1 ongoing study may be able to provide further information relating to the impact of ProKnow on plan quality assurance, treatment planning time, and resource use (Shepherd et al. 2022). However, this is a small non-UK-based sample (n=55) and the anatomical cancer location was not specified (Table 4). No data are currently available, and no study end date has been specified, however even if results were available, they may not be applicable to the NHS in England.

There is no UK data available on the outcomes relevant to the resource use and subsequent micro-costing or DES modelling of radiotherapy treatment planning in standard NHS care (such as time of treatment planning, number of peer reviews undertaken, proportion of treatment plans changed following peer review, or time of staff involved).

9.6. *Key areas for evidence generation*

There are currently 51 NHS Acute Trusts delivering external beam radiotherapy in England. Given that all specialist cancer centres in England have been commissioned by NHSE to use ProKnow (Appendix D3), the EAG proposes that a range of pragmatic study designs, utilising real world evidence, could be conducted to address the key areas of uncertainty, Table 10. The EAG consider that the outcomes of interests could be addressed through national data collection as part of service evaluations associated with the commissioning of ProKnow across the NHS in England. Evidence generated as part of a large national evaluation would be reflective of practise across the UK NHS and likely robust for future decision-making. Furthermore, to assess aspects of ProKnow as a facilitator of quality assurance of radiotherapy treatment plans ethical approval and power calculations would likely not be needed because of its widespread use and if information were gathered as part of a service evaluation or audit.

Additional uses of ProKnow may facilitate the use of other technologies in the NHS. For example:

- AI-based treatment planning, which has been highlighted as a useful tool to support quality assurance and reduce planning time for radiotherapy treatment;

- wider adoption of SABR, through the availability of treatment plan scorecards, based on national guidelines, to offer a quality assurance tool without possible reliance on staff-based peer review (Appendix D2c).

Table 10: Evidence generation recommendations

Outcome of interest	Study design	Population	Intervention	Comparator	Outcome measures	EAG Comments
• The impact of ProKnow on radiotherapy treatment planning QA • Number of internal and external peer reviews performed	Interrupted time-series	Services delivering radiotherapy	ProKnow for peer review.	Local protocol for conducting peer review.	• Description of how ProKnow was used • Proportion of radiotherapy treatment undergoing peer review each year (as a surrogate marker of adherence to national guidelines) • Surrogate markers of plan quality (for example dose to organs at risk, planned target volume) • Proportion of radiotherapy undergoing major, minor, and no changes at peer review (as a marker of improvement of treatment	Robustness of comparative conclusions relies on the availability of data preceding the introduction of ProKnow. The EAG considers that the change in the outcomes of interest following the introduction of ProKnow may be beneficial in addressing some of the uncertainties highlighted. A before-and-after study could only be conducted in centres where ProKnow is not already fully implemented. A large sample size or follow-up time may be needed because of the large variance in clinical practise and service delivery, however this may be addressed by the widespread use of ProKnow across the NHS and the EAG consider a year of data collection could be appropriate based on the estimations of patient throughput per linac, and the number of linacs per centre, although note this would depend on the number of services participating. Data linkage to routinely collected data would allow for tests of association between conduct and impact of peer review on subsequent short, medium and long-term

Outcome of interest	Study design	Population	Intervention	Comparator	Outcome measures	EAG Comments
					plan quality) • NHS Trust of reviewer (also as surrogate of measuring inequality of access at a centre-level) • RTTT	patient outcomes. Therefore, data linkage may enable cost-effectiveness analysis of peer review. The Clinical Experts and RCR recognises that there is currently no standardised definitions of major and minor changes (Appendix D2c, RCR 2022), which would need to be consistently applied to determine meaningful outcomes. Appendix 6 in the RCR guidance (2022) provides definitions of major and minor changes that could be nationally adopted.
• Usability and ease of retrieving and archiving patient data	Qualitative study	Radiotherapy professionals involved with treatment planning	ProKnow	None	• Likert scale	A large sample size representative of ProKnow users could be achievable because of the availability of ProKnow as part of the NHSE Commissioned Pilot. Study activities could be evaluated at different stages of ProKnow implementation and familiarity depending on the uptake timing of different professionals.
• Radiotherapy treatment planning time • Impact on staffing & treatment plann	Time and motion study or survey data	Radiotherapy professionals involved with treatment planning	ProKnow	Local protocol regarding peer review.	• Time • Job title/band of staff • Number of staff	This would allow accurate resource use and therefore costing to be undertaken for the integration of ProKnow into the treatment planning pathway.

Outcome of interest	Study design	Population	Intervention	Comparator	Outcome measures	EAG Comments
ing resources						
• Impact of the system on clinical oncology training	Training evaluation	Healthcare professionals undergoing radiotherapy treatment planning training	ProKnow CA and PS for contouring and treatment planning training.	Standard training within NHS	• Number of treatment plans meeting national guidelines (in terms of dose to target order and organs at risk) • Scorecards	The EAG consider that a well-designed before-and-after study could be considered to address this outcome.
• Inequality of access (patient)	Cross-sectional cohort	Patients undergoing radiotherapy treatment planning (as need for specialist oncologist will vary by type of cancer)	Patients where ProKnow was used during treatment planning	Patients where ProKnow was not used during treatment planning	• Type of cancer where ProKnow used • Trusts using ProKnow • Prospective data linkage to routinely collected data (such as RTDS, HES, and Civil Mortality registration datasets which all include patient identifiers: NHS number, date of birth, postcode, gender), to determine differences in dose to target organs, adverse events	The EAG consider that this evidence could show whether ProKnow enables equal opportunity for individual treatment plans to undergo peer review or lead to similar quality plans or outcomes. Because of the existing variation in peer review practises across services, including the availability of local agreements and resources, these outcomes are unlikely to be addressed outside of real world evidence.

Outcome of interest	Study design	Population	Intervention	Comparator	Outcome measures	EAG Comments
					related to damage to non-target organs, or survival	
Abbreviations: EAG, External Assessment Group; HES, hospital episode statistics; RTDS, National Radiotherapy Dataset; RTTT, ready-to-treat treatment time.						

10. Conclusions

10.1. *Conclusions from the clinical evidence*

No evidence was identified that reported on 5 of the 9 outcomes identified within the NICE Final Scope (2022) (radiotherapy treatment planning time; number of internal and external peer reviews performed; impact on staffing and treatment planning resources; ability for data linkage to national registries; reduction in inequality of access). These outcomes are likely to be key factors in the demonstration of the claimed benefits of ProKnow, such as the ability to conduct and improve efficiency of peer reviews extending accessibility to high-quality treatment plans and the collection data that can be audited in a centralised place.

Two studies were set exclusively within the UK, including Taylor and Richmond (2020) that included 44 NHS and 4 private radiotherapy services. The implementation of ProKnow within the NHS may be hampered by issues with information governance and IT constraints, which may not be experienced in other settings such as private healthcare or other countries. None of the Clinical Experts reported any information governance issues when implementing ProKnow within NHS services, however a prospective qualitative study could be implemented across the NHS to capture this information (Appendix D2b).

The published evidence highlighted the versatility of ProKnow to enable sharing of radiotherapy treatment plans, between staff, between centres and between countries in some examples, to enable quality assurance and review of treatment plans either through peer-to-peer review or scoring metrics. The

evidence also highlights the functionality of ProKnow as a training tool for treatment planning and contouring, which the Clinical Experts have highlighted as a possible benefit to improve the quality and skill of clinicians and planners and reduce interoperator variability (Appendix D2c). There remains a lack of evidence to quantify the impact of ProKnow (increased peer review, improved quality of professional training) on patient care, however improvement in the quality of radiotherapy treatment plans then resulting in better patient outcomes is plausible, but difficult to quantify.

It is important that information, including the number and timings associated with peer review, impact on overall treatment planning, and impact on resources, is captured related to the use of ProKnow in the UK to identify key aspects for effectiveness and the impact on subsequent costs. This data could be captured within the 3-year commissioned pilot by NHSE, which includes all NHS radiotherapy centres across England.

10.2. *Conclusions from the economic evidence*

Based on the reviewed literature by EAG, there are no economic evaluations or cost analyses of ProKnow. Therefore, the full cost implications and economic benefits of ProKnow compared with standard practise of radiotherapy treatment planning is unknown. Therefore, the economic benefits of ProKnow within radiotherapy treatment planning remain unclear. An interrupted time series would pragmatically enable an evaluation of peer review practises in services not currently implementing ProKnow.

Clinical Experts have advised that the main benefit of ProKnow is that it can facilitate the peer review process of treatment planning, increasing adherence to national RCR guidance. The EAG identified 4 studies which evaluated the radiotherapy treatment plan peer review process which highlighted further variation. The EAG consider that a DES would be the most appropriate approach for a future economic evaluation comparing the use of ProKnow with standard care and would allow the incorporation of staff and machine resource capacity to be incorporated into the decision problem.

The EAG recommends data generation for following parameters:

- number of peer reviews performed, including re-review (external or internal);
- duration of peer review (including number and band of staff involved);
- proportion of treatment plans requiring change and magnitude of change;
- ready-to-treat to treatment time.

11. Summary of the combined clinical and economic sections

There is currently no comparative evidence available to show the clinical or economic benefits of the use of ProKnow within the NHS. The EAG recommends a well-designed before-and-after study or interrupted time series to capture the impact on clinical outcomes and resources use when compared to current NHS practise, and monitoring of radiotherapy treatment plan quality over time. The widespread commissioning of ProKnow across England creates an opportunity to collect this additional evidence prospectively.

12. References

Albert AA, Duggar WN, Bhandari RP et al. (2018) Analysis of a real time group consensus peer review process in radiation oncology: an evaluation of effectiveness and feasibility. Radiation Oncology. Dec;13(1):239

Babashov V, Aivas I, Begen MA et al. (2017) Reducing patient waiting times for radiation therapy and improving the treatment planning process: a discrete-event simulation model (radiation treatment planning). Clinical Oncology. 29(6): 385-91

Becksfort J, Wilson L, Xie F, et al. (2021) A federated database design for pediatric outcomes modelling. Medical Physics 48(6): e117-e635 (abstract)

Bertero M, González Armesto R, De Brida J et al. (2021) Optimization parameters in bladder and rectum for gynecologic cancer treatment with VMAT Technique through ProKnow platform. [abstract]. In: International Conference on Advances in Radiation Oncology. 16-19 February 2021: Abstract 83

Bisgaard A, van Lier A, Coolens C et al. (2022) PO-1754 Delineation-related ADC variation between centres in the Elekta Unity MR linac Consortium. [poster]. In: Physical Aspects of Quantitative Functional and Biological Imaging. 01 May 2022; 170(Suppl1): S1557-S1558

Byrne J, Walker C, Richmond N. (2021) NHS England Evaluation of Proknow – Lung SABR Scorecards [abstract]. In: Institute of Physics and Engineering in Medicine Stereotactic Ablative Radiotherapy Conference, 22 April 2021: 12

CADTH (2022) Economic evaluations and models – Embase. CADTH search filters database. [online; accessed 28 November 2022]

Chamberlain M, Krayenbuehl J, van Timmeren JE, et al. (2021) Head and neck radiotherapy on the MR linac: a multicentre planning challenge amongst MRIdian platform users. Strahlentherapie und Onkologie. 197(12): 1093-103

Fairchild A, Straube W, Laurie F, et al. (2013) Does quality of radiation therapy predict outcomes of multicentre cooperative group trials? A literature

review. International Journal of Radiation Oncology, Biology, Physics. 87(2): 246-60

Gao Y, Shen C, Gonzalez Y, et al. (2022) Intelligent automatic treatment planning for prostate cancer stereotactic body radiation therapy. Medical Physics. 49(6): e445 (abstract)

Hardcastle N, Nelms B, O'Connor L, et al. (2019) OC-0521 SRS plan quality with variation in modality: results of an international planning competition. Radiotherapy and Oncology. 133(Supplement 1); S272-S273 (abstract)

Hardcastle N, Bignell F, Nelms B et al. (2020) The challenge of planning vertebral body SBRT: Optimizing target volume coverage. Medical Dosimetry. 45(3): 302-7

Henson L, Li B, Rees H. (2020) Development of a pilot head and neck contouring and plan evaluation telehealth curriculum for existing radiation oncology centers in the Philippines [abstract]. In: Radiation Oncology Education Collaborative Study Group Symposium, 15 May 2020: 12

Hill SR, Bhattarai N, Tolley CL, et al. (2022) Eliciting willingness-to-pay to prevent hospital medication administration errors in the UK: a contingent valuation survey. BMJ Open 12(2): e053115

Hayakawa T, Kawakami S, Soda I, et al. (2019) Dosimetric factors associated with long-term patient-reported outcomes after definitive radiotherapy of patients with head and neck cancer. Radiation Oncology 14(1): 221

Irabor O, Swanson W, Oladeru OT, et al. (2019) The educational impact of web-based platforms for therapeutic radiology in Sub-Saharan Africa. Journal of Global Radiology. 5(1): 1

Johnson P, Schubert L, Kim G, Faught J, Buckey C, Conroy L et al. (2022). Experience and survey results from a national hands-on workshop on simulated error training for the physics plan review. Medical Physics. 49(6): e302-e303 (abstract)

Jordan P, Adamson P, Bhattbhatt V et al. (2022) Pediatric chest-abdomen-pelvis and abdomen-pelvis CT images with expert organ contours. Medical Physics. 49(5): 3523-8

Kapamara T, Sheibani K, Petrovic D et al. (2007). A simulation of a radiotherapy treatment system: A case study of a local cancer centre. InORP3 meeting Sep 12.

Lewis PJ, Court LE, Lievens Y et al. (2021) Structure and processes of existing practice in radiotherapy peer review: a systematic review of the literature. Clinical Oncology. 33(4):248-60

Li B, Engwo A, Perez T, et al. (2020) Variability of current clinical practices for locally advanced cervical cancer through assessment of contouring, prescription, and IMRT/VMAT planning abilities. International Journal of Radiation Oncology Biology Physics 108 (supplement 3): e423-4 (abstract)

Lin D, Wahid KA, Nelms E, et al. (2022) “E Pluribus Unum”: prospective acceptability benchmarking from the Contouring Collaborative for Consensus in Radiation Oncology (C3R0) crowdsourced initiative for multi-observer segmentation. medRxiv. 2022.09.23.22280295

Martin-Garcia E, Celada-Álvarez F, Pérez-Calatayud MJ, et al. (2020) 100% peer review in radiation oncology: is it feasible?. Clinical and Translational Oncology. 22(12):2341-9

McLaren KR, Ryan J, Jager C, Carmichael MA (2021) Colouring outside the lines: a visionary digital teaching tool for students. Journal of Medical Radiation Sciences. 68: 86 (abstract)

McClelland S, Achiko FA, Bartlett GK, et al. (2021) Analysis of virtual versus in-person prospective peer review workflow in a multisite Academic Radiation Oncology Department. Advances in Radiation Oncology. 6(6):100766

Moghanaki D, Slotman B, Swaminath A, et al. (2020) Assessing the variability and quality of lung stereotactic radiation therapy treatment plans using a web-based Crowdsourcing platform. Practical Radiation Oncology. 10(3): e118-27

Norum J, Bruland ØS, Spanne O, et al. (2005) Telemedicine in radiotherapy: a study exploring remote treatment planning, supervision and economics. Journal of Telemedicine and Telecare. 11(5): 245-50

Ohri N, Shen X, Dicker AP, et al. (2013) Radiotherapy protocol deviations and clinical outcomes: a meta-analysis of cooperative group clinical trials. Journal of the National Cancer Institute. 105(6): 387-93

Penoncello G, Gao Y, Sensoy L, et al. (2022) A multi-institutional multi-platform inter-comparison of dose volume histograms construction differences on eight commercial treatment planning and dose reporting systems. Medical Physics. 49(6): e921 (abstract)

Pepin MD, Penoncello GP, Brom KM, et al. (2022) Assessment of dose-volume histogram precision for five clinical systems. Medical Physics. 49(10): 6303-18

Powell T, Kulakiewicz A, Baker C. (2022) Access to radiotherapy. House of Commons Library Debate Pack 2022/0003, available at https://researchbriefings.files.parliament.uk/documents/CDP-2022-0003/CDP-2022-0003.pdf [accessed 21/12/2022]

Qureshi BM, Mansha MA, Karim MU, Et al. (2019) Impact of peer review in the radiation treatment planning process: experience of a tertiary care university hospital in Pakistan. Journal of global oncology. 5:1-7.

Roumeliotis M, Morrison H, Conroy L, et al. (2022) Competency-based medical education in radiation therapy treatment planning. Practical Radiation Oncology. 12(3): e232-8

Schmidt M, Folkerts M, Abraham C, et al. (2021) API driven plan scorecard designer for the evaluation of external beam planning quality. Medical Physics. 48(6): e581 (abstract)

Shen C, Nguyen D, Chen L, et al. (2020) Operating a treatment planning system using a deep-radiation reinforcement learning-based virtual treatment

planner for prostate cancer intensity-modulated radiation therapy treatment planning. Medical Physics. 47(6): 2329-36

Shen C, Men C, Gao Y, et al. (2021a) AI agent competing with hyman in planning challenge: a human-expert level virtual treatment planner network for prostate cancer stereotactic body radiation therapy (SBRT). Medical Physics. 48(6): e125 (abstract)

Shen C, Chen L, Gonzalez Y, et al. (2021b) Improving efficiency of training a virtual treatment planner network via knowledge-guided deep reinforcement learning for intelligent automatic treatment planning of radiotherapy. Medical Physics. 48(4): 1909-20

Shepherd M, Podreka A, Porter B et al. (2022) Uniting plan quality metrics using a cloud-based software for improving radiotherapy planning efficiency and quality Journal of Medical Radiation Sciences. 65(4): 445-63 (abstract)

Spencer K, Jones CM, Girdler R, et al. (2021) The impact of the COVID-19 pandemic on radiotherapy services in England, UK: a population-based study. Lancet Oncology 22: 309-20

Sprouts D, Shen C, Chi Y. (2021) Inverse treatment planning using a virtual treatment planner (VTP) for prostate cancer treated with intensity modulated radiation therapy. Medical Physics. 48(6): e121 (abstract)

Sprouts. D (2022a) Advancing the radiation oncology clinic with motion management and automatic treatment planning. [PhD thesis] University of Texas Arlington Libraries Research Commons Online Repository.

Sprouts D, Gao Y, Wang C, et al. (2022b) The development of a deep reinforcement learning network for dose-volume-constrained treatment planning in prostate cancer intensity modulated radiotherapy. Biomedical Physics and Engineering Express. 8(4): 045008

Sritharan K, Akhiat H, Cahill D, et al. (2022) PD-0571 Determining interobserver variability in prostate bed CTV target delineation using MRI. Radiotherapy and Oncology. 170(Supplement 1): S500-S501 (abstract)

Taylor T and Richmond N. (2020) A UK wide study of current prostate planning practice. British Journal of Radiology. 2020; 93(1111): 20200142

Vieira B, Demirtas D, B van de Kamer J, Hans EW, van Harten W (2019) Improving workflow control in radiotherapy using discrete-event simulation. BMC medical informatics and decision making. 19(1):199

Wahid KA, Lin D, Nelms BE, et al. (2022) Large-scale crowdsourced radiotherapy segmentations across a variety of cancer anatomic sites: interobserver expert/non-expert and multi-observer composite tumor and normal tissue delineation annotation from a prospective educational challenge. medRxiv. 2022.10.05.22280672

Zheng D, Liang X, Smith A, et al. (2018) The effect of dose calculation algorithms on lung SBRT optimization and plan quality scoring. Medical Physics. 45(6): e120-e706 (abstract)

13. Appendices

Appendix A: Clinical literature search

Appendix A1 - Search strategy (clinical evidence)

Database/Source	Platform/URL	Date range	Date searched	Retrieved Results
MEDLINE(R) and In-Process, In-Data-Review & Other Non-Indexed Citations	OVID	1946 to November 07, 2022	08/11/2022	16
Embase	OVID	1988 to 2022 Week 44	08/11/2022	35
CENTRAL	Cochrane Library	Issue 10 of 12, October 2022	08/11/2022	28
International HTA Database	https://database.inahta.org/	Up to 8th November 2022	08/11/2022	3
NIHR Database	https://www.nihr.ac.uk/health-and-care-professionals/search-our-evidence.htm	Up to date	08/11/2022	2
Google Scholar	https://scholar.google.com/	Up to date	08/11/2022	35
Google advanced search	https://www.google.co.uk/advanced_search	Up to date	08/11/2022	9
Journal of Applied Clinical Medical Physics from American Association of Physicists in Medicines (AAPM)	https://aapm.onlinelibrary.wiley.com/journal/15269914	Up to November 2022	08/11/2022	3
The International Journal of Medical Physics Research and Practice by the American Association of Physicists in Medicines (AAPM)	https://aapm.onlinelibrary.wiley.com/journal/24734209	Up to October 2022	08/11/2022	11
Engrxiv (Pre-print repository)	https://engrxiv.org/index	Up to date	08/11/2022	0

MedRxiv (Pre-print repository)	https://www.medrxiv.org/	Up to date	08/11/2022	2
FDA Devices Database	https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm	Up to date	18/10/2022	1
ScanMedicine	https://scanmedicine.com/	Up to date	08/11/2022	26
NIH Clinicaltrials.gov	https://clinicaltrials.gov/	Up to date	08/11/2022	27
EU Clinical Trials Register	https://www.clinicaltrialsregister.eu/ctr-search	Up to date	10/11/2022	0
The Australian and New Zealand trial registry database	https://anzctr.org.au/TrialSearch.aspx	Up to date	08/11/2022	4

DATABASE/PLATFORM: Ovid MEDLINE(R) and In-Process, In-Data-Review & Other Non-Indexed Citations 1946 to November 07, 2022
Platform/URL: OVID
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 16
SEARCH STRATEGY: The full (more sensitive) search strategy that combined terms for ProKnow functionality with the company name, retrieved many irrelevant records, and a pragmatic approach to search for device name was taken in agreement with reviewers. The final search strategy consisted of searching for device name in Medline OVID all fields.
1 (Proknow* or Pro know*).af. (16)
All 16 results were downloaded into Endnote 2.0 for de-duplication.

DATABASE/PLATFORM: Embase 1988 to 2022 Week 44
Platform/URL: OVID
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 35
SEARCH STRATEGY:
1 (Proknow* or Pro know*).af. (35)
All 35 downloaded into Endnote 2.0 for de-duplication and further assessment.

DATABASE/PLATFORM: Cochrane Library CENTRAL Issue 10 of 12, October 2022
Platform/URL: https://www.cochranelibrary.com/advanced-search
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 28 from CENTRAL
SEARCH STRATEGY:
ID Search Hits
#1 Proknow* OR (Pro NEXT know) OR "Pro-know" 0

#2 MeSH descriptor: [Radiotherapy] explode all trees 6696
#3 (radiotherap* or (radiation NEXT therap*)):ti,ab 32597
#4 #2 OR #3 34750
#5 (Elekta) 68
#6 #4 AND #5 48
#7 MeSH descriptor: [Radiotherapy Planning, Computer-Assisted] this term only 334
#8 MeSH descriptor: [Radiotherapy, Image-Guided] this term only 76
#9 MeSH descriptor: [Image Processing, Computer-Assisted] explode all trees 3802
#10 MeSH descriptor: [Imaging, Three-Dimensional] explode all trees 1211
#11 ((treatment NEXT plan*) OR (therapy NEXT plan*) OR VTPN):ti,ab 4204
#12 (target* or contour* or delineat* or segment* or outlin* or autosegment* or auto-segment*):ti,ab 131302
#13 ((dose NEXT volume NEXT histogram*) or DVH or (radiation NEXT dose) or (radiation NEXT dosage) or (radiation NEXT dosimet*)):ti,ab 2717
#14 {OR #7-#13} 139861
#15 #6 AND #14 28
#16 MeSH descriptor: [Organs at Risk] this term only 90
#17 (contour* NEAR/3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)):ti,ab 164
#18 (delineat* NEAR/3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)):ti,ab 293
#19 (segment* NEAR/3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)):ti,ab 469
#20 (outlin* NEAR/3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)):ti,ab 75
#21 (autosegment* or auto-segment*):ti,ab 50
#22 {OR #16-#21} 1034
#23 #6 AND #22 4
#24 ((learn* or teach* or educat* or train*) and (contour* or protocol* or plan* or treat* or DVH or imag*)):ti,ab 101950
#25 #6 AND #24 4
#26 MeSH descriptor: [Cloud Computing] this term only 6
#27 MeSH descriptor: [Algorithms] explode all trees 4863
#28 MeSH descriptor: [Big Data] this term only 5
#29 MeSH descriptor: [Machine Learning] explode all trees 274
#30 MeSH descriptor: [Data Warehousing] this term only 0
#31 ("cloud-based" or (cloud NEXT based) OR "cloud-native" or (cloud NEXT native) OR "cloud-enabled" or (cloud NEXT enabled) OR "cloud-computing" or (cloud NEXT computing)):ti,ab 168
#32 ((data NEXT mining) or (data NEXT retrieval) or (data NEXT storage) or (data NEXT warehous*) or dataset* or (data NEXT management) or (data NEXT set*) or (data NEXT repositor*) or (big NEXT data) or (deep NEXT reinforcement NEXT learning) or DRL OR DICOM):ti,ab 9831
#33 {OR #26-#32} 14657
#34 #6 AND #33 5
#35 #1 OR #15 OR #23 OR #25 OR #34 in Trials 28

All downloaded into Endnote 2.0 for further assessment. No time limits used or focussed search by product name.

DATABASE/PLATFORM: International HTA Database
Platform/URL: https://database.inahta.org/
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 3
SEARCH STRATEGY:
Searching in All fields:
(elekta) OR (proknow*) OR ('pro know*')
Retrieved records exported and downloaded into Endnote 2.0 for further assessment.

DATABASE/PLATFORM: National Institute for Health and Care Research (NIHR)
Platform/URL: https://www.nihr.ac.uk/health-and-care-professionals/search-our-evidence.htm
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 2
SEARCH STRATEGY:
Searching on 'Search our evidence' by ProKnow* across all NIHR websites retrieved no results.
Searching on 'Search our evidence' by 'Pro know*' across all NIHR websites retrieved no results.
Search on 'Search our evidence' by 'Elekta' across all NIHR websites retrieved 2 records that were downloaded for further assessment.

DATABASE/PLATFORM: Google Scholar
URL: https://scholar.google.com/
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 35
SEARCH STRATEGY:
(proknow* OR 'pro know*' OR Elekta) AND (radiotherapy OR radiation)

DATABASE/PLATFORM: Google Advanced search interface
URL: https://www.google.co.uk/advanced_search
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 9
SEARCH STRATEGY:
A very focussed search was used as Google advanced search retrieved many hundreds of results that couldn't be exported due to lack of functionality. The final search included the product name and excluded the 'false positive' product name of Proknow-C. Limits were applied to this search for country UK and time from 01/01/2020 to 08/11/2022 date when the search was run. File type was pdf.
proknow -proknow-c filetype:pdf

DATABASE/PLATFORM: Journal of Applied Clinical Medical Physics from American Association of Physicists in Medicines (AAPM)
URL: https://aapm.onlinelibrary.wiley.com/journal/15269914

DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 3
SEARCH STRATEGY:
Using the advanced search interface (https://aapm.onlinelibrary.wiley.com/action/doSearch?field1=AllField&text1=proknow*&field2=AllField&text2=&field3=AllField&text3=&publication%5B%5D=15269914&Ppub=) a search for "proknow*" retrieved 3 results that were exported into Endnote 2.0 for further assessment.

DATABASE/PLATFORM: The International Journal of Medical Physics Research and Practice by the American Association of Physicists in Medicines (AAPM)
URL: https://aapm.onlinelibrary.wiley.com/journal/24734209
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 11
SEARCH STRATEGY:
Using the advanced search interface (https://aapm.onlinelibrary.wiley.com/action/doSearch?AllField=proknow*) a search for proknow* retrieved 11 records that were downloaded for further assessment into Endnote 2.0

DATABASE/PLATFORM: Engrxiv (Pre-print repository)
URL: https://engrxiv.org/index
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 0
SEARCH STRATEGY:
Proknow* - yielded no results
Elekta – yielded no results

DATABASE/PLATFORM: MedRxiv (Pre-print repository)
URL: https://www.medrxiv.org/
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 2
SEARCH STRATEGY:
Using the advanced search interface searched for Proknow* in Search terms and Keywords field retrieved 2 results that were exported into Endnote 2.0. for further assessment.
Using the same interface and parameters a search for Pro know* retrieved over 30,000 and was deemed unsuitable for this review.

DATABASE/PLATFORM: FDA Devices Database
URL:
https://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfpmn/pmn.cfm
DATE SEARCHED: 18/10/2022
NUMBER OF RECORDS RETRIEVED: 1
SEARCH STRATEGY:
Searched for Proknow in Device name field retrieved one record that was downloaded for further assessment.

DATABASE/PLATFORM: ScanMedicine

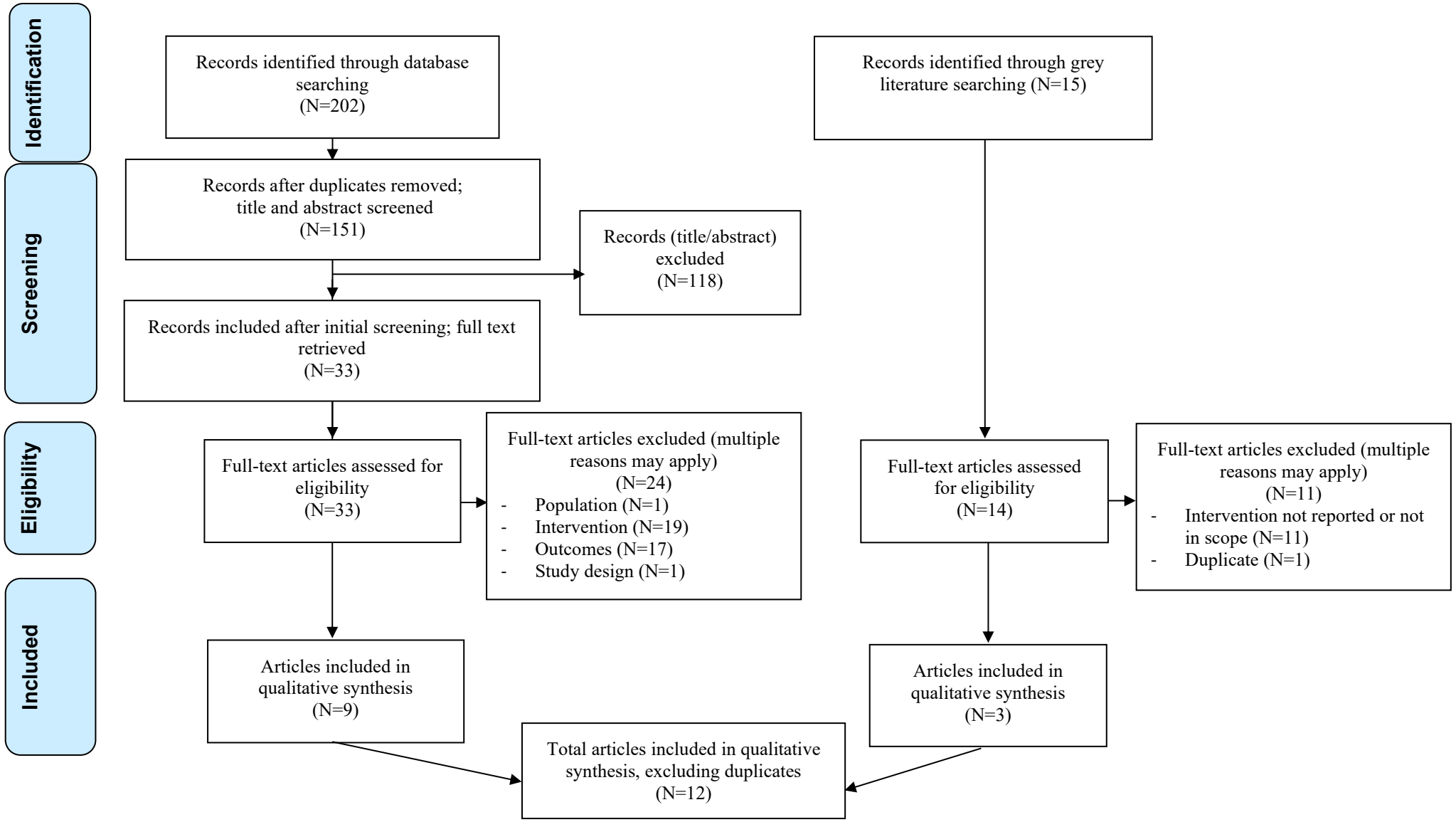
URL: https://scanmedicine.com/
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 26
SEARCH STRATEGY:
A search for Proknow* retrieved 0 results for clinical trials and 1 results for Devices. This document has been already identified by manually searching the FDA devices database.
A second search for clinical trials Active not recruiting, enrolling by invitation, completed or recruiting by search term 'elekta' retrieved 26 trials that were downloaded in a csv file, these were de-duplicated on screen and 3 remaining trials manually added to Endnote for further assessment.

DATABASE/PLATFORM: Clinicaltrials.gov
URL: https://clinicaltrials.gov/
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 27
SEARCH STRATEGY:
Search for Proknow* in Other terms fields yields 0 results
Search for Elekta in Other terms field yields 27 clinical trials that were downloaded in csv format for further assessment.

DATABASE/PLATFORM: EU Clinical Trials Register
URL: https://www.clinicaltrialsregister.eu/ctr-search
DATE SEARCHED: 10/11/2022
NUMBER OF RECORDS RETRIEVED: 0
SEARCH STRATEGY:
Searching independently for Proknow or Elekta retrieved 0 results.

DATABASE/PLATFORM: The Australian and New Zealand trial registry database
URL: https://anzctr.org.au/TrialSearch.aspx
DATE SEARCHED: 08/11/2022
NUMBER OF RECORDS RETRIEVED: 4
SEARCH STRATEGY:
Searching in advanced search interface only ANZCTR trials by 'Proknow' or 'Pro Know' in intervention/exposure yields no search results.
Searching in advanced search interface only ANZCTR trials by 'Elekta' in intervention/exposure field return 4 trials. Manually added to Endnote for further assessment.

Appendix A2 - PRISMA diagram (clinical evidence); N=217



Appendix B: Excluded studies (N=24)

#	Source	Study reference	Reason for exclusion
1	EAG search	Becksfort et al. (2021) Medical Physics†	Study outcomes: development of independent patient database which extracted information from multiple databases. Included within Section 5.3.8 to highlight data linkage to other systems.
2	EAG search	Bisgaard et al. (2022) Radiotherapy and Oncology†	Study outcomes: quantifying delineation variability and not quality assurance. Included within Section 5.3.10 to highlight data linkage to other systems.
3	EAG search	Gao et al. (2022) Medical Physics†	Study outcomes: evaluation of performance of AI-based treatment planning. Included within Section 5.3.10 to highlight other possible uses of ProKnow.
4	EAG search	Jordan et al. (2022) Medical Physics	Population: Contouring of healthy organs in existing paediatric CT dataset. Included within narrative in Section 5.3.10 to highlight possible other uses of ProKnow.
5	EAG search	Lin et al. (2022) medRvix	Study outcomes: quantifying interobserver variability of contouring and not quality assurance. Included within Section 5.3.10 to highlight data linkage to other systems.
6	EAG search	Mitchell et al. (2022) Radiotherapy and Oncology†	Intervention: ProKnow not explicitly used.
7	EAG search	Mohajer et al. (2021) Clinical and Translational Radiation Oncology	Intervention: ProKnow not explicitly used.
8	EAG search	Nabi et al. (2022) Radiotherapy and Oncology†	Intervention: ProKnow not explicitly used.
9	EAG search	Opie et al. (2021) Journal of Medical Imaging and Radiation Oncology	Intervention: ProKnow not explicitly used.
10	EAG search	Penoncello et al. (2022) Medical Physics†	Study outcomes: evaluation of dose volume histogram construction between 8 systems. Included within Section 5.3.10 to highlight other possible uses of ProKnow.
11	EAG search	Pepin et al. (2022) Medical Physics†	Study outcomes: quantifying variation of dose volume histogram construction between 5 systems (Eclipse, MIM Maestro, Mobius3D, ProKnow, RayStation). Included within Section 5.3.10 to highlight other possible uses of ProKnow.
12	EAG search	Schmidt et al. (2021) Medical Physics†	Study outcomes: evaluation of scorecards between 2 systems (Eclipse Planning Scorecard, ProKnow). Included within Section 5.3.10 to highlight other possible uses of ProKnow.
13	EAG search	Shen et al. (2020) Medical Physics	Study outcomes: evaluation of performance of AI-based treatment planning. Included within Section 5.3.10 to highlight other possible uses of ProKnow.
14	EAG search	Shen et al. (2021a) Medical Physics†	Study outcomes: evaluation of performance of AI-based treatment planning.

#	Source	Study reference	Reason for exclusion
			Included within Section 5.3.10 to highlight other possible uses of ProKnow.
15	EAG search	Shen et al. (2021b) Medical Physics	Study outcomes: evaluation of performance of AI-based treatment planning. Included within Section 5.3.10 to highlight other possible uses of ProKnow.
16	EAG search	Shepherd et al. (2022) Journal of Medical Radiation Services†	Study outcome: protocol outlining treatment planning and contouring evaluation using ProKnow, no results reported (plan comparison of ProKnow and Eclipse to follow). Included within narrative in Section 8.2 highlighting ongoing or planned study.
17	EAG search	Sprouts et al. (2021) Medical Physics†	Study outcomes: evaluation of performance of AI-based treatment planning. Included within Section 5.3.10 to highlight other possible uses of ProKnow.
18	EAG search	Sprouts (2022a) University of Texas Arlington Online Repository	Study outcomes: evaluation of performance of AI-based treatment planning. Included within Section 5.3.10 to highlight other possible uses of ProKnow.
19	EAC search	Sprouts et al. (2022b) Biomedical Physics and Engineering Express	Study outcomes: evaluation of performance of AI-based treatment planning. Included within Section 5.3.10 to highlight other possible uses of ProKnow.
20	EAG search	Sritharan et al. (2022) Radiotherapy and Oncology	Study outcomes: quantifying interobserver variability of contouring and not quality assurance. Included within Section 5.3.10 to highlight other possible uses of ProKnow.
21	EAG search	Wahid et al. (2022) medRxiv	Study outcomes: quantifying interobserver variability of contouring and not quality assurance. Included within Section 5.3.10 to highlight data linkage to other systems.
22	EAG search	Wright et al. (2022) Technical Innovations and Patient Support in Radiation Oncology	Study design: discussion of learning models, ProKnow referred to as an example of software only.
23	EAG search	Zawlodzka et al. (2020) Physical and Engineering Sciences in Medicine†	Intervention: ProKnow not explicitly used.
24	EAG search	Zheng et al. (2018) Medical Physics†	Study outcomes: evaluation of dose calculation algorithms using ProKnow. Included within Section 5.3.10 to highlight other possible uses of ProKnow.
Key: †abstract only			

Appendix C: Economic literature search

Appendix C1 - Search strategy (economic evidence)

Database/Source	Platform/URL	Date range	Date searched	Retrieved Results
MEDLINE(R) and In-Process, In-Data-Review & Other Non-Indexed Citations	OVID	1946 to November 07, 2022	10/11/2022	26
Embase	OVID	1988 to 2022 Week 44	10/11/2022	265
RePEC IDEAS	https://ideas.repec.org/	Up to date	10/11/2022	4
CEA Registry, the Tufts Medical Center Cost-Effectiveness Analysis (CEA) Registry	https://cear.tuftsmedicalcenter.org/	Up to date	10/11/2022	0

DATABASE/PLATFORM: Ovid MEDLINE(R) and In-Process, In-Data-Review & Other Non-Indexed Citations 1946 to November 09, 2022
DATE SEARCHED 10/11/2022
NUMBER OF RECORDS RETRIEVED 26
SEARCH STRATEGY:
1 (Proknow* or Pro know*).af. 16
2 exp Radiotherapy/ 203939
3 (radiotherap* or radiation therap*).ti,ab,kf,fs. 367301
4 2 or 3 423508
5 Elekta.ci. 359
6 Elekta.go. 41
7 Elekta.in. 181
8 or/5-7 573
9 4 and 8 410
10 Radiotherapy Planning, Computer-Assisted/ 24362
11 Radiotherapy, Image-guided/ 3815
12 exp "Image Processing, Computer-Assisted"/ 255835
13 exp Imaging, Three-Dimensional/ 90001
14 (treatment plan* or therapy plan* or VTPN).ti,ab,kf. 72738
15 (target volume* or contour* or delineat* or segment* or outlin* or autosegment* or auto-segment*).ti,ab,kf. 725585
16 (dose volume histogram* or DVH or radiation dose or radiation dosage or radiation dosimet*).ti,ab,kf. 35979
17 or/10-16 1047289
18 9 and 17 229
19 Organs at Risk/ 4528

20 (contour* adj3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)).ti,ab,kf. 2766
21 (delineat* adj3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)).ti,ab,kf. 6678
22 (segment* adj3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)).ti,ab,kf. 14967
23 (outlin* adj3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)).ti,ab,kf. 2577
24 (autosegment* or auto segment*).ti,ab,kf. 467
25 or/19-24 30506
26 9 and 25 48
27 ((learn* or teach* or educat* or train*) and (contour* or protocol* or plan* or treat* or DVH or imag*)).ti,ab,kf. 508260
28 9 and 27 42
29 Cloud Computing/ 1224
30 exp Algorithms/ 411845
31 Big Data/ 2546
32 exp Machine Learning/ 50726
33 Data warehousing/ 232
34 (cloud-based or cloud-native or cloud-enabled or cloud-computing or cloud computing).ti,ab,kf. 3341
35 (data mining or data retrieval or data storage or data warehous* or dataset* or data management or data set* or data repositor* or big data or deep reinforcement learning or DRL or DICOM).ti,ab,kf. 322019
36 or/29-35 673570
37 9 and 36 73
38 1 or 18 or 26 or 28 or 37 261
39 Economics/ 27469
40 exp "Costs and Cost Analysis"/ 260862
41 Economics, Nursing/ 4013
42 Economics, Medical/ 9229
43 Economics, Pharmaceutical/ 3084
44 exp Economics, Hospital/ 25641
45 Economics, Dental/ 1920
46 exp "Fees and Charges"/ 31234
47 exp Budgets/ 14051
48 budget*.ti,ab,kf. 33968
49 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kf. 264426
50 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 351460
51 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kf. 193967
52 (value adj2 (money or monetary)).ti,ab,kf. 2813
53 exp models, economic/ 16154
54 economic model*.ab,kf. 3891

55 markov chains/ 15829
56 markov.ti,ab,kf. 26958
57 monte carlo method/ 31678
58 monte carlo.ti,ab,kf. 56693
59 exp Decision Theory/ 12978
60 (decision* adj2 (tree* or analy* or model*)).ti,ab,kf. 33082
61 or/39-60 844508
62 38 and 61 26

DATABASE/PLATFORM: Embase 1988 to 2022 Week 44
DATE SEARCHED: 10/11/2022
NUMBER OF RECORDS RETRIEVED: 265
SEARCH STRATEGY:
Embase <1988 to 2022 Week 44>

1 (Proknow* or Pro know*).af. 35
2 Elekta.dm. 3648
3 Elekta.dq. 334
4 Elekta.ga. 1106
5 Elekta.go. 146
6 Elekta.in. 479
7 or/2-6 5199
8 exp radiotherapy/ 577400
9 (radiotherap* or radiation therap*).ti,ab,kf,fs. 586414
10 8 or 9 742089
11 7 and 10 4195
12 radiotherapy software/ 346
13 radiotherapy planning system/ 8121
14 planning target volume/ 5892
15 radiotherapy dosage/ or dose volume histogram/ 10006
16 computer assisted radiotherapy/ or image guided radiotherapy/ 16400
17 "radiology picture archiving and communication system"/ 137
18 (treatment plan* or therapy plan* or VTPN).ti,ab,kf. 109775
19 (target volume* or contour* or delineat* or segment* or outlin* or autosegment* or auto-segment*).ti,ab,kf. 877604
20 (dose volume histogram* or DVH or radiation dose or radiation dosage or radiation dosimet*).ti,ab,kf. 55948
21 or/12-20 1025304
22 11 and 21 2467
23 organs at risk/ 10690
24 (contour* adj3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)).ti,ab,kf. 5053
25 (delineat* adj3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)).ti,ab,kf. 10731
26 (segment* adj3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)).ti,ab,kf. 19310
27 (outlin* adj3 (anatomy or organ* or anatomical or structure* or variation or accuracy or accurate* or correct* or target*)).ti,ab,kf. 3050
28 (autosegment* or auto-segment*).ti,ab,kf. 1201
29 or/23-28 46191

30 11 and 29 568
31 ((learn* or teach* or educat* or train*) and (contour* or protocol* or plan* or treat* or DVH or imag*)).ti,ab,kf. 758211
32 11 and 31 231
33 cloud computing/ 2918
34 exp dose calculation algorithm/ 1215
35 big data/ 4972
36 machine learning/ or classification algorithm/ 79619
37 data warehouse/ 2531
38 (cloud-based or cloud-native or cloud-enabled or cloud-computing or cloud computing).ti,ab,kf. 5020
39 (data mining or data retrieval or data storage or data warehous* or dataset* or data management or data set* or data repositor* or big data or deep reinforcement learning or DRL or DICOM).ti,ab,kf. 414307
40 or/33-39 478080
41 11 and 40 301
42 1 or 22 or 30 or 32 or 41 2628
43 Economics/ 210873
44 Cost/ 47823
45 exp Health Economics/ 932404
46 Budget/ 30868
47 budget*.ti,ab,kw. 41859
48 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ti,kw. 275431
49 (economic* or cost or costs or costly or costing or price or prices or pricing or pharmacoeconomic* or pharmaco-economic* or expenditure or expenditures or expense or expenses or financial or finance or finances or financed).ab. /freq=2 482257
50 (cost* adj2 (effective* or utilit* or benefit* or minimi* or analy* or outcome or outcomes)).ab,kw. 262112
51 (value adj2 (money or monetary)).ti,ab,kw. 3769
52 Statistical Model/ 171731
53 economic model*.ab,kw. 5746
54 Probability/ 131240
55 markov.ti,ab,kw. 33771
56 monte carlo method/ 47620
57 monte carlo.ti,ab,kw. 57144
58 Decision Theory/ 1614
59 Decision Tree/ 18775
60 (decision* adj2 (tree* or analy* or model*)).ti,ab,kw. 44810
61 or/43-60 1793801
62 42 and 61 265

DATABASE/PLATFORM: RePEC IDEAS database
URL: https://ideas.repec.org/
DATE SEARCHED 10/11/2022
NUMBER OF RECORDS DOWNLOADED 4
SEARCH STRATEGY:

Log In not available at the time of running these searches which has affected the ability to save and export results. Therefore results have been sifted on screen and only those deemed relevant have been downloaded.
Searching in All fields for “ProKnow” retrieved 28 results. Limiting to 2020-2022 retrieved 9 results. None of the 28 results were relevant there were all for PROKNOW (in German) or ProKnow-C a tool for selection of literature.
Searching in All fields for “Pro Know” retrieves 0 results.
Searching in All fields for Elekta retrieves 7 results. Limiting to 2020 to 2022 retrieves 0 records.
All results downloaded into Endnote for deduplication.

DATABASE/PLATFORM: CEA Registry, the Tufts Medical Center Cost-Effectiveness Analysis (CEA) Registry
URL: https://cear.tuftsmedicalcenter.org/
DATE SEARCHED 10/11/2022
NUMBER OF RECORDS DOWNLOADED 0
SEARCH STRATEGY:
Searching on Methods using the basic search interface.
Search for Proknow retrieved 0 results
Search for Pro Know retrieved 0 results
Search for Elekta retrieved 0 results

Appendix D: Correspondence Log

Appendix D1 – Company

#	Questions (21/10/2022)	Response (31/10/2022)
1	The EAG acknowledge that the costs provided in the standard information request to NICE were relevant to the NHS England contract, but were shared CiC. Therefore, for transparency in our report: a. What is the cost of ProKnow per site per year out with the NHS England contract? b. The EAG recognises that the NHS England contract included unlimited number of users. However is there a "standard" number of users in centres purchasing ProKnow outwith the NHS England contract? c. The EAG recognises that the NHS England contract included unlimited data storage. However is there a "standard" storage provided to centres purchasing ProKnow outwith the NHS England contract?	[redacted] a. No, pricing is based on base package plus number of linacs b. Yes, 1TB is provided in the base package with each 1TB of extra data storage chargeable.
2	Do the Company offer any training? Is this included in the costs or extra?	Training is included
3	Is there any maintenance? Are software upgrades included in the annual cost?	ProKnow is provided as a SaaS (Software as a Service) therefore all maintenance and upgrades are included.
4	What happens to the data if the annual contract was not renewed? Are the Hospitals the data controllers, or does ProKnow retain the data?	The hospital remains the data controller and owner, the bulk of the data in ProKnow will be in DICOM format which the user can easily download at any time and transfer to a PACS for long term storage, Elekta will keep the account active for 30 days after the end of the contract to allow customers to do this.
5	Is there any hardware/software/formatting pre-requisites to using ProKnow?	No, ProKnow is accessed through standard internet browsers.
6	Can we please have a copy of the following documentation?: a. the latest CE certification, b. declaration of conformity, c. instructions for use	a. ProKnow 1.0 is a Class 1 product, Class 1 products require self-certification in the EU which means the manufacturer signs a declaration of conformity allowing it to be CE marked. b. Attached

		c. Click link: Useful Information – ProKnow
7	What month and year was ProKnow available commercially?	February 2020

#	Questions (11/11/2022)	Response (15/11/2022)
1	Is ProKnow DS currently only able to export structures that are closed and located on a single plane? The EAG notes that non-axial CT slices are used with brachytherapy; will ProKnow DS be able to support these images? If so, what is the expected timescale?	It is correct that at this point ProKnow only supports axial structures. Supporting non-axial structures is currently on our enhancement list, although I do not have a firm date on when it will be implemented.
2	Thank you for clarifying the ProKnow commercialisation date. The EAG have identified evidence relating to ProKnow prior to commercialisation; what are the key differences between versions prior to and following commercialisation?	The majority of the work that has been done has been iterative improvements to the software based on customer feedback. ProKnow has had a steady cadence of releases since initial commercialization in which we have significantly improved our permission system – for improved collaboration and control of data, improved DICOM upload capabilities including anonymization upon upload to the cloud while keeping PHI locally if desired, improved plan comparison, and many other features. These iterative improvements have added up to a significant number of changes. Release notes can be found here: https://proknow.com/product-roadmap/
3	Are you able to provide a reference list for published literature relating to ProKnow?	The following is one example of a published article relating to ProKnow. There is at least one more being worked on at this time. A UK wide study of current prostate planning practice - PubMed (nih.gov)
4	Are there any ongoing or completed clinical trials relating to ProKnow?	There are no ongoing or completed clinical trials related to ProKnow, however TROG, cancer research organization in Australia is a ProKnow user.
5	Was ProKnow ever known by another name prior to commercialisation?	No, as mentioned there are two distinct products that go under the name ProKnow. There is the ProKnow quality systems for contour and plan quality analysis (or ProKnow CA as it is referred to below), as well as ProKnow DS, which is the cloud-based RT PACS and big data analysis system.

6	Does the Company have any use case data relating to ProKnow and peer review of treatment plans either within or outside the NHS?	Elekta are the data processors and do not have access to the data hosted within the domains we do not have examples of its use, Elekta are interviewing ProKnow customers with a view to producing customer testimonials, the NHSE National ProKnow administrators will be able to provide specific NHSE ProKnow use examples. I will send on the St Jude's Children's Research hospital video (sent via seismic) and the RMIT Uni slide also (attached with this email).
7	Is the ProKnow CA module only intended for training use or is the intention to move this module into treatment planning use? If so, what is the expected timescale?	ProKnow Systems, or ProKnow CA as it is referred to here is solely used for training and educational use in contouring and treatment planning. There are some institutions that have dedicated deployments for internal training that are hosted and maintained by Elekta, but the use for internal education and validation of skills of internal staff and not for clinical use.

#	Questions (18/11/2022)	Response (21/11/2022)
1	The commercialisation date previously stated is February 2020, however the version and release notes extend to 07 September 2018; please can you clarify any major differences between the pre- and post-commercialised versions of ProKnow?	February 2020 is the date that ProKnow achieved CE mark, so that would be the official commercialization date for Europe. The changes done to ProKnow since inception have largely been iterative improvements, and have not been of the type that have required change of intended use or any sort of regulatory re-submission. It is important to note, however, that two of our most important changes that have been made since commercialization were done specifically with the intent of accommodating the needs of the NHS. The first was the addition of Audit Logging. This will allow administrators to view activities of users on the system for the purpose of monitoring what data users are accessing and what actions they are taking in the system. The second was the expansion of our permissions system to allow for very granular control over user rights – what can be accessed by individual users or groups of users, while also providing

		individual trusts with great control over the data within their Trust.
2	The EAG note from the most recent ProKnow DS Release Notes (version 1.31.1 dated 10 June 2022) that there was a bug fix to correct 'a security defect that could expose a patient's MRN and name to unauthorised users in the organisation'; please can you clarify what is meant by the organisation – is this the same NHS Trust or would this be across all NHS users?	The Release Note regarding the security defect, this was a very specific feature where the user had to be using a workflow management tool within ProKnow. In this case, the patient name would show up in the workflow, but if user did not have access to the patient, they would not be able to link to the patient to find out any other relevant information. We had spoken to users at the NHS and at the time nobody was using that particular tool, so the NHS was not affected, but of course we still fixed the issue.

#	Questions (25/11/2022)	Response (28/11/2022)
1	Does ProKnow capture a patient's date of birth, NHS number, gender, and postcode as part of the data collection?	All of the mentioned PHI data can be stored in ProKnow, when choosing to share a patient plan(s) in ProKnow the person sending the plan has the full control and choice of which PHI data is shared.

Appendix D2 - Clinical Experts

Appendix D2a: Questions discussed at meeting (07/11/2022)

MT770 ProKnow EVA

Meeting with clinical expert John Byrne [MS Teams]

Monday 07 November 2022 @ 11:00-12:15

NOTES

In Attendance:

EAG: Kim Keltie (KK), Emma Belilios (EB)

HEG: Gurdeep Sagoo (GP), Sedighe Hosseinijebeli (SH)

NuTH: John Byrne (JB) - Deputy Head of Section, Radiotherapy at NuTH

Background

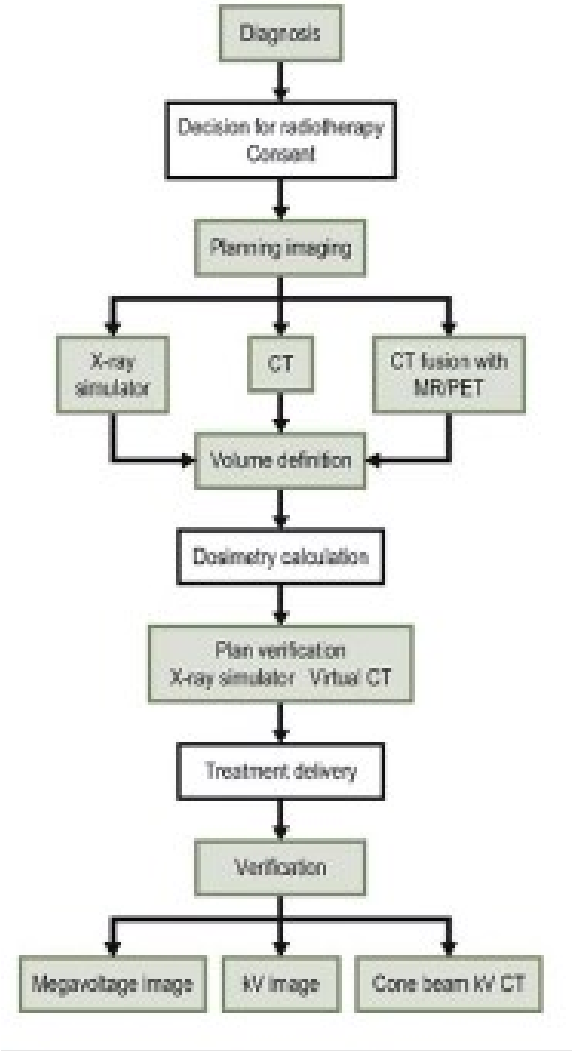
Newcastle EAG has been commissioned by NICE to carry out an Early Value Assessment (EVA) of ProKnow. As the EAG are expecting little to no direct evidence on ProKnow, we require extensive clinical input to help our health economics group better understand the cost of the current standard of care pathway. Purpose of this meeting is to discuss list of clinical questions with John Byrne to help HEG with costing up standard care pathway, so can attempt comparison with ProKnow.

Questions for JB

1. **Radiotherapy treatment planning**:

    a. **What staff role (including band) is involved in this step? This can be further broken down by steps within the treatment planning pathway if needed.**

GS has looked at different papers and websites to get an idea of the pathway. He has come up with the following flow diagram:



JB - ProKnow is most relevant to the step that is missing from the flow diagram currently - peer review of 'volume definition' (in the above diagram). Volume definition can include delineation of target, organs at risk, other body parts at risk. It is recommended that that the 'weak link' (that one person makes the decision on treatment target and dosage) is strengthened by peer review. This step should sit within volume/target definition box. Peer review is recommended (once treatment is delivered, cannot be undone, so want to get it right), but doesn't always happen. Most of the other steps have checking processes. ProKnow allows clinician to share with peers what they are planning to do and invite comment. This is where ProKnow is likely to be of greatest value currently.

ProKnow can also make available large amounts of data about the impact of previous treatments for analysis to inform future decision making. KK asked if this data analysis process would also sit within

target definition box (to inform decision making)? JB thought this should sit outside the clinical process diagram and happen periodically as separate audits.

Staff role - treatment planning covers a very wide set of processes (which span different complexities and time), from a skin cancer on the hand (very quick and straightforward to plan, approx. 15 minutes) through to cancer wrapped around the spinal cord where you will need multiple imaging modalities to plan treatment (could 2 weeks to develop treatment plan). Process would also depend on the outcome intention (curative or palliative), location and type of cancer. At NuTH, staff involved in treatment planning range from Band 6 to consultant clinical oncologist. At some Trusts, staff from Band 3 upward can upload some data. This would be difficult to generalise in an economic model. Peer review is currently not conducted in all patients, and not in all cancers.

b. On average what is the typical duration (minutes or hours as appropriate) that radiotherapy treatment planning takes per patient?

For the economic model, GS will need to understand processes involved and how long they take in order to measure benefits of ProKnow implementation (and gain understanding of where new 'bottle necks' may be). As per previous response, can take from 15 minutes to 2+ weeks depending on specific example.

GS asked if ProKnow may have some benefits to the treatment pathway itself. JB clarified that it may do in future. ProKnow can also help with auto-contouring to help with planning process; however this functionality has not yet been released by the Company. JB acknowledged there are competitive auto-contouring software options available. KK thought this would be an important gap in evidence which could be highlighted for future data collections.

c. What is the range associated with b?

As above. If ProKnow leads to additional peer review, this will be an additional cost. There is the cost of the software, also, review will be carried out by Consultant clinical oncologist. Their time has a high cost. But, peer review will lead to patient benefit. Could also potentially reduce litigation costs, though litigation cases concerning treatment planning are rare, so this would be hard to quantify.

d. Does this depend on cancer type (which cancer takes longest, shortest typically)?

Yes, will be affected by cancer type (and other factors) as discussed.

e. Does this depend on the planning software and IT infrastructure used? If so what in particular?

ProKnow is an online platform - this can lead to Information Governance issues, and there are costs associated with Trust IT. Trust IT's interpretation of GDPR and other relevant legislation can be different to NHS Digital's. KK noted that there can be additional IG issues with AI as the system is learning from patient data. JB clarified that data owner/controller is defined in the ProKnow contract.

f. What impact is ProKnow likely to have on any of the above?

Almost nil just now. KK - ProKnow will not inherently change the process. 'Doing it better' is hard to cost. JB agreed.

g. Specifically, would the use of ProKnow increase or reduce the time taken to develop (or peer review) plans for treatment planning or for quality assurance? If so, can you estimate the range of time saved/added and any other benefits/harms you think are relevant?

Peer review will increase the time taken in planning. This does not necessarily mean that treatment will start or finish at a later time (review can take place in parallel and should not delay treatment). Will increase number of people involved in the planning process and should reduce likelihood of errors. Centres currently do not peer review as much as they should because of constraints in number of clinical oncologists. Some centres may not have anyone locally with the necessary knowledge. NuTH treat patients with some very rare cancers. There may only be a couple of experts in the country qualified to peer review treatment plans for these patients. Peer review of a treatment plan by a Consultant clinical oncologist can take 15-45 minutes depending on complexity.

Consultants will still need to broker the relationships with peer reviewers themselves, but ProKnow will help with standardisation and transfer of data. It will also add value to the process. Clinicians can share their patient data directly with the reviewer(s), and give them control so that they can directly edit it. Before, even if you had acceptable IG use of a video tool, the peer reviewer couldn't directly edit the plan (for example extend contours).

KK - any potential harm from using ProKnow? JB - if you look at ProKnow from an audit viewpoint, the calculation of the dose received by the target area may be different to the amount in the plan, simply because it's a different software, using different algorithms. The Scorecard might then say the treatment plan has 'failed', purely because the amount has been calculated in a different way. This is likely to reduce harm though as it highlights the inherent uncertainties and this can be taken into account.

KK asked if once the AI functionality is available, there will also be differences between earlier and later calculations in ProKnow as AI learning updates the algorithms. JB agreed, part of testing will be understanding these uncertainties. Prepare planning systems, use of phantoms, and compare with what we actually find. Would need to do the same testing on ProKnow as on the planning system.

JB clarified that even with ProKnow, peer review will not be considered necessary/appropriate for every patient. Would focus on the higher risk cases first. Initially, likely to do more peer review. Later on (as learning increases) would need to do less. Stereotactic radiosurgery delivers a very high dose of treatment to a small area - get one shot at this, so peer review of the treatment plan would be helpful.

The Royal College of Radiologists (RCR) issued guidance on what should be peer reviewed and its frequency. JB will send link. GS asked if this can be taken as the gold standard? JB clarified that it is the minimum Trusts should be doing.

ACTION (JB): to share link to relevant and recent guidance from RCR

h. Do you think ProKnow will have any impact on the ready-to-treat-to-treatment-time (RTTT)?

It is possible we will improve our peer review and definition of target processes (reduction in margins). If you can safely increase dose to

target this reduces number of treatments needed. It is possible that through ProKnow, clinicians will gain an improved understanding of the impact of different treatment options, which could lead to changes in fractionation regimes, and improvement in training, but this requires access to big data.

ProKnow has the functionality to create Scorecards that allow plans to be evaluated against pre-defined metrics. Scorecards coupled with quality checklists may mean that, in future, ProKnow will help with the quality control of plans. JB has translated national guidance (lung SABR consortium) into 20 Scorecards - these are now nationally available. Clinicians will get green light if their treatment plan meets recommendations of the published guidelines. Tools for comparing multiple Centres are available to enable to compare against best practice and potentially improve their own practice. The functionality is not widely enough adopted yet to have an impact on planning but may have an impact in the future.

2. Technology:

a. Is ProKnow CA (contouring module) only used in training? Or is there an AI element which is used directly in patient care?

JB: This cannot be used for anything other than training. Module takes a set of contours defined by experts, trainee can get their plans compared with this 'ideal' set.

KK asked what steps clinicians need to complete to maintain competency? JB - there is, regular re-validation required in the UK. An oncologist would have to comment on this process but ProKnow could potentially play a part

b. Are you aware of any UK institutions, such as University programmes, using ProKnow CA for training?

Possibly used by radiographer courses, but not known.

3. **Equalities section:**

   b) **Brachytherapy doesn't appear to be an exclusion of the final scope, however is it correct to state that the current version of ProKnow struggles with non-axial CT slices, which is commonly used with brachytherapy, which is used most frequently with gynaecological cancers and therefore potential higher exclusion of people with female sex. Does Proknow have any other impact that would be specific for the type of therapy use like Proton beam?**

JB – peer review would be conducted another way, therefore no one is disadvantaged by this.

4. **Evidence:**

Are you aware of any grey literature sources publishing use or outcomes of ProKnow (e.g. key conference abstracts, presentation, local service documentation)? Are you aware of any data which may help with this evaluation that is routinely collected in the audit data?

May be something in conference abstracts. Have found peer reviewed papers. JB has a publication in progress which will be helpful when published. Audits tend to be carried out for very specific purposes.

NHSE funded the roll out and have some specific requirements. However, the Trusts now own the licences so can use the software as they want.

5. **Scorecards:**

a. **How can scorecards be produced and/or validated? We note that scorecards used for used SABR guidelines to develop scorecards for use in ProKnow, is it best practice to use clinical guidance, where available?**

JB clarified that the Conference (**Byrne et al. (2021**) did not go ahead (lockdown). JB has done some talks online but not yet at a meeting. Scorecards are set up (there is a template provided) but can be shared on ProKnow. JB is presenting at a Lung SABR meeting in Sheffield on 24 November 2022. NHSE are coordinating clinical groups to decide on

metrics that should either define or inform best practice and the dosimetric elements of these can be converted to ProKnow scorecards.

b. How long does it take to produce and upload scorecards to ProKnow?

Process is relatively quick once you know what you want to do the Scorecard for (approximately 2 weeks with validation). Need to decide what you want, get it checked, then entered into the system. There are some breast screening Scorecards currently in development. The delay has been in getting clinical agreement on dose metrics.

Scorecards can be available locally only, or, can make templates, and add to national collections. This is likely to be useful support for smaller Centres, and to help with standardisation nationally.

Can analyse ProKnow data retrospectively, to learn lessons from patients in the past, looking at how problems reported correlate with treatment decisions. Could have access to treatment plans and long-term outcomes (likely via National Cancer Registry) for thousands of people. KK asked if patient consent was needed for this data analysis. JB - no, would consider this work to be audit/service evaluation, not research. Patients consent to their data being used for audit purposes as part of their consent to therapy.

6. Stereotactic ablative radiotherapy:

The EAG have come across the terms 'Stereotactic Ablative Radiotherapy SABR' and 'Stereotactic Body Radiotherapy SBRT', are these the same and if so, which is the preferred term?

Yes. Treat as the same thing.

3. Any Other Business

None.

Appendix D2b: Questions sent to Clinical Experts 18/11/2022

Expert #1	Samantha Warren
Expert #2	John Byrne
Expert #3	Amanda Webster
Expert #4	Nicky Whilde
Expert #5	Alex Beardmore
Expert #6	Ian Boon

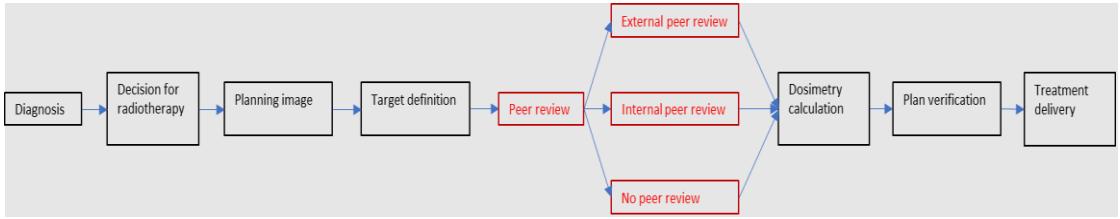
#	Questions (sent 21/10/2022)	Response
NHS England commissioned pilot		
1	Can you confirm that as part of the NHS England ProKnow commissioned pilot that no specific data collection requirements were requested?	Expert 1: Not within my scope of expertise
		Expert 2: Sorry. I don't know what this question means. ProKnow is specifically required to collect dicom data.
		Expert 3: I am unaware of the answer to this. I was not involved in the commissioned pilot. I can imagine that the time required DICOM data to commission the system.
		Expert 4: I don't understand the question sorry.
		Expert 5: None that I am aware of.

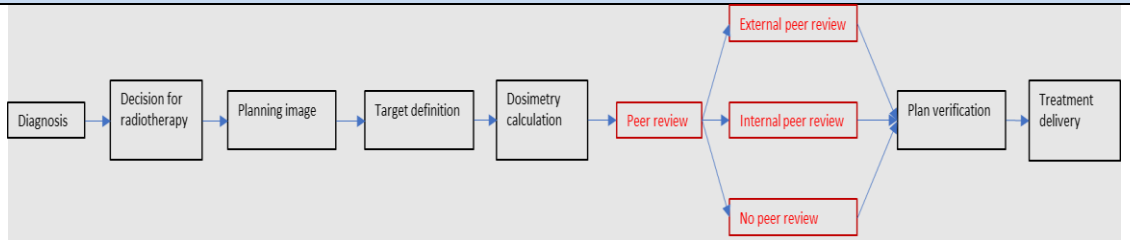
#	Questions (sent 21/10/2022)	Response
		Expert 6: Yes, after discussing within the department, the pilot has not mandated specific data collections.
Economic considerations		
2	For the economic modelling we estimate the peer review process using ProKnow takes 30 minutes (range 15 to 45 minutes) per case; is this an acceptable range?	Expert 1: This will vary hugely depending on the complexity of the plan and patient clinical characteristics, as well as expertise of peer reviewers.
		Expert 2: This is probably a good working estimate. Without a full study of the peer review value and practice of ProKnow, it's not possible to get an accurate value.
		Expert 3: Yes, for the actual review. I have found that what can add time is preparing the data, sending it, uploading it etc.
		Expert 4: Yes
		Expert 5: Probably this range is narrow. Straight forward cases could be correct, but complex cases could take much longer.
		Expert 6: There is considerable variations in peer review availability among tumour sites. In my clinical practice, we do not use Proknow to peer review cases. We have weekly peer review sessions ranging from 30-45 minutes to discuss 3-5 cases. The time range 15-45 minutes seem reasonable.
3	What systems or methods do you currently use to perform or conduct peer review (e.g., in person, online meetings, data sharing)?	Expert 1: In person, and online (teams)
		Expert 2: In person, online meetings, telephone.
		Expert 3: In person, teams meetings – both mainly on Eclipse. Sometimes on Velocity. For radiotherapy trials will move toward using XNAT.
		Expert 4: MSTeams for remote online PR. There is no other way of doing offline PR with different

#	Questions (sent 21/10/2022)	Response
		centres at the moment, than Proknow. Face to face at a single centre is a conversation around the TPS.
		Expert 5: In person mostly. Occasional using software like teams during times when covid precautions have been high. Occasionally data has been shared with colleagues from other centres regarding particularly complex and rare cases.
		Expert 6: We have used our local Pinnacle radiotherapy planning software. We have online meeting over teams to review the contours via sharing screens. We discussed among the department on using Proknow but for peer review but decided this was not feasible as would meant transferring images across our local radiotherapy planning system onto Proknow and then needed to be transferred back onto local planning software. This is not practical and logistically Proknow would alter the naming convention and therefore not safe or even feasible to use Proknow to peer review in our centre.
4	Can you estimate the time it takes to conduct peer review using methods other than ProKnow?	Expert 1: See reply to question 2.
		Expert 2: Not really! If it involves sending data securely across the country it could be quite involved. If it's just asking a colleague then a few minutes. Let's say 15 to 500 minutes.
		Expert 3: The peer review process itself is quite quick. A straightforward internal review can be done in about 15 minutes especially when the review is being undertaken in the clinical system and the team are aware of the patient. For external reviews, my experience in trials is that it can be up to 45 minutes.

#	Questions (sent 21/10/2022)	Response
		This is often because trial outlining may be new and a formal report is often required.
		Expert 4: N/A as there are no other ways of doing offline remote PR.
		Expert 5: No. We have not taken a record of this. We would expect it would be more expedient to use ProKnow for peer review with external colleagues.
		Expert 6: In my centre, would be quicker as does not need to transfer images across onto Proknow. As a head and neck oncologist, I am not aware on any other centres using Proknow to peer review head and neck cases.
5	We understand there is a large variation in radiotherapy treatment planning time depending on the complexity of the diagnosis; is it reasonable to consider a range of 15 minutes to 2 weeks for planning time?	Expert 1: 15 minutes would be (probably) a very simple palliative plan, so this seems very short. Could even be longer than 2 weeks, as often the rate determining step is finding a time slot when all appropriate MDT staff are available at the same time.
		Expert 2: Depends on what is included in the term “planning”. A reasonable minimum might be 1hr, assuming that checking is part of planning
		Expert 3: No response
		Expert 4: Strangely worded question. You would need to clarify the meaning of radiotherapy treatment planning time and if you mean time logged on, or time from CT scan to treatment start.
		Expert 5: Yes, this seems reasonable.
		Expert 6: Again, these questions would need to be caveated at what radiotherapy cases is involved- is it a palliative simple plan or complex advanced radiotherapy. This question is too generic to be meaningful for radiotherapy community. Certain subsites of head and neck (for eg nasopharynx

#	Questions (sent 21/10/2022)	Response
		would require much longer time due to complexity) and certain radiotherapy plan needs to have a number of iterations before can be finalised (particular cases of compromise between treating primary tumours and doses to organ at risks). This question would need to recognise large variation in radiotherapy contouring.
6	On average, how many linacs does a centre have? What is the range across centres in England?	Expert 1: This information should be available via RTDS / or e.g. IPEM or RCR survey.
		Expert 2: Don't know average. Range is, I think 2-11. Probably mode is around 4 and the median would be 6.5. It would be possible to calculate the average with a bit of digging around.
		Expert 3: No response
		Expert 4: From 2 to 15 – depends on population covered.
		Expert 5: Small private centres may have 1 linac. The smallest NHS centres have 2 linacs. The largest centres in England have around 13 linacs. I'm not aware of up-to-date cencus type information.
		Expert 6: I do not have this data on individual level. This could be obtained from the Royal College of Radiologists or NHS England reports.
7	On average, per year, per centre, how many TB of data storage for ProKnow would be needed? What is the range across centres in England?	Expert 1: This is almost impossible to answer, as it will depend on what each centre decides to send to ProKnow – can be a very large amount of data, (e.g. multi-modality imaging for each patient) , or bare minimum.
		Expert 2: Don't know. Rough guesstimate would be 1TB/yr if every radiotherapy dep't was putting all patient images in.
		Expert 3: No response

#	Questions (sent 21/10/2022)	Response
		Expert 4: I don't know.
		Expert 5: I wouldn't know. ProKnow is meant to be cloud based so it shouldn't be a concern for individual centres.
		Expert 6: This question again has significant variations due to the level of uptake of Proknow system. In our centre, we do not use Proknow to peer review. We are beginning to upload lung SABR cases to compare outcomes.
8	Relating to peer review for treatment planning, do either of Figure 1a or 1b simplistically capture the position of the process with the overall treatment planning pathway? We appreciate that this is possibly a simplification of what occurs, is there anything additional that should be captured or is incorrect within these figures? Figure 1a:  Figure 1b:	Expert 1: Both are feasible, but they are possibly doing different things. Fig 1a is more of a consultant oncologist peer review – probably fits better with literal interpretation of RCR guidelines. Fig 1b might be for the oncologist + physics team to verify plan quality. For some complex cases, or at start of roll-out of new technique, it may be both processes – i.e. peer review of contours Fig 1a, and also peer review of plan with dose distribution Fig 1b.
		Expert 2: Yes. Both are simplistic views of the peer review options. 1a for peer review of target definition and 1b for peer review of both target definition and therapeutic intention.
		Expert 3: No response
		Expert 4: There are several checks between the Dosimetry calculation and Treatment delivery. The plan needs to be approved, an independent check done and pre-treatment check. Plan verification – in current terminology is something different and is not used for all but the most complex plans in many hospitals.
		Expert 5: 1b appears the more reasonable approximation.

#	Questions (sent 21/10/2022)	Response
		Expert 6: Largely accurate. However, I would highlight after the peer review process, the radiotherapy plan is handed over to the physics department to come up with a radiotherapy plan for dosimetry calculations. This would be quality assurance checked by at least 2 physicists and then back to clinician for final checks for final authorisation prior to delivery.
General queries		
9	What version of the National Radiotherapy Dataset RTDS are you currently using?	Expert 1: Not within my scope of expertise. Expert 2: 5 Expert 3: No response Expert 4: V5 Expert 5: I don't know. Expert 6: 5
10	If you are using version 6 of RTDS, where and how (free text/yes/no/drop down menu) do you enter whether peer review has been conducted and conducted using ProKnow (data item numbers)?	Expert 1: Not within my scope of expertise. Expert 2: N/A Expert 3: No response Expert 4: N/A Expert 5: I don't know. Expert 6: 6 is not ready.
11	Are you able to submit data to ProKnow as of 18/11/2022?	Expert 1: Yes Expert 2: Yes, for most of our patients/processes. Expert 3: No response Expert 4: Yes Expert 5: Yes Expert 6: Yes but we do not use ProKnow for peer review

#	Questions (sent 21/10/2022)	Response
12	Have you or are you having any difficulties implementing the system within your Trust due to information governance, IT constraints, or other?	Expert 1: Some logistical issues with (some very specific) treatment planning systems, which do not easily allow a connection to ProKnow. Would require these external software manufacturers to intervene / upgrade software etc
		Expert 2: No.
		Expert 3: No response
		Expert 4: No.
		Expert 5: We use it in a limited capacity, currently. I'm not aware of any difficulties but it is not my area of expertise.
		Expert 6: As previous, it is not feasible/ safe to use Proknow for peer review. Discussions in our local department would require the plans to be uploaded onto Proknow and then downloaded back onto local planning system. The naming convention could be changes during this process and therefore introducing an unnecessary step that is unsafe. Peer review process does not require a specific software- all it needs is for the contours (delineated in whichever software) and the be reviewed by fellow other oncologists/ physicists. This could be facilitated by any communication software (Zoom/ Teams). I do not see peer review as a unique selling point of Proknow.

Appendix D2c: Questions sent to Clinical Experts 29/11/2022

A summary outlining the approach to economic conceptual modelling was outlined as follows:

Background

The conceptual model for the treatment planning pathway can be seen in Figure 1. The ProKnow technology can facilitate the peer review process within this pathway (impacting the boxes with red text only).

The model has allowed for the possibility of splitting the peer review of the target definition and the dosimetry calculations but it is appreciated that this process currently happens together (at the same time) in practise. The model can simply 'silence' the 'target definition' peer review process and focus on the second peer review (dosimetry calc) process as the combination of the two. The rationale for splitting them in this conceptual model is that in the future there may be a ProKnow module that could incorporate AI auto-contouring which acts as a first target volume definition with what is currently the initial treating clinician then becoming the 'peer review' - so no second person required for peer reviewing the target definition. Allowing for such a possibility in the conceptual model would speed up any future evaluation with such a change evaluated within the current structure and allow any data that may be required for this to be collected now. This does not however remove the requirement for peer reviewing the dosimetry calculation when peer review is required.

The peer review process has been further split into internal/external peer review to capture the difference between large centres (where most if not all peer review will be done in person and 'internally') and small centres (where there is no second person or the complexity of the treatment requires national expertise) and more complex or difficult to plan cancer versus 'simpler' cancers. The rationale would be that external peer reviews are only conducted with very expert individuals (consultant oncologists) and may be focused on more complex and difficult treatment plans which would take longer to review whereas internal peer reviews may be simpler and take less time.

There is currently an evidence gap between using ProKnow for peer review, a resulting change in treatment plan, and the impact (both financial and health-related) of that changed treatment plan on the individual patient.

Key assumptions:

1. The model represents a simplification of reality (which is complex due to heterogeneity in type of cancer, treatment intention etc).
2. ProKnow currently only directly impacts on the boxes with red text (the peer review process itself).
3. Due to large uncertainty regarding the proportion of treatment plans which undergo peer review, this will be varied between 10-100%.
4. ProKnow has no expected impact on the internal peer review process in terms of the outcome (e.g. increasing or decreasing the % major change).
5. For every 10 peer reviews conducted 9 will be internal and 1 will be external.

6. External peer reviews will be 25% more expensive due to their ‘complexity’ which will require more staff time and therefore cost more.

Expert #1	Samantha Warren
Expert #2	Amanda Webster
Expert #3	Nicky Whilde
Expert #4	Ian Boon
Expert #5	John Byrne
Expert #6	Alex Beardmore

#	Questions (sent 29/11/2022)	Response
1	Does the model structure look appropriate? If No, please describe why.	Expert 1: No, this model is not correct. There is also an element of peer review in the decision to treat and/or which structures should be included as targets. This can be iterative. I'm not sure what you mean by 'major' or 'minor' change? It is also not correct, as I would expect a major change to cause a loop back to the beginning of the process for TD (target definition) and then repeat (perhaps) of peer review to check that changes have been made. This might also be the case for a 'minor change'?
		Expert 2: What I am most concerned with is the definition of major change, minor change and no change. How are these being defined? In trials, this is for the most part straight forward as there is a protocol and guidelines that all centres have to be compliant with and this makes defining changes quite straight forward. However, in non-trial patients centres may be utilising different guidelines and may have different clinical goals. Additionally "minor change" reads as if a change is required, however, this may lead to a lot of additional unnecessary work for centres. I am especially concerned about this in the planning process as different centres may have different hardware and software which can impact on their plans. As in trials should an alternative be considered such as: Acceptable Acceptable variation (amendments recommended but not mandated) Unacceptable variation (amendements required) It is also not clear who defines when a peer review is required. Finally, do internal peer reviews have to be undertaken in ProKnow?
		Expert 3: Mostly - see response to question 2
		Expert 4: Just to point out once peer review has happened or not- this plan is passed onto physics department for plan to be done by physicists before dosimetry and clinician authorisation. For our department, the peer review happens only once that is prior for the plan being sent off to physicist to come up with a plan. We do not perform peer review twice. We do not routinely peer review replan cases (requires due to patient weight changes or contours position changes requiring replan). I do not think peer review process can happen multiple times in the current radiotherapy workflow. Some cancer subsites do not even implement

#	Questions (sent 29/11/2022)	Response
		peer review routinely due to staff shortages or smaller cancer sites managed single handily.
		Expert 5: If focussed on the TD and dose distribution review then yes though there needs to be a feedback look if a change is proposed because that should trigger an acceptance or not of the proposed change.
		Expert 6: I appreciate the split between target volume delineation and dose calc peer review, however, splitting down by the degree of change (which is subjective) seems to over complicate the pathway, in my view.
2	Do the listed assumptions seem appropriate? If No, please explain.	Expert 1: No. see comments above.
		Expert 2: In the clinical I am not sure that the assumptions will work. For example: • ProKnow has no expected impact on the internal peer review process in terms of the outcome (e.g. increasing or decreasing the % major change) – If things were black and white this assumption could hold but in reality it is not and I can imagine there may be overlap and things may seep into each other. I am also surprised by: • For every 10 peer reviews conducted 9 will be internal and 1 will be external. What about centres who can't undertake 9 internal peer-reviews as they simply do not have the appropriate staff to do so?
		Expert 3: No, see bold text below • *The model has allowed for the possibility of splitting the peer review of the target definition and the dosimetry calculations* ***but it is appreciated that this process currently happens together (at the same time) in practice***. - this is not true, PR usually happens separately • *in the future there may be a ProKnow module that could incorporate AI auto-contouring which acts as a first* ***target volume definition*** - Also not true – as it is unlikely that AI will ever be able to outline primary target volumes. • *This does not however remove the requirement for* ***peer reviewing the dosimetry calculation when peer review is required.*** - There are already programs out there that can review dosimetry calculations against protocol. Dosimetric 'Peer Review' is rarely if ever done currently.

#	Questions (sent 29/11/2022)	Response
		• *external peer reviews are only conducted with **very expert individuals** (consultant oncologists)* - Experts may also be at 'smaller' centres. It is unfortunate to split like this; and likely to cause upset! • ***ProKnow currently only directly impacts on the boxes with red text (the peer review process itself*** - Internal peer review is very unlikely to use Proknow, but the local planning system
		Expert 4: There is a point mentioned that external peer review may be more difficult and complex than internal peer review which may be misconstrued as that local oncologists are not as good as external oncologist. I would disagree with this. Every clinical oncologist would offer a ground truth to come up with a specific radiotherapy plan. It is through the peer review process where we check for any major deviations or errors. Not all oncologists will agree with cases or cancer sites with less numbers and less consensus than others. There are differences in cancer sites in terms of contouring consensus and variability. Smaller and rarer subsites such as sinonasal (head and neck subsite) would have very little consensus as these cases are rare and would be encounter rarely by individual oncologists.
		Expert 5: See above.
		Expert 6: The added cost of external peer reviews could be clarified. Is this considered nationally or locally? At a local level an external peer review may actually be less expensive than an internal review.
3	In your clinical opinion, on average what percentage of all treatment plans across all cancers need peer review?	Expert 1: Variable, and difficult to answer. A new indication, or new protocol (or new for that group of staff) might benefit from a lot of peer review initially. We might hope this would be minimised as training and competence increased.
		Expert 2: Is this question relating to any type of peer review (i.e., internal and external?). If yes, then in an ideal situation we should be aiming for 100%. If external only I think 10% of all is a good goal.
		Expert 3: All radical tumours EXCEPT standard breasts, where a selection of retrospective PR would be appropriate
		Expert 4: In my own clinical practice, we would mandate peer review of all radical head and neck cases (except early stage larynx). We do not peer review palliative cases. We do not review replan cases. There is a mandatory review of all nasopharynx cases. There will be variation to other centres and cancer sites- in my practice perhaps 60-70%.

#	Questions (sent 29/11/2022)	Response
		Expert 5: Don't know.
		Expert 6: More complex or rare disease sites/presentations may be more likely to benefit from peer review. Also clinicians or planners with less experience may benefit from their plans/delineations being peer reviewed, particularly during and soon after training. Intuitively, I think between 20-50% of cases could benefit from peer review.
4	In your clinical opinion, is the use of ProKnow likely to increase the proportion of radiotherapy treatment plans which undergo peer review?	Expert 1: It is possible that PK will facilitate data sharing, to enable peer review for more plans
		Expert 2: Yes, I think it does but I don't necessarily think it is a bad think as it may enable shared practice, collaboration etc.
		Expert 3: Yes
		Expert 4: No. As exampled by my own practice. Peer review requires clinicians to review contours drawn. Proknow does not offer any advantage over local radiotherapy softwares which already can be used for peer review process. In fact, Proknow would hamper peer review workflow as current team would need to upload the contours planned by clinicians onto Proknow and then after changes download back onto local planning system. This is not practical or safe for clinical implementation. I do not believe Proknow offers any unique advantages for peer review process.
		Expert 5: It has the potential to.
		Expert 6: External peer review may be much easier with a tool like ProKnow, as a result clinicians may be more likely to go through the process given a less burdensome option. Internal peer review might not change so much directly, however, if centres build a training database within ProKnow they may be able to improve quality and the ease that clinicians and planners feel with peer review. So indirectly the proportion might increase in time.
5	Is it possible that using ProKnow will also increase the proportion of peer reviews which are conducted externally versus internally?	Expert 1: It's possible.
		Expert 2: Yes, especially for smaller centres.
		Expert 3: Yes
		Expert 4: This begs the question why you need peer review. Peer review is to increase accuracy of radiotherapy for our patients, avoiding any major human errors and standardising radiotherapy plans for patients. In my centre very little external peer review is required. The only reason why external peer review is requires is there is no peer in your local centre. I do not think Proknow will impact the uptake of peer review be it internally or

#	Questions (sent 29/11/2022)	Response
		externally. Proknow do not contribute to peer review which already been adopted in our local centre,
		Expert 5: If adopted for peer review then yes because external peer review will be as easy as internal peer review.
		Expert 6: Yes, I feel this is likely. The currently available options make external peer review very difficult to accomplish.
6	Is it possible that using ProKnow can lead to changes in the proportion of treatment plans which require major or minor changes following peer review?	Expert 1: Without knowing what you are defining as 'major' or 'minor' this is almost impossible to answer. In any process, I would anticipate that review should pick up changes than not doing any review – there might be an expectation that this would diminish over time for a selected sub-set of patients or protocols, once expertise and experience had improved. Nonetheless, some light-touch peer review could still be beneficial to guard against any kind of drift away from standard protocols over time.
		Expert 2: Yes, and as per question 1 this is something I am most concerned about.
		Expert 3: Yes
		Expert 4: No. Peer review in my centre happen outside of Proknow. Proknow offers an alternative more cumbersome conduit to perform peer review but does not impact on increase or reduction of changes following peer review. The process of peer review is driven by oncologists contributing. The quality of contribution depends on local oncologists / teams.
		Expert 5: It's possible.
		Expert 6: If ProKnow is used to its full potential, it will also be a tool to improve the quality and skill of clinicians and planners. Improved skill may, in time, lead to fewer major changes being required (so the proportion of minor change may be higher) Initially, however, the availability of peer review may lead to a greater proportion of potential errors being observed. There may also be more harmonisation of practice nationally. This could lead to a greater proportion of major changes being seen.
7	Is the need for major or minor change in treatment plan (following peer review) currently recorded routinely either locally or nationally?	Expert 1: In our department at least = YES. Although it is perhaps recorded as free text in a document, and may not be easy to extract quantitatively. The recent version of RCR peer review guidelines stipulate that this should be done, although I don't know how long this will take to be implemented.

#	Questions (sent 29/11/2022)	Response
		Expert 2: My experience is that different centres have their own in-house way of recording this, but there isn't a "routine" way of recording.
		Expert 3: Not recorded locally here, but has been at other centres I have worked. Not recorded nationally
		Expert 4: No. There is no mandated documentation of this. Although locally, in my practice, I document this as evidence of local peer review process and self-improvement.
		Expert 5: Not nationally. Possibly locally in some places.
		Expert 6: There is no requirement for this to happen. Our centre does record peer-review activities including changes that are discussed. This is recorded on a form within the oncology management system ([redacted]). The degree of the change is subjective and not usually qualified in the record.
8	In the future, could widespread adoption of score cards lead to a potential reduction in peer review in the future?	Expert 1: ? if you mean peer review of the dose calculation at the end, then *possibly* (it's a bit of a stretch to say this, to be honest – it depends on how score cards are implemented). In terms of peer review of decision to treat, and of target definition, then absolutely not, as these are separate processes and need to be carefully reviewed separately.
		Expert 2: I need to know more on what is meant by score cards.
		Expert 3: No
		Expert 4: May or may not. Peer review happens prior to submission of radiotherapy contours to physics department which comes up with a radiotherapy plan which is the final plan used for dosimetric assessment. This is then used to be compared to the scorecard. However, these scorecards to not capture radiotherapy coverage. This is the same at present where dosimetry information does not capture radiotherapy coverage and needs to be assessed by looking at the actual radiotherapy plans. This question suggest that the person who asked this question does not fully understand the nuances and complexity of radiotherapy workflow.
		Expert 5: I don't think so.
		Expert 6: I am unable to answer.
9	In the future, could widespread adoption of ProKnow lead to facilitation of more AI software to support contouring?	Expert 1: NO. and this really does seem like the company trying to artificially inflate use of their product. *if * the PK manufacturers implement this (and it is not sure) it could potentially have a negative effect if it locks users into only a very limited range of AI software to use. It would also oblige all clinical users to insert use of PK into their clinical

#	Questions (sent 29/11/2022)	Response
		workflows for all patients in quite a rigid way. I predict you would get A LOT of kick back from clinical departments if this was enforced, and rightly so. I am really opposed to this being mentioned anywhere in any of the PK assessment documents
		Expert 2: Maybe, but there are a lot of vendors and researchers looking at different systems.
		Expert 3: No
		Expert 4: A few possible answers to this- if Proknow can resolve issues with inter-operability and being compatible to a streamlined radiotherapy planning software then can it offer any clinical utility to our current radiotherapy delivery workflow. With current rapid rate of development, if AI auto-contouring software can overcome interoperator variability and be adopted seamlessly into any oncology workflow- this would replace the need for Proknow.
		Expert 5: If Elekta build in an AI tool to ProKnow then it could increase the use of AI, especially if it was competitively priced. This doesn't have any impact on peer review though. See above.
		Expert 6: Yes. Possibly a barrier to AI supported contouring is a lack of trust in the outcome. Peer review via ProKnow could help to engage clinicians with AI contouring tools. Peer review processes will need to be robust to observe errors from AI contouring which may not be predictable – using ProKnow as part of a peer review process may help formalise the process and make it more robust. (This is in my opinion, not based on any evidence)
10	What is the number of new treatment starts per linac per year on average?	Expert 1: Outside of my scope – but RTDS or IPEM or other sources of info will have this. You might want to differentiate between (say) palliative new starts and radical new start, or some other criteria.
		Expert 2: I don't have these numbers.
		Expert 3: Approx 750 -800
		Expert 4: I do not have the data personally for this question.
		Expert 5: Don't know. RTDS could tell you. Maybe 500?
		Expert 6: In our department our statistics indicate around 650 new treatment courses per linac in the last 12 months. This will vary significantly in other centres. We have inferred this by interrogating our database for day 1 treatment appointments – this figure roughly agrees with the number of referrals annually divided by the number of available linacs

#	Questions (sent 29/11/2022)	Response
		An alternative method would be to review the Cancer Stats website which holds data from the RTDS. This might show the national average. The big caveat to this answer is that we don't normally report on that specific statistic and we observed a large range of values between individual linacs.

Additional comments

Expert 1:

- *[Regarding peer review process and pathway]* You seem to have completed neglected any kind of peer review of decision to treat or what should be included in target. This can be in addition to review of target contours as they have been delineated, and in addition to review of plan dose calculation.
- *[Regarding planning timing]* It *may* happen together, but not always, and this may not be the preferred option
- *[Regarding possible future AI auto-contouring use]* I object to this on several levels. The ProKnow AI segmentation module does not yet exist, and it is not sure how and when this would work, or if it would fix the choice of AI software that could be used. (there would surely be issues with fair competition, if it was not compatible with many other software systems for AI). In addition, I do not think the community is yet ready to accept that review of AI contours by a single human consultant is the same as peer review by many human consultants, so I disagree quite strongly with this description.
- *[Regarding quantifying internal versus external peer review]* I don't really understand the need or advantage to splitting into internal and external peer review. Even in a larger centre – there could be value in an external peer review, to avoid 'group think' and true comparison of treatments across the country.
- *[Regarding Key Assumption 2]* PK could impact on the boxes in red, but could also impact other items, depending on how it is used, so not really sure if you are choosing to study PK for only a restricted application?
- *[Regarding Key Assumption 5]* I'm not sure where this number came from ?
- *[Regarding Key Assumption 6]* Also not sure if this is true? Or whay we think it might be true? Staff time probably costs the same whether it is internal or external review.

Expert 5:

- *[Regarding the rationale for splitting the peer review steps due to AI auto-contouring*] AI auto-contouring is likely to be independent of the oncologist target peer review (or decision to treat peer review). AI auto-contouring is unlikely to produce contours of the target but may commonly be used in contouring. You could safely remove this section.
- *[Regarding dosimetry calculation when peer review is required]* Perhaps you mean peer review of the oncologist's specification of dose coverage? All dosimetry calcs are already independently checked but not the choice of dose coverage of target vs OAR coverage and this is somewhere that different oncologists will differ in opinion on. However, there are protocols that specify dose constraints for OARs.

#	Questions (sent 29/11/2022)	Response
	• *[Regarding the expertise level of an external peer reviewer]* No. The expertise level needs to be the same. The only reason that external might be more complex is if there is no easy route to getting the data to the per reviewer. • *[Regarding Key Assumption 2]* ProKnow could be involved in the decision to treat part and the target definition part, both of which are separate from peer review. • *[Regarding Key Assumption 4]* If ProKnow is shown to be a useful tool for peer review then it could be used internally or externally without any difference between them. It is too early to make any comment on whether it will increase or decrease the amount of peer review. • *[Regarding Key Assumption 5]* I can't support or refute this. I've no idea where it comes from but does it matter? • *[Regarding Key Assumption 6]* I don't know what this is based on. If there's a convenient tool (like ProKnow) then there should be no difference between the 2. If not then the difference is down to the difficulty in getting the data to/from the peer reviewer. I can't see why the external ones would be more complex. There may be nobody local with the necessary expertise but that doesn't make the peer review more complex or expensive, it just means that the peer reviewer is elsewhere in the country and there are fewer experts available.	

Appendix D3 - NHS England

Questions sent 21/10/2022		
The EAG are aware that 49 specialist cancer centres in the NHS are using ProKnow, as funded by NHS England		
1	Can NHS England share the evaluation that led to the selection of ProKnow over other IT solutions to improve radiotherapy delivery across the NHS? This will help the EAG understand competitor/comparator technologies and the variation in current pathway across the NHS.	ProKnow was the only technology identified with the functionalities to support the Radiotherapy Transformation Programme.
2	What instructions have been sent to sites from NHS England? Are all sites/specialties using the same functionalities? The will help the EAG understand the context of the NHS England Real-World Evaluation of ProKnow and the potential biases or limiting factors that need to be considered.	Document already shared with EAG (expressions of interest).
3	What instructions have been sent to sites from NHS England? Are all sites/specialties using the same functionalities? The will help the EAG understand the context of the NHS England Real-World Evaluation of ProKnow and the potential biases or limiting factors that need to be considered.	No response.
Questions sent 18/11/2022		
In order for the EAG to recommend evidence generation within the EVA to fulfil the gaps identified in the evidence for ProKnow, we need a better understanding of its current use in the NHS. The RTDS website states that there are 51 NHS Acute Trusts delivering external beam radiation in England. However, NHS England have commissioned use ProKnow in 49.		
1	Which 2 centres are not commissioned, and why is this?	There are only 49 (1 is managed by Newcastle and 1 by Southampton) all have access to ProKnow.
2	Can you provide a list of the 49 centres that were commissioned?	To be sent separately (will advise once received).
3	We note, from the expression of interest form provided by NHS England, the intention to fully implement ProKnow across NHS radiotherapy providers no later than 31 December 2021; can you confirm how many centres were fully implemented and able to submit data on this date?	All commissioned and in use official start date was March 2022.
4	As of 17 November 2022, how many of the 49 commissioned centres are fully implemented and are able to submit data to ProKnow?	All have local administrators in place. We are just tying off a couple of issues with IG leads.
5	Does the commissioning stop for all centres on 31 December 2024?	We will stop paying for licences from March 2025.
6	Does NHS England routinely audit the use of ProKnow during this commissioned period?	Yes we are developing plan quality metrics some are in place to form national collections. We can monitor which trusts are submitting data.

		We have a clinical leadership group in place to receive overview reports (anonymised demonstrating range of compliance).

Appendix D4 – National Radiotherapy Dataset (RTDS)

MT770 ProKnow - Meeting with RTDS
Tuesday 29 November 2022 @ 13:00

In Attendance:
EAG: Kim Keltie (KK), Emma Belilios (EB), Susan Reece (SR)
RTDS: Catherine (Kat) Roe (CR), Danielle Fleet (DF)

1) **Background**
   The Newcastle External Assessment Group (EAG), hosted by NMPCE at the Freeman Hospital in Newcastle upon Tyne, provides independent support to the National Institute for Health and Care Excellence (NICE)'s Medical Technologies Evaluation Programme. NICE recently commissioned the EAG to carry out an Early Value Assessment (EVA) of the ProKnow Cloud-based system for radiotherapy data archiving, communications and management. Purpose of this meeting to clarify what information is routinely captured within RTDS, what is the quality and completeness of submission to RTDS.

2) **General**
   The EAG is aware that NHS England (NHSE) have funded the introduction of ProKnow at 49 specialist Centres across England and has been informed that information regarding conduct of peer review and use of ProKnow may be captured in the routine data submissions to the National Radiotherapy Dataset (RTDS), within additional data fields included in RTDS version 6.

   Response: CR clarified that there is no link between ProKnow and the RTDS, they are separate systems that are unlinked. The RTDS programme is part of the National Disease Registration Service (NDRS), currently hosted by NHS Digital (NHSD). NHSD and NHSE will soon merge together to form the new NHSE. There is no formal agreement to suggest outcomes data captured in ProKnow will be specifically included in a version of the RTDS. [redacted]

3) **Questions to RTDS**
   i. **Of the 51 acute NHS Trusts with specialist cancer services delivering external beam radiotherapy, can you estimate how many are still submitting to RTDS v5 and how many have moved to RTDS v6?**

The RTDS is reviewed and updated roughly every 3 years. Proposed updates go out for consultation to a variety of stakeholders before rollout. RTDS version 6 (RTDS v6) is currently still in its pilot phase (started April 2022). Due to a number of issues, full rollout has been delayed. Consultation for RTDS v6 began around 18 months ago. Results of the consultation is not currently publicly available.

Currently, all Trusts who are commissioned to deliver radiotherapy in England submit to v5. Submission to the RTDS is mandatory; certain data fields within the RTDS are also mandatory. All Trusts will eventually transition to v6 (similar to v5 with additional data fields). During the v6 pilot phase, v5 can still be submitted until a trust has transitioned fully to V6.

ii. **Our local trust (The Newcastle upon Tyne Hospitals NHS Foundation Trust) has informed us that they are still submitting to RTDS v5, as their Treatment Planning System is currently unable to export to v6 (awaiting updates from the supplier). Are you aware of the different Treatment Planning Systems used?**
We are aware of the different Treatment Planning Systems used. The two main oncology information systems used in the NHS are Aria and Mosaiq. Please note, that it is not the treatment planning system that has not been upgraded, but the record and verify system.

iii. **NICE shared with us** the list of data fields included in RTDS v6**, and we are unable to locate where confirmation of whether treatment plan was peer reviewed (Yes/No response) is documented, or where/how use of ProKnow to facilitate peer review would be documented. Are you able to direct us to the data item number(s) where peer review and how it was conducted would be recorded in RTDS v6?**

The RTDS is a dataset and programme that is part of NDRS and hosted by NHSD. All NHS Acute Trust providers of radiotherapy services in England or private facilities where delivery is funded by the NHS, are mandated to collect and submit standardised data monthly against this nationally defined data set. National Radiotherapy Dataset (RTDS) (ncin.org.uk)

ProKnow is a web tool that can store and analyse radiotherapy plans and associated patient metrics such as comorbidities and outcomes. NHS England have funded the introduction of ProKnow at 49 specialist Centres across England. ProKnow data capture is not directly linked to the RTDS programme. [redacted]

[redacted] RTDSv6 does not include an item that is specific to 'peer review'; such a field, subject to reaching consensus on its definition, could be considered for future iterations of the dataset. We have proposed using RLP9 to capture peer review in the short term.

iv. Are there any data completeness reports for RTDS submissions in the public domain that we can reference in our report to NICE?

CR clarified that there are not. RTDS take a snapshot of the data every month, and report back to Trusts what is missing. Trusts can see their own data, and which data they are missing.

KK - clinicians reported that data completeness in RTDS is not consistent across the NHS. CR thought that poor data completeness was not a systematic issue in RTDS. Certain fields are mandatory (so Trusts cannot submit unless they are complete). For other data fields there are various levels of completeness.

CR will write a summary around data validation and completeness. Trusts are mandated to submit to RTDS on a monthly basis. We have weekly and monthly reports on submissions and the RTDS teamwork with trusts who are having problems extracting and submitting their data. A submission cannot be uploaded and processed unless the validation on the upload portal is met. We have radiotherapy data publicly available on the Cancerdata website cancerdata.nhs.uk/radiotherapy/dashboard and we have further trust level data available via Cancerstats 2 (for people working within oncology in the NHS) where an HSCN network and account approval is required to review data. There is currently no publicly available reports on data submissions for RTDS.

v. Is the data from RTDS routinely data linked to other databases (National Cancer Registry for more detailed patient/disease characteristics, or Hospital Episode Statistics, Mortality databases for long-term outcomes)?

CR – RTDS data is collected at patient level with information on the tumour diagnosed using ICD -10 codes. This data is routinely linked to other data sources as part of the national cancer registration dataset and the Rapid Cancer Registration Dataset. Data Resource Profile: National Cancer Registration Dataset in England | International Journal of Epidemiology | Oxford Academic (oup.com) It can also be linked to HES, SACT, and other cancer or health care datasets via patient identifiers (e.g.

NHS Number, DOB, gender, postcode). Specific projects include assessment of SABR for lung cancer Stereotactic Ablative Body Radiotherapy Versus Radical Radiotherapy: Comparing Real-World Outcomes in Stage I Lung Cancer - PubMed (nih.gov) . Another example of a publication that utilises the RTDS data is, The impact of the COVID-19 pandemic on radiotherapy services in England, UK: a population-based study - PubMed (nih.gov).

KK: the company has advised that sharing of information within ProKnow can be adjusted by the users. There may be IG issues regarding sharing of identifiers between centres or uploading to a cloud-based system (where members may not be directly involved in the patients care).

CR advised that NHSD have the legal permissions to collect patient level data under the NDRS Directions (National Disease Registries Directions 2021 - NHS Digital) with the particular purpose and controls contained within those documents.

4) **Next Steps**

KK clarified that the EAG's EVA report will go to NICE on 23 December 2022, and will inform the Committee's discussions (MTAC meeting on 20 January 2023). The EVA process is still under development, however the EAG's report will be published on NICE website as supporting documentation (and available in the public domain).

CR will have a discussion NHSE and discuss with her what information can be shared with the EAG.

KK - notes from this meeting will be shared with CR and DF for checking, and will then inform the EVA report to NICE. The notes can be marked for redaction if any of the information shared is felt to be commercially sensitive (highlight in blue) or academic in confidence (highlight in yellow).

Appendix D5 – Royal College of Radiologists (RCR)

#	EAG e-mail correspondence (DD/MM/YYYY)	Response (DD/MM/YYYY)
1	**23/11/2022** Good afternoon, I hope that you are well? I am a member of a NICE External Assessment Group currently considering relevant evidence as part of an Early Value Assessment for ProKnow. I note from the RCR website that a forthcoming audit project for 2022 is 'Peer review and REALMS'. As ProKnow can facilitate peer review in this field, I would be interested to know whether this audit has been conducted, the main outcomes of interest, and whether any information is currently available? Should you have any queries or concerns please do not hesitate to ask. Kindest regards	**24/11/2022** Thank you for your email. This audit is scheduled to be conducted in Q1 next year.
2	**24/11/2022** Good afternoon, Many thanks for your prompt response and information. Please can you advise on the outcomes of interest and the focus of the audit? For example, frequency, duration, staff, and method of peer review, etc. Any information that you can provide that will help us understand more about what information is due to be collected as part of the audit will be greatly appreciated as NICE are keen to know more about any current or future data collections that may address the evidence gaps identified. Please can I also confirm that you are happy for your responses to be published as an appendix within our report to NICE, which will be published on NICE's website as supporting documentation when the EVA is published? Any information that is commercially sensitive ([redacted]) or academic in confidence ([redacted]) so that we can ensure this information is fully redacted before the report is published. Of course, e-mail addresses will not be included in the report. Should you have any questions or concerns, please don't hesitate to contact me. Kindest regards,	**30/11/2022** Outcomes of interest are answers to following: • Through which methods is peer review facilitated in your Radiology department? • Is peer feedback routinely provided in your imaging department? • If an addendum is provided for a Radiology study does your RIS or PACS notify the primary reporter of the addendum automatically? • Is there a designated peer feedback moderator that monitors the content of the peer feedback response sent to the primary reporter? • Do radiologists in your department create a reflective note routinely for both their positive and negative peer feedback? • What was your department's percentage attendance rate for discrepancy meetings last year? • How many discrepancy meetings were held in your trust in 2021? • Are individual REALM attendance records distributed to radiologists? • Is a formal annual report of the outcomes from the discrepancy meetings at your trust provided routinely, summarising the learning points?

#	EAG e-mail correspondence (DD/MM/YYYY)	Response (DD/MM/YYYY)
		• Is there a formal process for providing confidential feedback to individuals prior to their case being discussed at the REALM? • Is there a REALM lead/coordinator? • Does the a REALM lead/coordinator have the role formally acknowledged in their job plan? • Does the REALM co-coordinator or another nominated person submit at least one case per year for consideration for publication in the REALM newsletter? The focus of the audit is to assess compliance with the RCR standards for REALM and to analyse current methods utilised to deliver peer review and peer feedback.
	30/11/2022 Please can the EAG also confirm whether the audit results will be published or available on request following completion?	**01/12/2022** RCR usually publishes its audit results anonymised in peer-revied journals - we would be happy to provide a link to them if that's any use.
	09/12/2022 Many thanks again for your previous support and advice, it has been hugely appreciated. Following feedback from NICE on the EAG draft report, I would be very grateful if you could provide further information relating to the planned audit to address the following queries. 1. What time period will be covered by the audit? 2. Will the following aspects be captured within the audit: a. Capturing details of local arrangements regarding peer review of treatment plans: i. how are treatment plans shared/viewed by multiple individuals (e.g. in person, electronically via virtual meeting, electronically using specified software)? ii. how many individuals conduct peer review (staff involved, time taken)? iii. how frequently are treatment plans reviewed (scheduled weekly MDT, on demand)? iv. how are treatment plans edited (e.g. Teams, ProKnow, treatment planning software)? b. Number or proportion of external and peer reviews conducted?	**19/12/2022** The majority of the audit data is around systems that are currently in place so the data is a capture of the time at which the audit launches so in 2023. There is not much data input that requires a retrospective analysis over a specific time period. The few that are relates to attendance at discrepancy meeting over the last year and how many discrepancy meetings over the last year (this would be entire of 2022). 2a i) No but this has been captured in a previous audit I performed with Karl for the RCR on Cancer MDT: Balasubramaniam R, Drinkwater K, Howlett DC. A national audit of radiology practice in cancer multidisciplinary team meetings. Clin Radiol. 2020 Aug;75(8):640.e17-640.e27. doi: 10.1016/j.crad.2020.03.031. Epub 2020 Apr 20. PMID: 32327228. Standard 9: 58% of hospitals raised issue with the quality of the equipment for reviewing MDT cases via videoconferencing (this may have improved with COVID and remote

#	EAG e-mail correspondence (DD/MM/YYYY)	Response (DD/MM/YYYY)
	c. Adherence to local peer review protocols (e.g., percentage of plans requiring peer review undergoing review)? d. Time taken to perform peer review? e. Staff present (role, number) at peer review?	working increasing precedence). Standard 8 was attained as 98% had imaging projection facilities so MDT core members could see images. But in only 34% did the MDT co-ordinator always link their computer so summations and treatment decisions could be reviewed by all members. ii) Yes we will be assessing which parts of Radiology are peer reviewed and for which staff (radiology/radiographers, out sourcing companies) and by which methods iii) No but again some of this has been captured in a previous audit I performed with Karl for the RCR on Cancer MDT: Balasubramaniam R, Drinkwater K, Howlett DC. A national audit of radiology practice in cancer multidisciplinary team meetings. Clin Radiol. 2020 Aug;75(8):640.e17-640.e27. doi: 10.1016/j.crad.2020.03.031. Epub 2020 Apr 20. PMID: 32327228. Showed most MDT occurred once a week but I guess this does not fully answer what you are asking, the frequency of treatment plans reviewed will depend on how often the oncologist puts the case through the MDT. A good question maybe to ask which we have not to my knowledge: Are all cases of cancer discussed at MDT before commencing treatment and in the context of neo-adjuvant therapy are they always discussed after down-staging at MDT to determine the next treatment step. iv) No we are not collating anything related to this but again this decision making should be done via an MDT in my view. 2b. Yes we are assessing how often and what is peer reviewed. For NHS the percentage is not being asked because I believe this would be hard for departments to provide an accurate response. One of the issues with peer review in Radiology in the NHS is that the mechanisms for recording peer review appear to be inconsistent and therefore collating any data on percentage assessed will be poor. It is one of the major reasons for doing this

#	EAG e-mail correspondence (DD/MM/YYYY)	Response (DD/MM/YYYY)
		audit to show it is not well done and potentially suggest how we might improve. 2c. Yes we are asking if they do peer review routinely and how often and by what method 2d. No not directly but some inferences can be made based on the areas that undergo peer review (MDT review approx. 5-10 min per case versus proper double reporting which will require same time as given to report scan) 2e. As above we are assessing peer review in radiographer and radiologists over different areas of clinical practice. I am not sure if that is what you are looking for or if it is relevant to Radiology.