Clinical Radiology 74 (2019) 823–830

Contents lists available at ScienceDirect

Clinical Radiology

journal homepage: www.clinicalradiologyonline.net

Review

Can prostate cancer be NICE?

J. Richenberg*

Department of Imaging, Brighton & Sussex University Hospitals NHS Trust, Eastern Road, Brighton BN2 5BE, UK

On 9 May 2019, the National Institute for Health and Care Excellence (NICE) published its updated UK guidance on prostate cancer. The publication is the culmination of a 3 year process. It is an evidence-based, carefully crafted, comprehensive "book" to compliment the pre-existing 2014 guidance. It was born from new evidence on aspects of prostate cancer treatment and, most relevant for this special edition, diagnosis. This article provides a "behind-the-scenes" on how NICE operates, using the guideline as a case study. The piece sets out to demystify this august governance body's processes: from the decision to update the existing guidance, through the scoping and discussion stages to the principles and policies that shaped the whole process. This provides the backdrop to the second half of the article wherein the 85 page guideline is condensed in to a few highly pertinent recommendations. The areas that sparked the most debate during the committee's 24-month lifespan are highlighted, finishing by asking the UK radiology community: where do we go next in this new era of multi-parametric magnetic resonance imaging first?

Introduction

Every radiologist, radiographer, and imaging nurse is aware of the National Institute for Health and Care Excellence (NICE), but for many I suspect it is a rather shadowy and not necessarily well-understood Dr Jekyll–Mr Hyde organisation. As the good doctor, it works tirelessly to sift through evidence to issue national guidelines to promote and standardise high-quality, cost-effective treatment. As the not so NICE Mr Hyde, I believe it is misrepresented as being focussed on saving money and has been accused of stifling adoption of new treatments despite credible evidence that the treatment improves patient outcomes. This article in the special edition of *Clinical Radiology* attempts to demystify some aspects of the NICE–not NICE processes, using the publication (9 May 2019) of the updated national guidance on prostate cancer[1] as a case study. This personal summary recognises that NICE has (1) a *legal obligation* to consider cost-effectiveness when evaluating treatments and is also required to consider the likely cost impact of its recommendation; and (2) teams set up specifically to evaluate novel treatments and to encourage them to be brought to market.

Background

In 2008, NICE published clinical guideline *CG58 Prostate cancer: diagnosis and treatment*. In 2014, following a 2-year review process, the guidance was updated and replaced by CG175.[2] Imaging, more accurately, multiparametric magnetic resonance imaging (mpMRI) featured heavily in the guideline update, as summarised in Box 1. Although the guidance fell short of promoting prebiopsy mpMRI in all

* Guarantor and correspondent: J. Richenberg.
E-mail address: Jonathan.richenberg@nhs.net

https://doi.org/10.1016/j.crad.2019.06.009
0009-9260/

Box 1. **Summary of recommendations of CG175 (2012).**[1]

Chapter 3: Diagnosis and staging of prostate cancer
A core member of the urological cancer MDT should review the risk factors of all men who have had a negative first prostate biopsy, and discuss with the man that: • there is still a risk that prostate cancer is present **and** • the risk is slightly higher if any of the following risk factors are present: - the biopsy showed high-grade prostatic intra-epithelial neoplasia (HGPIN) - the biopsy showed atypical small acinar proliferation (ASAP) - abnormal digital rectal examination (DRE). **[new 2014]**
Consider multiparametric MRI (using T2- and diffusion-weighted imaging) for men with a negative transrectal ultrasound 10-2 core biopsy to determine whether another biopsy is needed. **[new 2014]**
Do not offer another biopsy if the multiparametric MRE (using T2- and diffusion-weighted imaging) is negative, unless any of the risk factors listed in the recommendation on page 135 are present. [new 2014]

cases, the recommendations were presented to make it inevitable that most patients under investigation for suspected prostate cancer would have an mpMRI at some stage, and played on the growing recognition that mpMRI before biopsy was better than mpMRI after biopsy because it did not suffer from post-biopsy haemorrhagic artefact.

Despite this quantum leap in the emphasis on imaging in the prostate cancer pathway between 2008 and 2014, many of the committee's experts shrugged their collective shoulders as they walked from the NICE offices in Cardiff to the station after the concluding meeting of the CG175 panel. They muttered to themselves that that the recommendations around mpMRI were already out of date. They knew the PROMIS trial results[3] were imminent and that these would support upfront mpMRI.

The natural cycle for guidance update review is 5–7 years, but expert advice spotlighting the rapid changes within prostate cancer diagnosis and treatment focussing on new evidence, prompted the publication of a NICE evidence summary, leading to an early look at updating CG175, culminating in the publication of *Surveillance report (exceptional review) 2016 — prostate cancer: diagnosis and management (2014) NICE guideline CG175*.

In October 2016, NICE stated: "After considering all the new evidence and views of topic experts, we decided that a partial update is necessary for this guideline…. We will plan an update of the following sections of the guideline:

- Scheduling of docetaxel added to standard treatment for the treatment of hormone-sensitive metastatic prostate cancer;

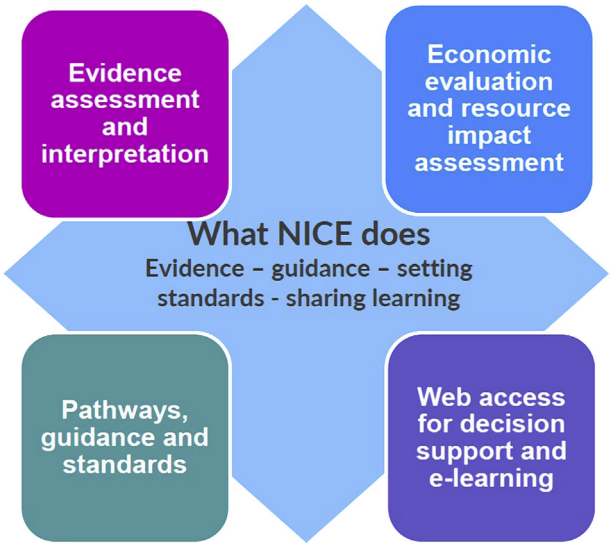

Figure 1 What NICE does.

- Scheduling of docetaxel added to standard treatment for the treatment of hormone-sensitive locally advanced prostate cancer;
- Multiparametric/functional MRI before transrectal ultrasound (TRUS) biopsy in people with suspected prostate cancer; and
- Optimal dose and fractionation schedule for people with localised prostate cancer (T1b–T3a N0 M0) who are treated with radical radiotherapy.

The decision was based on three randomised controlled trials (RCTs) included in ESUOM50[4] – STAMPEDE,[5] CHAARTED[6] and GETUG15, a meta-analysis by Vale,[7] the then ongoing PROMIS trial[3] (expected to publish in March 2017), and the CHHiP trial published in June 2016.[8] The acting Chair advised all other treatments for advanced disease were covered by NICE Technology Appraisals and therefore would not impact the guideline.

In addition, during the exceptional review, NICE was made aware of ongoing research in the areas of risk stratification and treatment for localised prostate cancer (ProtecT trial)[9,10] which was identified as having a possible near-future impact on current recommendations. During the scoping of the update, these areas would be checked to assess if an update was required.

NICE watchwords

NICE does much more than issue clinical guidelines (Fig 1). The guidelines work is core business; however, the remaining focus is on management of diseases/conditions, concentrating on care, and support for patients. The guidelines are based on the best available effectiveness evidence, informed by practitioners and people with direct experience of services. They do not replace clinical or professional judgement and are not designed to be a textbook on any particular condition.

Each guideline is considered in the wider perspective so that the final recommendations will have been influenced by considerations around cost-effectiveness, legal, and policy constraints, practicalities of implementation, equality of access, and acceptance. The overarching NICE credo is based on three principles: evidence, integrity (verging at times on extreme political correctness), and QALYs (quality-adjusted life years — a health economic term).

Evidence

The strength of NICE is the rigour that underpins the development of all its guidance. Every recommendation is justified, evidence based, and crafted meticulously. The thorough literature search is presented, critiqued, and subject to bias analysis, validity, and other methodological checks far beyond those applied even in respected peer-reviewed, high-impact-factor journals. Each recommendation is given an evidence grade, limitations of the evidence highlighted, and once the content agreed, serial editorial checks aim to eliminate any ambiguity in what is written.

The PICO table features strongly in the NICE approach. The Population (P) is defined, Interventions (I) compared against a Comparator (C), against an agreed set of Outcomes (O; see the Electronic Supplementary Material).

Integrity

NICE are phobic about the concept of "bias". Every potential committee member is vetted. Before, during, and after the guideline production a log of members' potential conflicts of interest is published and updated; a small forest has been consumed in the production of the comprehensive, regularly served conflict of interest (CoI) declaration forms.

The concern is understandable as any (even perceived) motivation of a key expert member to influence the recommendations could torpedo the whole guideline, and all the solid benefits that the guideline may otherwise confer on patient care. The obsession with integrity mirrors that within NHS control bodies in general, doubtless in turn a reflection of the laudable move to freedom of information and encouragement of external scrutiny.

There is, however, a price to pay as the issue of integrity and probity becomes ever more politically correct. NICE relies on expert opinion, and the experts are, almost by definition, recognised through their publications and presentations. Committee members may feel they have the right to promote good practice as they see it, ahead of a thorough but extended period of guideline production. The understandable paternalistic attitude within NICE to convey absolute objectivity from its experts sometimes, in my opinion, blurs with a concern that committee members might say something that anticipates the guideline. In a rather tautological way, recommending an approach subsequently published in the guideline could be construed as not being objective.

QALYs

The QALY is defined in the NICE Glossary as "a measure of the state of health of a person or group in which the benefits, in terms of length of life, are adjusted to reflect the quality of life. One QALY is equal to 1 year of life in perfect health. QALYs are calculated by estimating the years of life remaining for a patient following a particular treatment or intervention and weighting each year with a quality-of-life score (on a 0 to 1 scale). It is often measured in terms of the person's ability to carry out the activities of daily life, and freedom from pain and mental disturbance."

The various interventions and treatments within the PICO are commonly compared on a cost-effectiveness plane, with axes of clinical effectiveness and cost: interventions that are effective and cheaper than current practice always do well, but therapies more effective yet more expensive than current practice are also considered, and a threshold of ~£20,000–30,000 per QALY usually becomes the threshold above which a new treatment would be rejected. This is, to be fair to NICE, a vast over-simplification of what the very sophisticated health economic team contribute to the guideline. The 'NICE says "no" because it costs too much' is a widely, but not justifiably, held view that invests NICE with its Hyde persona. I cannot pretend to be anywhere competent in the science that is health economics, but my exposure to it during the guideline production has made me appreciate how complex yet necessary it is in influencing clinical practice in a cash-challenged National Health Service.

The update begins: the importance of scoping

Having resolved to update, the NICE machinery rumbled in to action at the end of 2016. The committee with a 2–3-year lifespan gained a very able NICE committee chair (a general practitioner) and standing personnel from NICE, including health economists and statisticians and editors and evidence/research experts. Expressions of interest were sought and after interviews led by the chair, core experts were selected. In this case, the initial clinical experts comprised one of the urologists, one of the oncologists, and the radiologist that had been on the CG175 2012–2014 committee. This trio met in the spring of 2017 in London with the chair and the NICE team.

Guidance updates, it became apparent, are *not* necessarily equivalent to a full guidance development. Only the aspects of existing guidelines (in this case CG175) affected by subsequent publication of (high-level evidence/level 1 evidence) are considered.

The initial meetings are crucial as they define the terms of reference going forward, essentially what can and cannot be discussed within the limited areas that remain permissible to update. There was an acute awareness among the experts of the importance of this, having been frustrated at times during the CG175 guidance development process by the rigidity of the NICE rules of engagement, indeed feeling

that this inflexibility in part contributed to the "datedness" of the 2014 recommendations.

Despite the awareness that this overture phase determines in large part how the rest of the grand work is composed, and that choosing the correct melodies and identifying the best leit-motifs at this stage is crucial, I have to admit that we did not get the terms of reference entirely correct, and the final guidance suffers somewhat from this failing.

The "agenda" setting at the initial meetings is detailed: apart from agreeing on the composition and number of expert members that should comprise the committee (lay members, oncologists, radiologists, urologists, patient interest groups, specialist cancer nurses, radiotherapy radiographers, and radiotherapy experts), the statements for discussion are meticulously fashioned. The initial set of questions — the lines of enquiry — had been drafted by the NICE team during the preliminary review process, based on the existing guidelines and the newly published trials.

In June and July 2017, the draft scope went to registered stakeholders for consultation. After a very intense, bordering on obsessive, set of discussions following the stakeholder comments, nine topics or review questions were agreed (Electronic Supplementary Material). There were nine research questions (RQs), each topic discussion based around the material within the comprehensive evidence review.

The process for updating the prostate cancer guideline

The nine RQs were tackled over a series of eight meetings October 2017 to December 2018, during which comprehensive literature reviews were picked apart, robust discussions were had between the experts and the NICE staff on phrasing and impact, strongly held views were expressed, and recanted, headaches were assuaged with copious tea and several biscuits. By the end of the summer of 2018, a document worthy of sending out to the commissioning team (internal quality assurance [QA]) and the stakeholders came in to being.

In the autumn of 2018, the guideline having been updated with individual chapters and a short guideline version, including appendices, was submitted to the commissioning team for internal QA. Their "return" ranged from editorial comments to queries around rationale for individual recommendations and areas of concern around resource impact and implementation.

The draft guidelines were scrutinised by the stakeholders (the list had been circulated in October 2018 to the committee to ensure it was inclusive) between 12 December 2018 and 16 January 2019: many stakeholders remarked at length. The NICE team collated the replies into 85 pages of comments, which were discussed in detail by the full committee in February 2019, and the adapted final draft submitted to commissioning for validation and publication (9 May 2019). My impression was that about 20% of the comments led to a minor change in the guidance and 5% to a moderate change in the phrasing. The key stages of guideline development are summarised in Fig 2.

The emphasis on quality

QA in guideline development is intrinsic and extrinsic. The guidelines themselves are taken as the benchmark for good practice in the health and social care sector altering how care is delivered and how resources are used. Externally, NICE is funded with public money: NICE's reputation (respected internationally) is fragile and only as good as its latest publication. It is hardly surprising that quality controls are applied at all stages of the process. Pre-consultation queries focus on:

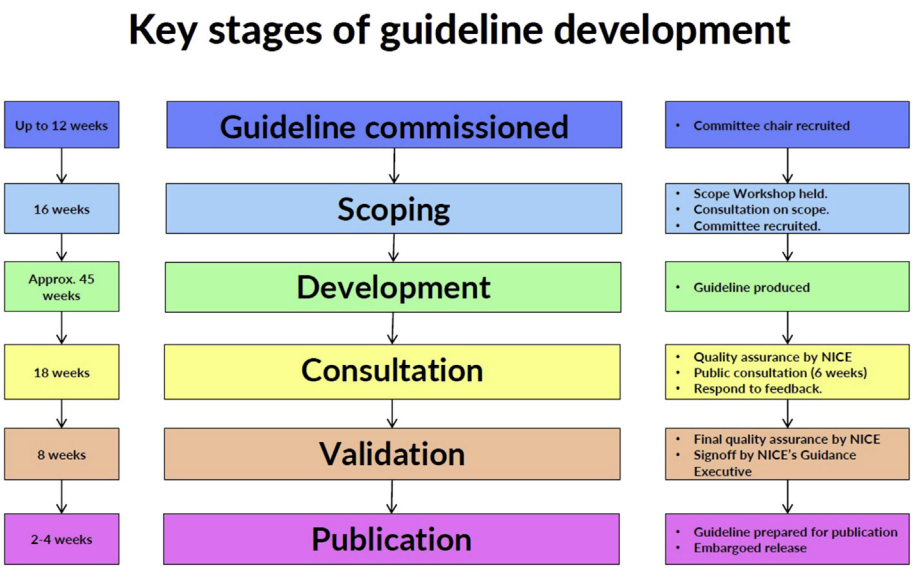

Figure 2 Steps in guideline update development.

- Does the evidence support the strength of the recommendations?
- Are you allocating additional resources without sufficient justification?

The post-consultation period scrutinises the adequacy of the responses to the stakeholders. Ultimately, NICE has to be prepared to promote and defend publicly any guidance it publishes.

The outcome

The guideline summary

The guideline *Prostate cancer: diagnosis and management (update)*[Short version] runs to 85 pages, announcing "This guideline covers diagnosing and managing prostate cancer in secondary care. It offers information on the best way to diagnose and identify different stages of the disease, and how to manage adverse effects of treatment. It includes recommendations on follow-up in primary care for people with a diagnosis of prostate cancer." The recommendations are presented in five different chapters: Information and decision support for people with prostate cancer, their partners and carers; Assessment; Localised and locally advanced prostate cancer; People having hormone therapy; and Metastatic prostate cancer.

In each chapter, recommendations still relevant from the 2008 and 2014 publications are presented alongside the new (2019) recommendations.

There follows a summary of the key points from the section 1.2[2] where mpMRI and biopsy are discussed. The summary only contains the 2019 recommendations.

Prostate mpMRI: key points.

- Only offer mpMRI to patients able to have radical treatment;
- Offer mpMRI as the first-line investigation for people with suspected clinically localised PCa; and
- Report mpMRI using a five-point Likert scale.

Prostate biopsy: key points.

- Offer prostate biopsy to men with a Likert score of $\geq$3 on mpMRI; and
- Consider omitting biopsy for men with a Likert score of $\leq$2 after discussion with the patient, and taking into account life expectancy and comorbidities.

Follow-up: key points.

- Review cases of a Likert score of $\geq$3 on mpMRI with a negative biopsy result in the MDT setting;
- For men with a Likert score of $\leq$2 on mpMRI who have not had a prostate biopsy, repeat PSA test at 3–6 months, and then every year; and
- Follow-up in primary care if the level of suspicion is low; set a PSA level at which to re-refer based on PSA density (0.15 ng/ml/ml) or velocity.

See Box 2 for a full transcript of the guideline section "Magnetic resonance imaging and biopsy".

Box 2. **Radiology-focussed recommendations in the updated guideline**

Magnetic resonance imaging and biopsy

1.2.1 Do not routinely offer multiparametric MRI to people with prostate cancer who are not going to be able to have radical treatment. [2019]

1.2.2 Offer multiparametric MRI as the first-line investigation for people with suspected clinically localised prostate cancer. Report the results using a five-point Likert scale. [2019]

1.2.3 Offer multiparametric MRI-influenced prostate biopsy to people whose Likert score is 3 or more. [2019]

1.2.4 Consider omitting a prostate biopsy for people whose multiparametric MRI Likert score is 1 or 2, but only after discussing the risks and benefits with the person and reaching a shared decision (see table 4 below, table 1 in original). If a person opts to have a biopsy, offer systematic prostate biopsy. [2019]

1.2.5 Do not offer mapping transperineal template biopsy as part of an initial assessment, unless as part of a clinical trial. [2019]

If the MRI or biopsy is negative

1.2.10 For people with a negative biopsy who have an MRI Likert score of 3 or more, discuss the possibility of significant disease in an MDT meeting with a view to repeating the prostate biopsy. [2019]

1.2.11 For people who have a raised PSA and MRI Likert score of 1 or 2, and who have not had a prostate biopsy, repeat PSA test at 3–6 months and: offer prostate biopsy if there is a strong suspicion of prostate cancer (for example, PSA density greater than 0.15 ng/ml/ml or PSA velocity greater than 0.75 ng/year, or strong family history), taking into account their life expectancy and comorbidities discharge the person to primary care if the level of suspicion is low; advise PSA follow-up at 6 months and then every year, and set a PSA level for primary care at which to re-refer based on PSA density (0.15 ng/ml/ml) or velocity (0.75 ng/year). [2019]

1.2.12 For people who have a raised PSA, an MRI Likert score of 1 or 2 (or a contraindication to MRI), and negative biopsy, repeat PSA at 3–6 months and: offer prostate biopsy if there is a strong suspicion of prostate cancer (for example, PSA density greater than 0.15 ng/ml/ml or PSA velocity greater than 0.75 ng/year, or strong family history), taking into account their life expectancy and comorbidities discharge the person to primary care if the level of suspicion is low; advise PSA follow-up every 2 years, and set a PSA level for primary care at which to re-refer, based on PSA density (0.15 ng/ml/ml) or velocity (0.75 ng/year). [2019]

Factors to consider when discussing the options for people whose mpMRI Likert score is 1 or 2.

This very important topic is covered in some detail in the guideline, presenting the pros and cons of prostate biopsy in this setting. In short, the guideline:

- Acknowledges that between 11–28 people per hundred low-risk mpMRI cases may have clinically significant cancers;

- Notes that prostate biopsies find less than half of the clinically significant prostate cancers that are missed at MRI; and
- Points out that between 18 and 23 out of 100 people with a low-risk MRI get a diagnosis of clinically insignificant prostate cancer if they have a prostate biopsy.

Detail on the different types of biopsy, including the route and targeting technique together with complication rates, are also provided.

mpMRI and protocol for active surveillance

The increasing role of mpMRI in active surveillance is treated in Chapter 3 "Localised and locally advanced prostate cancer". Similar to the 2014 guidance, MRI should be performed prior to enrolment on active surveillance programmes and in cases where higher-grade disease is suggested at MRI, an early targeted biopsy should be considered. The follow-up regime is more proscriptive than the 2014 guidelines, suggesting initial follow-up MRI at 12–18 months and that MRI should be the first investigation when there is a clinical concern for disease progression on AS.

The research recommendations

In addition to the more widely recognised output as a large guideline and set of updated recommendations, the development group also identified areas where key questions are difficult to answer because of a lack of evidence. The shortfall in evidence prompted the committee to make a series of research recommendations. As part of the 2019 update, the guideline committee made additional research recommendations on the follow-up, diagnosis, and progression of prostate cancer (Electronic Supplementary Material). I hope that the key recommendations for research will initiate collaborative research in the UK, especially in addressing: what is the natural history of people with a Likert score on MRI of <3 without biopsy at long-term follow-up and in patients with negative MRI (Likert score 1 or 2), what is the next best diagnostic investigation to rule out clinically significant prostate cancer?

The real wrangles during the process

PIRADS versus Likert

PIRADS now in version 2.1[11-13] is a widely accepted and reliable scale for evaluating lesions identified on mpMRI. Its widespread use has been key in the promotion of mpMRI as a critical tool in diagnosing prostate cancer, and its consistency has meant that meta-analysis of imaging techniques in those with suspected prostate cancer are now realistic; however, PIRADS is limited in the setting of a guideline as it is a radiology-only tool; it pointedly ignores the larger clinical, demographic, and biochemical data. The Likert approach combines lesion analysis, essentially according to the PIRADS system, and then takes in to account clinical gestalt, family history, and validated risk evaluation metrics notably prostate-specific antigen (PSA) density.[14,15] Likert, in other words, offers a more holistic way of making a risk assessment that any particular individual harbours a clinically significant prostate cancer. Crucially, level 1 evidence for the value of pre-biopsy mpMRI has provided by studies using Likert rather than PIRADS scoring.[3,16,17] The last meta-analysis of MRI first,[17] reported both systems, but defaulted to Likert over PIRADS scoring. Ultimately, the estimated risk has to be translated into a binary decision: biopsy now or postpone biopsy (possibly indefinitely). Likert won out and the guideline reflects the UK bias toward Likert rather than PIRADS.

Category 2 versus category 3

In both the Likert and PIRADS schemes, there are five categories, boiled down in practical terms to low risk, intermediate risk, and high risk by combining categories 1 & 2 and categories 4 & 5. Setting the threshold for biopsy to level 2 (within the low-risk category) increases the sensitivity of detection of significant cancer, but at the considerable cost of over-diagnosis of clinically insignificant cancer, and at the human and economic cost of sending many for an unnecessary biopsy. The reduction in missing important disease runs counter to using mpMRI as a sound triage test. The committee looked in great detail at economic and outcome modelling setting biopsy threshold at 2 and 3 (intermediate risk). The mind-bending complexity of these meetings and the natural aversion to "missing" important disease have been succinctly captured in the recommendations. The 3s have it. The significance of setting the threshold at 3 becomes apparent when noting that the prevalence of score 1 was only 1% (6/626) in the 4M study,[18] and when using Likert in the PROMIS study only 4% (23/576). Thus setting the threshold at 2 would mean almost everyone received a biopsy negating the triage effect of pre-biopsy mpMRI.

Risk

At no point during the 2-year process did the committee, or indeed the European or UK or US health professionals, come up with a universally accepted set of criteria for what constituted low, intermediate, or high risk for clinically significant prostate cancer. Worse still, the definition of "clinically significant" is yet to be universally agreed upon. Ultimately, the arguably obsolete D'Amico classification[19] had to be used as it had been used in the 2014 guidance; this was supplemented by the definitions used in the PROMIS trial.[1]

[1] Clinically significant cancer was defined as Gleason score $\geq 4 + 3$ or a maximum cancer core length 6 mm or longer.

An insider's appraisal of why NICE is NICE

I would describe the NICE process as very fair, obsessively so; unimpeachable; evidence based (and this within a very narrow definition of what is allowed as evidence); and thorough. I would also add rigid, process-driven, and heavy-going at times. Ultimately, and this a reflection of the chair and the composition of the NICE standing team, a suitable amount of sense checking was allowed, so that the recommendations were not, in my opinion, too limited.

The committee, as is often the case, took on a personality and grew with the guideline. My experience was of a harmonious, respectful, engaged, and highly informative set of individuals. Everyone contributed, everyone listened, everyone learnt, and everyone showed determination to write the best possible guideline.

A huge amount of work goes in to the guidelines: behind the scenes and from the committee members. Many give up their time (thank you to the Trusts and clinical colleagues), including patients and charity sector workers. In recognition for this, and the sincerity expressed at all stages of the process, I would say NICE is 95% Jekyll with only a 5% trace of Hyde.

Post-guidance: the next steps

The recommendation that is going to have the largest impact on imaging practice is "1.2.2: Offer multiparametric MRI as the first-line investigation for people with suspected clinically localised prostate cancer. Report the results using a five-point Likert scale."

The Royal College of Radiologists (RCR), British Society of Uroradiology, and Prostate Cancer UK have in anticipation of this seismic change in practice — the primacy of mpMRI — been working diligently to highlight resource gaps, put in place training and mentoring schemes, offer web-based learning material, and explore a voluntary self-certification scheme within a fuller framework of QA based on Multi-disciplinary meeting (MDM) attendance and audited practice. The initiatives include a series of RCR workshops, an East of England mentoring programme, a capacity and demand analysis, work with the Welsh Assembly on resource improvement, and e-learning course. The capacity demand analysis and the wide variation in mpMRI provision across the UK highlighted by this freedom of information exercise that is summarised in this edition.[20]

There remains much to be done: increasing stock of modern MRI machines within the UK, updating the RCR curriculum, promoting a kite-mark assured teaching and training programme for consultants delivered across the country, and generally, getting recognition and appreciation of the benefits radiology services bring to clinical care. There will also be a need to work closely with urology colleagues on developing a biopsy service, shared between urology and radiology, in this new era of target/mpMRI influenced biopsy, based on a lesion depicted on mpMRI, not on a sextant of the prostate on whole-gland ultrasound.

In answer to the question: why get involved with this guideline process? I hope that the high-quality and highly respected care offered to people with prostate cancer in several NHS Trusts can be duplicated across the UK through national guidance, education, training, and QA programmes. Being able to do this through NICE and having the opportunity to update the original guidelines, so that they are current, is a key step worth the effort in 2012–2014 and 2017–2019.

And in answer to the question: would you do it again? Please take this personal review as my sign-off!

Conflict of interest

The authors declare no conflict of interest.

Acknowledgements

The guideline referred to in this article was produced by the Guideline Updates Team for the National Institute for Health and Care Excellence (NICE). The views expressed in this article are those of the author and not necessarily those of NICE.

{National Institute for Health and Care Excellence (2019) PROSTATE CANCER: DIAGNOSIS AND MANAGEMENT. Available from https://www.nice.org.uk/guidance/ng131} I thank fellow committee members and the NICE employees for their dedication, humour and expertise. It was a privilege to be part of this committee.

Appendix A. Supplementary data

Supplementary data to this article can be found online at https://doi.org/10.1016/j.crad.2019.06.009.

References

1. *Prostate cancer: diagnosis and management NICE guideline [NG131]*. May 2019 https://www.nice.org.uk/guidance/ng131. CG175 [Background].
2. *NICE. Prostate cancer: diagnosis and management Clinical guideline [CG175]*. 2014 Jan.
3. Ahmed HU, El-Shater Bosaily A, Brown LC, *et al*. Diagnostic accuracy of multi-parametric MRI and TRUS biopsy in prostate cancer (PROMIS): a paired validating confirmatory study. *Lancet* 2017;**389**(10071):815–22.
4. *Hormone-sensitive metastatic prostate cancer: docetaxel, Evidence summary published January*. 2016 https://www.nice.org.uk/advice/esuom50/0063hapter/Key-points-from-the-evidence.
5. James ND, Sydes MR, Clarke NW, *et al*. Addition of docetaxel, zoledronic acid, or both to first-line long-term hormone therapy in prostate cancer (STAMPEDE): survival results from an adaptive, multiarm, multistage, platform randomised controlled trial. *Lancet* 2016;**387**(10024):1163–77.
6. van Soest RJ, de Wit R. Irrefutable evidence for the use of docetaxel in newly diagnosed metastatic prostate cancer: results from the STAMPEDE and CHAARTED trials. *BMC Med* 2015;**13**:304.
7. Vale CL, Burdett S, Rydzewska LHM, *et al*. Addition of docetaxel or bisphosphonates to standard of care in men with localised or metastatic, hormone-sensitive prostate cancer: a systematic review and meta-analyses of aggregate data. *Lancet Oncol* 2016;**17**(2):243–56.
8. Dearnaley D, Syndikus I, Mossop H, *et al*. Conventional versus hypofractionated high-dose intensity-modulated radiotherapy for prostate

cancer: 5-year outcomes of the randomised, non-inferiority, phase 3 CHHiP trial. *Lancet Oncol* 2016;**17**(8):1047–60.
9. Donovan JL, Young GJ, Walsh EI, *et al*. A prospective cohort and extended comprehensive-cohort design provided insights about the generalizability of a pragmatic trial: the ProtecT prostate cancer trial. *J Clin Epidemiol* 2018;**96**:35–46.
10. Johnston TJ, Shaw GL, Lamb AD, *et al*. Mortality among men with advanced prostate cancer excluded from the ProtecT trial. *Eur Urol* 2017;**71**(3):381–8.
11. Padhani AR, Weinreb J, Rosenkrantz AB, *et al*. Prostate imaging-reporting and data system steering committee: PI-RADS v2 status update and future directions. *Eur Urol* 2019;**75**(3):385–96.
12. Turkbey B, Rosenkrantz AB, Haider MA, *et al*. Prostate imaging reporting and data system version 2.1: 2019 update of prostate imaging reporting and data system version 2. *Eur Urol* 2019.
13. Barrett T, Rajesh A, Rosenkrantz AB, Choyke PL, Turkbey B. PI-RADS version 2.1 – One small step for prostate MRI. *Clin Radiol* 2019;**74**:841–52.
14. Brizmohun Appayya M, Sidhu HS, Dikaios N, *et al*. Characterizing indeterminate (Likert-score 3/5) peripheral zone prostate lesions with PSA density, PI-RADS scoring and qualitative descriptors on multiparametric MRI. *Br J Radiol* 2018;**91**(1083):20170645.
15. Nordstrom T, Akre O, Aly M, *et al*. Prostate-specific antigen (PSA) density in the diagnostic algorithm of prostate cancer. *Prostate Cancer Prostatic Dis* 2018;**21**(1):57–63.
16. Kasivisvanathan V, Rannikko AS, Borghi M, *et al*. MRI-targeted or standard biopsy for prostate-cancer diagnosis. *N Engl J Med* 2018.
17. Rouviere O, Puech P, Renard-Penna R, *et al*. Use of prostate systematic and targeted biopsy on the basis of multiparametric MRI in biopsy-naive patients (MRI-FIRST): a prospective, multicentre, paired diagnostic study. *Lancet Oncol* 2019;**20**(1):100–9.
18. van der Leest M, Cornel E, Israel B, *et al*. Head-to-head comparison of transrectal ultrasound-guided prostate biopsy versus multiparametric prostate resonance imaging with subsequent magnetic resonance-guided biopsy in biopsy-naive men with elevated prostate-specific antigen: a large prospective multicenter clinical study. *Eur Urol* 2019;**75**(4):570–8.
19. D'Amico AV, Renshaw AA, Cote K, *et al*. Impact of the percentage of positive prostate cores on prostate cancer-specific mortality for patients with low or favorable intermediate-risk disease. *J Clin Oncol* 2004;**22**(18):3726–32.
20. Davies C, Castle JT, Stalbow K, Haslam PJ. Prostate mpMRI in the UK: the state of the Nation. *Clin Radiol* 2019;**74**:894.e11–8.