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Research Letters

Study Protocol for the DETECTIVE Study: An International Collaborative Study To Develop Consensus Statements for Deferred Treatment with Curative Intent for Localised Prostate Cancer

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Deferred active treatment (DAT) strategies for men with localised prostate cancer have emerged as a viable alternative to radical intervention as we aim to avoid the consequences of overtreatment. Nevertheless, such strategies remain controversial, with significant uncertainty and heterogeneity in all domains, including criteria for patient selection, the nature and timing of interventions during follow-up, criteria and thresholds for reclassification, and which outcome measures should be prioritised [1–3]. These are important barriers to the conduct and uptake of DAT by clinicians and patients as they prohibit comparison of the clinical effectiveness of different protocols. In order to address these issues in a comprehensive, robust, and systematic manner, the European Association of Urology (EAU) Prostate Cancer Guidelines Panel, in partnership with other leading guideline authorities and organisations (listed in Appendix A), has commissioned a project to develop consensus statements for all domains relating to DAT to standardise clinical practice and research.

The specific objectives are to achieve consensus for the following domains: (1) criteria for patient selection (including patient and disease characteristics, imaging criteria, and type of biopsies); (2) the nature and timing of investigations and assessments during follow-up (such as repeat imaging and repeat biopsies); (3) criteria and thresholds for reclassification; and (4) the type of outcome measures that should be prioritised.

To address these objectives, we will utilise transparent consensus methods involving a large, international cohort of stakeholders, broadly divided into two groups: (1) health care professionals (HCPs) consisting of urologists, clinical or radiation oncologists, medical oncologists, radiologists, pathologists, primary care physicians, and nurse specialists; and (2) patients. The research will be divided into three distinct but inter-related phases, and is expected to last for 12 mo.

Phase 1 is a systematic review conducted according to PRISMA guidelines [4]. The aim is to describe, explore, and assess clinical heterogeneity in DAT studies to inform the statements for the consensus processes. The review protocol has been published [5]. In brief, all prospective single-arm case series of DAT (including active surveillance and active monitoring but excluding watchful waiting) and all prospective comparative studies involving DAT will be included. The review will summarise eligibility and selection criteria, characteristics of monitoring and follow-up (including the type, frequency, and timing of repeat imaging and repeat biopsies), reclassification definitions and thresholds, and primary outcomes measured in studies. English language articles published after 1990 will be included.

Summary-of-findings tables including details of the pre-specified domains and subdomains will be developed. From these tables, a list of statements organised according to the different domains and subdomains relating to all aspects of DAT will be generated.

Phase 2 will comprise of a two-round online Delphi survey involving a large, international cohort of key stakeholders (HCPs and patients). The consensus methods used have been described previously in consensus studies in prostate cancer [6,7]. HCPs involved with DAT identified through international specialist societies (Appendix A) will be invited to participate. Patients throughout Europe with localised prostate cancer and eligible for DAT will be recruited through patient advocacy organisations (Appendix A). Up to 150 HCPs and 50 patients will be invited to participate. Patients will be asked to complete the patient-relevant parts of the survey only (identification of the most important outcomes). Participants will be asked to vote according to their level of agreement on a nine-point scale, ranging from strongly disagree (1) to strongly agree (9) (ie, 1–3 disagree; 4–6 uncertain; 7–9 agree). There will also be an "Unable to answer" option. An online questionnaire will be developed for the Delphi process using the COMET Initiative DelphiManager tool [8]. Two iterative rounds will be conducted anonymously, with anonymised feedback provided to all participants at the end of each round showing the percentage scoring for each response option. In round 1, participants will have the opportunity to add further statements for incorporation into round 2. With an anticipated response rate of 80% for both stakeholder groups and an expected overall completion rate of 80%, the total number of participants involved is expected to be at least 128 (96 HCPs and 32 patients). The results for each stakeholder group will be analysed and presented separately in each round. After the final round, statements scored as "strongly agree" (score 7–9) by $\geq$70% of the participants and with minimal disagreement scored by the rest (defined as $<$15% of participants scoring "strongly disagree", ie, 1–3) will be considered to have reached the threshold for consensus agreement. Conversely, statements scored as "strongly disagree" (score 1–3) by $\geq$70% of participants and with minimal agreement scored by the rest (defined as $<$15% of participants scoring "strongly agree", ie, 7–9) will be considered to have reached the threshold for consensus disagreement. All other statements not falling in the above categories will be classified as equivocal. Statements reaching consensus (either agreement or disagreement) will be collated for review in phase 3, while equivocal statements will be brought forward for discussion and voting in phase 3.

Phase 3 is the final stage of the consensus process, involving a 1-d meeting attended by representatives of each stakeholder group and chaired by a nonvoting methodologist and a clinician moderator. We will use structured discussion and live voting sessions. Representatives from each stakeholder group and subgroup (ie, urologists, oncologists, radiologists, pathologists, and patients) will be purposively sampled from those completing all rounds of the Delphi survey to ensure proportional representation. The voting panel will consist of 25 voting participants (7 patients and 18 HCPs). Statements reaching consensus (either agreement or disagreement) in phase 2 will be reviewed by the panel. Consensus decisions from the Delphi survey cannot be overturned by the panel without sound reasoning (eg, misleading statements). Equivocal statements from phase 2 will be discussed and voted on by the panel. Scoring thresholds will be the same as in phase 2 (level of agreement on a nine-point scale: 1–3 disagree; 4–6 uncertain; 7–9 agree; and "Unable to answer"). Voting will be anonymous using Poll Everywhere [9], which participants can access during the meeting using personal computers and a shared IP address. Definitions of consensus will be the same as in phase 2. Results for all statements will be conveyed in real time, and final consensus statements will be prepared. A final list of consensus statements organised according to the DAT domains and subdomains will be issued.

The consensus statements are expected to be adopted by guideline developers and disseminated through clinical practice guidelines issued by the EAU Prostate Cancer Guidelines Panel and other organisations (Appendix A), and are intended to provide authoritative guidance to clinicians and researchers by standardising definitions, thresholds, and terminology; characteristics for patient selection, monitoring, reclassification, and changes in management; and outcome measures that should be prioritised in DAT programmes in clinical practice and research, at least until higher levels of evidence emerge from initiatives such as GAP3 [10].

Conflicts of interest: Thomas B.L. Lam is a company consultant for and has received company speaker honoraria from Pfizer, GSK, Astellas, and Ipsen. Malcolm D. Mason is a company consultant for Ellipses Pharma and Oncotherics. Philip Cornford is a company consultant for Astellas, Ipsen, and Ferring; receives company speaker honoraria from Astellas, Janssen, Ipsen, and Pfizer; participates in trials run by Ferring; and receives fellowships and travel grants from Astellas and Janssen. Erik Briers has received grant and research support from Ipsen, the European Association of Urology, and Bayer; is an ex officio board member for Europa UOMO; is an ethics committee and advisory group member for REQUITE; is a patient advisory board member for PAGMI; and is a member of SCA and EMA PCWP. Stefano Fanti is a company consultant for Bayer and ANMI; has received speaker honoraria from Bayer, Genzyme, ANMI, and GE Healthcare; and participates in trials run by Amgen, Bayer, BMS, Genzyme, Janssen, Merck, and Novartis. Maria De Santis is a company consultant for Amgen, Astellas, AstraZeneca, Bayer, Bristol-Myers Squibb, Celgene, Dendreon, Eisai Inc, ESSA, Ferring, GSK, Incyte, IPSEN, Janssen Cilag, Merck, MSD, Novartis, Pfizer, Piere Fabre Oncologie, Roche, Sanofi Aventis, SeaGen, Shionogi, Synthon, Takeda, Teva, OncoGenex, and Sandoz; receives speaker honoraria from Amgen, Astellas, AstraZeneca, Bayer, Bristol-Myers Squibb, Ferring, GSK, IPSEN, Janssen Cilag, Merck, MSD, Novartis, Pfizer, Pierre Fabre Oncologie, Roche, Sanofi Aventis, Synthon, and Takeda; participates in trials run by the Technical University Munich, Amgen, Astellas, AstraZeneca, Bayer, Bristol-Myers Squibb, Celgene, Dendreon, Eisai Inc, Ferring, GSK, IPSEN, Incyte, Janssen Cilag, Merck, MSD, Novartis, Pfizer, Pierre Fabre Oncologie, Roche, Sanofi Aventis, and SOTIO; and as a member of the EORTC GU group participates in various trials. She has received research grants from Pierre Fabre Oncologie, and travel grants from Amgen, Astellas, AstraZeneca, Bayer, Bristol-Myers Squibb, Celgene, Dendreaon,

Ferring, GSK, IPSEN, Incyte, Janssen Cilag, Merck, MSD, Novartis, Pfizer, Pierre Fabre Oncologie, Roche, Sanofi Aventis, SeaGen, Shionogi, Synthon, Takeda, and Teva/OncoGenex. Silke Gillessen is a company consultant for AAA International, Astellas Pharma, Bayer, Bristol-Myers Squibb, Clovis, CureVac, Ferring, Innocrin Pharmaceuticals, Janssen Cilag, MaxIVAX SA, Orion, Roche, Sanofi Aventis Group, Nectar, and ProteoMediX; has received speaker honoraria from Janssen and Novartis; and participates in multiple trials run by different companies. Ann M. Henry is a company consultant for Nucletron-Elektra; participates in trials run by Cancer Research UK and the National Institute of Health Research (UK); ahs received travel grants from the Medical Research Council, the National Institute of Health Research (UK), and Cancer Research UK; and has received research grants from Cancer Research UK and the Sir John Fisher Foundation. Henk G. van der Poel is a company consultant for Intuitive Surgical; has participated in trials for Astellas and Steba Biotech; and has received grant and research support from Astellas. Thomas Wiegel is an advisory board member for IPSEN; receives company speaker honoraria from IPSEN and Hexal; is a member of the Janssen Steering Committee; and has participated in the ATLAS/AUO trial. Olivier Rouvière has received company speaker honoraria from EDAP-TMS; participates in trials run by ESAO-TMS and Vermon; and has received research and travel grants from Philips. Derya Tilki is a company consultant for Steba Biotech and MDx Health; has received speaker honoraria from Mundipharma, Astellas, and Ribosepharm; participates in trials run by MDx Health; has received travel and research grants from Janssen; and is a member of the PIONEER consortium. Nicolas Mottet is a company consultant for Janssen, GE, BMS, Sanofi and Astellas; has received speaker honoraria from Astellas, Pierre Fabre, Steba, Janssen and Ferring; and has received fellowships and travel grants from Astellas, IPSEN, Sanofi, Janssen and Roche. The remaining authors have nothing to disclose.

Appendix A. Collaborator list

The official collaborators include the following organisations and patient advocacy groups:

European Association of Urology (EAU)
European Association of Urology Nurses (EAUN)
EAU PIONEER
European Urology Editorial Board
American Urological Association (AUA)
Canadian Urological Association (CUA)
European Society for Radiotherapy and Oncology (ESTRO)
International Society of Urological Pathology (ISUP)
Urological Society of Australia and New Zealand (USANZ)
European Society of Urogenital Radiology (ESUR)
EAU Section of Oncological Urology (ESOU)
Urological Association of Asia (UAA)
American Society for Radiation Oncology (ASTRO)
American Society of Clinical Oncology (ASCO)
European Forum for Primary Care (EFPC)
EAU Research Foundation (EAU RF)
UCAN UK
Tackle Prostate Cancer UK
Europa UOMO
Movember Foundation

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Prevalence of and Predictive Factors for Burnout Among French Urologists in Training

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The burnout rate among young doctors currently seems to be increasing [1]. It is essential to be able to diagnose and prevent this condition to better take care of young caregivers. Burnout is defined as a "feeling of intense exhaustion, loss of control and inability to achieve concrete results at work" according to the World Health Organisation. The assessment questionnaire used most often is the Maslach Burnout Inventory (MBI), which covers (1) emotional exhaustion, (2) depersonalisation, and (3) personal accomplishment [2]. The aim of our study was to assess the prevalence of burnout among young urologists in training in 2018 and to identify its prognostic factors.

In 2018, the MBI self-administered assessment questionnaire was sent to members of the French Association of Urologists in Training (Association Française des Urologues en Formation). To evaluate the degree of burnout, the three components were analysed separately. Global burnout was defined as a high occupational exhaustion score combined with a high depersonalisation score and/or low personal accomplishment score. Multivariate analysis was performed to identify factors predictive of burnout.

Among the 501 members of the association, 48% (n = 239) replied to the questionnaire. One-quarter (n = 59) of them suffered from global burnout, while 21 (9%) had severe impairment in relation to the three components, 91% had at least moderate impairment for one of the components, and only 22 (9%) had no burnout symptoms at all.

Emotional exhaustion was reported by 55% of responders and three protective factors were identified: having a pastime (odds ratio [OR] 0.06), a feeling of being well trained (OR 0.004), and male gender (OR 0.02; Table 1). Some 75% of respondents suffered from depersonalisation, for which a feeling of being well trained was the only protective factor (OR 0.03). Personal accomplishment was low for 30% of the responders, and three protective factors were identified: a regular pastime (OR 4.84), sexual intercourse (OR 2.22), and a feeling of being well trained (OR 9.16). A feeling of being well trained was the only protective factor for all the burnout components (Table 1).

Table 1 – Multivariate analysis according to the three components of burnout

	OR (95% CI)	p value
Emotional exhaustion		
Sex (male)	0.02419 (0.001251–0.4678)	0.015
Nightshift work	2.55 (0.4989–13.04)	0.26
Regular pastime	0.06876 (0.009453–0.5001)	0.0087
Sexual intercourse	0.6029 (0.2728–1.332)	0.21
Alcohol consumption	0.2148 (0.0132–3.496)	0.28
Illicit drug consumption	25.5 (2.036–319.4)	0.013
Feeling of being well trained	0.0044 (0.00056–0.034)	<0.0001
Depersonalisation		
Sex (male)	3.547 (0.5701–22.07)	0.17
Nightshift work	0.7817 (0.2856–2.139)	0.63
Regular pastime	0.7213 (0.212–2.454)	0.6015
Sexual intercourse	0.7539 (0.4622–1.23)	0.26
Alcohol consumption	6.251 (1.118–34.96)	0.038
Illicit drug consumption	2.423 (0.5092–11.53)	0.27
Feeling of being well trained	0.032 (0.009–0.1139)	<0.0001
Personal accomplishment		
Sex (male)	2.05 (0.2026–20.74)	0.55
Nightshift work	0.4547 (0.1271–1.627)	0.23
Regular pastime	4.84 (1.027–22.81)	0.048
Sexual intercourse	2.224 (1.197–4.133)	0.012
Alcohol consumption	8.388 (0.9486–74.17)	0.057
Illicit drug consumption	0.4951 (0.06871–3.567)	0.49
Feeling of being well trained	9.166 (1.841–45.63)	0.0073

OR = odds ratio; CI = confidence interval.