RV: Remisión dictamen pericial - EXPEDIENTE: 50001333300320170001600

Juzgado 03 Administrativo - Meta - Villavicencio
<j03admvcio@cendoj.ramajudicial.gov.co>

Lun 26/02/2024 7:37 AM

Para:Juzgado 03 Administrativo - Meta - Villavicencio <jadmin03vvc@notificacionesrj.gov.co>

De: Peritajes de Vicedecanatura de Investigación y Extensión De La Facultad De Medicina <peritajes_fmbog@unal.edu.co>
Enviado: viernes, 23 de febrero de 2024 17:22
Para: Giancarlo Buitrago <gbuitragog@unal.edu.co>; Decanatura Facultad De Medicina <decfacm_bog@unal.edu.co>; Vicedecanatura de Investigación y Extensión Facultad de Medicina <viceinv_fmbog@unal.edu.co>; Juzgado 03 Administrativo - Meta - Villavicencio <j03admvcio@cendoj.ramajudicial.gov.co>; abgalisguerrero@hotmail.com <abgalisguerrero@hotmail.com>
Asunto: Fwd: Remisión dictamen pericial - EXPEDIENTE: 50001333300320170001600

Buenas tardes

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EXPEDIENTE: 50001333300320170001600

Asunto: Remisión dictamen pericial

Por medio del presente oficio se da repuesta al caso de la referencia.

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MRI y biopsia de prostata Cochrane 2020.pdf

MRI y biopsia sistematica Una revisión sistematica Go…

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Cordialmente:

Anabel Angarita Pinto
Asesora- Oficina Jurídica
Facultad de Medicina
UNIVERSIDAD NACIONAL DE COLOMBIA

Bogotá D.C.20 de febrero de 2024

B.F.M.1.002-112-24

Señor(as)(es)

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DEMANDANTE: ERNESTO ROMÁN
DEMANDADO: NACIÓN-MINISTERIO DE EDUCACIÓN NACIONAL SERVIMEDICOS FIDUPREVISORA SAS S.A. COOPERATIVA DE URÓLOGOS DEL META Y LA ORINOQUIA CUMO (LLAMADO EN GARANTÍA POR SERVIMEDICOS). ASEGURADORA CONFIANZA S.A. (LLAMADA EN GARANTÍA POR CUMO Y POR EMCOSALD) Y OTROS
EXPEDIENTE: 50001333300320170001600

Asunto: Remisión de dictamen pericial en el proceso de la referencia.

ANTECEDENTES

En respuesta a la petición esgrimida por usted, mediante la cual solicita lo siguiente:

> *"De conformidad con la remisión a su dependencia hace un año aproximadamente (febrero de 2023) de manera atenta y respetuosa solicito de manera urgente se haga entrega del mentado dictamen, toda vez que, con fecha de ayer 05 de febrero de 2024, el juzgado a través de requerimiento concedió 15 días para la entrega o de lo contrario declarar desistimiento tácito por falta de tan importante prueba"*

Como Vicedecanatura de Investigación y Extensión; otorgamos respuesta con base en los siguientes hechos:

El día 02 de octubre de 2023, fue recibida la reiteración de su solicitud de realización de dictamen pericial, por medio de la dirección de correo electrónico peritajes_fmbog@unal.edu.co. La cual fue tramitada al interior de nuestra Alma Matér, atendiendo los presupuestos del Acuerdo 01 de 2023 expedido por el Consejo de Facultad de Medicina. Sobre la petición mencionada como Vicedecanatura advertimos lo siguiente:

> *"De igual modo, nos permitimos manifestar que, debido a las múltiples funciones de docencia asistenciales que prestan los profesores de la Facultad de Medicina de la Universidad Nacional en los diferentes hospitales del país, junto con las diferentes labores académicas, administrativas y de investigación a cargo de los mismos, sumado al cierre del*

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> *campus por casi dos años debido a la situación de la pandemia, se han ocasionado retrasos para adelantar la gestión de los múltiples requerimientos periciales a nivel nacional, y del encomendado por su Honorable Despacho."*

Consecuentemente luego del análisis realizado por el Departamento de Cirugía se comunicó a las partes interesadas y a su honorable despacho el correspondiente valor establecido para la rendición de la pericia, según la complejidad del caso, junto con la solicitud de los documentos necesarios para realizar el trámite financiero al interior de la Universidad Nacional . Lo anterior se realizado por medio del oficio B.F.M. 1.002.514.23, enviado el 26 de octubre del año 2023.

Sobre lo anterior, se recibió respuesta el 07 de diciembre del 2023, en donde nos anexan los soportes de pago solicitados, razón por la cual se remitió el caso a el docente RODOLFO VARELA RAMIREZ especialista en Urología del Departamento de Cirugía de la Facultad de Medicina.

De esta forma se le indica al Doctor Varela, que en el término de 20 días hábiles, contados a partir del 15 de enero de 2024 emita el concepto técnico requerido, atendiendo lo establecido en la Resolución 1243 de 2023 "*Por la cual se ordena la suspensión de términos de las actuaciones administrativas para el Nivel Nacional, Sede Bogotá,(...) de la Universidad Nacional de Colombia, por el periodo comprendido entre el 14 de diciembre de 2023 y el 10 de enero de 2024, inclusive*" emitida por la Rectoria de La universidad Nacional de Colombia, en donde se suspenden los términos de las actuaciones administrativas, en razón del periodo de vacaciones colectivas de los docentes y administrativos de la institución.

CONSIDERACIONES

En cuanto a la Autonomía Universitaria:

La Universidad Nacional es un ente autónomo universitario del orden nacional, vinculado al Ministerio de Educación Nacional, con un régimen especial, cuyo objeto es la educación superior y la investigación (Decreto 1210 de 1993, artículo 1). A la luz de lo definido en la Constitución Política de Colombia, la Ley y los Estatutos Internos, el concepto de Autonomía Universitaria desarrollado en el artículo 69 de la Constitución Política, establece lo siguiente:

> *"Se garantiza la autonomía universitaria. Las universidades podrán darse sus directivas y regirse por sus propios estatutos, de acuerdo con la ley. La ley establecerá un régimen especial para las universidades del Estado (...)".*

El concepto de Autonomía Universitaria se desarrolla además, en el Artículo 28 de la Ley 30 de 1992 "*Por la cual se organiza el servicio público de la Educación Superior*", que recoge el concepto y lo define de la siguiente manera:

> *"La autonomía universitaria consagrada en la Constitución Política de Colombia y de conformidad con la presente Ley, reconoce a las universidades el derecho a darse y modificar sus estatutos, designar sus autoridades académicas y administrativas, crear, organizar y desarrollar sus programas académicos, definir y organizar sus labores*

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formativas, académicas, docentes, científicas y culturales, otorgar los títulos correspondientes, seleccionar a sus profesores, admitir a sus alumnos y adoptar sus correspondientes regímenes y establecer, arbitrar y aplicar sus recursos para el cumplimiento de su misión social y de su función institucional".

En el mismo sentido, el artículo 3° del Decreto 1210 de 1993, "*Por el cual se reestructura el régimen orgánico especial de la Universidad Nacional de Colombia*", dispone sobre el régimen de autonomía de la Universidad Nacional de Colombia lo siguiente:

"***Artículo 3. Régimen de autonomía.*** *En razón de su misión y de su régimen especial, la Universidad Nacional de Colombia es una persona jurídica autónoma, con gobierno, patrimonio y rentas propias y con capacidad para organizarse, gobernarse, designar sus propias autoridades y para dictar normas y reglamentos, conforme al presente decreto".*

En cuanto a las disposiciones normativas internas

Expuesto lo anterior, y atendiendo los presupuestos de autonomía universitaria, cabe precisar que el Consejo de la Facultad de Medicina en uso de sus atribuciones legales y estatutarias por medio del Acuerdo 01 de enero de 2023, en donde se establecieron las directrices académicas y administrativas para la gestión de los requerimientos periciales, junto con el Memorando N°1256 de 2003 expedido por la Oficina Jurídica de Sede Bogotá ; precisan que, el proceso interno que se debe surtir para el trámite de los requerimientos periciales es el siguiente:

"

1. *La recepción y el registro del peritaje se llevará a cabo por la Vicedecanatura de Investigación y Extensión de la Facultad. Será en esta dependencia donde se determinará a que Departamento se debe enviar en reparto, teniendo en cuenta la(s) especialidad(es) que solicite el Despacho de Conocimiento (juzgado, fiscalía, tribunal, corte, autoridad administrativa, entre otras) o las que técnicamente se considere deben intervenir en la resolución del asunto*
2. *Una vez determinada la(s) especialidad(es) que interviene(n) desde la Vicedecanatura se remitirá con memorando al director del Departamento, quien previa revisión del asunto de que se trata, decidirá la(s) especialidad(es) que deben conocer, decidirá el asunto y designará al (los) docente(s) que estarán a cargo de emitir el Concepto. A partir de este momento se podrán presentar los siguientes casos:*

   A. *Si a juicio del Director del Departamento el asunto no cumple con los criterios definidos en el literal c) del artículo 4 del Acuerdo 01 de 2023 del Consejo de Facultad de Medicina; lo devolverá a la Vicedecanatura, con la justificación de su decisión, mediante comunicado, esta última se encargará de dar respuesta al solicitante del dictamen informando tal situación.*
   B. Si el expediente no contiene el cuestionario y la historia clínica la Vicedecanatura inmediatamente devolverá con oficio al juzgado de conocimiento o parte interesada para que aporte la documentación faltante.
   C. Si el expediente viene completo (cuestionario e historia clínica legible y completa con los soportes que se consideren necesarios), el director del departamento recibirá el expediente, lo revisará y determinará si el asunto cumple con los requisitos contemplados a continuación:
      I. Si la solicitud versa "sobre materias propias de la actividad" académica.
      II. Si cuenta con los expertos en el tema o,
      III. Si aunque cuente con los expertos, las labores ya asignadas o la carga académica no permiten abordar con los tiempos y la responsabilidad requeridos para rendir la experticia.

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IV. Si la colaboración solicitada se enmarca en la función social, en los fines que está llamada a cumplir y existe un interés colectivo que incumba al Estado.

3. ***Una vez valoradas las condiciones anteriores, el Director del Departamento decidirá si acepta o no la solicitud*** *y definirá a qué docente de su Departamento lo designa, situación que deberá comunicar de manera inmediata a la Vicedecanatura mediante oficio, informando además la tasación de la prueba y los datos de la cuenta institucional para realizar la consignación. La Vicedecanatura se encargará de allegar la respuesta al solicitante."*

En este orden de ideas, es dable manifestar también que el servicio de peritajes que se brinda desde los servicios de extensión de la Universidad(numeral 4, literal b articulo5, Acuerdo 036 de 2009 del Consejo Superior Universitario) no es absoluto, pues el mismo se enmarca en la medida de los recursos disponibles en la institución, y dentro los limites contemplados por el fin misional de la Universidad de prestar con autonomía, en los órdenes científico, tecnológico, cultural y artístico; apoyo y asesoría al Estado.

Por consiguiente, para tomar la decisión de rendir el dictamen pericial o concepto solicitado por parte de la autoridad judicial o administrativa interesada ante esta Universidad; la Facultad de Medicina debe entrar a considerar si se llena el juicio de razonabilidad, según los criterios anteriormente expuestos.

Sobre el pago de honorarios y los hechos cumplidos:

Una vez verificado que el procedimiento descrito para solicitar un peritaje se cumpla en debida forma y se tengan la totalidad de documentos señalados para emitir un concepto pericial. Se hará la gestión administrativa para efectuar el pago de los honorarios del perito encargado según lo regulado por el Acuerdo 036 de 2009 ***"Por el cual se reglamenta la Extensión en la Universidad Nacional de Colombia",*** donde establece la figura de "Servicios Académicos Remunerados" (en adelante SAR) como el acto administrativo por medio del cual se tramita la retribución por los conceptos técnicos emitidos por nuestros docentes en desarrollo de la función de extensión de nuestra alma mater.

Por lo tanto, se hace necesario que previamente a la emisión el dictamen pericial, se identifiquen los dineros consignados por el interesado, para de esta forma realizar la solicitud del SAR a la Unidad Administrativa de la Facultad de Medicina, cumpliendo con el lleno de los requisitos legales establecidos para emitir el pago correspondiente. Así remunerar la dedicación, el tiempo y los conocimientos; invertidos en la emisión del concepto técnico y científico expedido por el docente asignado.

Por lo tanto para poder identificar el dinero ingresado, es necesario que el solicitante y depositante brinde los siguientes documentos:

1. *Formato diligenciado de creación de terceros.*
2. *Formato diligenciado de autorización de tratamiento de datos.*
3. *Comprobante de consignación bancaria.*
4. *Registro Único Tributario (RUT).*
5. *Copia de la cédula del representante legal.*
6. *Dirección, teléfono y correo electrónico de contacto*

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En conexidad con lo mencionado, Los documentos enunciados anteriormente son solicitados en cada respuesta de tasación, lo cual para el caso en concreto se mencionó en el oficio expedido por esta dependencia con consecutivo "B.F.M. 1.002.514.23" del 26 de octubre de 2023.

Adicional a lo anterior, el acuerdo 153 de 2014 "***Por el cual se adopta el régimen financiero de la Universidad Nacional de Colombia".*** Establece la prohibición de tramitar hechos cumplidos de la siguiente manera:

> **"ARTÍCULO 47. *Hechos cumplidos.*** *Prohíbase tramitar actos administrativos u obligaciones que afecten el presupuesto de gastos cuando no reúnan los requisitos legales o se configuren como hechos cumplidos.*
>
> *El ordenador del gasto responderá disciplinaria, fiscal y penalmente por incumplir lo establecido en el presente artículo."*

Atendiendo la norma citada, podemos concluir que es un riesgo jurídico emitir dictámenes periciales sin cumplir con el lleno de los requisitos legales, ya que el omitir alguno de los pasos para constituir el SAR que conlleva al pago de los honorarios y exigirle al Docente que emita el dictamen solicitado, conllevaría a ejecutar una obligación que afecta el presupuesto de la Universidad sin que exista un acto administrativo que lo respalde, tal y como lo es la figura del SAR cuando es solicitado en debida forma.

Por lo tanto solo se le indico al docente que debía rendir el dictamen cuando se obtuvo la totalidad de la documentación como se evidencia en el apartado de antecedentes del presente oficio.

RESPUESTA:

Teniendo en cuenta las consideraciones esbozadas, como Vicedecanatura de Investigación y Extensión; en aras de apoyar el esclarecimiento de los elementos científicos para garantizar la protección y efectividad de los derechos fundamentales de las partes interesadas, nos permitimos allegar respuesta frente al requerimiento, anexando el dictamen pericial elaborado por el Doctor ***RODOLFO VARELA RAMIREZ***, especialista en Urología perteneciente al Departamento de Cirugía de la Facultad de Medicina de nuestra preciada institución.

De igual forma nos permitimos adicionar las declaraciones e informaciones exigidas por el artículo 226 del Código General del Proceso, a saber:

1. **Identidad del perito encargado:**
   Rodolfo Varela Ramírez, Identificado con número de cedula 79.244.111 de Suba (Cundinamarca).
2. **Información de contacto:**
   - **Dirección**: Cra 19 A No 82 – 85 Cons 704 edificio CMC
   - **Teléfono** 3115321154
3. **Profesión:** Médico cirujano especializado en Urología Oncológica desde el año 2002
4. **Casos en los que fue designado como perito**:

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Participo en enero 2020 , que fue el proceso con código interno VIEFM-003-06-03-2019, del Juzgado Sexto Administrativo Oral del Circuito de Villavicencio relacionado con el señor BRAYAN STIVEN CARDOZO OSORIO. EL caso estuvo relacionado con la extracción de un testículo, mediante cirugía, por haber presentado una torsión testicular.

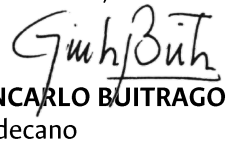
5. **Causales articulo 50 C.G.P:** No se encuentra incurso en ninguna de las causales de exclusión de la lista.
6. Los exámenes, métodos, experimentos e investigaciones efectuados son los usados en el ejercicio normal de su profesión.
7. **La bibliografía usada para la emisión del dictamen es:**

Goldberg, H. et al. (2020) Comparison of Magnetic Resonance Imaging and Transrectal Ultrasound Informed Prostate Biopsy for Prostate Cancer Diagnosis in Biopsy Na€ıve Men: A Systematic Review and Meta-Analysis. THE JOURNAL OF UROLOGY. 203.1085-1093

Drost F-JH, et al. (2019) Prostate Magnetic Resonance Imaging, with or Without Magnetic Resonance Imaging-targeted Biopsy, and Systematic Biopsy for Detecting Prostate Cancer: A Cochrane Systematic Review and Meta-analysis. Eur Urol.

Agradecemos su amable atención quedando atentos a las inquietudes y observaciones que sean del caso.

Cordialmente,



GIANCARLO BUITRAGO GUTIÉRREZ
Vicedecano
Vicedecanatura de Investigación y Extensión
Facultad de Medicina

Anexos:

- **Goldberg, H. et al. (2020) Comparison of Magnetic Resonance Imaging and Transrectal Ultrasound Informed Prostate Biopsy for Prostate Cancer Diagnosis in Biopsy Na€ıve Men: A Systematic Review and Meta-Analysis. THE JOURNAL OF UROLOGY. 203.1085-1093**
- **Drost F-JH, et al. (2019) Prostate Magnetic Resonance Imaging, with or Without Magnetic Resonance Imaging-targeted Biopsy, and Systematic Biopsy for Detecting Prostate Cancer: A Cochrane Systematic Review and Meta-analysis. Eur Urol.**
- Diploma Médico Cirujano Universidad Nacional de Colombia
- Diploma especialidad en Urología Universidad Nacional de Colombia
- Diploma especialidad en Urología Oncológica Pontificia Universidad Javeriana
- Diploma especialista en Urología Oncológica Pontificia Universidad Javeriana
- Acta de grado Pontificia Universidad Javeriana
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European Association of Urology

Review – Prostate Cancer

Prostate Magnetic Resonance Imaging, with or Without Magnetic Resonance Imaging-targeted Biopsy, and Systematic Biopsy for Detecting Prostate Cancer: A Cochrane Systematic Review and Meta-analysis

Frank-Jan H. Drost [a,b], *Daniel Osses* [a,b], *Daan Nieboer* [b,c], *Chris H. Bangma* [b], *Ewout W. Steyerberg* [c], *Monique J. Roobol* [b], *Ivo G. Schoots* [a,*]

[a] *Department of Radiology & Nuclear Medicine, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands;* [b] *Department of Urology, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands;* [c] *Department of Public Health, Erasmus University Medical Center Rotterdam, Rotterdam, The Netherlands*

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Abstract

Context: Magnetic resonance imaging (MRI), with or without MRI-targeted biopsy (MRI pathway), is an alternative test to systematic transrectal ultrasonography-guided biopsy in men suspected of having prostate cancer. At present, evidence on which test to use is insufficient to inform detailed evidence-based decision making.
Objective: To determine the diagnostic accuracy of the index tests MRI only, MRI-targeted biopsy, MRI pathway, and systematic biopsy, as compared with template-guided biopsy (reference standard), in detecting clinically significant prostate cancer, defined as International Society of Urological Pathology grade 2 or higher, in biopsy-naive men or those with a prior-negative biopsy (or mix of both).
Evidence acquisition: We systematically searched the literature and considered for inclusion any cross-sectional study if it investigated (1) one or more index tests verified by the reference standard, and (2) paired testing of the MRI pathway with systematic biopsy. Quality and certainty of evidence were assessed by the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) and Grading of Recommendations Assessment, Development and Evaluation, respectively.
Evidence synthesis: *Accuracy analyses:* Using a baseline cancer prevalence of 30%, MRI pathway (sensitivity 0.72 [95% confidence interval {CI}: 0.60–0.82]; specificity 0.96 [0.94–0.98]; eight studies) may result in 216 (180–246) true positives, 28 (14–42) false positives, 672 (658–686) true negatives, and 84 (54–120) false negatives per 1000 men. Systematic biopsy (sensitivity 0.63 [0.19–0.93]; specificity 1.00 [0.91–1.00];

☆ This article is based on a Cochrane Review published. Drost FH, Osses DF, Nieboer D, Steyerberg EW, Bangma CH, Roobol MJ, et al. Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer. The Cochrane Database of Systematic Reviews 2019;4: Cd012663. https://www.cochranelibrary.com/cdsr/doi/10.1002/14651858.CD012663.pub2/full. Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and the Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

* Corresponding author. Department of Radiology & Nuclear Medicine (Room Ns-549), Erasmus University Medical Centre, P.O. Box 2040, Rotterdam 3000 CA, The Netherlands; Dr. Molenwaterplein 40, 3015GD Rotterdam, The Netherlands. Tel. +31 10 7042006.
E-mail address: i.schoots@erasmusmc.nl (I.G. Schoots).

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four studies) may result in 189 (57–279) true positives, 0 (0–63) false positives, 700 (637–700) true negatives, and 111 (21–243) false negatives per 1000 men. *Agreement analyses:* With a direct comparison of the MRI pathway with systematic biopsy concerning significant disease, we found pooled detection ratios of 1.05 (95% CI: 0.95–1.16; 20 studies) in biopsy-naive men and 1.44 (1.19–1.75; 10 studies) in men with a prior-negative biopsy. Concerning insignificant disease, we found detection ratios of 0.63 (95% CI: 0.54–0.74), and 0.62 (95% CI: 0.44–0.88), respectively.
Conclusions: MRI pathway had the most favourable outcome in significant and insignificant prostate cancer detection compared with systematic biopsy. The certainty in our findings was reduced by study limitations.
Patient summary: We reviewed recent advances in prostate biopsy by magnetic resonance imaging (MRI) guidance and targeting for prostate cancer detection in comparison with standard diagnosis by systematic biopsies. The findings of this Cochrane review suggest that MRI pathway is better than systematic biopsies in making a correct diagnosis of clinically important prostate cancer and reducing redundant biopsies and the detection of unimportant cancers substantially. However, MRI pathway still misses some men with important prostate cancer. Therefore, further research in this area is important.

1. Introduction

To reduce overdiagnosis and overtreatment of indolent prostate cancer, while improving the detection of clinically significant prostate cancer and reducing the number of biopsy procedures, we need more accurate diagnostic methods and better risk stratification [1]. In a recent international multicentre randomised controlled trial, magnetic resonance imaging (MRI) in combination with MRI-targeted biopsy (MRI pathway) detected an absolute 12% more clinically significant prostate cancer and 13% less indolent prostate cancer than systematic biopsy in biopsy-naive men, and achieved 28% reduction of biopsies, because men with negative MRI did not receive prostate biopsy [2]. These results indicate that prebiopsy MRI and MRI-targeted biopsy in the presence of an MRI-suspicious lesion would be superior to a systematic biopsy. If this is confirmed by other studies and longer follow-up of men who were not biopsied, it may initiate a change to guidelines.

Previous systematic reviews on diagnostic performances of the MRI pathway or prebiopsy MRI approach [3–11] have been based on study designs that did not accurately capture target conditions and index or reference test definitions, leading to a number of biases and inaccurate findings. Studies in these reviews included mainly men with positive MRI and disregarded men with negative MRI, inevitably leading to inaccurate true- and false-negative values of the MRI pathway. In addition, these reviews used systematic biopsy or radical whole-mount surgical specimens as reference standards, which inherently have a number of biases. Furthermore, the established definitions of clinically significant prostate cancer, based on histology from systematic biopsy and possibly additional nonhistological parameters, cannot be applied to results from the MRI pathway [12]. In this (copublished) Cochrane review and meta-analysis [13] we have largely overcome these limitations.

2. Evidence acquisition

For further detailed information on methods, we refer to the original Cochrane review [13].

2.1. Objectives

We aimed to determine the diagnostic accuracy of the index tests MRI only, MRI-targeted biopsy, MRI pathway (MRI with or without MRI-targeted biopsy), and systematic biopsy, as compared with template-guided biopsy as the reference standard, in detecting International Society of Urological Pathology (ISUP) grade 2 or higher (primary target condition), grade 3 or higher, and grade 1 prostate cancer (secondary target condition). Furthermore, we aimed to determine the agreement and disagreement, and the potential change in the number of biopsy procedures between the two index tests, MRI pathway, and systematic biopsy, for detecting the primary and secondary target conditions.

2.2. Inclusion criteria

2.2.1. Types of studies

We considered any cross-sectional study, if it investigated (Fig. 1) the following: (1) diagnostic test accuracy of one or more of the index tests (MRI, MRI pathway;including MRI-targeted biopsy], or systematic biopsy) verified by the reference standard (template-guided biopsy), with each index test and reference standard performed in the same men or compared as in a randomised trial of test accuracy; or (2) agreement evidence between the MRI pathway and systematic biopsy, with each test performed in the same men.

Studies involving MRI had to report on both MRI-positive and MRI-negative men. The primary target condition had to be reported on a per-participant basis for all studies (Fig. 2).

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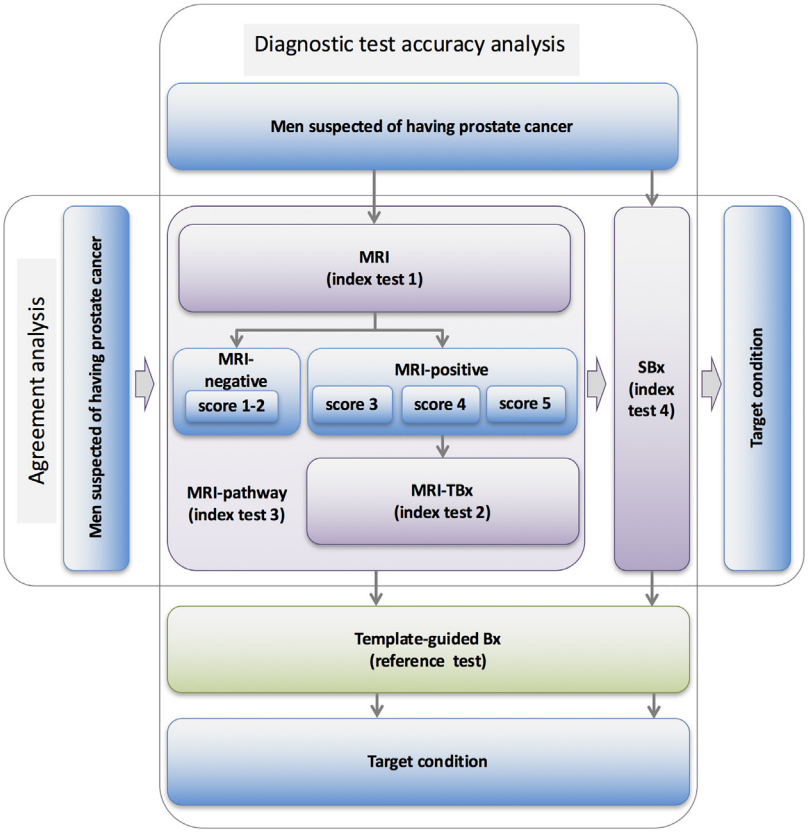

Fig. 1 – Clinical pathway flow diagram and study design.

2.2.2. *Study population*

The study population consisted of men with a clinical suspicion of prostate cancer (based on prostate-specific antigen or digital rectal examination outcome) in the biopsy-naive or prior-negative biopsy setting (or a mix of both).

2.2.3. *Index tests*

MRI (index test 1) comprised at least T2-weighted imaging and one functional imaging technique (diffusion-weighted imaging or dynamic contrast-enhanced imaging), reported according to any MRI-scoring system, mainly based on a five-point scale (Likert or Prostate Imaging Reporting and Data System) [14,15]. We defined the default threshold for MRI-positivity as 3/5 or more where possible. MRI-targeted biopsy (index test 2) included only MRI-positive men. The MRI pathway (index test 3) included MRI-positive men (in whom MRI-targeted biopsy was performed) and MRI-negative men (in whom no MRI-targeted biopsy was performed). Systematic biopsy (index test 4) included either systematic transrectal or transperineal ultrasound-guided biopsies. We defined the MRI pathway and systematic biopsy as positive when histopathology of one of the target conditions in the biopsy cores was confirmed.

2.2.4. *Reference standard*

Template-guided biopsy, including transperineal template-guided mapping biopsy and the template-guided saturation biopsy, served as the reference standard [16,17]. We defined a positive template-guided biopsy as histopathological confirmation of one of the target conditions within the biopsy cores.

2.2.5. *Target conditions*

We solely focused on target conditions based on histological definitions according to the ISUP grading, as was recommended by International Working Group on Standards of Reporting for MRI-targeted biopsy studies (START) in order to overcome differences between definitions and biopsy methods [18]. The primary target condition was clinically significant prostate cancer, defined as ISUP grade 2 or higher based on histopathology findings, and scored as Gleason score (GS) 3 + 4 or higher [19]. Secondary target conditions were grade 1 (GS 3 + 3, indolent prostate cancer) and grade 3 or higher (GS 4 + 3 or higher).

2.3. *Search strategy*

We performed a comprehensive search with no restriction on language or status of publication (including on-going studies), in electronic databases (CENTRAL, MEDLINE, Embase, and nine other databases), and updated to 31 July 2018 (Supplementary material, Appendix 1).

2.4. *Data collection and analysis*

2.4.1. *Selection of studies, data extraction, and management*

Two reviewers independently screened all abstracts and full-text articles for eligibility, and extracted data using a

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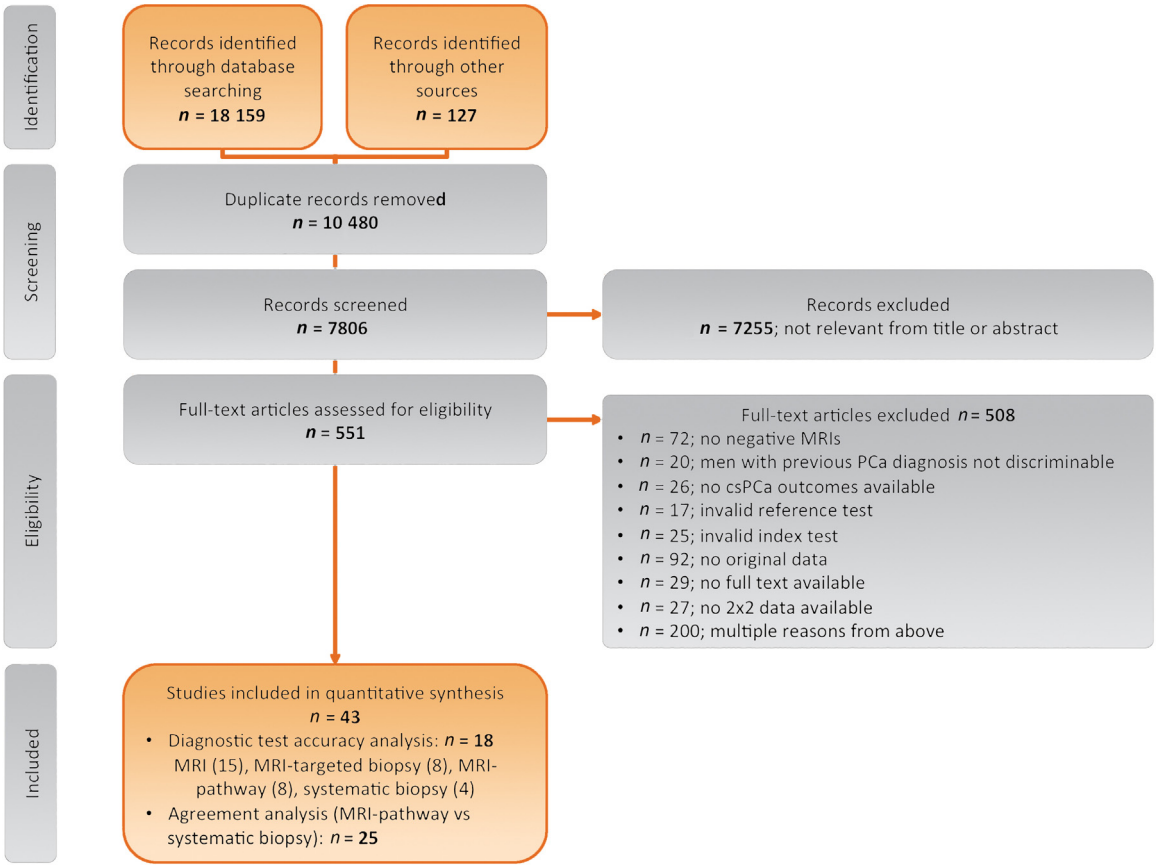

Fig. 2 – Study flowchart. csPCa = clinically significant prostate cancer; MRI = magnetic resonance imaging; MRI pathway = magnetic resonance imaging with subsequent magnetic resonance imaging-targeted biopsy; PCa = prostate cancer.

predefined data-extraction form. We constructed two-by-two tables for cross-classification of the index tests versus reference standard for test accuracy data and the MRI pathway versus systematic biopsy for agreement data, based on per-participant data (Supplementary material, Appendix 2).

2.4.2. *Assessment of methodological quality*

Two reviewers independently assessed all included studies for methodological quality using the Quality Assessment of Diagnostic Accuracy Studies (QUADAS-2) tool [20], tailored to this Cochrane review [13].

2.4.3. *Statistical analysis and data synthesis*

For the test accuracy analysis, we calculated pooled estimates of sensitivity and specificity using the bivariate model [21]. For the agreement analysis (MRI pathway vs systematic biopsy), we calculated the proportion of detected cases (total number of cancers) as the number of concordant positive results plus the number of discordant positive results of both tests (Supplementary material, Appendix 2). We calculated the detection rate of either test as the number of positive results of that test divided by the total number of cancers detected. We synthesised pooled estimates of detection ratios (detection rate of MRI pathway/detection rate of systematic biopsy) by performing random-effect meta-analyses. We used mixed models (multinomial logistic regression models with a random intercept for study effects) to calculate pooled proportions of concordance and discordance between tests (Cochrane review [13]). Added value (discordance) data were constructed such that we assessed the tests as add-on tests (ie, considering reclassification by each test; Supplementary material, Appendix 3). We used Statistical Analysis Software (SAS), version 9.3, for Windows and R version 3.5.0 to perform all statistical analyses.

2.4.4. *Investigations of heterogeneity and sensitivity analyses*

To explore sources of heterogeneity, we assessed covariates by adding them one by one in our bivariate model: population setting, MRI magnet strength, MRI sequences, MRI-positivity threshold, endorectal coil, MRI-targeted biopsy method, biopsy approach, and radiologists' experience. We tested the same covariates using meta-regression techniques for the detection ratio in the agreement analysis.

2.4.5. *Certainty of evidence*

We rated the certainty of evidence on a per-outcome basis according to Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidance for studies of diagnostic accuracy [22]. For the four main

comparisons, we rated the certainty of evidence using GRADEpro GDT.

3. Evidence synthesis

For further detailed information on results, we refer to the original Cochrane review [13].

3.1. Results of the search

A total of 43 studies were eligible for inclusion in this review (Fig. 1) and provided data for multiple tests (Supplementary material, Appendix 4). Eighteen studies addressed the test accuracy analysis (index tests vs reference standard): 15 studies on MRI, eight studies on MRI, MRI-targeted biopsy, and MRI pathway in the same men and four studies on systematic biopsy (Table 1). These studies included 6871 men, of whom 5075 were biopsy naive, and 1796 had a history of at least one prior-negative biopsy. Twenty-five studies addressed the agreement analysis between MRI pathway and systematic biopsy in detecting prostate cancer with 6944 men, of whom 5353 were biopsy naive and 1591 had a history of at least one prior-negative biopsy (Table 1).

3.2. Methodological quality of included studies

As a result of QUADAS-2 assessment (Supplementary Fig. 2), we acknowledge overall concerns about the independence and applicability of tests in both test accuracy and agreement analyses, for which we performed sensitivity analyses to exclude studies with such quality concerns.

3.3. Findings

3.3.1. Test accuracy analysis (index tests verified by reference standard)

3.3.1.1. Detection of grade 2 or higher prostate cancer. MRI (pooled sensitivity of 0.91 [95% confidence interval {CI} 0.83–0.95], specificity of 0.37 [0.29–0.46]; 12 studies, 3091 men; Table 2) at a baseline prevalence of 30% (300/1000) may result in 273 (249–285) true positives, 441 (378–497) false positives, 259 (203–322) true negatives, and 27 (15–51) false negatives per 1000 men (Table 3). Hence, MRI did not identify 9% (27/300) of men with grade 2 or higher prostate cancer.

These accuracy and predictive metrics are also presented for the index tests MRI-targeted biopsy, MRI pathway, and systematic biopsy (Tables 2 and 3). MRI-targeted biopsy, MRI pathway, and systematic biopsy missed, respectively, 20% (60/300), 28% (84/300), and 37% (111/300) of men with grade 2 or higher prostate cancer at the prevalence of 30% (300/1000), identified by the reference standard. Implications of these results, taking into account each step in the MRI pathway (MRI with subsequent MRI-targeted biopsy in MRI-positive men only) and systematic biopsy, are shown in Fig. 3.

A comparison of MRI with MRI pathway showed a substantial decrease in sensitivity (from 0.91 to 0.72; Fig. 4) and an increase in specificity (from 0.37 to 0.96), which were both statistically significant ($p < 0.01$; Table 2). Comparing MRI pathway with systematic biopsy showed a substantial decrease in sensitivity (0.72 vs 0.63; $p = 0.06$; Table 2) and similar specificities (Fig. 4).

At a baseline prevalence of 30% grade 2 or higher prostate cancer, the negative predictive values for MRI, MRI-targeted biopsy, MRI pathway, and systematic biopsy are 91% (86–94%), 92 (88–94%), 89% (85–92%), and 86% (65–95%), respectively (Table 2). Consequently, in the MRI pathway, negative MRI falsely predicts the absence of grade 2 or higher prostate cancer in 9% of men, while a negative systematic biopsy falsely predicts the absence of grade 2 or higher prostate cancer in 14% of men.

3.3.1.2. Detection of grade 1 prostate cancer. The pooled sensitivity and specificity for detecting grade 1 prostate cancer of all index tests are shown in Table 2. Comparing the sensitivity of the MRI pathway and systematic biopsy, the MRI pathway potentially avoided the detection of 66% of men with grade 1 prostate cancer, whereas systematic biopsy potentially avoided 45% of men with grade 1 prostate cancer ($p = 0.52$).

3.3.1.3. Detection of grade 2 or higher prostate cancer at a higher MRI-positive threshold. In clinical practice, lesions with an MRI suspicion score of 3 (likelihood for clinically significant cancer is equivocal [23]) might or might not be targeted with biopsies. By increasing the threshold of MRI positivity from 3/5 to 4/5, the proportion of negative MRI increased from 30% (23–38%) to 59% (43–74%). The pooled sensitivity of MRI for detecting grade 2 or higher prostate cancer decreased from 0.89 (0.82–0.94) to 0.72 (0.52–0.86). The pooled specificity increased from 0.39 (0.32–0.47) to 0.78 (0.68–0.86). Consequently, with a threshold 4/5 for MRI positivity, negative MRI missed identifying 28% of men with grade 2 or higher prostate cancer.

3.3.2. Agreement analysis between MRI pathway and systematic biopsy

In this section, we focused on agreement and disagreement (concordance and discordance) in the number of target conditions identified by the MRI pathway and systematic biopsy.

3.3.2.1. Detection of grade 2 or higher prostate cancer. In a mixed population (of biopsy-naive and prior-negative biopsy men), the pooled detection ratio of grade 2 or higher prostate cancer was 1.12 (1.02–1.23; 25 studies, 6944 men), meaning that the MRI pathway increased the detection rate of grade 2 or higher prostate cancer by 12% compared with systematic biopsy.

For men in the biopsy-naive setting, cancer proportion (total prostate cancer detected by both tests) was 27.7% (23.7–32.6%; 20 studies, 5219 men) versus prior-negative biopsy setting of 22.8% (20.0–26.2%; 10 studies, 1564 men; Table 4). The pooled detection ratios for grade 2 or higher prostate cancer were 1.05 (0.95–1.16), and 1.44 (1.19–1.75), respectively ($p < 0.01$; Fig. 5). When focusing on only MRI-positive men in both subgroups, the pooled detection ratio

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Table 1 – Characteristic of the diagnostic test accuracy and agreement studies

Study	Tests						Target condition	Recruitment			Patient characteristics			
	Index tests				Reference standard									
Author (year)	Index tests analysed	MRI scale; threshold	MRI TBx, technique	Route	Technique	Independence	ISUP grade (G)	Study design[a]	Consecutive enrolment	Population	No. of participants	Median age (range/SD)	Median PSA ng/ml (range)	Median prostate volume cm^3 (range)
Diagnostic test accuracy studies														
Abd-Alazeez (2014)	MRI	1–5; ≥3	Cognitive	Transperineal	TTMB	No	G = 1, ≥1, ≥2, ≥3	Retrospective	No	Prior-negative Bx	54	64 (39–75)	10 (2–23)	53 (19–136)
Ahmed (2017)	MRI, SBx	1–5; ≥3	NA	Transrectal	TTMB	Yes	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	576	63 (7.6)[b]	7.1 (2.9)[b]	NR
Dal Moro (2019)	MRI, MRI TBx, MRI pathway	1–5; ≥3	Cognitive	Transrectal	TSB[c]	Yes	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Prior-negative Bx	123	62 (57–68[d])	6.3 (4.8–8.9[d])	55 (20–149)[b]
Distler (2017)	MRI, MRI TBx, MRI pathway	1–5; ≥3	Software	Transperineal	TSB[e]	No	G ≥ 2	Prospective	Yes	Mixed[f]	1040 (597/443)	65 (60–71[d])	7.2 (5.3–10.4[d])	45 (34–64[d])
Grey (2015)	MRI	1–5; ≥3	Cognitive	Transperineal	TSB[e]	No	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Mixed [f]	83	64 (6.8)[b]	13.3 (12.1)[b]	68 (35)[b]
											103	65 (7.6)[a]	12.6 (13.7)[a]	54 (31)[a]
Hansen (2016)	MRI, MRI TBx, MRI pathway	1–5; ≥3	Software/ transperineal	Transperineal	TSB[e]	Unclear	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Prior-negative Bx	295	65 (59–69[d])	7.8 (6.0–12[d])	65 (44–83[d])
Hansen (2018)	MRI	1–5; ≥3	Software	Transperineal	TSB[e]	No	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive (centre 1)	163	64 (57–69[d])	6.6 (4.6–9.0[d])	44 (33–55[d])
			Cognitive							Bx naive (centre 3)	242	65 (60–70[d])	5.9 (4.6–8.0 [d])	25 (24–47[d])
Hansen (2017)	MRI, MRI TBx, MRI pathway	1–5; ≥3	Software/ transperineal	Transperineal	TSB[e]	Unclear	G ≥ 2	Prospective	Unclear	Prior-negative Bx	287	66 (61–72[d])	9.7 (7.1–13.9[d])	52 (36–75[d])
Kesch (2017)	MRI, MRI TBx, MRI pathway	1–5; ≥3	Software/ transperineal	Transperineal	TSB[g]	Yes	G = 1, ≥1, ≥2, ≥3	Prospective	Unclear	Mixed [f]	146 (95/51)	65 (58–71[d])	7.2 (5.4–10.2[d])	46 (36–60[d])
Lawrence (2014)	MRI, MRI TBx, MRI pathway	1–4; ≥2	Software	Transperineal	TSB[e]	No	G = 1, ≥1, ≥2	Retrospective	No	Prior-negative Bx	39	64 (47–77)[b]	10 (1.2–36)	NR
Mortezavi (2018)	MRI, MRI TBx, MRI pathway	1–5; ≥3	Software	Transrectal	TSB	No	G = 1, ≥1, ≥2, ≥3	Retrospective	Yes	Bx naive	163	63 (57–68[d])	5.8 (4.4–8.9[d])	44 (34–60[d])
										Prior-negative Bx	86	64 (60–69[d])	8.6 (5.7–13[d])	54 (41–70[d])
Muthuveloe (2016)	MRI	1–5; ≥3	NA	NA	TSB[h]	Unclear	G = 1, ≥1, ≥2, ≥3	Retrospective	Unclear	Bx naive	9	68 (46–81)	11.5 (1.2–92.5)	NR
										Prior-negative Bx	162	65 (47–78)	10 (2.7–61)	NR
Pepe (2013)	MRI, MRI TBx, MRI pathway	0–1: ≥1	Cognitive	Transrectal	TSB[h]	No	G = 1, ≥1, ≥2	Prospective	Unclear	Prior-negative Bx	78	63 (49–72)	11 (3.7–45)	NR
Thompson (2016)	MRI	1–5; ≥3	Software, cognitive	Transperineal	TTMB	No	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	344	63 (56–67[d])	5.2 (3.7–7.1[d])	40 (30–54[d])
Tsivian (2017)	MRI	1–5; ≥3	NA	NA	TTMB	Yes	G = 1, ≥1, ≥2, ≥3	Retrospective	Unclear	Prior-negative Bx	33	65 (61–69[d])	7.1 (5.1–13.6[d])	44 (32–65[d])
Nafie (2014)	SBx	NA	NA	Transrectal	TSB[h]	Yes	G = 1, ≥1, ≥2, ≥3	Prospective	Unclear	Bx naive	50	67 (54–84)[b]	8 (4–18)[b]	58 (19–165)[b]

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Table 1 (*Continued*)

Study	Tests						Target condition	Recruitment			Patient characteristics			
	Index tests				Reference standard									
Author (year)	Index tests analysed	MRI scale; threshold	MRI TBx, technique	Route	Technique	Independence	ISUP grade (G)	Study design[a]	Consecutive enrolment	Population	No. of participants	Median age (range/SD)	Median PSA ng/ml (range)	Median prostate volume cm^3 (range)
Nafie (2017)	SBx	NA	NA	Transrectal	TSB[h]	Yes	G = 1, ≥1, ≥2	Prospective	Unclear	Prior-negative Bx	42	65 (50–75)[b]	8.3 (4.4–19)[b]	59 (21–152)[b]
Ploussard (2014)	SBx	NA	NA	Transrectal	TSB[c]	No	G = 1, ≥1, ≥2	Prospective	Yes	Bx naive	2753	64 (8)[b]	12.5 (7.2)[b]	46 (25)[b]
Agreement studies														
Alberts (2017)	MRI pathway vs SBx	1–5; ≥3	Software	Transrectal	NA	Yes	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	74	73 (72–74[d])	4.2 (3.4–5.8[d])	53 (37–71[d])
										Prior-negative Bx	84			
Boesen (2017)	MRI pathway vs SBx	1–5; ≥3	Software	Transrectal	NA	Yes	G = 1, ≥1, ≥2, ≥3	Prospective	Unclear	Prior-negative Bx	206	65 (58–68[d])	12.8 (8.9–19.6[d])	NR
Boesen (2018)	MRI pathway vs SBx	1–5; ≥3	Software	Transrectal	NA	Yes	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	1020	67 (61–71[d])	8 (5.7–13[d])	53 (40–72[d])
Castellucci (2017)	MRI pathway vs SBx	1–5; ≥3	Cognitive	Transrectal	NA	Unclear	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	168	61 (8)[f]	8.3 (6.1)[f]	49 (7)[f]
Chang (2017)	MRI pathway vs SBx	1–5; ≥3	Cognitive	Transrectal	NA	No	G = 1, ≥1, ≥2, ≥3	Retrospective	Yes	Prior-negative Bx	65	64 (60–68[d])	10.9 (7.2–14.7[d])	48 (34–63[d])
Chen (2015)	MRI pathway vs SBx	1–5; ≥3	Cognitive	Transperineal	NA	Yes	G ≥ 2	Prospective	Yes	Bx naive	420	67 (45–91)	9.7 (2.4–35.7)	45 (21–83)
Cool (2016)	MRI pathway vs SBx	Other	Software	Transrectal	NA	Unclear	G = 1, ≥1, ≥2	Prospective	Unclear	Bx naive	50	59 (8)[f]	6.0 (3.5)[f]	38 (18)[f]
										Prior-negative Bx	50	62 (7)[f]	7.9 (3.9)[f]	56 (27)[f]
Costa (2013)	MRI pathway vs SBx	1–5; ≥4	Cognitive	Transrectal	NA	No	G ≥ 2, ≥3	Retrospective	No	Prior-negative Bx	38	64 (48–77)[f]	14.4 (1.8–33.1)[f]	NR
Delong-champs (2013)	MRI pathway vs SBx	1–5; ≥3	Software	Transrectal	NA	Unclear	G ≥2	Prospective	Yes	Bx naive	391	64 (7)[f]	8.5 (3.9)[f]	56 (30)[f]
Filson (2016)	MRI pathway vs SBx	1–5; ≥3	Software	Transrectal	NA	Unclear	G ≥ 2, ≥3	Prospective	Yes	Bx naive	329	64 (59–69[d])	5.8 (4.4–8.1[d])	45(33–62[d])
										Prior-negative Bx	324	66 (59–70[d])	7.6 (5–11.5[d])	58 (40–84[d])
Garcia Bennett (2017)	MRI pathway vs SBx	1–5; ≥3	Cognitive	Transperineal	NA	Yes	G = 1, ≥1, ≥2, ≥3	Prospective	Unclear	Bx naive	60	64 (6.7)[f]	7.2 (6–9.4[d])	48 (35–63[d])
Grönberg (2018)	MRI pathway vs SBx	1–5; ≥3	Software	Transrectal	NA	No	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	387	64 (45–74)[f]	6.3 (4.4[d])	(32–70)[i]
										Prior-negative Bx	145			
Jambor (2015)	MRI pathway vs SBx	1–5; ≥4	Cognitive	Transrectal	NA	Yes	G = 1, ≥1, ≥2, ≥3	Unclear, unclear	Unclear	Bx naive	53	66 (47–76)	7.4 (4–14)	42 (17–107)
Jambor (2017)	MRI pathway vs SBx	1–5; ≥3	Cognitive	Transrectal	NA	No	G = 1, ≥1, ≥2, ≥3	Prospective	Unclear	Mixed	134	65 (6)[f]	7.5 (5.7–9.6[d])	37 (28–49[d])

Table 1 (*Continued*)

Study	Tests						Target condition	Recruitment			Patient characteristics			
	Index tests				Reference standard									
Author (year)	Index tests analysed	MRI scale; threshold	MRI TBx, technique	Route	Technique	Independence	ISUP grade (G)	Study design[a]	Consecutive enrolment	Population	No. of participants	Median age (range/SD)	Median PSA ng/ml (range)	Median prostate volume cm^3 (range)
											27			
Kim (2017)	MRI pathway vs SBx	1–5; ≥4	Software, cognitive	Transrectal	NA	No	G = 1, ≥1, ≥2, ≥3	Retrospective	Unclear	Bx naive	183	64 (7)[f]	10.2 (15.1)[f]	NR
										Prior-negative Bx	154			
Lee (2016)	MRI pathway vs SBx	1–4; ≥2	Cognitive	Transrectal	NA	No	G = 1, ≥1, ≥2, ≥3	Retrospective	Unclear	Bx naive	76	66 (43–83)	6.4 (3.3–9.8)	39 (17–127)
Lee (2017)	MRI pathway vs SBx	1–4; ≥2	Cognitive	Transrectal	NA	No	G = 1, ≥1, ≥2, ≥3	Retrospective	Unclear	Bx naive	123	62 (10)[f]	6.4 (1.8)[f]	40 (18)[f]
Okcelik (2016)	MRI pathway vs SBx	0–1: ≥1	Cognitive	Transrectal	NA	Unclear	G = 1, ≥1, ≥2	Prospective	Unclear	Bx naive	52	62 (43–79)	5 (3–8.9)	45 (17–93)
Panebianco (2018)	MRI pathway vs SBx	1–5; ≥3	Cognitive	Transrectal	NA	Unclear	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	570	64 (51–82)	NR	NR
										Prior-negative Bx	355			
Peltier (2015)	MRI pathway vs SBx	1–4; ≥2	Software	Transrectal	NA	No	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	110	65 (7)[f]	8.4 (6.3)[f]	49 (22)[f]
Pokorny (2014)	MRI pathway vs SBx	1–5; ≥3	In-bore	Transrectal	NA	Unclear	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	223	63 (57–68[d])	5.3 (4.1–6.6[d])	41 (30–59[d])
Rouvière (2019)	MRI pathway vs SBx	1–5; ≥3	Software	Transrectal	NA	Yes	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	251	64 (59–68[d])	6.5 (5.6–9.6[d])	50 (38–63[d])
Say (2016)	MRI pathway vs SBx	1–4; ≥2	Software	Transrectal	NA	Unclear	G = 1, ≥1, ≥2, ≥3	Retrospective	Yes	Prior-negative Bx	143	64 (47–82)[f]	11.59 (0.4–96.9)[f]	69 (17–309)[f]
Tonttila (2016)	MRI pathway vs SBx	1–4; ≥2	Cognitive	Transrectal	NA	Yes	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	53	63 (60–66[d])	6.1 (4.2–9.9[d])	28 (24–37[d])
Van der Leest (2018)	MRI pathway vs SBx	1–5; ≥3	In-bore	Transrectal	NA	Yes	G = 1, ≥1, ≥2, ≥3	Prospective	Yes	Bx naive	626	65 (59–68[d])	6.4 (4.6–8.2[d])	55 (41–77[d])

Bx = biopsy; ISUP G = International Society of Urological Pathology grade; MRI = magnetic resonance imaging; MRI pathway = magnetic resonance imaging with or without magnetic resonance imaging-targeted biopsy; MRI TBx = magnetic resonance imaging-targeted biopsy; N = number; NA = not applicable; NR = not reported; PSA = prostate-specific antigen; SBx = systematic biopsy; SD = standard deviation; TSB = transperineal saturation biopsy; TTMB = transperineal template mapping biopsy.

[a] Included participants were part of the same study cohort (no randomised populations were included).
[b] Included participants were part of the same study cohort (no randomised populations were included).
[c] Transrectal.
[d] Interquartile range (as opposed to range).
[e] Ginsburg biopsies.
[f] Mean value (as opposed to median value).
[g] Transperineal optimised prostate biopsy.
[h] In-house transperineal saturation biopsy.
[i] Range of interquartile ranges across three centres.

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Table 2 – Diagnostic accuracy and predictive metrics of the index tests verified by template-guided biopsy as the reference standard for different target conditions

Target condition	Index test[a]	No. of participants (studies)	Proportion negative MRI (95% CI)	Accuracy metrics			Prevalence[b] (95% CI)	Assumptive prevalence[c]	Predictive metrics	
				Sensitivity (95% CI)	Specificity (95% CI)	*p* value			NPV[d] (95% CI)	PPV[d] (95% CI)
ISUP G ≥ 2 prostate cancer	MRI	3091 (12)	0.29 (0.22–0.37)	0.91 (0.83–0.95)	0.37 (0.29–0.46)	$p < 0.01$[e]	0.29 (0.22–0.38)	0.30	0.91 (0.86–0.94)	0.38 (0.36–0.40)
	MRI Tbx[f]	1553 (8)	NA	0.80 (0.69–0.87)	0.94 (0.90–0.97)		0.34 (0.24–0.46)		0.92 (0.88–0.94)	0.85 (0.77–0.91)
	MRI pathway	2257 (8)	0.29 (0.24–0.35)	0.72 (0.60–0.82)	0.96 (0.94–0.98)	$p = 0.06$[g]	0.26 (0.18–0.36)		0.89 (0.85–0.92)	0.90 (0.83–0.94)
	SBx	3421 (4)	NA	0.63 (0.19–0.93)	1.00 (0.91–1.00)		0.34 (0.21–0.51)		0.86 (0.65–0.95)	1.00 (0.73–1.00)
ISUP G ≥ 3 prostate cancer	MRI	1438 (7)	0.31 (0.21–0.42)	0.95 (0.87–0.99)	0.35 (0.26–0.46)	ID[e]	0.14 (0.08–0.23)	0.15	0.98 (0.95–0.99)	0.21 (0.19–0.23)
	MRI Tbx[f]	428 (3)	NA	ID	ID		0.21 (0.12–0.35)		ID	ID
	MRI pathway	604 (3)	0.29 (0.26–0.33)	ID	ID	ID[g]	0.16 (0.09–0.27)		ID	ID
	SBx	626 (2)	NA	ID	ID		ID		ID	ID
ISUP G = 1 prostate cancer	MRI	1764 (10)	0.28 (0.20–0.38)	0.70 (0.59–0.80)	0.27 (0.19–0.37)	$p < 0.01$[e]	0.20 (0.17–0.23)	0.20	0.79 (0.74–0.82)	0.20 (0.18–0.21)
	MRI Tbx[f]	497 (5)	NA	0.51 (0.21–0.81)	1.00 (0.77–1.00)		0.22 (0.19–0.26)		0.89 (0.80–0.94)	0.97 (0.21–1.00)
	MRI pathway	681 (5)	0.24 (0.16–0.36)	0.34 (0.19–0.53)	1.00 (0.90–1.00)	$p = 0.52$[g]	0.21 (0.18–0.24)		0.86 (0.82–0.89)	0.95 (0.37–1.00)
	SBx	3421 (4)	NA	0.55 (0.25–0.83)	0.99 (0.81–1.00)		0.20 (0.16–0.25)		0.90 (0.81–0.95)	0.94 (0.37–1.00)

CI = confidence interval; ISUP G = International Society of Urological Pathology grade; ID = inadequate data; MRI = magnetic resonance imaging; MRI pathway = magnetic resonance imaging with or without magnetic resonance imaging-targeted biopsy; MRI TBx = magnetic resonance imaging-targeted biopsy; NA = not applicable; NPV = negative predictive value; PPV = positive predictive value; SBx = systematic biopsy.

[a] Data did not allow differentiation between the mix of included participants (biopsy-naive and prior-negative biopsy men).

[b] Prevalence is pooled estimate of all detected cancer by template-guided biopsy.

[c] Assumptive prevalence is an extrapolation from the pooled estimates of all detected cancer by template-guided biopsy per target condition. This assumptive prevalence is necessary for adequate comparison of PPVs and NPVs between index tests.

[d] Based on the Bayes' theorem using the point estimates and 95% confidence intervals of the pooled positive and negative likelihood ratio and the point estimate of the prevalence.

[e] Comparing sensitivity between MRI and the MRI pathway.

[f] MRI-positive men only, instead of MRI-positive + MRI-negative men, implicating a higher risk profile and increased prevalence of clinically significant prostate cancer.

[g] Comparing sensitivity between the MRI pathway and SBx.

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Table 3 – Summary of Grading of Recommendations Assessment, Development and Evaluation (GRADE) guidance for diagnostic test accuracy of individual index tests

Population:	Men suspected of having clinically significant prostate cancer undergoing their first biopsy (biopsy-naive men) or a repeat biopsy (prior-negative biopsy men)
Setting:	University hospitals and specialised care centres
Reference test:	Template-guided biopsy, which comprehensively samples all zones of the prostate
Threshold:	ISUP grade ≥2 prostate cancer

Index test:	MRI	MRI-targeted biopsy	MRI pathway	Systematic biopsy
Threshold:	MRI score ≥3 out of 5	ISUP grade ≥2 prostate cancer	ISUP grade ≥2 prostate cancer	ISUP grade ≥2 prostate cancer
Population:	3091 (12)	1553 (8)	2257 (8)	3421 (4)
Pooled sensitivity:	0.91 (95% CI: 0.83–0.95)	0.80 (95% CI: 0.69–0.87)	0.72 (95% CI: 0.60–0.82)	0.63 (95% CI: 0.19–0.93)
Pooled specificity:	0.37 (95% CI: 0.29–0.46)	0.94 (95% CI: 0.90–0.97)	0.96 (95% CI: 0.94–0.98)	1.00 (95% CI: 0.91–1.00)
Results per 1000 men tested (95% CI): at a baseline prevalence of 30% ISUP grade ≥2 prostate cancer by the reference test				
True positives:	273 (249–285)	240 (207–261)	216 (180–246)	189 (57–279)
False negatives:	27 (15–51)	60 (39–93)	84 (54–120)	111 (21–243)
True negatives:	259 (203–322)	658 (630–679)	672 (658–686)	700 (637–700)
False positives:	441 (378–497)	42 (21–70)	28 (14–42)	0 (0–63)
Certainty of evidence (tp/fn):	●●○○ Low[a,b]	●●○○ Low[a,b]	●●○○ Low[a,b]	●●●○ Moderate[a,b,c]
Certainty of evidence (tn/fp):	●●○○ Low[a,b]	●●○○ Low[a,b]	●●○○ Low[a,b]	●●○○ Low[a,b,c]

CI = confidence interval; fn = false negative—test indicates that clinically significant prostate cancer is not present but patient actually has clinically significant prostate cancer; fp = false positive—test indicates clinically significant prostate cancer but patient actually does not have clinically significant prostate cancer; ISUP = International Society of Urological Pathology; MRI = magnetic resonance imaging; tn = true negative—test indicates that clinically significant prostate cancer is not present and patient actually does not have clinically significant prostate cancer; tp = true positive—indicates clinically significant prostate cancer and patient actually has clinically significant prostate cancer.

[a] A considerable number of studies had a high or unclear risk of bias, mainly in the participant selection and reference standard domains.

[b] Considerable, clinically relevant, heterogeneity was observed across pooled study results.

[c] Important imprecision was noted, which contributed to decision to downgrade for inconsistency.

increased from 1.05 to 1.12 (1.01–1.23) and from 1.44 to 1.49 (1.22–1.82), respectively.

3.3.2.2. Detection ratios for grade 1 prostate cancer. For men in the biopsy-naive and the prior-negative biopsy settings, cancer proportions of grade 1 prostate cancer were 27.2% (23.9–31.1%; 17 studies, 4079 men) and 23.0% (18.0–30.2%; eight studies, 1202 men), respectively; the pooled detection ratio was 0.63 (0.54–0.74) and 0.62 (0.44-0.88), respectively (Table 4).

3.3.2.3. Added values (discordance) in detection of grade 2 or higher prostate cancer. Per 100 biopsy-naive men, the MRI pathway detected approximately 23 men with grade 2 or higher prostate cancer (23.4% [19.4–28.2]; Table 4). In addition to the MRI pathway, systematic biopsy detected four additional men (4.3% [2.6–6.9%]). The total number of detected cases was 27 (27.7% [23.7–32.6%]). Conversely, systematic biopsy detected 21 men (21.4% [17.2–26.5%]) and the MRI-pathway detected six additional men (6.3% [4.8–8.2%]). Further details on mixed population and prior-negative biopsy men are shown in the Cochrane review [13].

3.3.2.4. Added values (discordance) in detection of grade 1 prostate cancer. Per 100 biopsy-naive men, the MRI pathway detected approximately 11 men with grade 1 prostate cancer (11.2% [8.4–14.9%]; Table 4). In addition to the MRI pathway, systematic biopsy detected 10 additional men (9.8% [8.0–11.8%]). The total number of detected cases was 21 (20.9% [18.0–24.7%]). Conversely, systematic biopsy detected 19 men (18.5% [15.6–22.2%]) and the MRI pathway detected two additional men (2.4% [1.4–4.0%]).

3.3.2.5. Added values (discordance) in detection of grade 2 or higher prostate cancer in MRI-positive and MRI-negative men. Stratifying men further into having positive or negative MRI aids in interpreting the added value in each of these categories. The pooled proportions of positive and negative MRI were respectively 67.0% (58.7–74.4%) and 33.0% (25.6–41.3%) in the biopsy-naive setting, and were equivalent in the prior-negative biopsy setting (Table 4).

Per 100 biopsy-naive men with positive MRI, the MRI pathway detected approximately 39 men with grade 2 or higher prostate cancer (39.2% [33.3–45.7%]). In addition to the MRI pathway, systematic biopsy detected five men (4.9% [2.8–8.3%]). The total number of detected cases was 44 (44.2% [38.6–50.4%]). Conversely, systematic biopsy detected 34 men (34.4% [28.3–41.3%]) and the MRI pathway detected 10 additional men (9.8% [7.1–13.2%]).

Per 100 biopsy-naive men with negative MRI, systematic biopsy detected eight additional men with grade 2 or higher prostate cancer (8.1% [5.6–11.6%]) and 18 additional men with grade 1 prostate cancer (18.4% [14.2–23.7%]).

3.4. Heterogeneity analyses and sensitivity analyses

For the test accuracy analyses (index tests vs reference standard [template-guided biopsy]), we observed considerable heterogeneity in all index tests (Cochrane review [13]). For the agreement analyses (MRI pathway vs systematic biopsy), the heterogeneity (total tau-square = 0.03) is illustrated in Figure 5. We found a statistically significant difference in the detection ratio of the MRI pathway versus systematic biopsy between the subgroups of population (prior-negative biopsy vs biopsy

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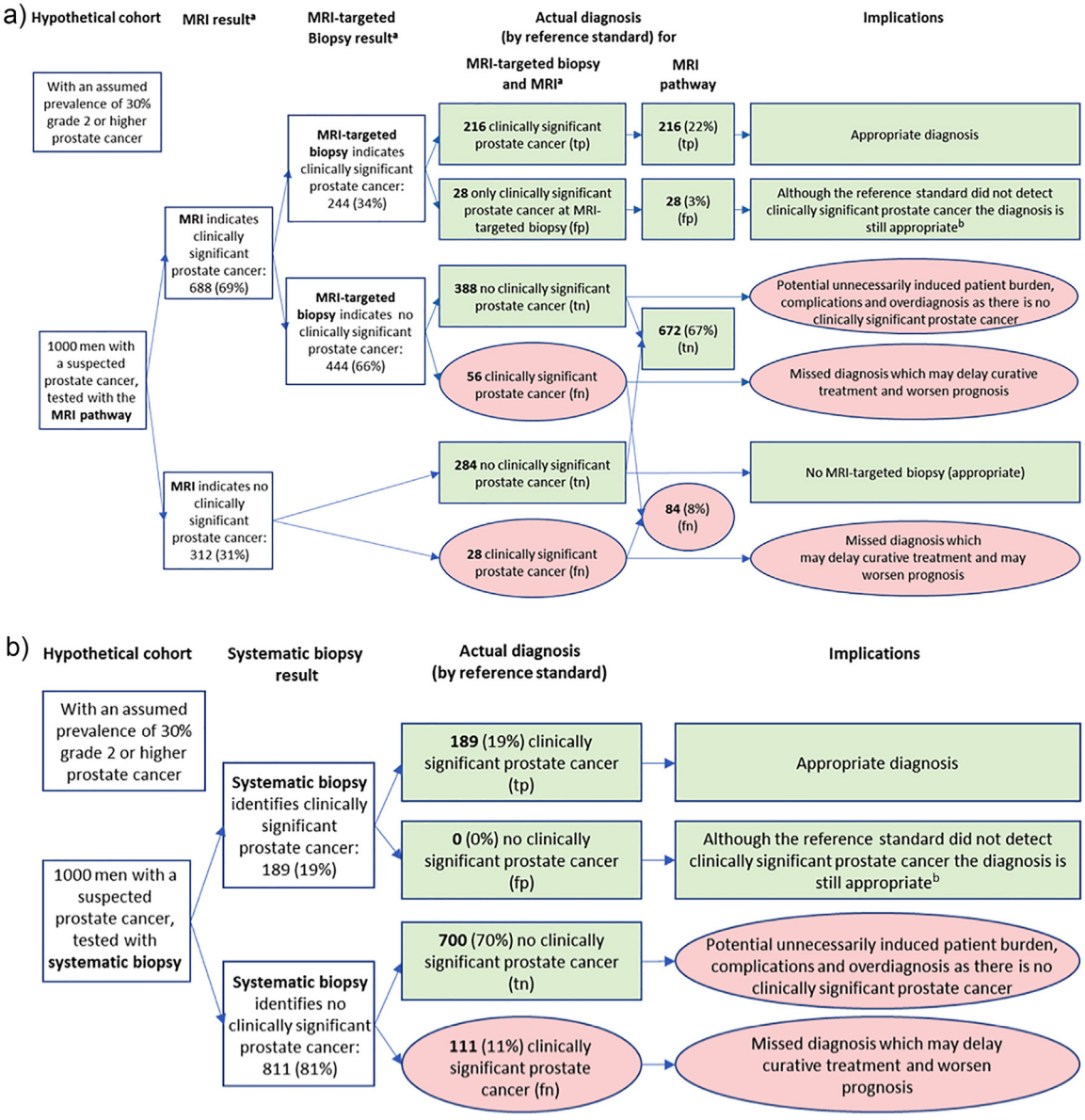


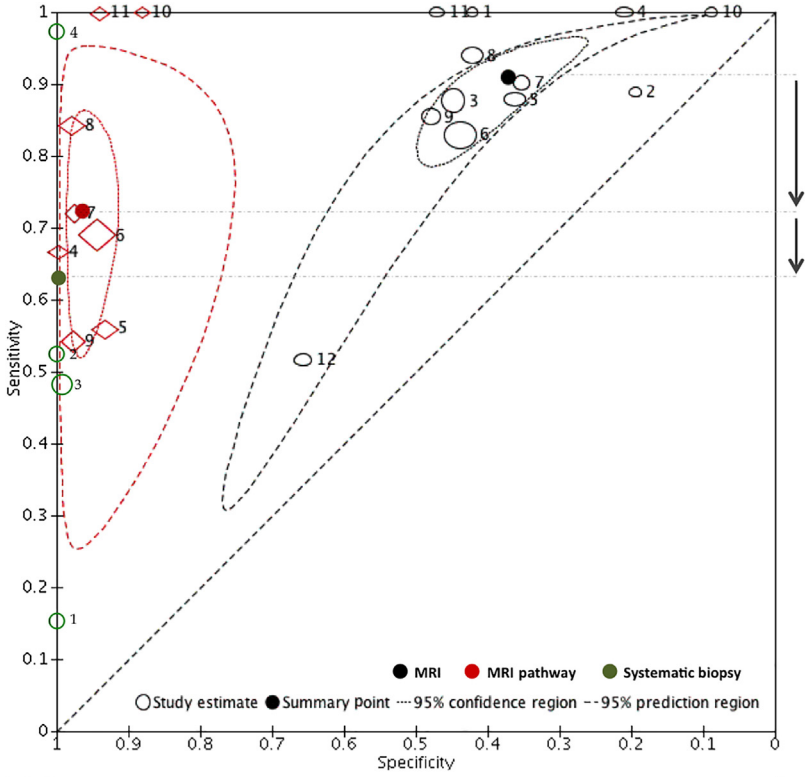
Fig. 3 – Test results and implications of a hypothetical cohort of 1000 men tested for prostate cancer using the (A) MRI pathway and (B) systematic biopsy. fn = false negative—test indicates that clinically significant prostate cancer is not present but patient actually has clinically significant prostate cancer; fp = false positive—test indicates clinically significant prostate cancer but patient actually does not have clinically significant prostate cancer; MRI = magnetic resonance imaging; tn = true negative—test indicates that clinically significant prostate cancer is not present and patient actually does not have clinically significant prostate cancer; tp = true positive—indicates clinically significant prostate cancer and patient actually has clinically significant prostate cancer. [a] The numbers in this figure are based on findings of the MRI pathway; therefore, MRI and MRI-targeted biopsy results differ slightly from the numbers in Table 3. [b] Diagnoses by the MRI pathway and reference standard are based on biopsy histopathology, with equal chance of up- or downgrading following radical prostatectomy.

naive), suggesting that they may be sources of heterogeneity (Cochrane review [13]).

We performed sensitivity analyses for the detection of grade 2 or higher prostate cancer by excluding studies based on certain quality and additional criteria. Excluding studies with a high or an unclear risk of bias or applicability concern in one of the four QUADAS-2 domains did not substantially change the accuracy results of MRI, MRI-targeted biopsy, and the MRI pathway (Cochrane review [13]).

3.5. Discussion

This copublished Cochrane review presents the test accuracy of prostate MRI, MRI-targeted biopsy, MRI pathway (MRI with or without MRI-targeted biopsy), and current standard testing with systematic biopsies in prostate cancer diagnosis, using template-guided biopsy sampling of the whole prostate as the reference standard. This analysis provides evidence to determine their discriminative value in current clinical practice. Both the MRI



Index test:	MRI	MRI pathway	Systematic biopsy
Threshold:	MRI score ≥ 3 out of 5	ISUP grade ≥ 2 prostate cancer	ISUP grade ≥ 2 prostate cancer
Population:	3091 (12)	2257 (8)	3421 (4)
Pooled sensitivity:	0.91 (95% CI: 0.83—0.95)	0.72 (95% CI: 0.60—0.82)	0.63 (95% CI: 0.19—0.93)
Pooled specificity:	0.37 (95% CI: 0.29—0.46)	0.96 (95% CI: 0.94—0.98)	1.00 (95% CI: 0.91—1.00)

Fig. 4 – Comparison of diagnostic test accuracy between MRI, MRI pathway, and systematic biopsy for detecting ISUP grade 2 and higher prostate cancer. Summary ROC plots of MRI, MRI pathway, and systematic biopsy, verified by template-guided biopsy, with references to included studies (see original review for further details [1]). A comparison of MRI with MRI pathway showed a substantial decrease in sensitivity (from 0.91 to 0.72) and an increase in specificity (from 0.37 to 0.96), both of which were statistically significant ($p < 0.01$; Table 3). A comparison of the MRI pathway with systematic biopsy showed a substantial decrease in sensitivity (from 0.72 to 0.63; $p = 0.06$; Table 3), and similar specificities. CI = confidence interval; ISUP = International Society of Urological Pathology; MRI = magnetic resonance imaging; ROC = receiver operating characteristics.

pathway and the systematic biopsy missed considerable proportions of grade 2 or higher prostate cancer, but the MRI pathway missed less than the systematic biopsy.

Furthermore, the agreement analyses for detecting prostate cancer between two index tests (the MRI pathway and the current practice of systematic biopsy) provide additional evidence for biopsy decision making, indicating that the MRI pathway is more favourable than systematic biopsy. The difference between the detection rates of the MRI pathway and systematic biopsy was largest in men with a prior-negative biopsy and insignificant in biopsy-naive men. Evidence further suggested that the MRI pathway beneficially missed more grade 1 prostate cancer than systematic biopsy in both population types. Therefore, the MRI pathway could potentially reduce the amount of overdiagnosis, and harms related to surveillance and overtreatment.

3.5.1. *MRI-directed biopsy management*

The benefits of using MRI (reducing biopsy procedures and the overdiagnosis of grade 1 prostate cancer with improving the detection of grade 2 and higher prostate cancer) are largest if MRI has a direct impact on biopsy decision management and shared decision making. In other words, the MRI before any biopsy and the MRI pathway as the replacement for systematic biopsy, thus omitting systematic biopsy in specified circumstances, might provide the most favourable diagnostic strategy.

Approximately one-third of all men had negative MRI. This is a substantially large population in whom additional systematic biopsies may potentially be avoided. Some expert centres even report up to 50% MRI-negative men, suggesting that an even larger population may benefit when experience in MRI reading may improve [24]. The added value of performing systematic biopsy in MRI-negative men for the detection of grade 2 or higher prostate cancer could be considered as limited with regard to total detection and additional harms. As a prostate biopsy is associated with patient burden, infection, morbidity, overdiagnosis, and related overtreatment, it should be avoided when possible. Omitting systematic biopsy in men with negative MRI might be considered acceptable in some clinical situations. However, benefits and harms are difficult to balance on an individual basis. Therefore, men with negative MRI could

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Table 4 – Agreement analysis of proportion of prostate cancer detected by the MRI pathway and systematic biopsy tests in biopsy-naive men

Population		Target condition (ISUP grade)	Patients (studies)	Proportion prostate cancer detected in % (95% CI)						Detection ratio (95% CI)[b]		Difference between populations, *p* value[c]
Biopsy status	MRI in % (95% CI)[a]			Combined MRI pathway + SBx (total cancer detected)	MRI pathway	SBx	Both MRI pathway and SBx	Only by MRI pathway (added value)	Only by SBx (added value)	MRI pathway versus SBx	*p* value	
Biopsy-naive men	Positive + negative (100 [100–100])	G = 1	4079 (17)	NA	13.5 (10.7–17.2)	22.4 (19.1–26.3)	NA	NA	NA	0.630 (0.535–0.742)	0.000	0.905
		G = 1[d]	4079 (17)	20.9 (18.0–24.7)	11.2 (8.4–14.9)	18.5 (15.6–22.2)	8.8 (6.2–12.3)	2.4 (1.4–4.0)	9.8 (8.0–11.8)	0.611 (0.485–0.769)	0.000	–
		G ≥ 1	4799 (19)	53.2 (48.7–57.9)	41.0 (35.8–46.4)	47.8 (42.8–52.9)	35.6 (30.2–41.2)	5.4 (3.6–8.0)	12.2 (8.7–16.7)	0.845 (0.767–0.930)	0.001	0.121
		G ≥ 2	5219 (20)	27.7 (23.7–32.6)	23.4 (19.3–28.1)	21.4 (17.2–26.5)	17.1 (13.0–22)	6.3 (4.8–8.2)	4.3 (2.6–6.9)	1.050 (0.948–1.162)	0.349	0.002
		G ≥ 3	4306 (16)	15.5 (12.6–19.5)	12.7 (9.9–16.5)	10.8 (8.0–14.8)	8.0 (5.4–11.6)	4.7 (3.5–6.3)	2.8 (1.7–4.8)	1.087 (0.937–1.261)	0.269	0.004
	Positive (67.0 [58.7–74.4])	G = 1	2682 (16)	NA	21.3 (17.0–26.9)	23.7 (19.6–29.1)	NA	NA	NA	0.854 (0.743–0.982)	0.026	0.347
		G = 1[d]	2682 (16)	21.1 (16.7–27.1)	17.0 (12.6–22.9)	17.7 (13.3–23.8)	13.6 (9.3–19.5)	3.4 (2.1–5.3)	4.1 (2.5–6.7)	0.909 (0.770–1.072)	0.257	–
		G ≥ 1	2955 (17)	70.9 (65.0–76.6)	63.7 (56.3–70.6)	63.8 (56.2–70.7)	56.6 (47.7–64.6)	7.1 (4.2–11.9)	7.2 (4.7–10.8)	0.994 (0.915–1.079)	0.881	0.053
		G ≥ 2	2955 (17)	44.2 (38.6–50.4)	39.2 (33.3–45.7)	34.4 (28.3–41.3)	29.5 (23.2–36.5)	9.8 (7.1–13.2)	4.9 (2.8–8.3)	1.119 (1.014–1.234)	0.025	0.005
		G ≥ 3	2899 (15)	24.8 (21.0–29.6)	21.2 (17.4–25.7)	17.5 (13.8–22.3)	13.9 (10.3–18.3)	7.3 (5.4–9.7)	3.7 (2.2–6.1)	1.158 (1.024–1.310)	0.020	0.007
	Negative (33.0 [25.6–41.3])	G = 1	1287 (16)	18.4 (14.2–23.7)	NA	18.4 (14.2–23.7)	NA	NA	18.4 (14.2–23.7)	NA	NA	NA
		G ≥ 1	1343 (17)	25.5 (20.7–30.9)	NA	25.5 (20.7–30.9)	NA	NA	25.5 (20.7–30.9)	NA	NA	NA
		G ≥ 2	1343 (17)	8.1 (5.6–11.6)	NA	8.1 (5.6–11.6)	NA	NA	8.1 (5.6–11.6)	NA	NA	NA
		G ≥ 3	1297 (15)	3.0 (1.6–5.5)	NA	3.0 (1.6–5.5)	NA	NA	3.0 (1.6–5.5)	NA	NA	NA

CI = confidence interval; ISUP = International Society of Urological Pathology; MRI = magnetic resonance imaging; MRI pathway = magnetic resonance imaging with or without magnetic resonance imaging-targeted biopsy; NA = not applicable; SBx = systematic biopsy.

[a] Proportion of participants with a positive or negative magnetic resonance imaging result, based on the studies reporting grade 2 or higher.

[b] Detection ratio is the detection rate of MRI pathway divided by the detection rate of systematic biopsy; the detection rate is the pooled number of positive results of the test divided by the pooled total number of positive results from both tests.

[c] Evaluating the difference in detection ratios between the populations (biopsy-naive men vs prior-negative biopsy) for each target condition.

[d] The tests are considered as "add-on tests", taking into account grade reclassification by each test. Therefore, G = 1e results differ from G = 1 results, where the tests are considered as "replacement tests", not taking into account grade reclassification.

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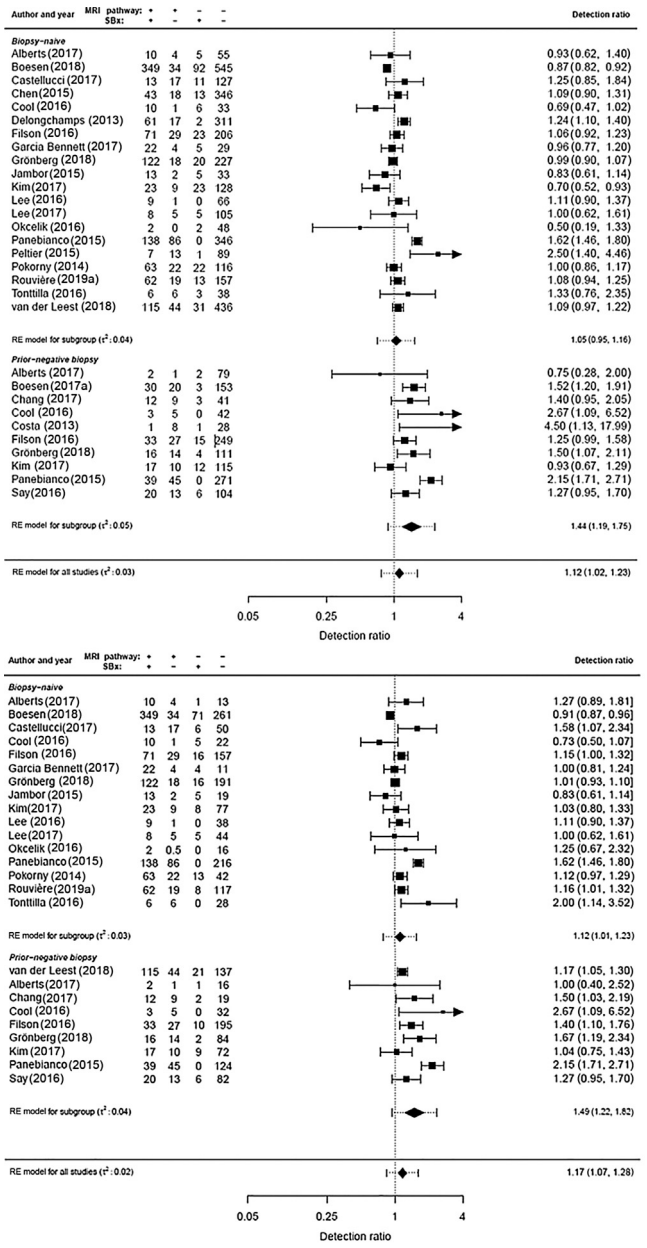

The upper plot is based on all included men; the lower plot is based on MRI-positive men. **MRI pathway:** magnetic resonance imaging with subsequent magnetic resonance imaging-targeted biopsy; **SBx:** systematic biopsy; **+:** positive test result; **-:** negative test result; **detection ratio:** detection rate MRI pathway divided by detection rate SBx; **detection rate:** pooled number of positive results of one test divided by the pooled total number of positive results from both tests; **RE model:** random effects model; τ^2: Tau² (heterogeneity). The continuous lines and brackets indicate study individual 95% confidence intervals; diamonds indicate the pooled summary estimate 95% confidence intervals; the dashed lines indicate the pooled 95% predicition intervals.

Fig. 5 – Forest plots of the agreement analysis (MRI pathway vs systematic biopsy) for detecting grade 2 and higher prostate cancer. The upper plot is based on all included men; the lower plot is based on MRI-positive men. Continuous lines and brackets indicate study individual 95% confidence intervals; diamonds indicate the pooled summary estimate 95% confidence intervals; and dashed lines indicate the pooled 95% prediction intervals. Detection rate = pooled number of positive results of one test divided by the pooled total number of positive results from both tests; detection ratio = detection rate of the MRI pathway divided by detection rate of SBx; MRI magnetic resonance imaging; MRI pathway: MRI with subsequent MRI-targeted biopsy; RE model = random-effect model; SBx = systematic biopsy; τ^2: tau-square (heterogeneity); + = positive result; – = negative result.

be counselled to pursue clinical and biochemical monitoring as a reasonable alternative for systematic biopsy, as also argued by others [25–27].

Men with positive MRI have a clear indication for MRI-targeted biopsy and can opt for additional systematic biopsy. The added value of performing systematic biopsy in MRI-positive men for the detection of grade 2 or higher prostate cancer, however, could be considered as limited with regard to total detection and additional harms. The conditions under which systematic biopsy could be safely avoided in men with positive MRI remain to be defined [26,28,29]. When in this population, the MRI pathway does not detect significant prostate cancer, a monitoring approach could be introduced (instead of systematic biopsy), based on clinical, biochemical, and imaging parameters, and would result in a "safety net". This safety net could easily be adopted in the shared decision making in current diagnostic work-up, as already recommended in international guidelines [30–32].

3.5.2. *Strength and weaknesses*

For the in-depth analysis of quantity and quality of evidence, strengths and weaknesses of included studies, and strengths and weaknesses of the review process, we refer to the original Cochrane review [13].

3.5.3. *Context of other research*

Distinguishing between biopsy-naive men and men with a prior-negative biopsy is paramount in daily practice. The agreement analysis, balancing the results of detecting grade 2 or higher prostate cancer, grade 1 prostate cancer, and reduction of biopsies in MRI-negative men, can be compared with selected high-quality studies (Supplementary Table 1). Recently, two multicentre randomised controlled trials in biopsy-naive men [2,33] investigated the MRI pathway and systematic biopsy. Furthermore, two large high-quality prospective multicentre cohort studies [24,34] investigated the agreement of prostate cancer detection between the MRI pathway and systematic biopsy.

The most remarkable differences are the following. Both randomised controlled trials showed that the MRI pathway detected significantly more grade 2 or higher prostate cancer than systematic biopsy [2,33], in contrast to the results from the agreement analyses in this review [13], including the two cohort studies [24,34]. Hence, while the randomised controlled trials showed superiority of the MRI pathway over systematic biopsy, the agreement studies did not. Despite these inconsistencies, none of the studies showed the MRI pathway to be inferior to systematic biopsy in detecting grade 2 or higher prostate cancer. In addition, in this Cochrane review, the proportion of men with grade 2 or higher prostate cancer detected by the MRI pathway was 23.4% (95% CI: 19.3–28.1%), while this was substantially higher in the two randomised controlled trials (Supplementary Table 1). Regarding the proportions of men with grade 1 prostate cancer, the MRI pathway in this review

detected 14% (95% CI: 11–17%), while this was lower in the two randomised controlled trials. Explanatory reasons might be multiple and are discussed within the context of this review (Cochrane review [13]).

3.5.4. Future research and perspectives

Quality control in the MRI pathway should be further employed to improve MRI acquisition, MRI reading, and MRI-targeted biopsy methods. The role of biparametric MRI as well as the different approaches for targeted biopsy (fusion, cognitive/visual, in bore), the route (transrectal/transperineal), and the clinical validity and utility of artificial intelligence with machine learning tools should be further investigated. Education, training, procedural standardisation, better imaging, and biopsy equipment require a multidisciplinary approach in the management of men with suspected prostate cancer [7,15,35,36]. This diagnostic chain is only as strong as its weakest link [37]. To improve the clinical utility of MRI-driven tests, factors influencing the outcome of the MRI pathway (such as per-lesion instead of a per-patient analysis, number of MRI-targeted biopsy cores, MRI positivity threshold in relation to clinical risk profiles, underlying MRI reading problems, and inaccurate MRI-targeted biopsy) should be further investigated. Risk calculators may aid in balancing harms and benefits by further refining the selection of those men who are at a risk of potentially life-threatening disease. Research should be initiated with recently introduced multivariable risk prediction models, including the MRI suspicion score as an extra input variable, to better identify those who would benefit from MRI and subsequent MRI-targeted biopsy, or an additional systematic biopsy, or both [38–42].

4. Conclusions

Balancing the potential benefits (reduction of biopsies and a decrease of grade 1 prostate cancer overdiagnosis) against the potential disadvantages (missing some grade 2 or higher prostate cancer), in disregard to further economic metrics (availability and costs), we conclude that the MRI pathway may represent a more favourable diagnostic test than systematic biopsy in all men suspected to have clinically significant prostate cancer. Therefore, performing prostate MRI before any biopsy should be structurally incorporated in the diagnostic work-up. Our certainty in our findings was reduced by study limitations. Furthermore, the MRI pathway relies on experience and skills in acquiring and reading MRI images, on targeting biopsy, and on high-end equipment of MRI and biopsy hardware and software, which are not yet widely available. Based on these considerations, further improvement of the prostate cancer diagnostic pathways should be pursued.

Author contributions: Ivo G. Schoots had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

Study concept and design: Drost, Roobol, Schoots.
Acquisition of data: Drost, Osses.
Analysis and interpretation of data: Drost, Osses, Nieboer, Roobol, Schoots.
Drafting of the manuscript: Drost, Schoots.
Critical revision of the manuscript for important intellectual content: Bangma, Steyerberg, Roobol.
Statistical analysis: Drost, Nieboer.
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Appendix A. Supplementary data

Supplementary data associated with this article can be found, in the online version, at https://doi.org/10.1016/j.eururo.2019.06.023.

References

[1] Alberts AR, Schoots IG, Roobol MJ. Prostate-specific antigen-based prostate cancer screening: past and future. Int J Urol 2015;22:524–32.
[2] Kasivisvanathan V, Rannikko AS, Borghi M, et al. MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med 2018;378:1767–77.
[3] De Rooij M, Hamoen EH, Futterer JJ, Barentsz JO, Rovers MM. Accuracy of multiparametric MRI for prostate cancer detection: a meta-analysis. Am J Roentgenol 2014;202:343–51.
[4] Futterer JJ, Briganti A, De Visschere P, et al. Can clinically significant prostate cancer be detected with multiparametric magnetic resonance imaging? A systematic review of the literature. Eur Urol 2015;68:1045–53.
[5] Gayet M, Van der Aa A, Beerlage HP, Schrier BP, Mulders PF, Wijkstra H. The value of magnetic resonance imaging and ultrasonography (MRI/US)-fusion biopsy platforms in prostate cancer detection: a systematic review. BJU Int 2016;117:392–400.

[6] Hamoen EH, de Rooij M, Witjes JA, Barentsz JO, Rovers MM. Use of the Prostate Imaging Reporting and Data System (PI-RADS) for prostate cancer detection with multiparametric magnetic resonance imaging: a diagnostic meta-analysis. Eur Urol 2015;67:1112–21.
[7] Moore CM, Robertson NL, Arsanious N, et al. Image-guided prostate biopsy using magnetic resonance imaging-derived targets: a systematic review. Eur Urol 2013;63:125–40.
[8] Schoots IG, Roobol MJ, Nieboer D, Bangma CH, Steyerberg EW, Hunink MG. Magnetic resonance imaging-targeted biopsy may enhance the diagnostic accuracy of significant prostate cancer detection compared to standard transrectal ultrasound-guided biopsy: a systematic review and meta-analysis. Eur Urol 2015;68: 438–50.
[9] Valerio M, Donaldson I, Emberton M, et al. Detection of clinically significant prostate cancer using magnetic resonance imaging-ultrasound fusion targeted biopsy: a systematic review. Eur Urol 2015;68:8–19.
[10] Van Hove A, Savoie PH, Maurin C, et al. Comparison of image-guided targeted biopsies versus systematic randomized biopsies in the detection of prostate cancer: a systematic literature review of well-designed studies. World J Urol 2014;32:847–58.
[11] Woo S, Suh CH, Kim SY, Cho JY, Kim SH, Moon MH. Head-to-head comparison between biparametric and multiparametric MRI for the diagnosis of prostate cancer: a systematic review and meta-analysis. AJR Am J Roentgenol 2018;211:W226–41.
[12] Robertson NL, Hu Y, Ahmed HU, Freeman A, Barratt D, Emberton M. Prostate cancer risk inflation as a consequence of image-targeted biopsy of the prostate: a computer simulation study. Eur Urol 2014;65:628–34.
[13] Drost FH, Osses DF, Nieboer D, et al. Prostate MRI, with or without MRI-targeted biopsy, and systematic biopsy for detecting prostate cancer. Cochrane Database Syst Rev 2019;4:Cd012663.
[14] Dickinson L, Ahmed HU, Allen C, et al. Magnetic resonance imaging for the detection, localisation, and characterisation of prostate cancer: recommendations from a European consensus meeting. Eur Urol 2011;59:477–94.
[15] Weinreb JC, Barentsz JO, Choyke PL, et al. PI-RADS Prostate Imaging-Reporting and Data System: 2015, version 2. Eur Urol 2016;69:16–40.
[16] Kuru TH, Wadhwa K, Chang RT, et al. Definitions of terms, processes and a minimum dataset for transperineal prostate biopsies: a standardization approach of the Ginsburg for Enhanced Prostate Diagnostics. BJU Int 2013;112:568–77.
[17] Sivaraman A, Sanchez-Salas R, Barret E, et al. Transperineal template-guided mapping biopsy of the prostate. Int J Urol 2015;22:146–51.
[18] Moore CM, Kasivisvanathan V, Eggener S, et al. Standards of reporting for MRI-targeted biopsy studies (START) of the prostate: recommendations from an International Working Group. Eur Urol 2013;64:544–52.
[19] Epstein JI, Egevad L, Amin MB, et al. The 2014 International Society of Urological Pathology (ISUP) consensus conference on Gleason grading of prostatic carcinoma: definition of grading patterns and proposal for a new grading system. Am J Surg Pathol 2016;40:244–52.
[20] Whiting PF, Rutjes AW, Westwood ME, et al. QUADAS-2: a revised tool for the quality assessment of diagnostic accuracy studies. Ann Intern Med 2011;155:529–36.
[21] Macaskill P, Gatsonis C, Deeks JJ, Harbord RM, Takwoingi Y. Chapter 10: analysing and presenting results. In: Deeks JJ, Bossuyt PM, Gatsonis C, editors. Cochrane handbook for systematic reviews of diagnostic test accuracy version 1.0. The Cochrane Collaboration; 2010,, srdta.cochrane.org/.
[22] Schünemann HJ, Oxman AD, Brozek J, et al. Grading quality of evidence and strength of recommendations for diagnostic tests and strategies. Br Med J 2008;336:1106–10.
[23] Barentsz JO, Richenberg J, Clements R, et al. ESUR prostate MR guidelines 2012. Eur Radiol 2012;22:746–57.
[24] 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;75:570–8.
[25] Moldovan PC, Van den Broeck T, Sylvester R, et al. What is the negative predictive value of multiparametric magnetic resonance imaging in excluding prostate cancer at biopsy? A systematic review and meta-analysis from the European Association of Urology Prostate Cancer Guidelines Panel. Eur Urol 2017;72:250–66.
[26] Padhani AR, Weinreb J, Rosenkrantz AB, Villeirs G, Turkbey B, Barentsz J. Prostate Imaging-Reporting and Data System Steering Committee: PI-RADS v2 status update and future directions. Eur Urol 2019;75:358–96.
[27] Panebianco V, Barchetti G, Simone G, et al. Negative multiparametric magnetic resonance imaging for prostate cancer: what's next? Eur Urol 2018;74:48–54.
[28] Richenberg J, Logager V, Panebianco V, Rouviere O, Villeirs G, Schoots IG. The primacy of multiparametric MRI in men with suspected prostate cancer. In press. https://doi.org/10.1007/s00330-019-06166-z.
[29] Rouvière O, Souchon R, Melodelima C. Pitfalls in interpreting positive and negative predictive values: application to prostate multiparametric magnetic resonance imaging. Diagn Interv Imaging 2018;99:515–8.
[30] Carter HB, Albertsen PC, Barry MJ, et al. Early detection of prostate cancer: AUA guideline. http://www.auanet.org/guidelines/prostate-cancer-early-detection-(2013-reviewed-for-currency-2018)-x26372018.
[31] Mottet N, Van den Bergh RCN, Briers E, et al. European Association of Urology: guideline on prostate cancer. 2018 In: https://uroweb.org/guideline/prostate-cancer/
[32] National Comprehensive Cancer Network (NCCN). Guidelines on prostate cancer: 2018, update. 2018 In: http://www.nccn.org/professionals/physician_gls/default.aspx
[33] Porpiglia F, Manfredi M, Mele F, et al. Diagnostic pathway with multiparametric magnetic resonance imaging versus standard pathway: results from a randomized prospective study in biopsy-naive patients with suspected prostate cancer. Eur Urol 2017;72: 282–8.
[34] Rouvière 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;20:100–9.
[35] Moore CM, Giganti F, Albertsen P, et al. Reporting magnetic resonance imaging in men on active surveillance for prostate cancer: the precise recommendations-a report of a European School of Oncology task force. Eur Urol 2017;71:648–55.
[36] Puech P, Randazzo M, Ouzzane A, et al. How are we going to train a generation of radiologists (and urologists) to read prostate MRI? Curr Opin Urol 2015;25:522–35.
[37] Rouvière O, Schoots IG, Mottet N, EAU-EANM-ESTRO-ESUR-SIOG Prostate Cancer Guidelines Panel. Multiparametric magnetic resonance imaging before prostate biopsy: a chain is only as strong as its weakest link. Eur Urol 2019;75:889–90.
[38] Alberts AR, Roobol MJ, Verbeek JF, et al. Prediction of high-grade prostate cancer following multiparametric magnetic resonance imaging: improving the Rotterdam European Randomized Study of Screening for Prostate Cancer risk calculators. Eur Urol 2019;75: 310–8.
[39] Ankerst DP, Straubinger J, Selig K, et al. A contemporary prostate biopsy risk calculator based on multiple heterogeneous cohorts. Eur Urol 2018;74:197–203.
[40] Foley RW, Maweni RM, Gorman L, et al. European Randomised Study of Screening for Prostate Cancer (ERSPC) risk calculators significantly outperform the Prostate Cancer Prevention Trial

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(PCPT) 2.0 in the prediction of prostate cancer: a multi-institutional study. BJU Int 2016;118:706–13.

[41] Mehralivand S, Shih JH, Rais-Bahrami S, et al. A magnetic resonance imaging-based prediction model for prostate biopsy risk stratification. JAMA Oncol 2018;4:678–85.

[42] Radtke JP, Wiesenfarth M, Kesch C, et al. Combined clinical parameters and multiparametric magnetic resonance imaging for advanced risk modeling of prostate cancer-patient-tailored risk stratification can reduce unnecessary biopsies. Eur Urol 2017;72:888–96.

Please cite this article in press as: Drost F-JH, et al. Prostate Magnetic Resonance Imaging, with or Without Magnetic Resonance Imaging-targeted Biopsy, and Systematic Biopsy for Detecting Prostate Cancer: A Cochrane Systematic Review and Meta-analysis. Eur Urol (2019), https://doi.org/10.1016/j.eururo.2019.06.023

Comparison of Magnetic Resonance Imaging and Transrectal Ultrasound Informed Prostate Biopsy for Prostate Cancer Diagnosis in Biopsy Naïve Men: A Systematic Review and Meta-Analysis

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Purpose: Multiparametric magnetic resonance imaging with informed targeted biopsies has changed the paradigm of prostate cancer diagnosis. Randomized studies have demonstrated a diagnostic benefit of clinical significance for targeted biopsy compared to standard systematic biopsies. We evaluated whether multiparametric magnetic resonance imaging informed targeted biopsy has superior diagnosis rates of any, clinically significant, high grade and clinically insignificant prostate cancer compared to systematic biopsy in biopsy naïve men.

Materials and Methods: Data were searched in Medline®, Embase®, Web of Science and Evidence-Based Medicine Reviews-Cochrane Database of Systematic Reviews from database inception until 2019. Studies were selected by 2 authors independently, with disagreements resolved by consensus with a third author. Overall 1,951 unique references were identified and 100 manuscripts underwent full-text review. Data were pooled using random effects models. The meta-analysis is reported according to the PRISMA statement and the study protocol is registered with PROSPERO (CRD42019128468).

Results: Overall 29 studies (13,845 patients) were analyzed. Compared to systematic biopsy, use of multiparametric magnetic resonance imaging informed targeted biopsy was associated with a 15% higher rate of any prostate cancer diagnosis (95% CI 10–20, p <0.00001). This relationship was not affected by the study methodology (p=0.11). Diagnoses of clinically significant and high grade prostate cancer were more common in the multiparametric magnetic resonance imaging informed targeted biopsy group (risk difference 11%, 95% CI 0–20, p=0.05 and 2%, 95% CI 1–4, p=0.005, respectively) while there was no difference in diagnosis of clinically insignificant prostate cancer (risk difference 0, 95% CI -3 to 3, p=0.96). Notably, the exclusion of systematic biopsy in the multiparametric magnetic resonance imaging informed targeted biopsy arm significantly modified the association between a multiparametric magnetic resonance imaging strategy and lower rates of clinically insignificant prostate cancer diagnosis (p=0.01) without affecting the diagnosis rates of clinically significant or high grade prostate cancer.

Conclusions: Compared to systematic biopsy a multiparametric magnetic resonance imaging informed targeted biopsy strategy results in a significantly higher

Abbreviations and Acronyms

CI = clinically insignificant
CS = clinically significant
GGG = Gleason Grade Group
HG = high grade
mpMRI = multiparametric magnetic resonance imaging
MRI = magnetic resonance imaging
PB = prostate biopsy
PCa = prostate cancer
RP = radical prostatectomy
SBX = systematic biopsy
TGBX = targeted biopsy
TRUS = transrectal ultrasound

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diagnosis rate of any, clinically significant and high grade prostate cancer. Excluding systematic biopsy from multiparametric magnetic resonance imaging informed targeted biopsy was associated with decreased rates of clinically insignificant prostate cancer diagnosis without affecting diagnosis of clinically significant or high grade prostate cancer.

Key Words: multiparametric magnetic resonance imaging, prostatic neoplasms, biopsy

PROSTATE cancer diagnosis by systematic, random, histological sampling of the prostate has, until recently, been the standard of care.[1] Transrectal ultrasound guided 12-core template systematic biopsy has been widely recommended for men at risk for PCa.[2] However, SBX templates are limited by inherent random and systematic errors. Specific regions of the prostate are consistently under sampled, including the anterior region and apex[3] and, unless hypoechoic lesions are seen on TRUS, sampling occurs by chance. Thus, SBX can miss up to 20% of CS PCa, resulting in under diagnosis.[4] Additionally, SBX detects a relatively high percentage of clinically insignificant PCa (GGG 1), which may result in overtreatment if proper use of active surveillance is not practiced.[2]

With the introduction of multiparametric prostate magnetic resonance imaging the pathways for PCa diagnosis have changed. mpMRI is unique in that it can risk stratify men for prostate biopsy and allow anatomical guidance for biopsy. The spatial information provided by mpMRI allows for precise mpMRI informed targeted biopsy, where clinically significant PCa (GGG 2 or greater[5]) is detected with fewer biopsy cores[6] and diagnosis of CI PCa decreases.[7] Randomized studies have demonstrated the superior diagnosis rate of TGBX in diagnosing CS PCa in biopsy naïve men.[8,9] However, TGBX has limitations, missing CS PCa in 2.1% to 15% of cases.[10–13] Although the most recent European Association of Urology[2] and National Institute for Health and Care Excellence[14] guidelines recommend performing mpMRI in biopsy naïve men with suspected PCa, these recommendations are not widely adopted in North America, where mpMRI is usually reserved for men with a previous negative biopsy. Furthermore, the added benefit of combining SBX with TGBX remains unclear with conflicting data supporting TGBX alone[7,15] as well as combining SBX with TGBX.[16] The combination appears to detect more CS PCa than TGBX alone.[4,7] The European Association of Urology and American Urological Association guidelines currently recommend adding SBX in men with a suspicious mpMRI lesion undergoing TGBX.[2,17]

To synthesize the available data on these questions we undertook a systematic review and meta-analysis of all studies comparing SBX and TGBX, alone or in combination with SBX, to assess the detection rate of any PCa, CS PCa, high grade PCa (GGG 4 or greater) and CI PCa in biopsy naïve men.

METHODS

This systematic review and meta-analysis is reported according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[18] The study protocol was registered with PROSPERO CRD42019128468.

Research Question

Is mpMRI informed TGBX with or without SBX associated with higher rates of any, CI, CS and HG PCa diagnosis than SBX alone in biopsy naïve men at risk for PCa?

Types of Studies

Randomized clinical trials and observational cohort studies were included. Other publications including editorials, commentaries, review articles, meeting abstracts and publications not subject to peer review (ie reports of data from vital statistics and dissertations or theses) were excluded. Only studies with paired cohorts, with patients with a positive mpMRI undergoing TGBX alone or together with SBX were included. To prevent duplication of patients used in our analyses we selected 1 study (when more than 1 was published on the same patient cohort) based on contemporary timing, cohort size and granularity of data reported. Our main interest was to compare the outcomes of mpMRI informed TGBX alone or in combination with SBX to SBX outcomes in biopsy naïve men. Thus, studies comparing mpMRI guided TGBX and SBX in biopsy naïve men were included and those in men with prior negative biopsy or with prior PCa diagnosis were excluded from analysis.

Outcome Measures

The primary outcome of interest was the rate of any PCa diagnosis. Secondary outcomes were rates of CS PCa (GGG 2 or greater), HG PCa (GGG 4 or greater) and CI PCa (GGG 1).

Search Strategy

Medline, Embase, Web of Science, Scopus® and Evidence-Based Medicine Reviews-Cochrane Database of Systematic Reviews databases were searched by a professional medical librarian using the OvidSP platform for studies indexed from database inception to February 15, 2019. We used subject headings and text word terms for "prostate cancer", "prostate neoplasm", "biopsy", "no prior", "no previous", "naïve", "ultrasound", "magnetic resonance imaging", "systematic", "targeted" and related and exploded terms including MeSH (medical subject headings) terms in combination with keyword searching. A full search strategy is presented in supplementary Appendix 1

(https://www.jurology.com). Only English language publications were included in analysis and all duplicates were excluded.

Study Review Methodology

The study selection was conducted by 2 authors (AEA and TC) independently. Disagreements were resolved by consensus with a third author (HG). Titles and abstracts were used to screen for initial study inclusion. Full-text review was used when abstracts were insufficient to determine if the study met inclusion criteria. A data extraction form was created and piloted prior data extraction, which was performed by a single author (AEA) and subsequently verified by 2 additional authors (HG and ZK) independently.

Risk of Bias Assessment

The Cochrane Collaboration tool for assessing risk of bias[19] and the NOS (Newcastle-Ottawa Scale) were used for risk of bias assessment in randomized clinical trials and cohort studies, respectively. The NOS assesses risk of bias in the domains of 1) selection of study groups, 2) comparability of groups and 3) ascertainment of exposure and outcome.[20,21] Studies with scores of 7 or greater were considered as having a low risk of bias, scores of 4 to 6 as having a moderate risk of bias, and scores less than 4 as having a high risk of bias.

Assessment of Heterogeneity

Heterogeneity was assessed using the Q test, estimated using the DerSimonian-Laird method and finally quantified using I^2 values.[22] Given the identified clinical heterogeneity, we used random effects models for each of our analyses.

Data Synthesis

We expressed the outcome as the risk difference for PCa diagnosis between mpMRI informed TGBX and SBX. This was determined as the proportion of patients diagnosed with PCa in the SBX group minus the proportion of patients diagnosed in the mpMRI informed TGBX group. Therefore, a risk difference less than zero (negative risk difference) indicates that PCa diagnosis was more frequent in the mpMRI informed TGBX group while a risk difference greater than zero (positive risk difference) indicates that PCa diagnosis was more frequent in the SBX group.

We used the Mantel-Haenszel method for meta-analysis of dichotomous data using the risk difference as our measure of effect. For each outcome we performed meta-analysis among 3 strata defined by study methodology (randomized controlled trials, prospective cohort studies and retrospective cohort studies) as differences in study methodology may reasonably be expected to affect study conclusions. We tested for subgroup differences between strata for each outcome using the chi-squared test. Where the chi-squared test for subgroup differences was insignificant, we pooled results for each outcome across the study methodologies to provide a single pooled effect estimate. Where the chi-squared test for subgroup differences was significant ($p < 0.05$) we deemed it inappropriate to pool results and, thus, reported pooled results among each stratum individually.

We performed a priori subgroup analysis to assess whether inclusion of SBX in the mpMRI informed TGBX arm would affect the risk difference for PCa diagnosis between mpMRI informed TGBX and SBX for each outcome. Again, we tested for subgroup differences between strata for each outcome using the chi-squared test to assess for effect modification due to this factor.

Meta-analysis was performed using Review Manager 5.3 (Copenhagen: The Nordic Cochrane Centre, The Cochrane Collaboration 2014) software. Statistical significance was determined at $p < 0.05$.

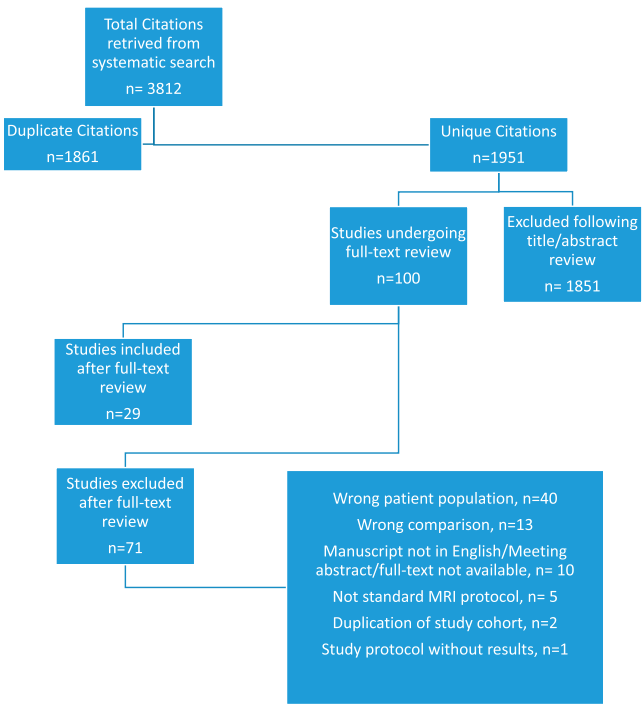
RESULTS

Literature Search Results

We identified 1,951 unique references (see figure). Overall 100 manuscripts underwent full-text review and 29 studies were selected for final analyses. Reasons for exclusion are provided in the figure. Of these studies 19 (65.5%) enrolled patients prospectively. However, only 5 studies (17.2%) randomly assigned patients to the mpMRI informed TGBX or SBX group. Publication details of all included studies can be found in supplementary Appendix 2 (https://www.jurology.com).

Characteristics of Identified Studies

Studies were conducted in 4 continents (65.5% in Europe, 20.7% in Asia, 6.9% in the U.S. and 6.9% in Australia) and 89.7% were conducted after 2010 (supplementary table, https://www.jurology.com). Overall 21 studies (72.5%) were from single centers,



PRISMA flow chart

3 studies (10.3%) analyzed 2 centers and 5 studies (17.2%) were multicenter.

Across the 29 included studies there were 13,845 patients, of whom 1,085 (7.8%) were enrolled in randomized trials. Nearly all studies included men based on an elevated prostate specific antigen and/or an abnormal digital rectal examination (supplementary table, https://www.jurology.com).

With respect to MRI performance and interpretation 21 studies (72.4%) used 3 Tesla mpMRI and 8 (27.6%) used 1.5 Tesla. PI-RADS (Prostate Imaging Reporting and Data System) was used in most studies (21, 72.4%), while 7 studies (24.1%) used the Likert and similar 4 or 5-point scales. A total of 14 studies (48.3%) included SBX in addition to mpMRI informed TGBX in the mpMRI arm. Targeted biopsy was performed with an ultrasound fusion biopsy technique in 18 studies (62.1%). Cognitive fusion biopsy and in-bore fusion biopsy were used in 8 (27.6%) and 2 studies (7%), respectively. Most studies (24, 82.7%) used transrectal biopsy.

All studies reported on overall PCa and CS PCa detection rate, defined based on Gleason score and/or maximum PCa core length (supplementary table, https://www.jurology.com). However, for our analysis we considered CS PCa to be GGG 2 or greater alone.[5]

Risk of Bias Assessment

All randomized controlled trials included concealed random sequence generation and were similarly at low risk for attrition and reporting bias (supplementary Appendix 3, https://www.jurology.com). While all studies were unblinded and, thus, potentially at risk for performance and detection bias, it is not likely that this would influence the outcome of PCa diagnosis.

The risk of bias in the prospective and retrospective cohort studies was low in all included studies (supplementary Appendix 4, https://www.jurology.com). In some studies patients with negative mpMRI were excluded, which may have potentially introduced selection bias. As the outcome of interest was overall PCa or CS PCa diagnosis rate, all studies were deemed to have adequate followup.

Quantitative Synthesis

Any prostate cancer diagnosis. Assessing the association between use of mpMRI informed TGBX or SBX and rates of any PCa diagnosis, we pooled results from 29 studies representing 31 unique patient cohorts and 13,845 participants. Among randomized controlled trials (5 studies; 1,085 participants) the use of mpMRI informed TGBX ± SBX was associated with a 16% increased likelihood of PCa diagnosis (risk difference -0.16, 95% CI -0.22 to -0.11, $p < 0.00001$, $I^2 = 4\%$) compared to SBX alone (supplementary fig. 1, *a*; https://www.jurology.com). Among 14 prospective cohort studies (5,508 participants) the use of mpMRI informed TGBX ± SBX was associated with a 20% increased likelihood of PCa diagnosis (risk difference -0.20, 95% CI -0.27 to -0.12, $p < 0.00001$, $I^2 = 89\%$) compared to SBX alone. Finally, among 10 retrospective cohort studies (7,252 participants) the use of mpMRI informed TGBX ± SBX was associated with a 9% increased likelihood of PCa diagnosis (risk difference -0.09, 95% CI -0.16 to -0.01, $p = 0.03$, $I^2 = 89\%$) compared to SBX alone. The test for subgroup differences was insignificant (chi-squared 4.40, $p = 0.11$, $I^2 = 54.5\%$). Thus, we pooled results across these strata. Assessing all 13,845 participants from 29 studies the use of mpMRI informed TGBX ± SBX was associated with a 15% increased likelihood of PCa diagnosis (risk difference -0.15, 95% CI -0.20 to -0.10, $p < 0.00001$, $I^2 = 89\%$) compared to SBX alone.

We then assessed whether inclusion of SBX in the mpMRI informed TGBX arm affected the observed association between mpMRI informed TGBX and any PCa diagnosis. Among cohorts in which data were available for patients in the mpMRI informed TGBX arm who underwent targeted biopsy alone (22 studies, 75.9%), the use of mpMRI informed TGBX was associated with a 12% increased likelihood of PCa diagnosis (risk difference -0.12, 95% CI -0.18 to -0.07, $p < 0.00001$, $I^2 = 89\%$) compared to SBX alone (supplementary fig. 2, *a*; https://www.jurology.com). For cohorts in which data were available for patients who underwent TGBX and SBX (14 studies, 48.3%) the use of mpMRI informed TGBX was associated with a 17% increased likelihood of PCa diagnosis (risk difference -0.17, 95% CI -0.24 to -0.09, $p < 0.00001$, $I^2 = 91\%$) compared to SBX alone. The test for subgroup differences was insignificant (chi-squared 0.78, $p = 0.38$, $I^2 = 0\%$), suggesting that the inclusion of SBX in patients undergoing mpMRI informed TGBX does not modify the association between mpMRI informed TGBX and rates of any PCa diagnosis.

Clinically significant prostate cancer diagnosis. A total of 27 studies (13,089 participants) provided data for meta-analysis of the outcome of CS PCa. There was an increased likelihood of CS PCa diagnosis among randomized controlled trials (risk difference -0.11, 95% CI -0.2 to 0.00, $p = 0.05$, $I^2 = 78\%$), among prospective cohort studies (risk difference -0.18, 95% CI -0.24 to -0.11, $p < 0.00001$, $I^2 = 81\%$) and among retrospective cohort studies (risk difference -0.07, 95% CI -0.12 to -0.02, $p = 0.004$, $I^2 = 77\%$) (supplementary fig. 1, *b*; https://www.jurology.com). However, the test for subgroup differences

was significant (chi-squared 6.35, p=0.04, I^2=68.5%). Thus, we did not pool results across strata of study methodology. We found no evidence of effect modification due to inclusion of SBX in the mpMRI informed TGBX arm on the relationship between mpMRI informed TGBX and rates of CS PCa diagnosis (test for subgroup differences chi-squared 0.18, p=0.67, I^2=0%) (supplementary fig. 2, *b*; https://www.jurology.com).

Clinically insignificant prostate cancer diagnosis. Similarly, 27 studies (13,089 participants) provided data for meta-analysis of the outcome of CI PCa. The use of mpMRI informed TGBX ± SBX was associated with no meaningful difference in the likelihood of CI PCa diagnosis, whether assessed among randomized controlled trials (risk difference 0.01, 95% CI -0.09 to 0.11, p=0.85, I^2=82%), prospective cohort studies (risk difference 0.00, 95% CI -0.05 to 0.05, p=0.99, I^2=79%) or retrospective cohort studies (risk difference -0.01, 95% CI -0.05 to 0.04, p=0.83, I =84%) (supplementary fig. 1, *c*; https://www.jurology.com). The test for subgroup differences was insignificant (chi-squared 0.08, p=0.96, I^2=0%). Thus, we pooled results across strata of study methodology and found no meaningful difference in the likelihood of CI PCa diagnosis (risk difference 0.00, 95% CI -0.03 to 0.03, p=0.96, I^2=80%).

Interestingly there was evidence of effect modification due to the inclusion of SBX in the mpMRI informed TGBX arm for this outcome (test for subgroup differences chi-squared 6.49, p=0.01, I^2=84.6%), while studies that included SBX in the mpMRI informed TGBX arm demonstrated a 4% higher rate of diagnosis of CI PCa among patients who underwent mpMRI informed TGBX+SBX compared to SBX alone (risk difference -0.04, 95% CI -0.08 to -0.00, p=0.05, I^2=77%). Using TGBX alone demonstrated a 3% lower rate of diagnosis of CI PCa among patients who underwent mpMRI informed TGBX compared to SBX alone (risk difference 0.03, 95% CI -0.01 to 0.06, p=0.11, I^2=75%) (supplementary fig. 2, *c*; https://www.jurology.com).

High grade prostate cancer diagnosis. A smaller subset of 19 studies (9,811 participants) provided data for meta-analysis of the outcome of HG PCa. The use of mpMRI informed TGBX ± SBX was associated with a significantly higher likelihood of HG PCa diagnosis among randomized controlled trials, albeit with a small effect size (risk difference -0.04, 95% CI -0.07 to -0.01, p=0.004, I^2=0%) compared to SBX alone (supplementary fig. 1, *d*; https://www.jurology.com). Among prospective cohort studies (risk difference -0.02, 95% CI -0.05 to 0.01, p=0.23, I^2=66%) and retrospective cohort studies (risk difference -0.02, 95% CI -0.06 to 0.01, p=0.12, I^2=38%) this effect was not significant, although the direction and magnitude were similar. The test for subgroup differences was insignificant (chi-squared 1.72, p=0.42, I^2=0%). Thus, we pooled results across strata of study methodology and found the use of mpMRI informed TGBX was associated with a small but significantly higher likelihood of HG PCa diagnosis (risk difference -0.02, 95% CI -0.04 to -0.01, p=0.005, I^2=47%) than SBX alone. We found no evidence of effect modification due to inclusion of SBX in the mpMRI informed TGBX arm on the relationship between mpMRI informed TGBX and rates of HG PCa diagnosis (test for subgroup differences chi-squared 0.40, p=0.53, I^2=0%) (supplementary fig. 2, *d*; https://www.jurology.com).

DISCUSSION

In this meta-analysis of biopsy naïve patients undergoing PB we compared rates of PCa diagnosis for those undergoing standard SBX and mpMRI informed TGBX. Our analyses demonstrate several findings. Patients who underwent a mpMRI informed TGBX ± SBX were 15% more likely to be diagnosed with any PCa than those who underwent standard SBX. Further, this improved diagnostic yield was not affected by whether a mpMRI informed biopsy was performed with TGBX alone or combined with SBX. In addition, patients who underwent mpMRI informed biopsy were more likely to be diagnosed with CS PCa and HG PCa, with no difference in the diagnosis rate of CI PCa compared to those who underwent SBX alone. The exclusion of SBX in the mpMRI informed TGBX arm was associated with decreased rates of CI PCa diagnosis (p=0.01) without meaningfully affecting diagnosis rates of any, CS or HG PCa.

Standard TRUS guided SBX remains the most common technique used worldwide in biopsy naïve patients deemed to warrant PB. While affected by characteristics of the population under study, PCa detection rates are approximately 40% to 45% for SBX.[23] Nevertheless, TRUS-SBX harbors low sensitivity and specificity in the diagnosis of PCa.[12] Repeat biopsy identifies PCa in 10% to 25% of men with an initially negative biopsy.[24] Furthermore, TRUS-SBX underestimates tumor grade in 36% of men compared to radical prostatectomy.[25] With the advent of mpMRI the sensitivity of PCa imaging has improved.[26] Previous meta-analyses have shown that mpMRI informed TGBX detects more CS PCA, with fewer cores than used in TRUS guided SBX.[13]

More than 70% of studies included in this analysis used 3 Tesla mpMRI and incorporated PI-RADS for interpretation of imaging. However, similar results were seen in studies using 1.5 Tesla mpMRI and other reporting systems such as the Likert scale. Included studies used numerous strategies for TGBX including ultrasound, cognitive and in-bore fusion biopsies, all of which have demonstrated an increased detection rate of CS PCa compared to SBX.[27–29] Presently there is no consensus on which strategy is superior.

We identified a higher rate of CS PCa diagnosed with mpMRI informed biopsy compared to SBX, ranging from 7% to 18%, with an 11% higher diagnostic rate among randomized controlled trials. This finding is on par with results of prior meta-analyses.[11–13,30] Uniquely, this analysis demonstrated that mpMRI informed biopsy identified higher rates of HG PCa.

More actionably, exclusion of SBX in the mpMRI informed TGBX arm significantly modified the association between mpMRI and CI PCa diagnosis ($p=0.01$), without meaningfully affecting diagnostic rates of CS or HG PCa. Thus, in contrast to the common hypothesis that the combination of TGBX+SBX yields a higher diagnosis rate of any and CS PCa,[31] these data suggest that SBX may be safely omitted in men undergoing mpMRI guided biopsy. This approach would be expected to decrease the over detection of clinically indolent PCa. Further, using TGBX only, a lower number of biopsy cores are required to reach a diagnosis, leading to less discomfort and morbidity.[32,33] Lastly, emerging data suggest that a decreased number of biopsy cores can lead to less blood loss during RP.[34]

This analysis strengthens the body of evidence supporting mpMRI as a risk stratification tool in biopsy naïve men, showing that a positive mpMRI can lead to a higher detection rate of CS PCa. Our study adds to the current knowledge and supports other recently published meta-analyses demonstrating that TGBX has a clear benefit over SBX alone in the diagnosis of CS PCa.[30,35–37] More than a million men in the United States undergo TRUS guided SBX each year,[38] at a cost of nearly $1 billion, with less than 10% of the 12 million biopsy core samples demonstrating cancer. According to the PROMIS study approximately 25% of the biopsies (250,000) could be avoided in patients with a negative pre-biopsy mpMRI.[39] However, for patients with a positive mpMRI our study shows that there could be a decrease from a 12-core biopsy to only a 4-core biopsy (provided there is only 1 mpMRI targeted lesion), resulting in a reduction of 8 million cores processed per year. This supports the concept of a mpMRI first strategy in biopsy naïve men as an effective and cost-effective approach for the diagnosis of CS PCa.[40] However, we must not forget that if a mpMRI first strategy in biopsy naïve men is adopted, the cost of mpMRI must be taken into consideration when analyzing the cost-effectiveness of this entire approach. Taken together, the added benefit of SBX is shown to be questionable in the setting of biopsy naïve men suspected to have PCa, and its role must be reconsidered, possibly omitted, as recommended in men with a previous negative biopsy.[2]

No difference was noted in the diagnosis rate of CI PCa between mpMRI informed biopsy and SBX. In contrast, 3 prior meta-analyses demonstrated a lower rate of CI PCa diagnosis with TGBX vs SBX,[11,12,30] while Valerio et al showed that most studies demonstrated a higher rate of CI PCa in the mpMRI informed biopsy pathology.[13] As previously discussed this may be affected using SBX in the TGBX group. In our meta-analysis TGBX alone or combined with SBX demonstrated an equal rate of CS PCa diagnosis but TGBX alone resulted in a 4% reduction in CI PCa diagnosis. The definition of CI PCa varies among studies, ranging from the Epstein criteria[41] to the combination of maximal cancer core length less than 6 mm with GGG 1.[42] In our analysis we used the simplified definition of GGG 1 alone, which could explain some of the discrepancies between our analysis and others.

The strength of our analysis includes a comprehensive search strategy and actionable data due to the use of mpMRI protocols in accordance with the current recommended imaging guidelines. However, there are several limitations. The multiparametric MRI informed biopsy procedure lacked standardization. There was significant variability across the studies with regard to the interpretation of suspicious MRI lesions, the decision on when to biopsy, the method of TGBX, the number of cores taken and the different learning curve stages of the radiologists who interpreted the imaging. There was significant heterogeneity among many of the comparisons included in this review. We used random effects models to pool these studies as a result. This analysis focused on biopsy naïve men and these results may not be applicable to those with a previous negative biopsy. This analysis only applies to patients with a positive mpMRI. For patients with a negative mpMRI the current role of SBX remains controversial. Notably, previous analyses have demonstrated a CS PCa diagnosis rate of 12% on systematic biopsy of men with negative mpMRI,[43] making the role of SBX far from obsolete, especially with a negative mpMRI. SBX is still crucial in many settings and understanding when it is mandatory and when it is not is imperative. Furthermore, when considering management with

focal therapy, SBX might have a critical role of ruling out additional disease outside the target lesion. Importantly, aside from the changing radiologist learning curve in interpreting mpMRI, the ease of properly obtaining a mpMRI targeted biopsy around the world varies due to a multitude of considerations and, thus, the conclusion of this study may not be applicable worldwide. Lastly, there is a potential methodological error in assuming that one type of biopsy diagnoses more CS PCa than another based on the results of PB alone. Deciphering which strategy is better from a diagnostic perspective would involve analyzing the RP specimens of all patients who underwent TGBX or SBX and comparing the rate of CS PCa in the final specimen to the preoperative biopsy result. Indeed, a recently published study showed that TGBX can sample the highest grade of a dominant lesion and perhaps even a tertiary high score location.[44] This resulted in reporting a higher biopsy GGG and subsequent downgrading of the final pathological specimen following RP.

CONCLUSIONS

Based on a comprehensive, current meta-analysis a mpMRI informed TGBX strategy in men undergoing their first PB resulted in a significantly higher diagnosis rate of any, CS and HG PCa compared to SBX. Furthermore, exclusion of SBX for men undergoing mpMRI informed TGBX was associated with decreased rates of CI PCa diagnosis without affecting diagnosis rates of clinically significant or high grade PCa.

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REFERENCES

1. Hodge KK, McNeal JE, Terris MK et al: Random systematic versus directed ultrasound guided transrectal core biopsies of the prostate. J Urol 1989; **142:** 71.

2. Mottet N, Bellmunt J, Bolla M et al: EAU-ESTRO-SIOG guidelines on prostate cancer. Part 1: screening, diagnosis, and local treatment with curative intent. Eur Urol 2017; **71:** 618.

3. Kongnyuy M, Sidana A, George AK et al: The significance of anterior prostate lesions on multiparametric magnetic resonance imaging in African-American men. Urol Oncol 2016; **34:** 254.

4. Schouten MG, van der Leest M, Pokorny M et al: Why and where do we miss significant prostate cancer with multi-parametric magnetic resonance imaging followed by magnetic resonance-guided and transrectal ultrasound-guided biopsy in biopsy-naive men? Eur Urol 2017; **71:** 896.

5. Zhao C, Gao G, Fang D et al: The efficiency of multiparametric magnetic resonance imaging (mpMRI) using PI-RADS version 2 in the diagnosis of clinically significant prostate cancer. Clin Imaging 2016; **40:** 885.

6. Fütterer JJ, Briganti A, De Visschere P et al: Can clinically significant prostate cancer be detected with multiparametric magnetic resonance imaging? A systematic review of the literature. Eur Urol 2015; **68:** 1045.

7. Siddiqui MM, Rais-Bahrami S, Turkbey B et al: Comparison of MR/ultrasound fusion-guided biopsy with ultrasound-guided biopsy for the diagnosis of prostate cancer. JAMA 2015; **313:** 390.

8. Kasivisvanathan V, Rannikko AS, Borghi M et al: MRI-targeted or standard biopsy for prostate-cancer diagnosis. N Engl J Med 2018; **378:** 1767.

9. Porpiglia F, Manfredi M, Mele F et al: Diagnostic pathway with multiparametric magnetic resonance imaging versus standard pathway: results from a randomized prospective study in biopsy-naive patients with suspected prostate cancer. Eur Urol 2017; **72:** 282.

10. Borofsky S, George AK, Gaur S et al: What are we missing? False-negative cancers at multiparametric MR imaging of the prostate. Radiology 2018; **286:** 186.

11. Schoots IG, Roobol MJ, Nieboer D et al: Magnetic resonance imaging-targeted biopsy may enhance the diagnostic accuracy of significant prostate cancer detection compared to standard transrectal ultrasound-guided biopsy: a systematic review and meta-analysis. Eur Urol 2015; **68:** 438.

12. Wegelin O, van Melick HHE, Hooft L et al: Comparing three different techniques for magnetic resonance imaging-targeted prostate biopsies: a systematic review of in-bore versus magnetic resonance imaging-transrectal ultrasound fusion versus cognitive registration. Is there a preferred technique? Eur Urol 2017; **71:** 517.

13. Valerio M, Donaldson I, Emberton M et al: Detection of clinically significant prostate cancer using magnetic resonance imaging-ultrasound fusion targeted biopsy: a systematic review. Eur Urol 2015; **68:** 8.

14. Wise J: NICE recommends MRI for suspected prostate cancer to reduce biopsies. BMJ 2018; **363:** k5290.

15. Baco E, Rud E, Eri LM et al: A randomized controlled trial to assess and compare the outcomes of two-core prostate biopsy guided by fused magnetic resonance and transrectal ultrasound images and traditional 12-core systematic biopsy. Eur Urol 2016; **69:** 149.

16. Rosenkrantz AB, Verma S, Choyke P et al: Prostate magnetic resonance imaging and magnetic resonance imaging targeted biopsy in patients with a prior negative biopsy: a consensus statement by AUA and SAR. J Urol 2016; **196:** 1613.

17. Fulgham PF, Rukstalis DB, Turkbey IB et al: AUA policy statement on the use of multiparametric magnetic resonance imaging in the diagnosis, staging and management of prostate cancer. J Urol 2017; **198:** 832.

18. Moher D, Liberati A, Tetzlaff J et al: Preferred reporting items for systematic reviews and meta-analyses: the PRISMA statement. J Clin Epidemiol 2009; **62:** 1006.

19. Higgins JPT, Altman DG, Gøtzsche PC et al: The Cochrane Collaboration's tool for assessing risk of bias in randomised trials. BMJ 2011; **343:** d5928.

20. Deeks JJ, Dinnes J, D'Amico R et al: Evaluating non-randomised intervention studies. Health Technol Assess 2003; **7:** iii.

21. Wells GA, Shea B, O'Connell D et al: The Newcastle-Ottawa Scale (NOS) for Assessing the Quality of Nonrandomised Studies in Meta-analyses. Ottawa, Ontario: Ottawa Hospital Research Institute; 2019. Available at http://www.ohri.ca/programs/clinical_epidemiology/oxford.asp. Accessed March 24, 2019.

22. Higgins JP, Thompson SG, Deeks JJ et al: Measuring inconsistency in meta-analyses. BMJ 2003; **327:** 557.

23. Lane BR, Zippe CD, Abouassaly R et al: Saturation technique does not decrease cancer detection during followup after initial prostate biopsy. J Urol 2008; **179:** 1746.

24. Welch HG, Fisher ES, Gottlieb DJ et al: Detection of prostate cancer via biopsy in the Medicare-SEER population during the PSA era. J Natl Cancer Inst 2007; **99:** 1395.

25. Epstein JI, Feng Z, Trock BJ et al: Upgrading and downgrading of prostate cancer from biopsy to radical prostatectomy: incidence and predictive factors using the modified Gleason grading system and factoring in tertiary grades. Eur Urol 2012; **61:** 1019.

26. Wu LM, Xu JR, Gu HY et al: Usefulness of diffusion-weighted magnetic resonance imaging in the diagnosis of prostate cancer. Acad Radiol 2012; **19:** 1215.

27. Pinto PA, Chung PH, Rastinehad AR et al: Magnetic resonance imaging/ultrasound fusion guided prostate biopsy improves cancer detection following transrectal ultrasound biopsy and correlates with multiparametric magnetic resonance imaging. J Urol 2011; **186:** 1281.

28. Moore CM, Robertson NL, Arsanious N et al: Image-guided prostate biopsy using magnetic resonance imaging-derived targets: a systematic review. Eur Urol 2013; **63:** 125.

29. Hoeks CM, Schouten MG, Bomers JG et al: Three-tesla magnetic resonance-guided prostate biopsy in men with increased prostate-specific antigen and repeated, negative, random, systematic, transrectal ultrasound biopsies: detection of clinically significant prostate cancers. Eur Urol 2012; **62:** 902.

30. Kasivisvanathan V, Stabile A, Neves JB et al: Magnetic resonance imaging-targeted biopsy versus systematic biopsy in the detection of prostate cancer: a systematic review and meta-analysis. Eur Urol 2019; **76:** 284.

31. Mannaerts CK, Kajtazovic A, Lodeizen OAP et al: The added value of systematic biopsy in men with suspicion of prostate cancer undergoing multiparametric MRI-targeted biopsy. Urol Oncol 2019; **37:** 298.

32. Pepe P and Aragona F: Morbidity after transperineal prostate biopsy in 3000 patients undergoing 12 vs 18 vs more than 24 needle cores. Urology 2013; **81:** 1142.

33. Simsir A, Kismali E, Mammadov R et al: Is it possible to predict sepsis, the most serious complication in prostate biopsy? Urol Int 2010; **84:** 395.

34. Carneiro A, Sivaraman A, Sanchez-Salas R et al: Higher number of transrectal ultrasound guided prostate biopsy cores is associated with higher blood loss and perioperative complications in robot assisted radical prostatectomy. Actas Urol Esp 2017; **41:** 155.

35. Elwenspoek MMC, Sheppard AL, McInnes MDF et al: Comparison of multiparametric magnetic resonance imaging and targeted biopsy with systematic biopsy alone for the diagnosis of prostate cancer: a systematic review and meta-analysis. JAMA Netw Open 2019; **2:** e198427.

36. Drost FH, Osses D, Nieboer D et al: Prostate magnetic resonance imaging, with or without magnetic resonance imaging-targeted biopsy, and systematic biopsy for detecting prostate cancer: a Cochrane systematic review and meta-analysis. Eur Urol 2019; doi: 10.1016/j.eururo.2019.06.023.

37. Woo S, Suh CH, Eastham JA et al: Comparison of magnetic resonance imaging-stratified clinical pathways and systematic transrectal ultrasound-guided biopsy pathway for the detection of clinically significant prostate cancer: a systematic review and meta-analysis of randomized controlled trials. Eur Urol Oncol 2019; doi: 10.1016/j.euo.2019.05.004.

38. Loeb S, Vellekoop A, Ahmed HU et al: Systematic review of complications of prostate biopsy. Eur Urol 2013; **64:** 876.

39. 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:** 815.

40. Faria R, Soares MO, Spackman E et al: Optimising the diagnosis of prostate cancer in the era of multiparametric magnetic resonance imaging: a cost-effectiveness analysis based on the Prostate MR Imaging Study (PROMIS). Eur Urol 2018; **73:** 23.

41. Epstein JI, Walsh PC, Carmichael M et al: Pathologic and clinical findings to predict tumor extent of nonpalpable (stage T1c) prostate cancer. JAMA 1994; **271:** 368.

42. Rouvière 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:** 100.

43. Rouse P, Shaw G, Ahmed HU et al: Multiparametric magnetic resonance imaging to rule-in and rule-out clinically important prostate cancer in men at risk: a cohort study. Urol Int 2011; **87:** 49.

44. Beksac AT, Sobotka S, Xu P et al: Downgrading of grade group after radical prostatectomy: comparison of multiparametric magnetic resonance imaging guided fusion biopsy and standard 12-core biopsy. Urology 2019; **127:** 80.

EDITORIAL COMMENT

With the advent of MRI guided biopsy new debate has arisen regarding the value of MRI in the diagnosis of prostate cancer, specifically with its well recognized success in detecting clinically significant cancers, but finding the tipping point where imaging can aid in avoiding biopsy and the downstream workup in cases without clinically impactful cancer. As one of the leading causes of cancer related mortality among men, prostate cancer continues to be a public health concern warranting continued optimization in the diagnostic algorithm for the early, actionable diagnosis of clinically significant cases. Goldberg et al report a meta-analysis comparing the utility of MRI targeted biopsy to systematic biopsy not only in the overall diagnosis of prostate cancer, but specifically in diagnosing clinically significant and high grade cancers.

Their study revealed significantly higher rates of detecting clinically significant and high grade prostate cancers with the MRI targeted biopsy technique. Interestingly the meta-analysis supported that excluding the pathological findings from systematic biopsy sampling would not affect the overall rate of detecting clinically significant and high grade cancers while only potentially decreasing detection of lower grade cancers. This begs the question as to the public health impact of performing target-only biopsy in cases where MRI demonstrates areas of suspicion, particularly at experienced centers with internally

proven high negative predictive values of their imaging protocols.[1]

Targeted sampling in the absence of a concurrent systematic biopsy has been supported by a prospective randomized trial and should be recognized as an equally good or ideally improved technique to the standard of care that has been in practice for decades (reference 8 in article). For widespread adoption, particularly in the setting of biopsy naïve men, the added cost of MRI technology, training and programmatic development should be counterbalanced by optimized selection of patients for biopsy sampling without compromising oncologic outcomes in the long term.[2]

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REFERENCES

1. Pietryga JA and Rais-Bahrami S: Role of systematic biopsy in the era of multiparametric magnetic resonance imaging and ultrasound fusion guidance. BJU Int 2016; **118:** 181.

2. Truong M, Wang B, Gordetsky JB et al: Multi-institutional nomogram predicting benign prostate pathology on magnetic resonance/ultrasound fusion biopsy in men with a prior negative 12-core systematic biopsy. Cancer 2018; **124:** 278.

REPLY BY AUTHORS

We thank the editorial writers for their insightful thoughts on the evolving role of mpMRI in the prostate cancer diagnostic pathway. As with other studies, these data support the paradigm of image guided biopsy in PCa diagnosis, similar to current practice in other solid organ malignancies. Our meta-analysis showed that omitting systematic biopsy and performing only targeted biopsies did not confer a lower rate of clinically significant cancer diagnosis. However, the role of SBX remains unclear in 2 settings, namely patients with a negative mpMRI and in the pretreatment setting of focal therapy. While a 12% rate of CS PCa has been found in patients with a negative mpMRI, the role of systematic biopsy before focal therapy needs to be further assessed.[1]

There are also concerns about whether the results can be translated to nonacademic and low volume centers, where the level of operator dependency with targeted biopsy techniques is unknown. However, a particular strength of the PRECISION trial is its generalizability. As it was not limited to highly experienced operators, most participants had modest experience with mpMRI targeted biopsies and nonacademic centers were included (reference 8 in article). The required level of radiologist expertise in interpreting mpMRI results also remains a critical issue to be addressed before embarking on the pathway of image guided PCa biopsy.

Lastly, despite initial concerns regarding the potential additional cost of up front use of mpMRI, available data to date demonstrate this to be a cost-effective approach,[2] likely due to a lower number of initial and repeat biopsies, fewer cores taken, earlier detection of CS PCa and less insignificant cancer diagnosed.

REFERENCES

1. Rouse P, Shaw G, Ahmed HU et al: Multi-parametric magnetic resonance imaging to rule-in and rule-out clinically important prostate cancer in men at risk: a cohort study. Urol Int 2011; **87:** 49.

2. Pahwa S, Schiltz NK, Ponsky LE et al: Cost-effectiveness of MR imaging–guided strategies for detection of prostate cancer in biopsy-naive men. Radiology 2017; **285:** 157.

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EN TESTIMONIO DE ELLO OTORGA EL PRESENTE

DIPLOMA

EN LA CIUDAD DE Santafé de Bogotá, Julio 24 DE 1992

DUPLICADO: Resolución No. 91 de septiembre 7 de 1995, del Consejo Directivo.

DECANO DE LA FACULTAD

RECTOR DE LA UNIVERSIDAD

SECRETARIO DE LA FACULTAD

SECRETARIO GENERAL DE LA UNIVERSIDAD

SECRETARIA DEL MINISTERIO

PONTIFICIA UNIVERSIDAD JAVERIANA

FACULTAD DE MEDICINA

ACTA DE GRADO Nº SG— 4027

En la ciudad de Bogotá el día 19 del mes de septiembre de 2002 se llevó a cabo el acto de graduación, presidido por el Doctor Jairo H. Cifuentes Madrid Vicerrector Académico en el cual la Pontificia Universidad Javeriana, previo el juramento reglamentario, confirió el título de

ESPECIALISTA EN UROLOGIA ONCOLOGICA

a RODOLFO VARELA RAMIREZ

identificado (a) con c.c. Nº 79'244.111 de ---------- quien cumplió con los requisitos académicos, las exigencias establecidas en los Reglamentos y las normas legales; y le otorgó el Diploma Nº 2628 que lo (la) acredita como tal.

La Universidad está autorizada para conferir este título por las normas legales vigentes en Colombia.

En fe de lo anterior se firma la presente Acta de Grado, en Bogotá el 19 de septiembre de 2002

Firmada por

GERARDO REMOLINA V., S.J.	JAIME BERNAL E., S.J.	FRANCISCO HENAO P.
Rector	Secretario General	Decano

Es fiel copia tomada del original, en lo pertinente.

Santa Fe de Bogotá, D.C. 19 de septiembre de 2002

PONTIFICIA UNIVERSIDAD JAVERIANA · COLOMBIA ·

Secretario General

116539

THOMAS GREG & SONS

UNIVERSIDAD NACIONAL DE COLOMBIA

ACTA DE GRADO NÚMERO 102

EL CONSEJO DE LA FACULTAD DE Medicina
EN SU SESIÓN DEL DÍA 30 DE Marzo DE 2000 ACTA No. 9

CONSIDERANDO QUE:

Rodolfo Varela Ramirez
C.C. No. 79.244.111 de Suba (Bogotá D.E.)

CUMPLIÓ SATISFACTORIAMENTE TODOS LOS REQUISITOS EXIGIDOS POR LOS ACUERDOS Y REGLAMENTOS DE LA UNIVERSIDAD RESUELVE OTORGARLE EL TÍTULO DE:

Especialista en Urologia

EN NOMBRE Y REPRESENTACIÓN DE LA UNIVERSIDAD NACIONAL DE COLOMBIA Y DE LA REPÚBLICA DE COLOMBIA Y PREVIO EL JURAMENTO DE RIGOR, EL DECANO DE LA FACULTAD HIZO ENTREGA DEL DIPLOMA CORRESPONDIENTE REGISTRADO EN EL FOLIO No. 21 L.1

ACUERDO No.33A DE 1973 DEL CONSEJO SUPERIOR UNIVERSITARIO

EN TESTIMONIO DE LO ANTERIOR SE FIRMA LA PRESENTE ACTA DE GRADO EN LA CIUDAD DE Santafé de Bogotá D.C. A LOS 13 DIAS DEL MES DE Abril DE 2000

CONSEJO DE FACULTAD
Presidente

CONSEJO DE FACULTAD
Secretario

0010418

UNIVERSIDAD NACIONAL DE COLOMBIA

FACULTAD DE

Medicina

ACTA DE GRADO NUMERO 8014

EL CONSEJO DIRECTIVO DE LA FACULTAD DE Medicina

EN SU SESION DEL DIA 7 DE julio DE 1992

ACTA No. 23 CONSIDERANDO QUE :

Rodolfo Varela Ramírez

C.C. No. 79.244.111. Suba

CUMPLIO SATISFACTORIAMENTE TODOS LOS REQUISITOS EXIGIDOS POR LOS ACUERDOS Y REGLAMENTOS DE LA UNIVERSIDAD RESUELVE OTORGARLE EL TITULO DE :

Médico Cirujano

EN NOMBRE Y REPRESENTACION DE LA UNIVERSIDAD NACIONAL Y DE LA REPUBLICA DE COLOMBIA Y PREVIO EL JURAMENTO DE RIGOR, EL DECANO DE LA FACULTAD HIZO ENTREGA DEL DIPLOMA CORRESPONDIENTE REGISTRADO AL FOLIO No. 39 L-54 Ñ

ACUERDO NUMERO 156 DE 1980 - CONSEJO SUPERIOR UNIVERSITARIO

EN TESTIMONIO DE LO ANTERIOR SE FIRMA LA PRESENTE ACTA DE GRADO

EN LA CIUDAD DE Bogotá, A LOS 24 DIAS DEL MES DE Julio DE 1992

DUPLICADO: Resolución Nº 91 de sept. 7 de 1995, del Consejo Directivo.

PRESIDENTE DEL CONSEJO DIRECTIVO

SECRETARIO DEL CONSEJO DIRECTIVO

0046110

1. Si se puede descartar totalmente una patología maligna con niveles persistentemente elevados de antígeno prostático, a pesar de múltiplestratamientos con DUTASTERIDE y LEVAFLOXACINA, considerando el diagnóstico inicial de prostatitis crónica.

   R/ Cuando se tiene un PSA elevado siempre se debe pensar que se tiene que descartar la posibilidad de la presencia de un cáncer de próstata, sin importar que se está recibiendo algún tratamiento farmacológico (como dutasteride o levofloxacina). El dutasteride reduce el PSA aproximadamente al 50% y podría enmascarar un PSA anormal.

2. Si se puede descartar completamente un cáncer de próstata después de dos sets de biopsias, con antígenos prostáticos persistentemente elevados y síntomas urinarios persistentes en un paciente de 75 años, con re consultas frecuentes por persistencia de la sintomatología en los últimos cuatro años (2012 a 2015)?

   R/ No se puede descartar completamente un cáncer de próstata después de dos biopsias negativas, ni con PSA persistentemente elevados, ni en un paciente de 75 años, ni con sintomatología urinaria por cuatro años.

3. Por qué con una sola biopsia, realizada en la ciudad de BOGOTÁ se hace un diagnóstico inmediato y certero de Cáncer de Próstata, en cambio enVillavicencio a pesar de los dos sets de Biopsias y de múltiples consultas,exámenes de laboratorio, nunca se pudo establecer este diagnóstico?

   R/ No es una sola biopsia realizada en Bogotá, sino que es la tercera biopsia realizada, ya que se realizó después de dos biopsias de Villavicencio. Además se tenía una guía adicional que fue haber realizado una Resonancia Magnética de próstata para poder dirigir más adecuadamente las muestras de la biopsia que se va a realizar.

4. Si la RESONANCIA MAGNÉTICA NUCLEAR CONTRASTADA, PREVIO A LA BIOPSIA, jugo un papel importante en el diagnóstico patológico del cáncer de próstata diagnosticado.

   R/ La Resonancia Magnética de la próstata favoreció la ubicación de la toma de las biopsias de la próstata en la tercera biopsia efectuada en Bogotá y así tener una diagnóstico conclusivo de cáncer de próstata.

5. ¿Si se hubiera realizado la resonancia magnética nuclear contrastada en Villavicencio, se habría podido detectar la formación tumoral descrita en los exámenes practicados en BOGOTA?

R/ La biopsia se realiza mediante la visualización de la glándula prostática por medio de una ecografía. El mejor rendimiento y positividad de la biopsia de próstata es cuando se toma una Resonancia Magnética de próstata que logra identificar nódulos anormales en la próstata que son sugestivos de presencia de cáncer de próstata. El proceso de fusión real entre la Resonancia Magnética y la ecografía, que significa que se superponen las imágenes de la Resonancia con la imagen de la Ecografía, es el que permite la mejor detección de cáncer de la próstata, pero esta tecnología de fusión no está disponible en Villavicencio.

Con relación a las preguntas adicionales las respondo a continuación:

1. La identidad de quien rinde el dictamen y de quien participó en su elaboración.

   R/ Dictaamen realizado por el Dr RODOLFO VARELA, URÓLOGO ONCÓLOGO.

2. La dirección, el número de teléfono, número de identificación y los demás datos que faciliten la localización del perito.

   R/ Dirección: Cra 19 A No 82 – 85 Cons 704 edificio CMC
   Teléfono 3115321154
   CC: 79244111

3. La profesión, oficio, arte o actividad especial ejercida por quien rinde el dictamen y de quien participó en su elaboración. Deberán anexarse los documentos idóneos que lo habilitan para su ejercicio, los títulos académicos y los documentos que certifiquen la respectiva experiencia profesional, técnica o artística.

   R/ Profesión: Médico cirujano especializado en Urología Oncológica desde el año 2002

4. La lista de publicaciones, relacionadas con la materia del peritaje, que el perito haya realizado en los últimos diez (10) años, si las tuviere.

   R/ No tengo publicaciones mías relacionadas con la materia de peritaje

5. La lista de casos en los que haya sido designado como perito o en los que haya participado en la elaboración de un dictamen pericial en los últimos

cuatro (4) años. Dicha lista deberá incluir el juzgado o despacho en donde se presentó, el nombre de las partes, de los apoderados de las partes y la materia sobre la cual versó el dictamen.

R/ En un caso he participado en Enero 2020 , que fue el proceso con código interno VIEFM-003-06-03-2019, del Juzgado Sexto Administrativo Oral del Circuito de Villavicencio relacionado con el señor BRAYAN STIVEN CARDOZO OSORIO. EL caso estuvo relacionado con la extracción de un testículo, mediante cirugía, por haber presentado una torsión testicular.

6. Si ha sido designado en procesos anteriores o en curso por la misma parte o por el mismo apoderado de la parte, indicando el objeto del dictamen.

   R/ No he sido designado por la misma parte ni por el mismo apoderado.

7. Si se encuentra incurso en las causales contenidas en el artículo 50, en lo pertinente.

   R/ No tengo causales según el artículo 50

8. Declarar si los exámenes, métodos, experimentos e investigaciones efectuados son diferentes respecto de los que ha utilizado en peritajes rendidos en anteriores procesos que versen sobre las mismas materias. En caso de que sea diferente, deberá explicar la justificación de la variación.

   R/ No hay variación con respecto a los otros peritajes.

9. Declarar si los exámenes, métodos, experimentos e investigaciones efectuados son diferentes respecto de aquellos que utiliza en el ejercicio regular de su profesión u oficio. En caso de que sea diferente, deberá explicar la justificación de la variación.

   R/ No son diferentes a los usados en la práctica habitual

10. Relacionar y adjuntar los documentos e información utilizados para la elaboración del dictamen."

RV: Documento compartido contigo: "DICTAMEN PERICIAL ERNESTO ROMAN 2024.pdf.docx"

Juzgado 03 Administrativo - Meta - Villavicencio
<j03admvcio@cendoj.ramajudicial.gov.co>

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Para:Juzgado 03 Administrativo - Meta - Villavicencio <jadmin03vvc@notificacionesrj.gov.co>

De: Peritajes de Vicedecan... (vía Documentos de Google) <drive-shares-noreply@google.com>
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Para: Juzgado 03 Administrativo - Meta - Villavicencio <j03admvcio@cendoj.ramajudicial.gov.co>
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Abrir

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   R/ No son diferentes a los usados en la práctica habitual

10. Relacionar y adjuntar los documentos e información utilizados para la elaboración del dictamen."