(Non)-Sense du Dépistage Précoce du Cancer de la Prostate?

em. Prof. Dr. Hein Van Poppel
Urologie, KU Leuven, Belgium
Chairman Policy Office EAU

27-10-2022

Urologues
Région Verviers

Gilles V. Cauwenberghe

CHR VERVIERS
EAST BELGIUM

Amandine Croux

Baudouin Heinrichs

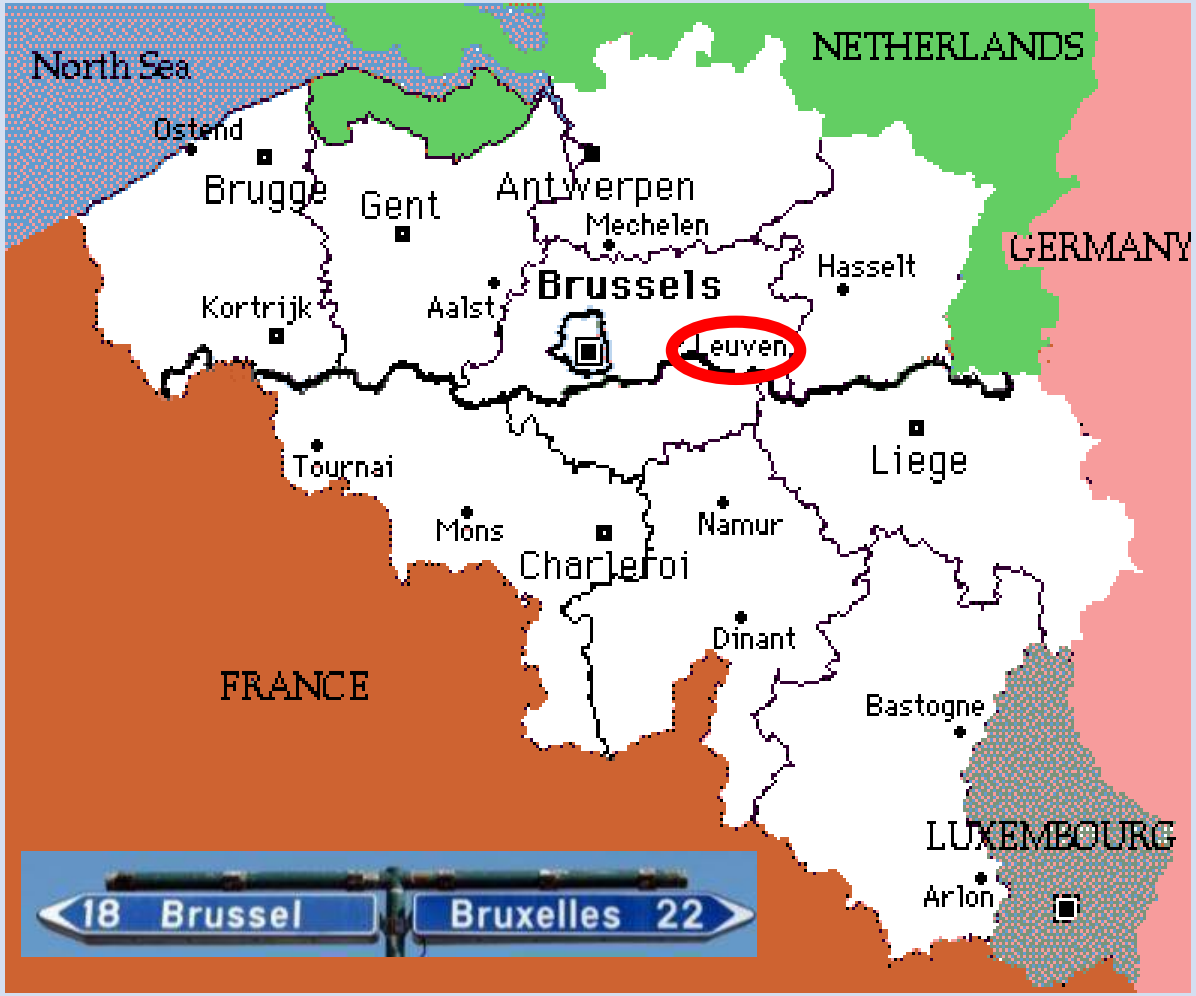
François Sohngen

- (Pierre Angenot +)
- Yves Gaspar
- Jean Paul Hans
- Hubert Nicolas
- …..?

European Association of Urology

België - Belgique - Belgien

België - Belgique - Belgien



Competition to become Capital of Brabant

Bruxelles

Leuven

Katholieke Universiteit Leuven (KU Leuven)

Founded 9-12-1425 by Pope Martin V

<u>on the initiative of Duke Jean IV of Brabant</u>

Retorica 1967

FNDP

1967-71

<u>Chirurgie Générale</u> Lacquet/Gruwez Kestens, Alexandre…

<u>Urologie</u> Verduyn, Vereecken, Baert Brenez, Hennebert, Van Cangh, Grégoire, Deleval, Schulman, Waltrégny, Roumeguère, Tombal…

Since 1970 two catholic universities

KU Leuven

38.000 Students
14% international
BMW 9400= 25%

UC Louvain

23.500 Students
17% international
BMW 6000= 25%

(Non)-Sense du Dépistage Précoce du Cancer de la Prostate?

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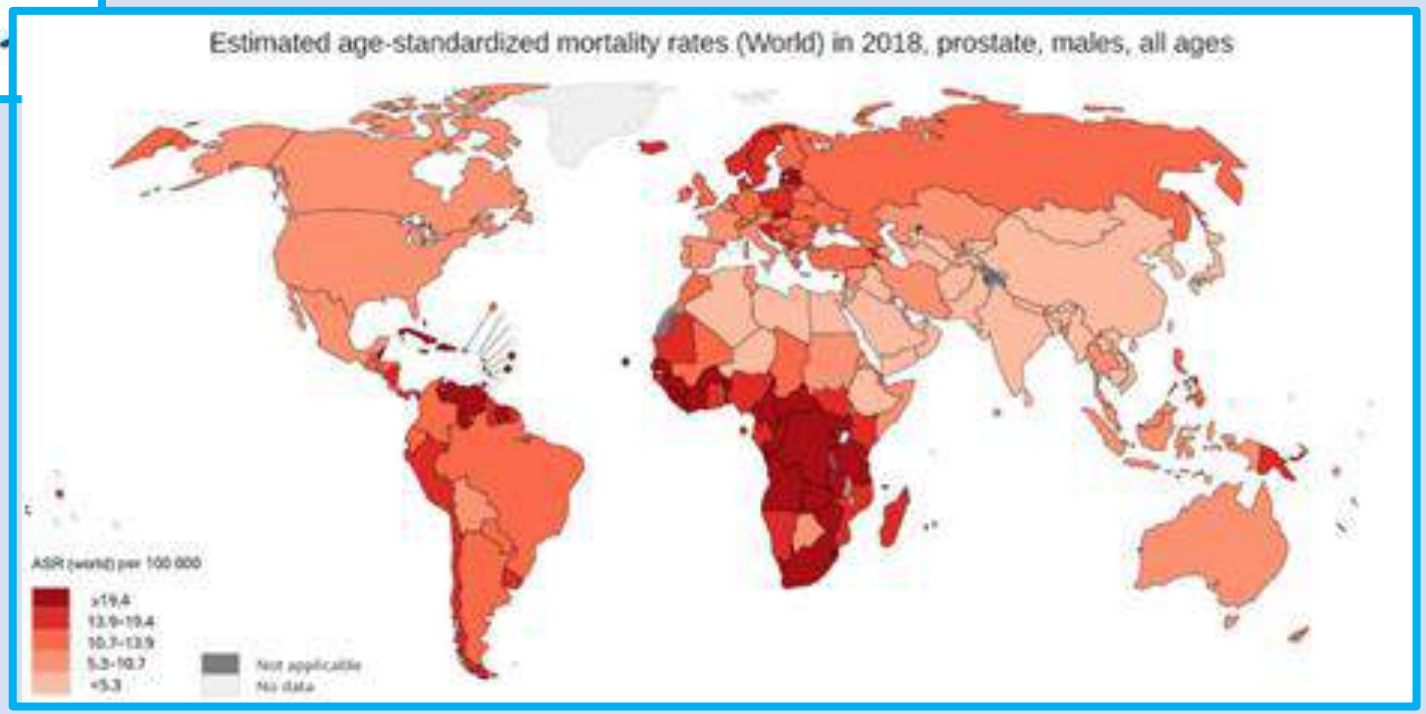
Cancer de prostate: Incidence et Mortalité

Incidence

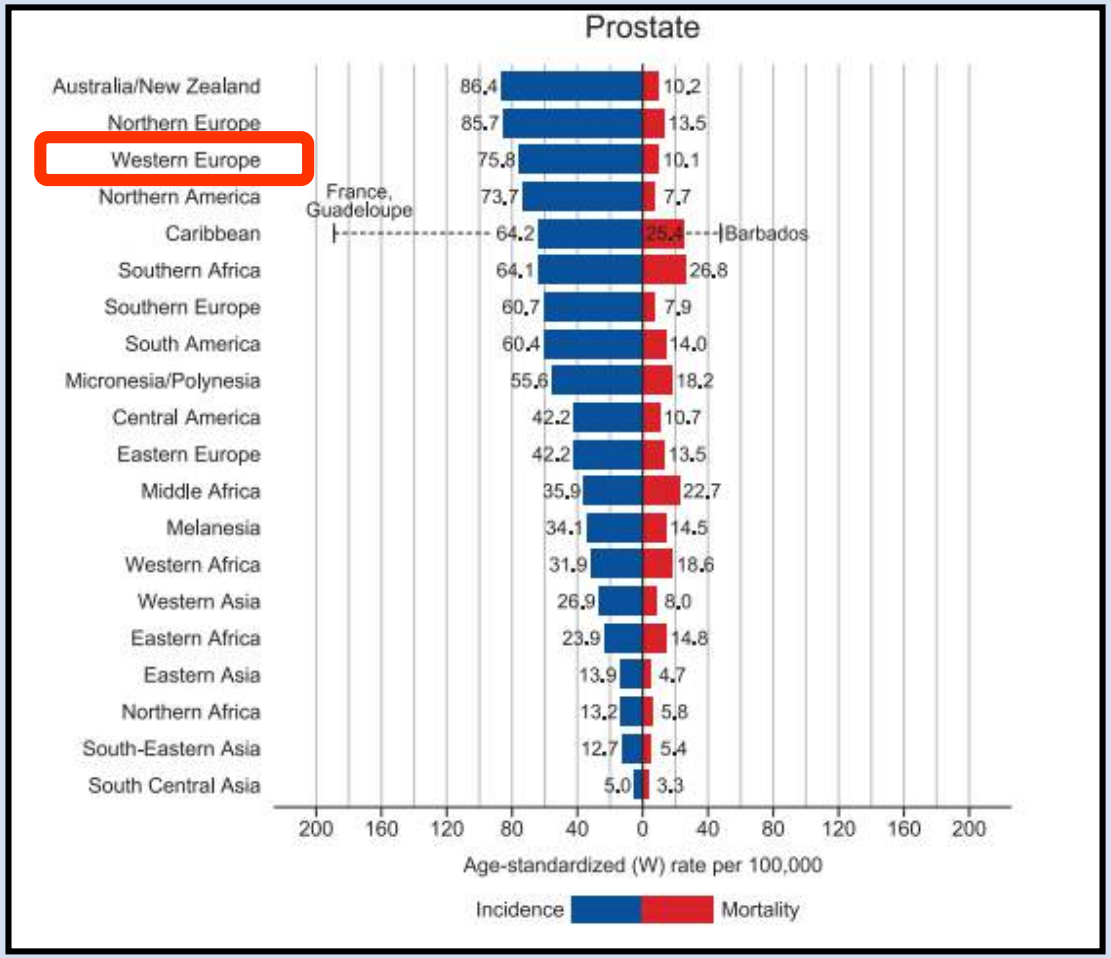
Mortalité



MBB Culp et al., Eur. Urol., 77, 38-52, 2020 (Globocan Database 2018)

European Association of Urology

Cancer de la prostate: Incidence et Mortalité



EU 28 = 514 Mio

I: 417.000 CaP/an

= 160/100.000

M: 107.000/an

= 37/100.000

Belgique = 11,5 Mio

I: 14.700 CaP/an

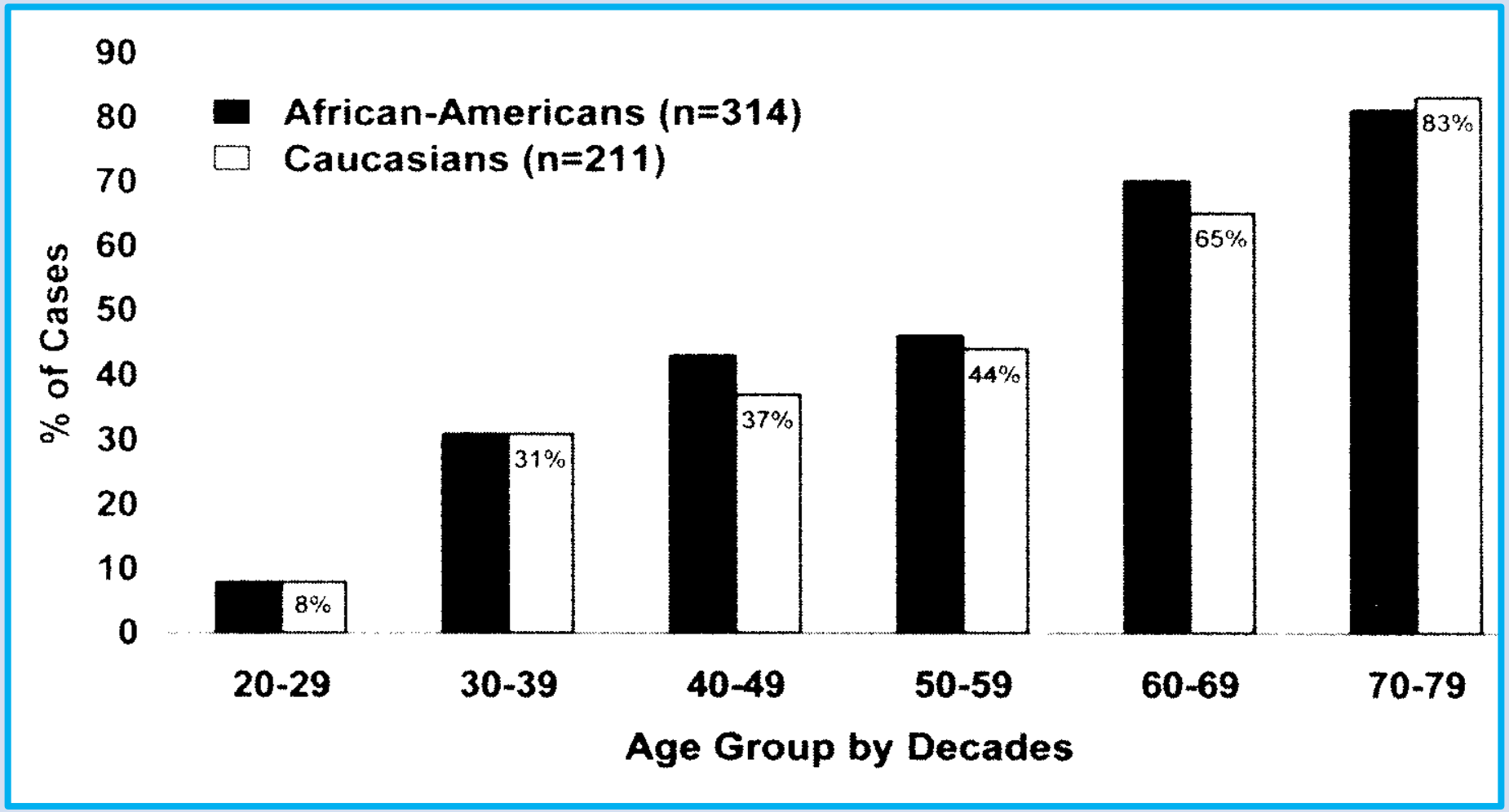
= 147/100.000

M: 1.500/an

= 32/100.000

Bray F et al. Global cancer statistics; CA Cancer J Clin. 2018; 68:394-424

CaP microscopique (autopsies)



Sakr W, Eur Urol 30:138, 1996

CaP≠CaP:
Noms identiques mais pathologies différentes

Il est vrai que…

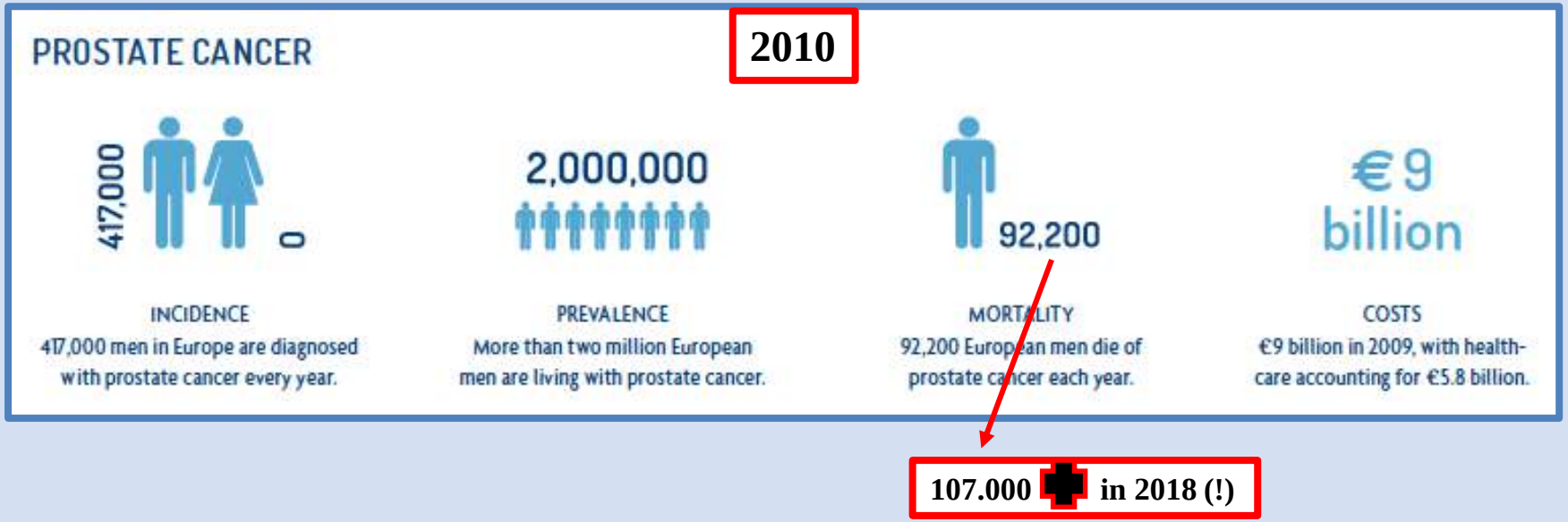
Incidence du CaP à l'autopsie: >50%

Mais n'oublions pas…

11% des décès par cancers masculins

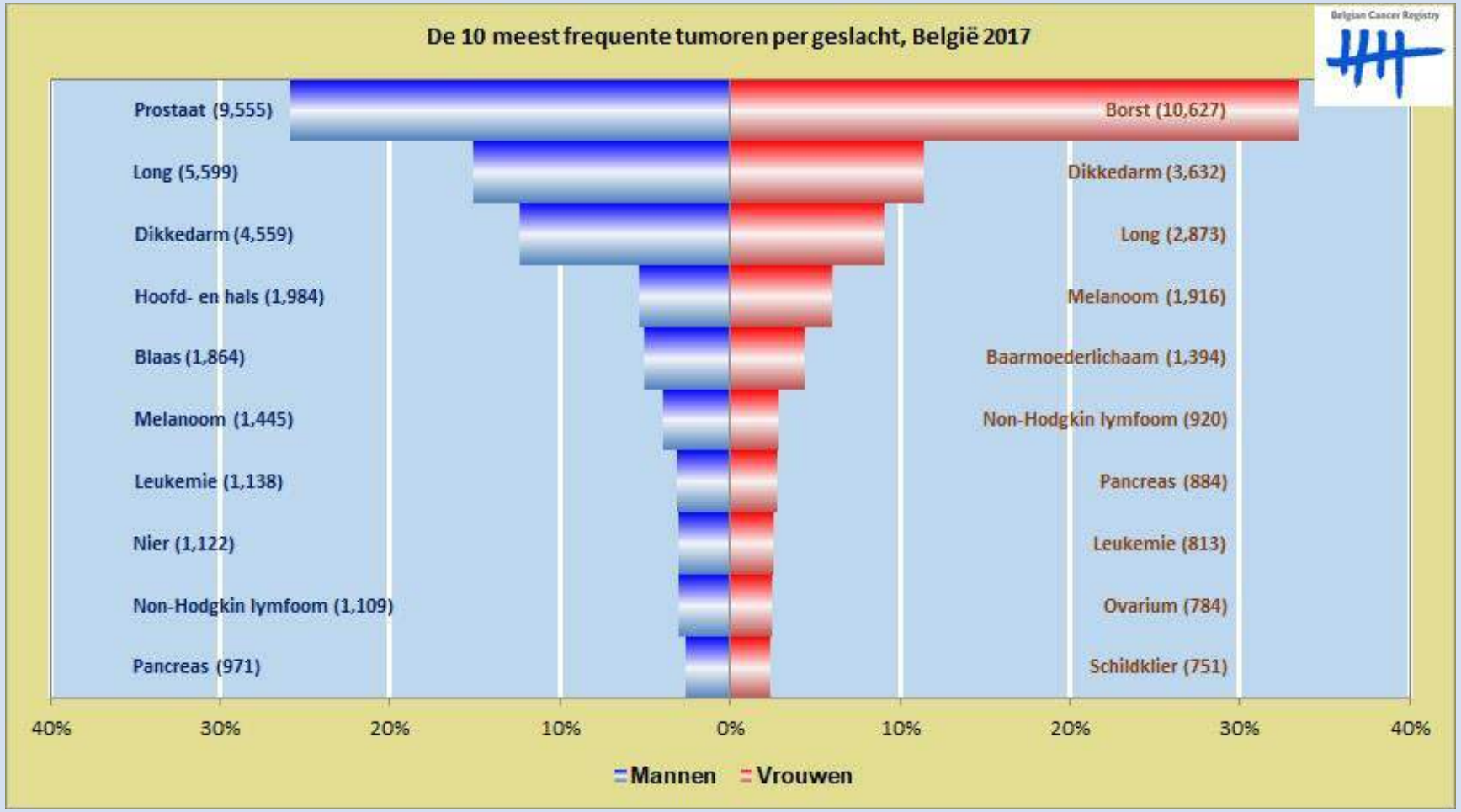
Siegel et al., CA Cancer Clin. 2019

CaP en Europe



- **Cancer masculin le plus fréquent dans l' Union Européenne**
- **1 / 7 hommes developpera un CaP en Europe**
- **CaP est inévitable et est asymptomatique dans les stades curables**
- **Il n'existe aucun programme de screening comme pour le sein,…**

Prostate cancer fact sheet



http://kankerregister.org

CaP en Belgique
Incidence et Mortalité

- **Aussi en Belgique CaP est le cancer masculin le plus fréquent**

EU 28	BE
160/100,000	147/100,000
37/100,000 décès	32/100,000 décès
107.000 décès/an	1500 déces/an = 4 par jour

- **Au stade précoce il est parfaitement curable, et nous en sommes capables**
- **Le PSA n'est pas cher et est faible**

Situation avant PSA (1985-86)

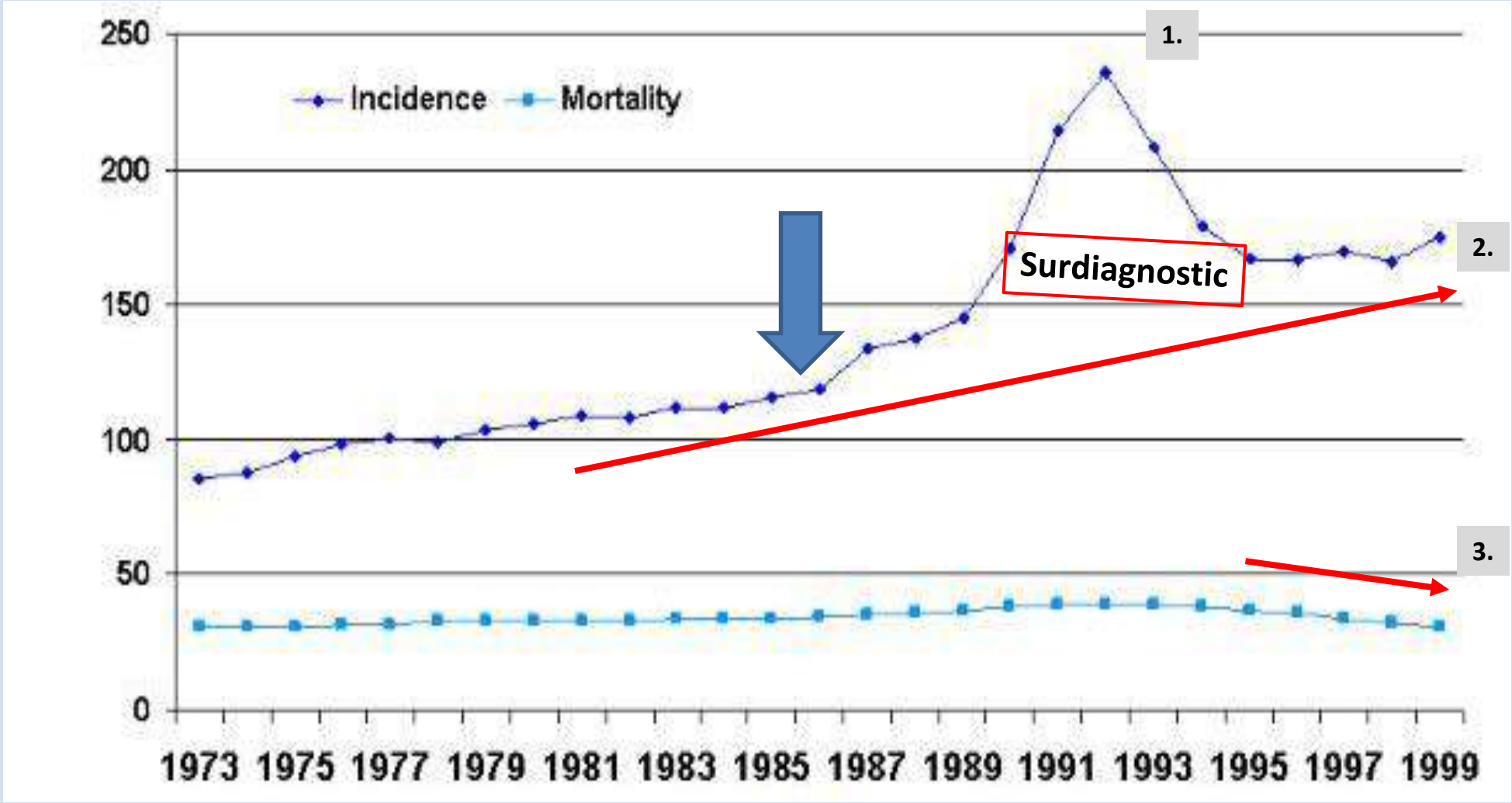
Table IV. MORTALITY-INCIDENCE RATE RATIOS[1] IN 13 COUNTRIES DURING 1973–77 TO 1988–92

Countries	1973–77[1]	1978–82	1983–87	1988–92
High risk				
U.S. blacks	0.35	0.33	0.39	0.25
U.S. whites	0.28	0.25	0.23	0.16
Canada				0.20
Sweden				0.38
Australia				0.33
France				0.36
Medium risk				
Denmark				0.60
England and				0.57
Italy				0.41
Spain				0.48
Israel				0.38
Low risk				
Singapore	0.40	0.44	0.55	0.38
Japan	0.49	0.44	0.42	0.42
Hong Kong	0.41	0.39	0.36	0.35

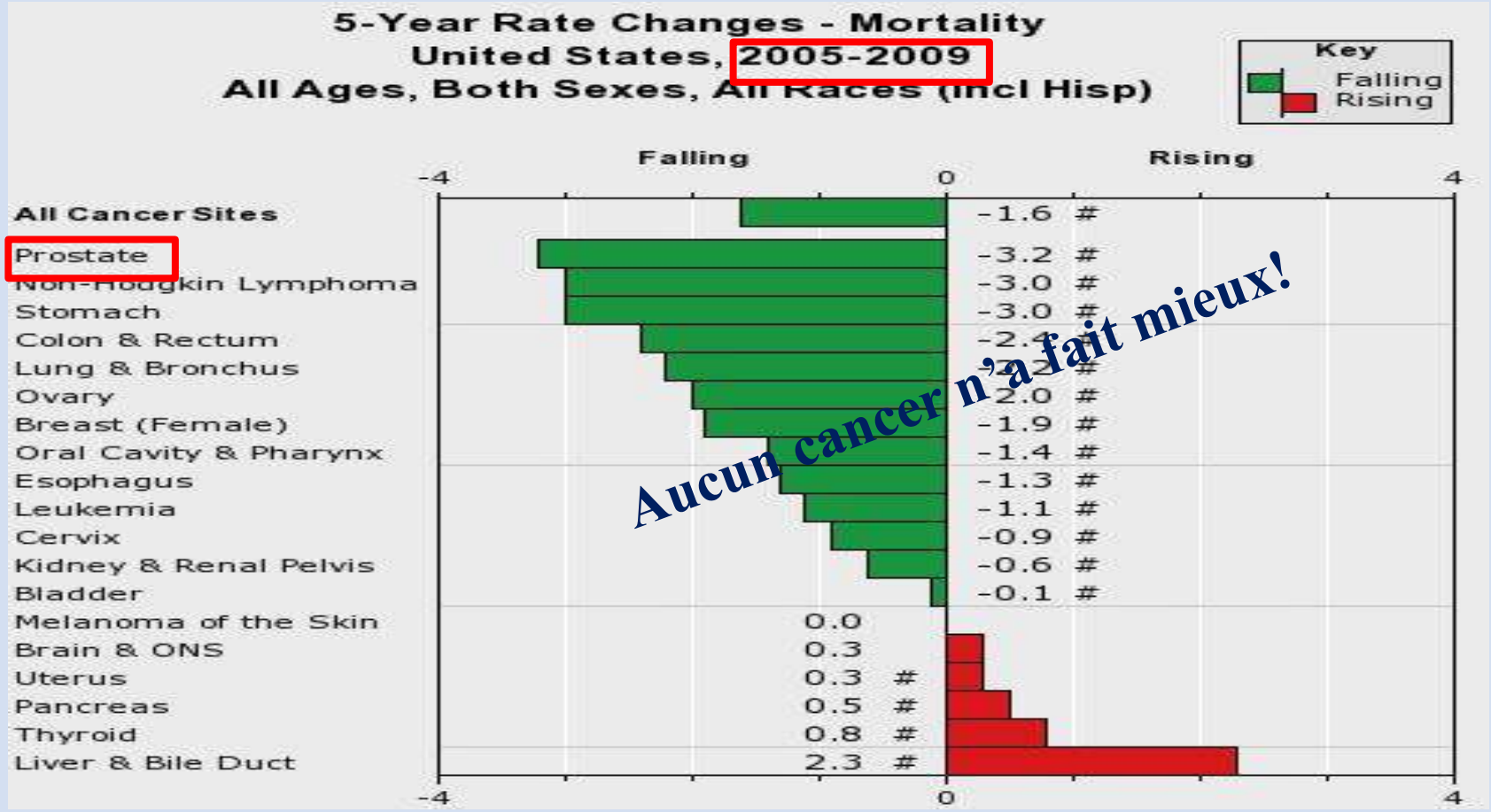
1 The ratio of mortality to incidence in each country, by time period.

1/3 à 1/2 patients diagnostiqués en mouraient

Et depuis l'introduction du PSA…



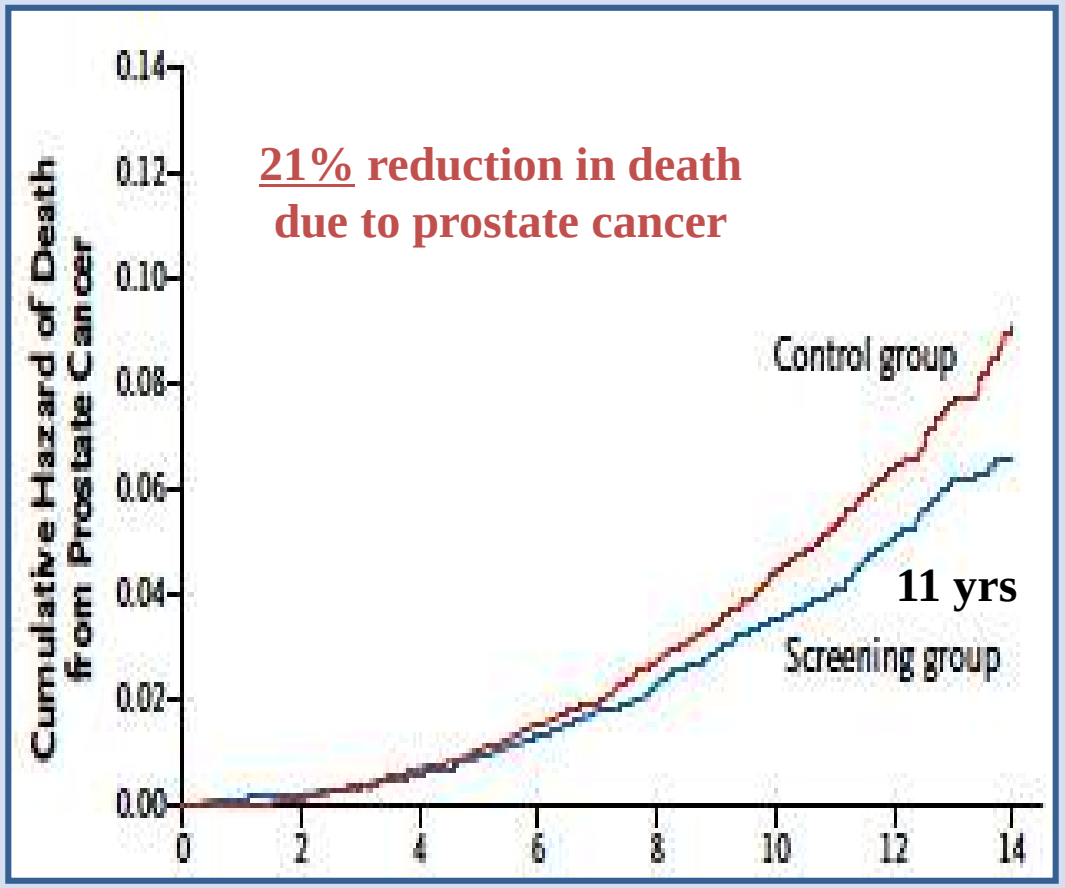
Evolution de la mortalité liée au cancer



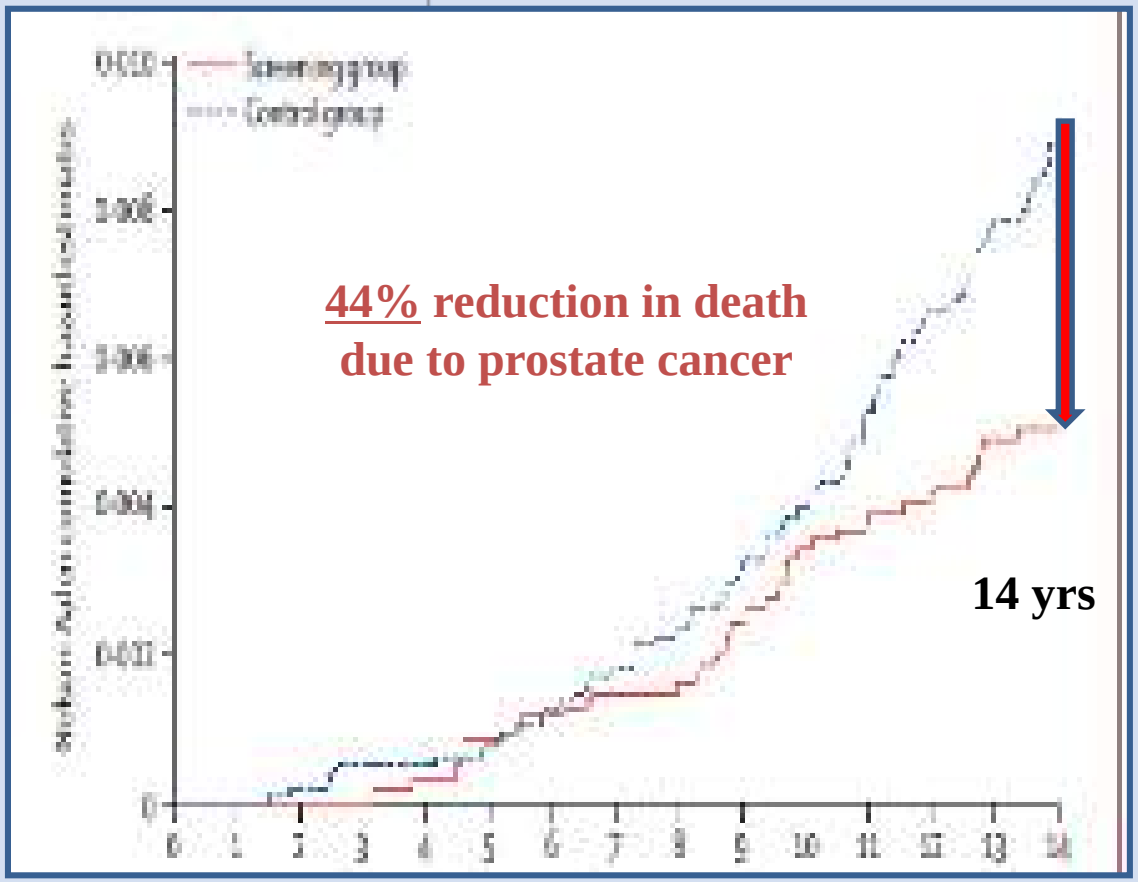
Alors, un dépistage précoce par moyen d'un screening de la population?

Screening dans les essais randomisés controlés (RCT)

Göteborg trial

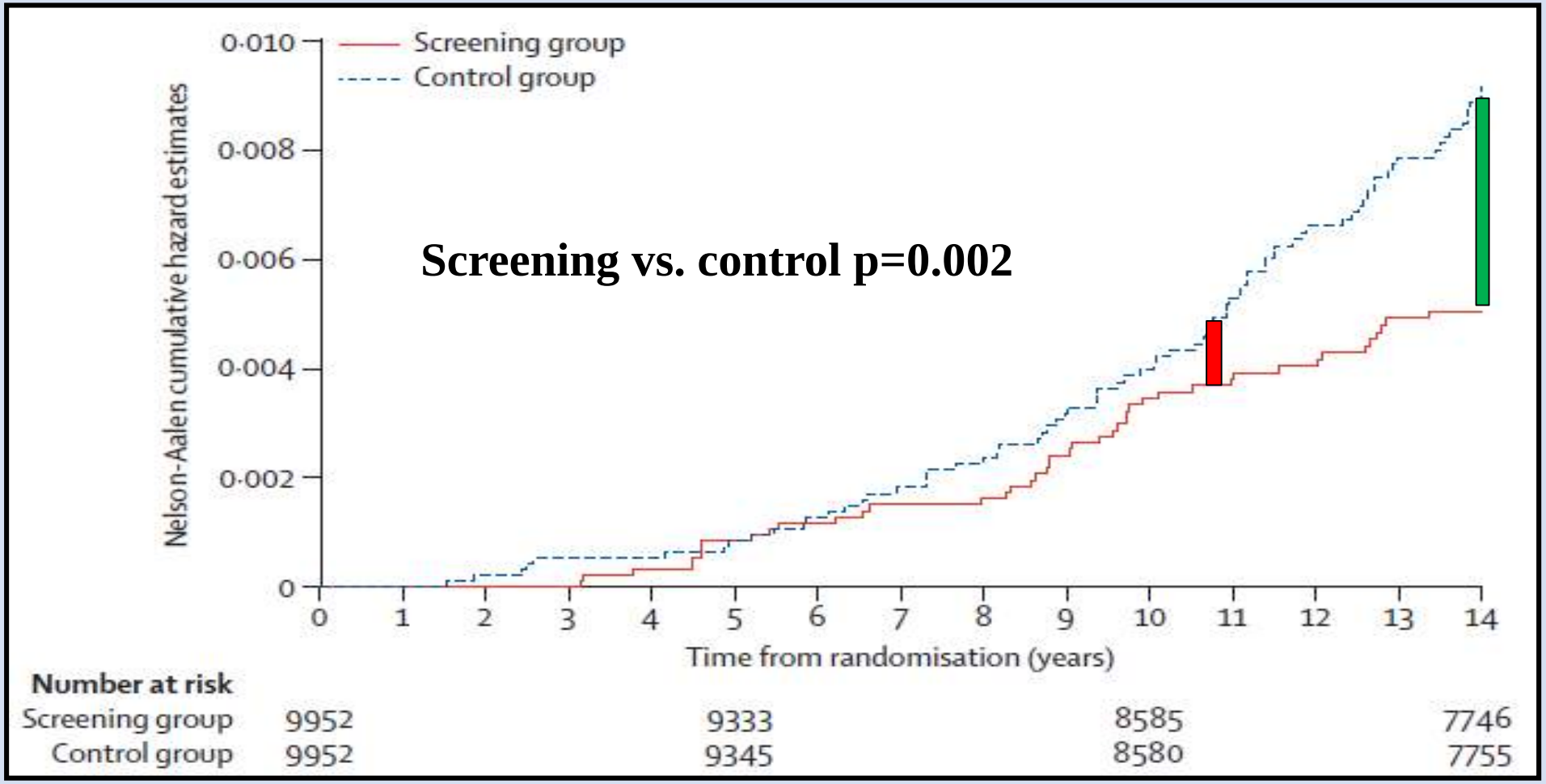


21% reduction in death due to prostate cancer



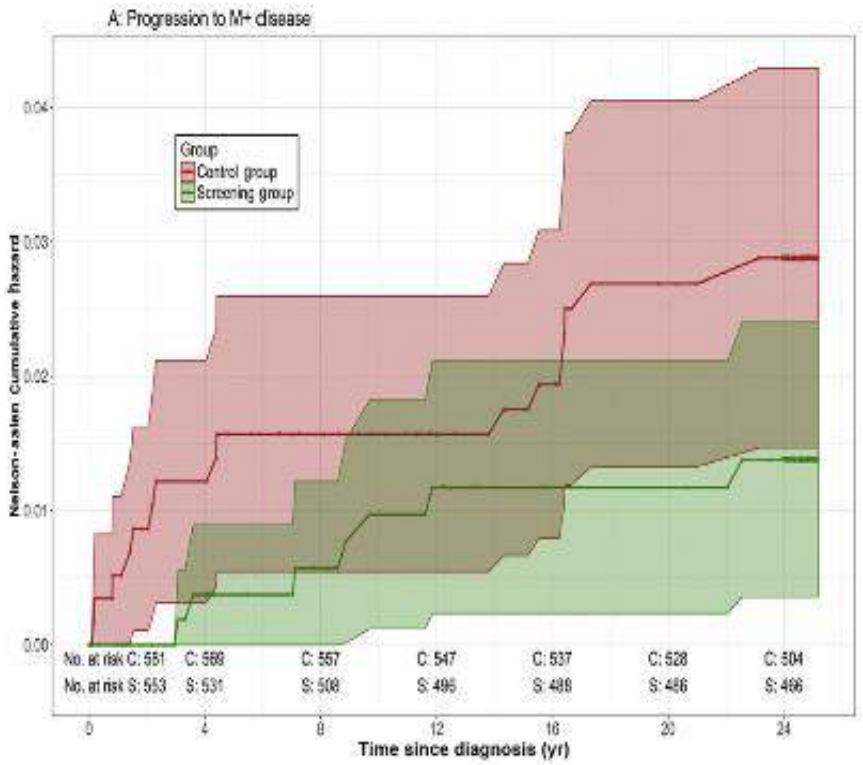
44% reduction in death due to prostate cancer

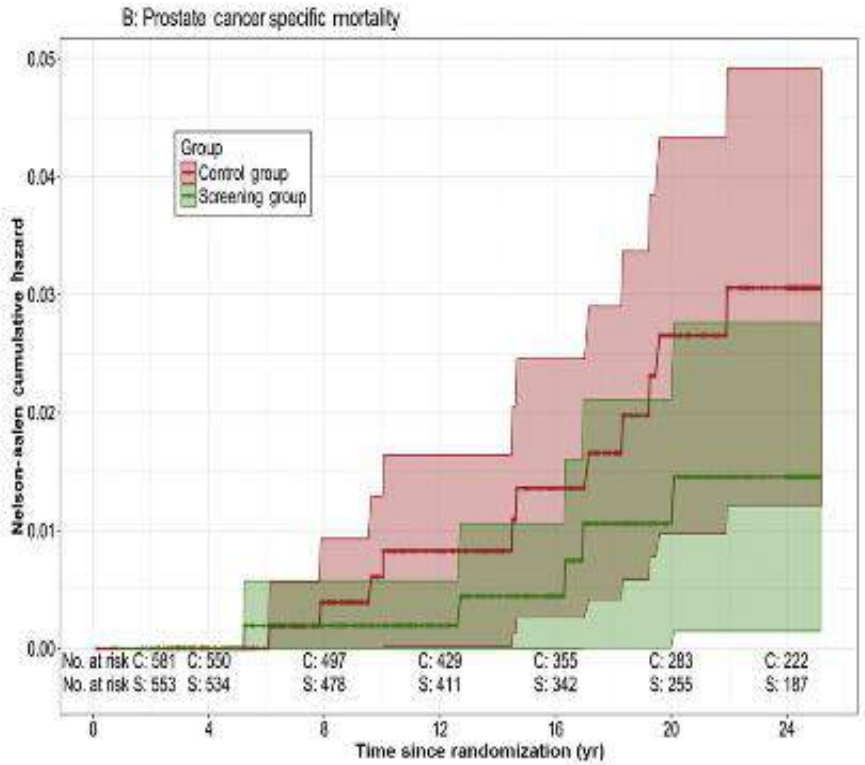
Göteborg: Mortalité Cancer Spécifique



Hugosson et al. Eur. Urol.2019

Cohorte ERSPC Rotterdam





19 ans de suivi, pas de contamination: - 54% M+ et - 52% mortalité CaP

Osses et al. Eur. Urol. 2019

PSA = Victime de son propre succès…

et son usage a été découragé

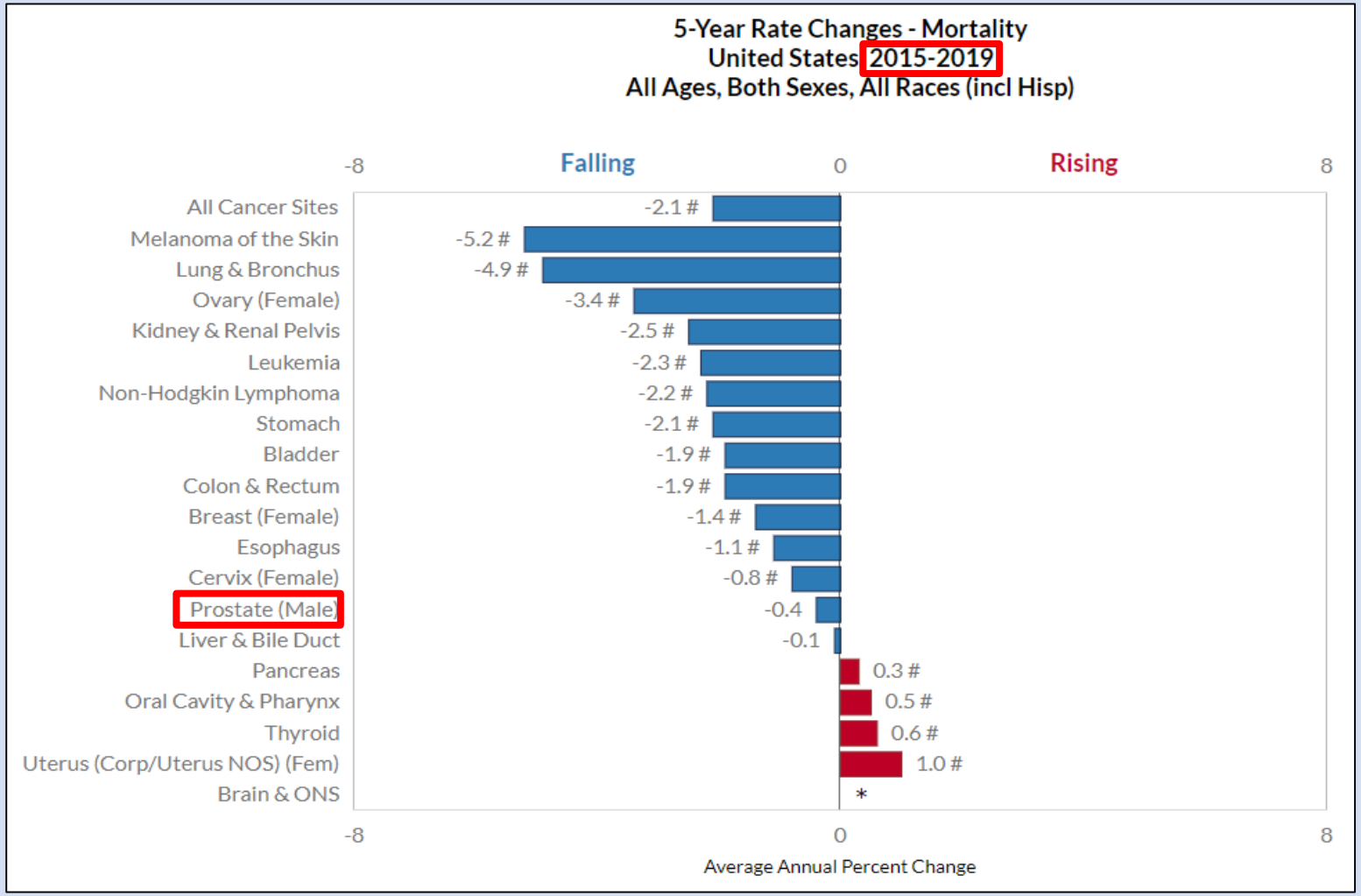
- “CaP touche le viellard et n’est pas une maladie mortelle :
  - Vous mourrez <u>avec</u> mais pas à cause du CaP…”
- Les traitements (non-nécessaires) peuvent induire des effets indésirables
- <u>Un diagnostic de CaP conduisait automatiquement à un traitement actif</u>

“Nous n’étions pas capables de distinguer un CaP significatif/non-significatif”

→ Propagande anti-PSA!

Mais que s’est-il passé avec moins de dosages de PSA ?

Evolution de la mortalité liée au cancer



https://statecancerprofiles.cancer.gov/recenttrend/index.php#results.

CaP 2019 Etats Unis

Incidence=n° 1

American Urological Association

Mortalité=n°2

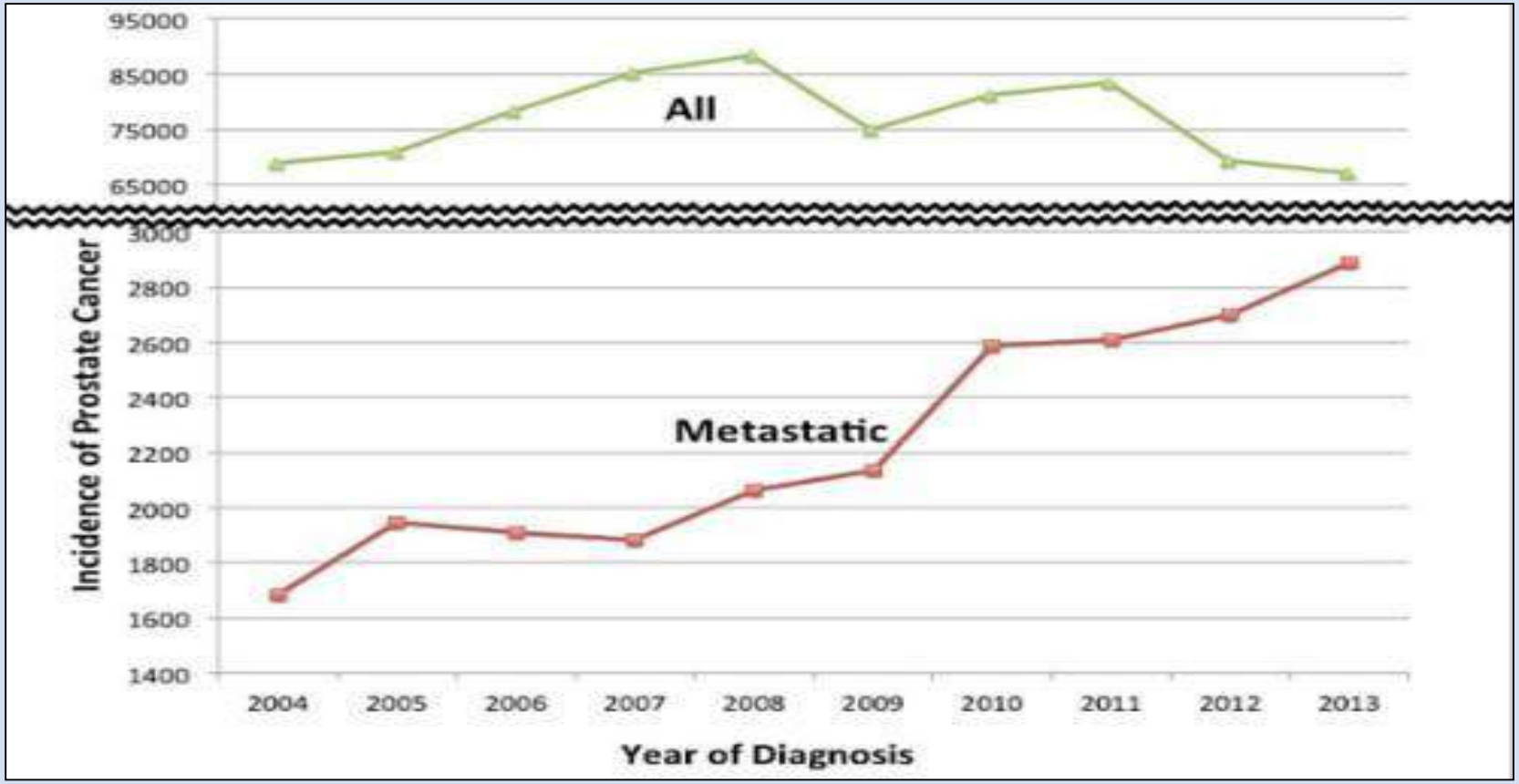
Prostate	174,650	20%
Lung & bronchus	116,440	13%
Colon & rectum	78,500	9%
Urinary bladder	61,700	7%
Melanoma of the skin	57,220	7%
Kidney & renal pelvis	44,120	5%
Non-Hodgkin lymphoma	41,090	5%
Oral cavity & pharynx	38,140	4%
Leukemia	35,920	4%
Pancreas	29,940	3%
All Sites	**870,970**	**100%**

Males

Lung & bronchus	76,650	24%
Prostate	31,620	10%
Colon & rectum	27,640	9%
Pancreas	23,800	7%
Liver & intrahepatic bile duct	21,600	7%
Leukemia	13,150	4%
Esophagus	13,020	4%
Urinary bladder	12,870	4%
Non-Hodgkin lymphoma	11,510	4%
Brain & other nervous system	9,910	3%
All Sites	**321,670**	**100%**

Siegel et al., CA Cancer Clin. 2019

Le nombre de patients diagnostiqués dans un stade métastatique augmente



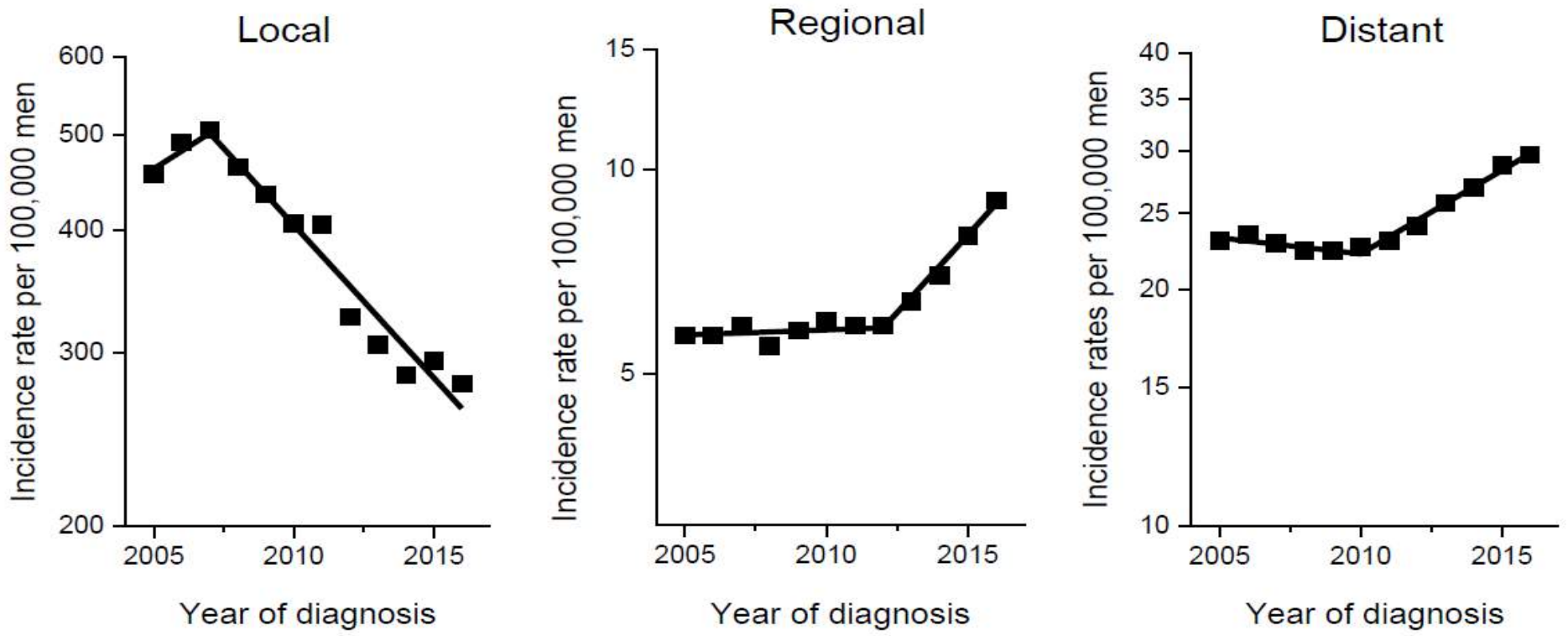
"Reverse Migration"

Le cancer de la prostate est de plus en plus détecté trop tard

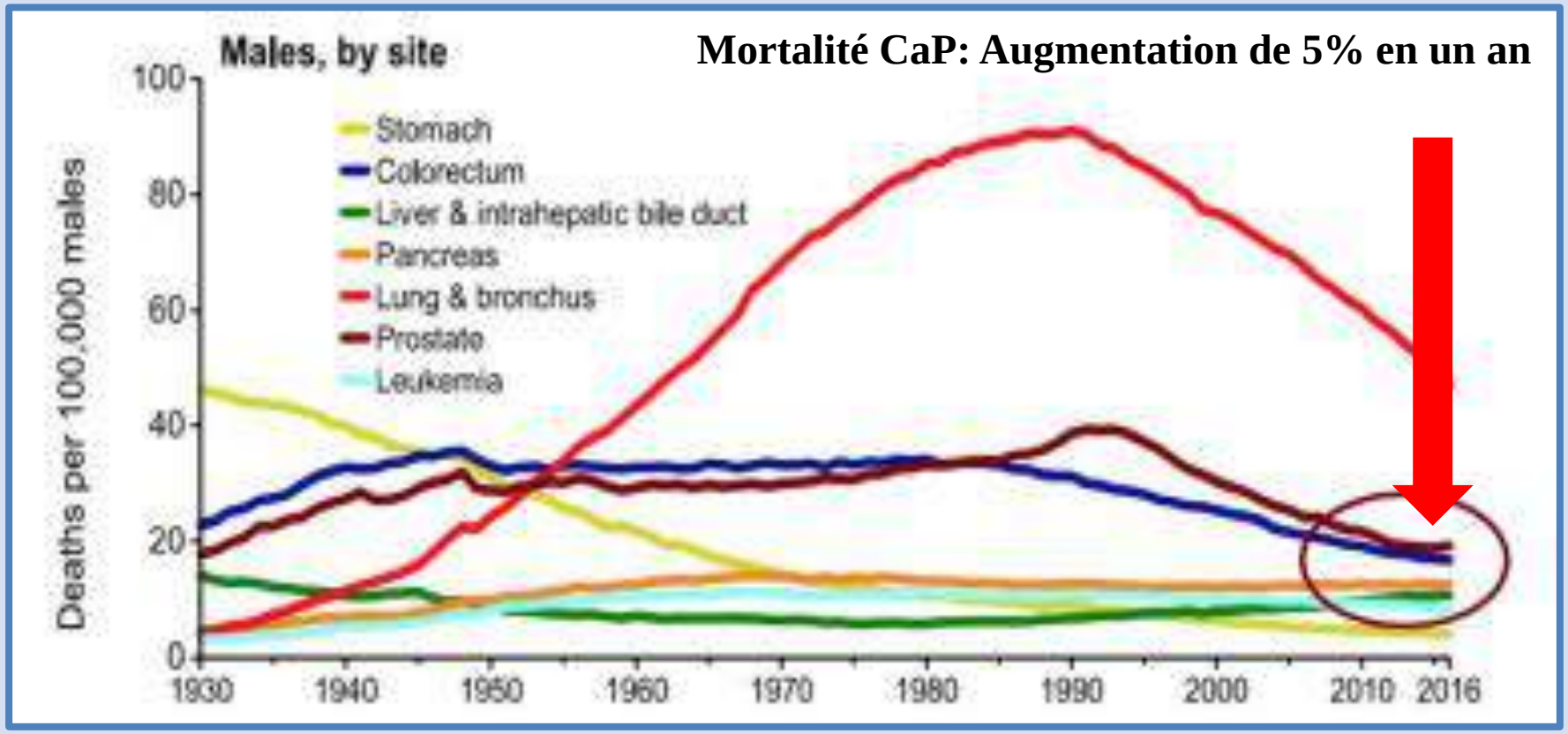
Weiner A. et al., Prostate Cancer and Prostatic Diseases, 2016

Incidence du CaP 5 ans après les recommandations de l'USPSTF contre le dépistage

Figure 1



Moins de PSA testing, quelles conséquences ?



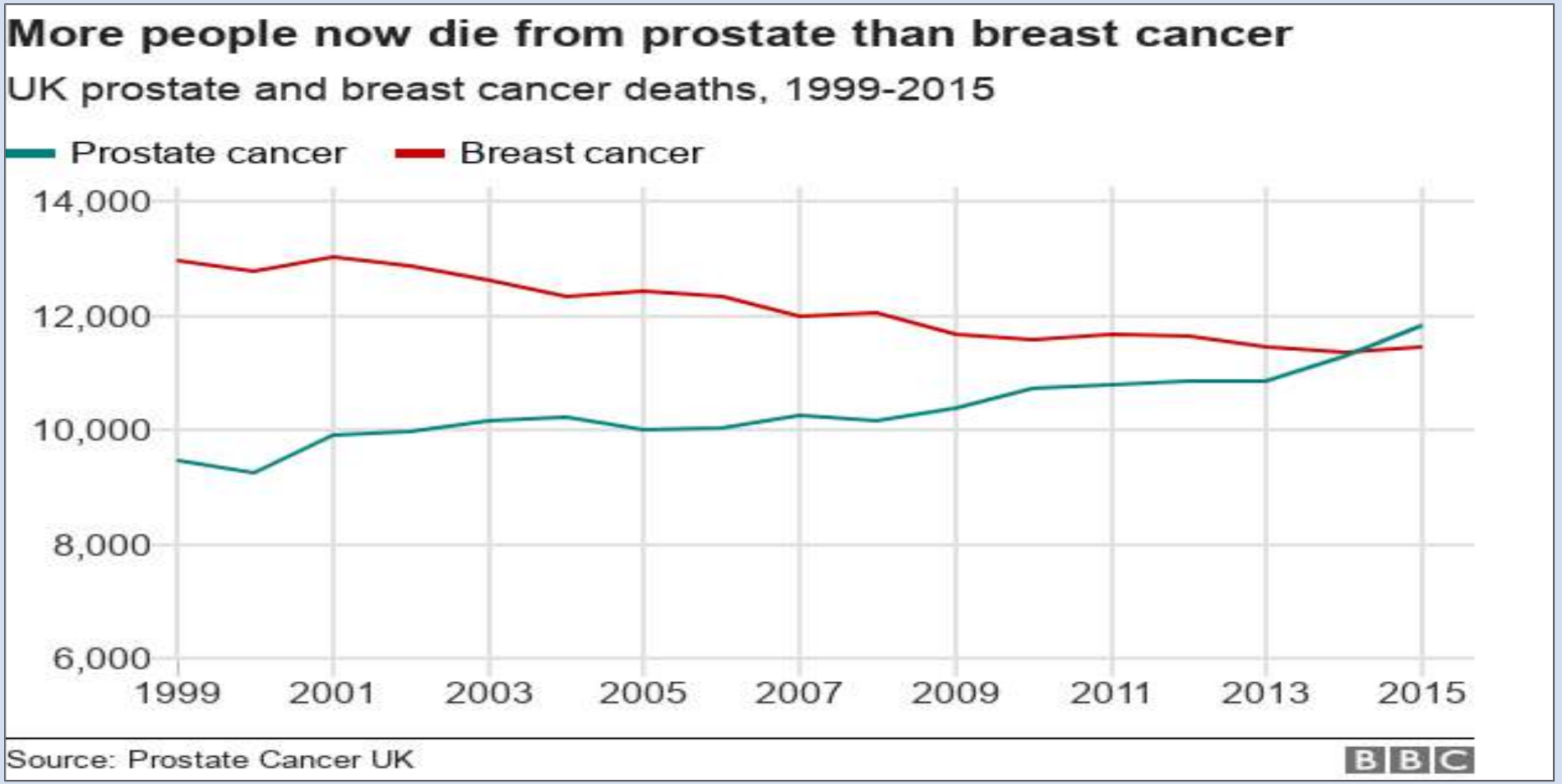
Mortalité CaP: Augmentation de 5% en un an

Et nous laissons cela se passer !?

Hu et al., JAMA Oncol. 2017 Butler et al., Cancer 2020 Am. Cancer Society 2020

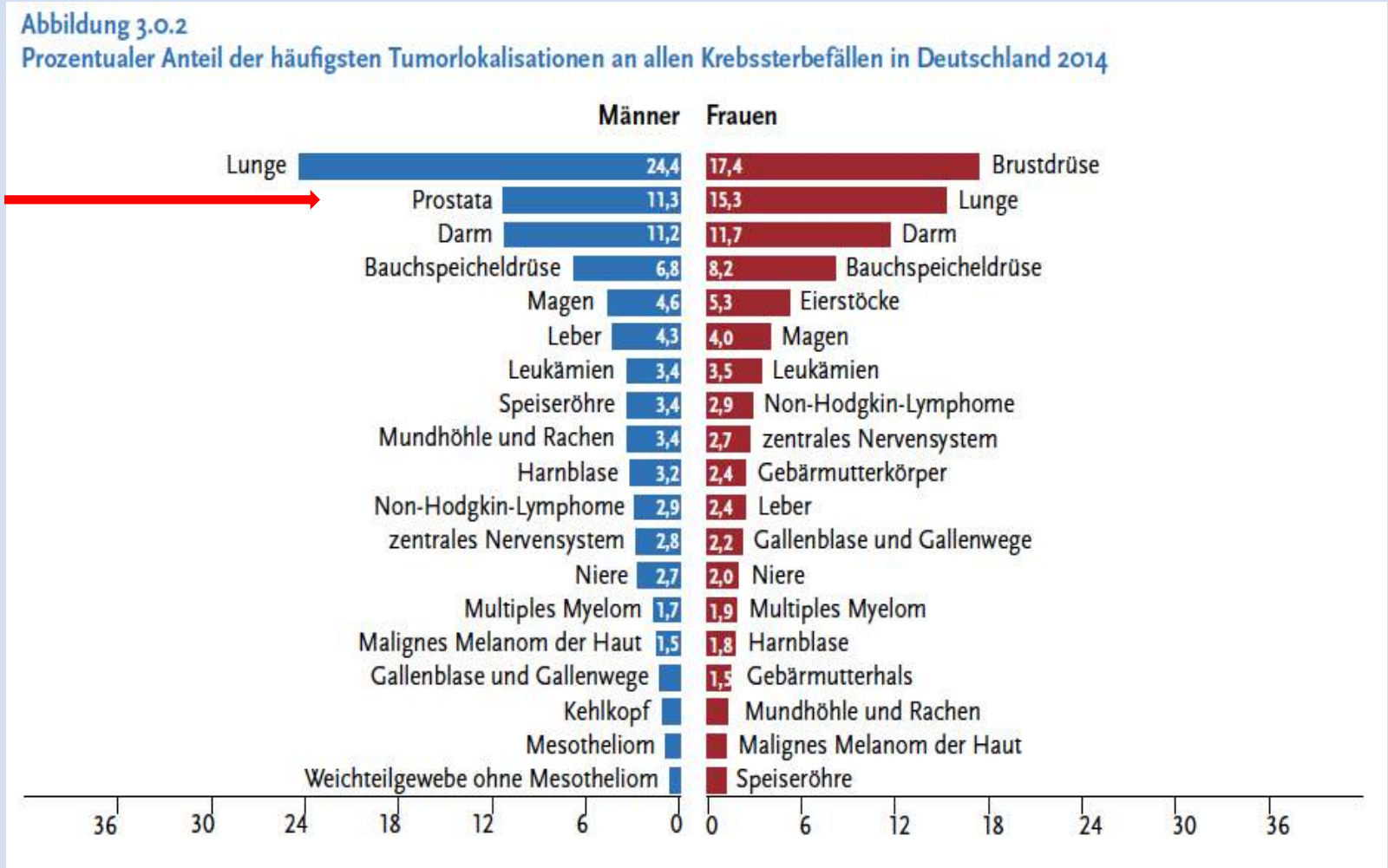
European Association of Urology

UK : Mortalité du CaP a augmenté de 17% en 10 ans



http://spcsg.ca/reading-material/prostate-cancer-deaths-overtake-breast-cancer/

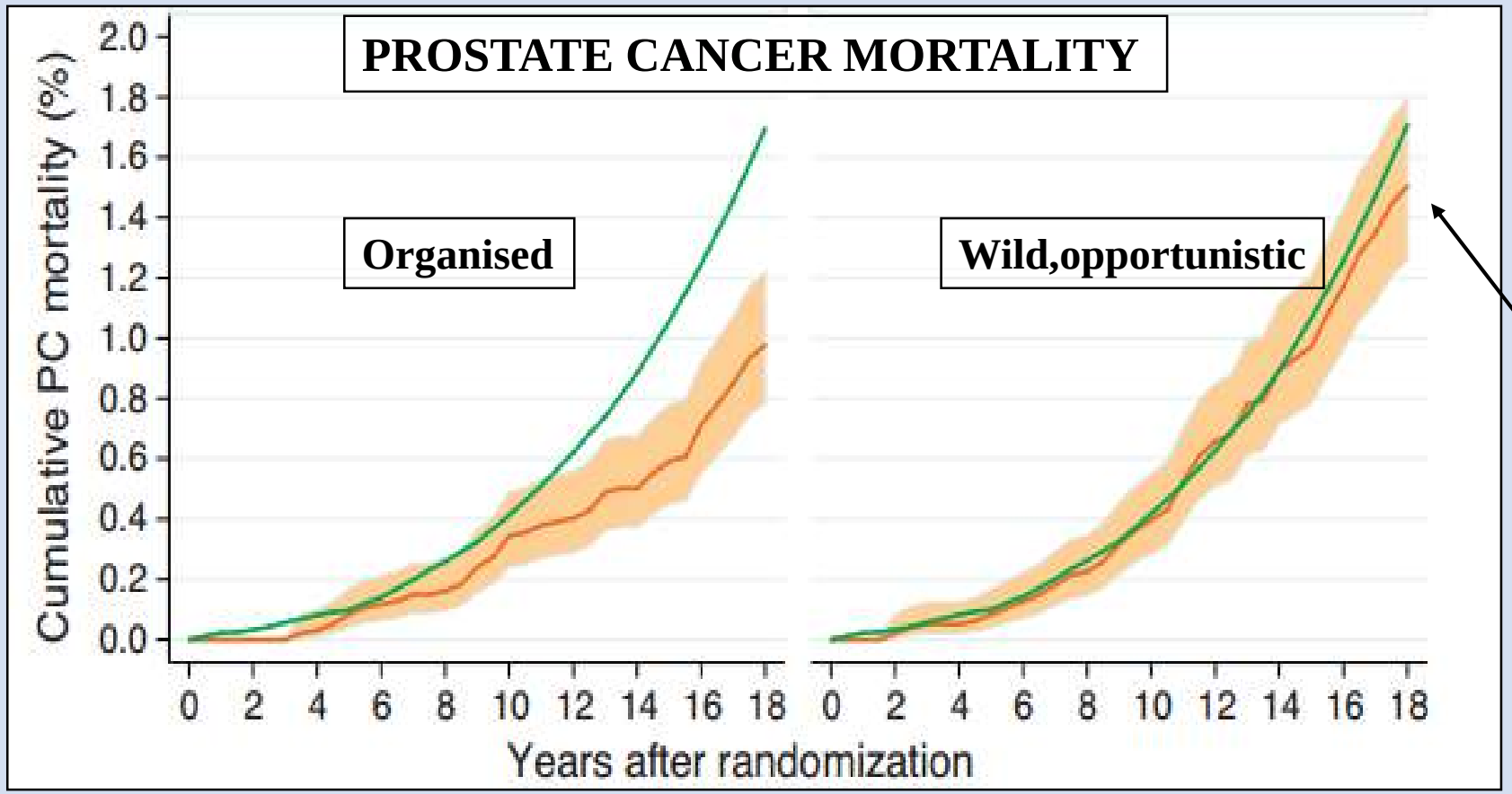
Allemagne : cancer mortel numéro 2



Stade T3 au diagnostic:
- 29% en 2008
- 49% en 2017

Lenzen-Schulte, Dtsch Arztebl. 2020

Screening non-organisé (opportunistic) n'évite pas le surdiagnostic et le surtraitement



Pas d'effet sur la mortalité

Arnsrud Godtman R, et al. Eur Urol. 2015;68(3):354-60

Sweden: N°1

EUROPEAN UROLOGY ONCOLOGY 4 (2021) 677–696

available at www.sciencedirect.com
journal homepage: euoncology.europeanurology.com

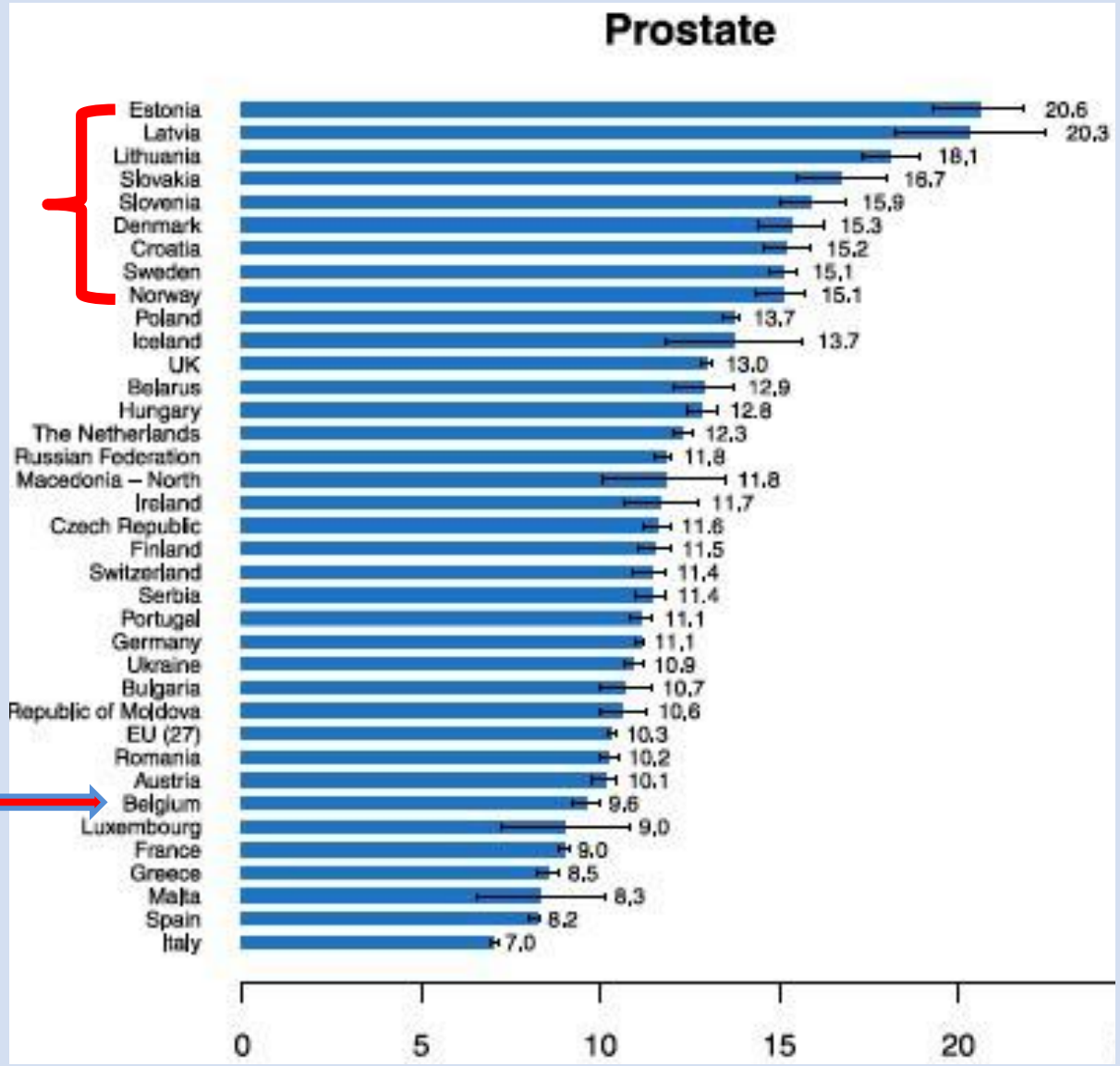
European Association of Urology

Priority Article

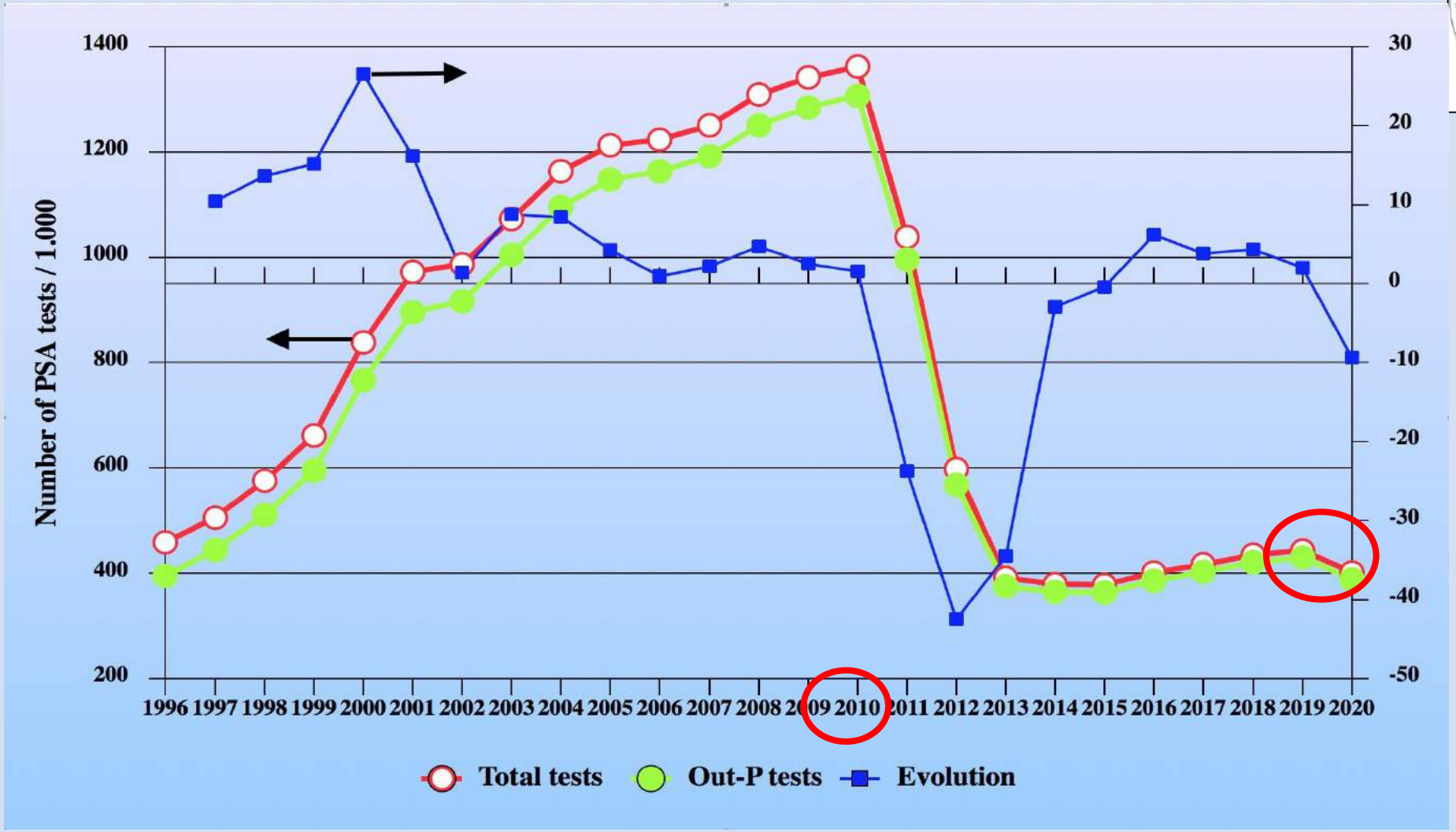
Mortality Trends from Urologic Cancers in Europe over the Period 1980–2017 and a Projection to 2025

Paola Bertuccio[a,*], *Claudia Santucci*[b], *Greta Carioli*[b], *Matteo Malvezzi*[b], *Carlo La Vecchia*[b], *Eva Negri*[b,c]

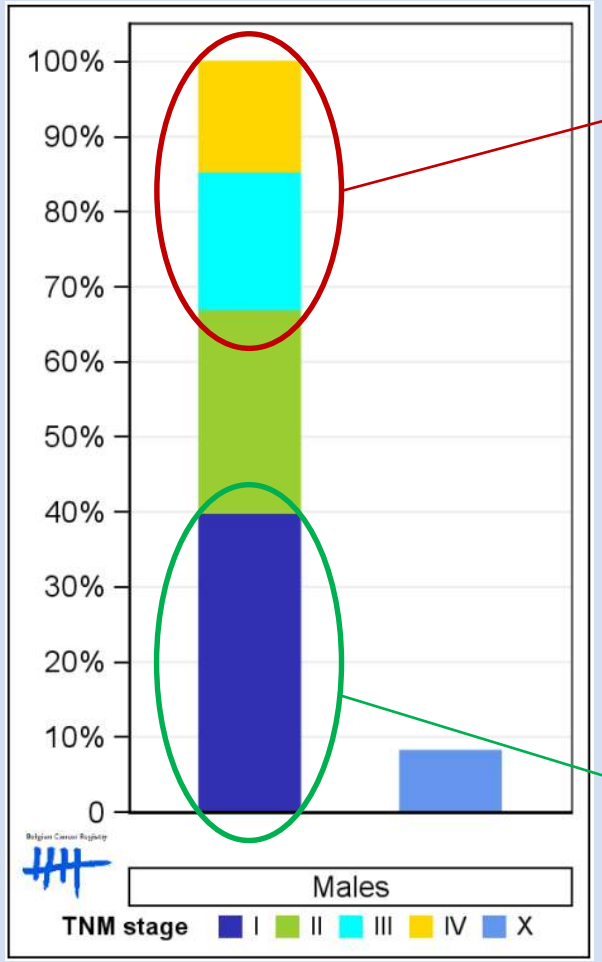
[a] Department of Biomedical and Clinical Sciences L. Sacco, Università degli Studi di Milano, Milan, Italy; [b] Department of Clinical Sciences and Community Health, Università degli Studi di Milano, Milan, Italy; [c] Department of Humanities, Pegaso Online University, Naples, Italy



PSA testing: l' histoire Belge



Prostate cancer fact sheet - Belgium



1/3 détectés au stade avancé

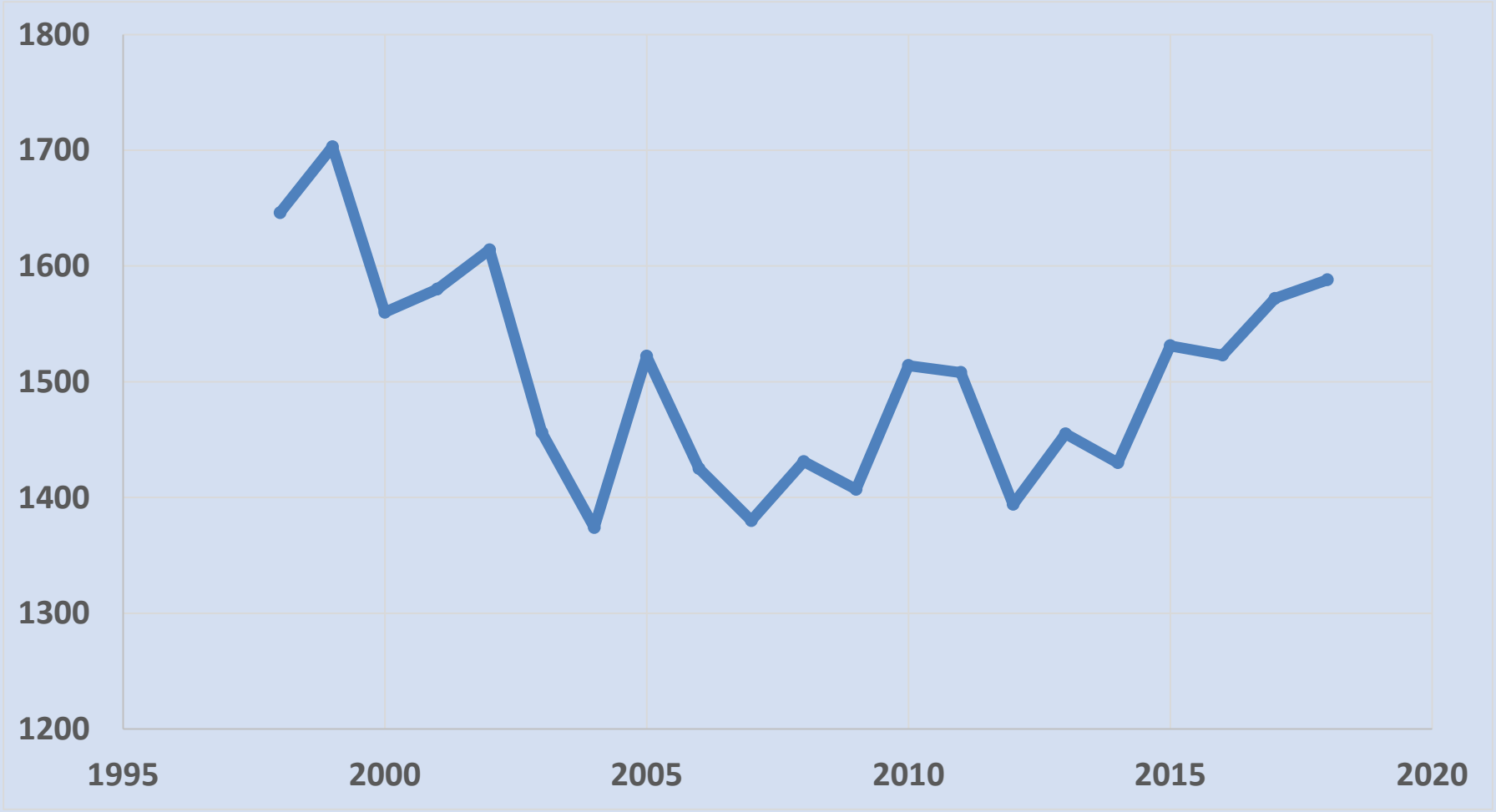
	Stage I	Stage II	Stage III	Stage IV	Stage X	Stage NA	Total
Males							
N	3,502	2,385	1,609	1,280	779	0	9,555
%	36.7	25.0	16.8	13.4	8.2	0.0	100

Staging according to the TNM 8th edition (Ref: Brierley JD, Gospodarowicz MK, Wittekind Ch. TNM classification of malignant tumours, UICC 8th edition)
Combined TNM stage : compilation of pathological (pTNM) and clinical (cTNM) stage. pTNM prevails over cTNM, except when cTNM stage is IV
Stage X: diagnoses with an unknown stage
Stage NA: diagnoses with a histological diagnosis where no stage can be evaluated (Not Applicable)

2/5 sont candidats pour la Surveillance Active (SA)

http://kankerregister.org

Et, la mortalité par CaP en Belgique?



Les temps ont changé !

1. Nous pouvons éviter le surdiagnostic:

- **Meilleur usage du PSA: lié à l'âge, la densité (volume prostatique)**
- **Calculateurs de risque (PCPT et ERSPC) +/- Biomarqueurs moléculaires**
- **mp(bp) IRM AVANT la biopsie** **Mannaerts et al., Eur. Urol. Oncol. 2018**

….diminue le nombre de biopsies
…...détecte plus de cancers significatifs et moins de cancers non-significatifs

Amin et al., J. Urol. 2020

2. Nour réduisons le surtraitement:

- **Surveillance active chez 65% des bas risques et risques intermédiaires**
- **Nomograms MAP (age, PSA, GG, MRI volume, PIRADS, MRI ECE)**

Lantz A, et al. Eur Urol Oncol 2022;5:187–94

EAU Lobbying au Parlement Européen

2017, 2019 and 2020

MOVEMBER® European Cancer Patient Coalition EUROPA UOMO The Voice of Men with Prostate Cancer in Europe European Alliance for Personalised Medicine eau European Association of Urology

available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

Platinum Opinion

Early Detection of Prostate Cancer in 2020 and Beyond: Facts and Recommendations for the European Union and the European Commission

Hendrik Van Poppel[a,†,*], *Renée Hogenhout*[b,†], *Peter Albers*[c,d], *Roderick C.N. van den Bergh*[e], *Jelle O. Barentsz*[f,‡], *Monique J. Roobol*[b,‡]

Eur. Urol. 79 (2021) 327-329

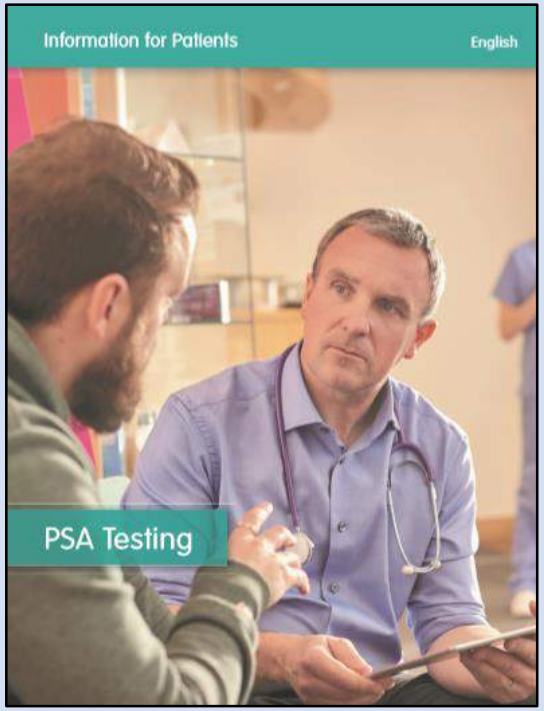
available at www.sciencedirect.com
journal homepage: www.europeanurology.com

European Association of Urology

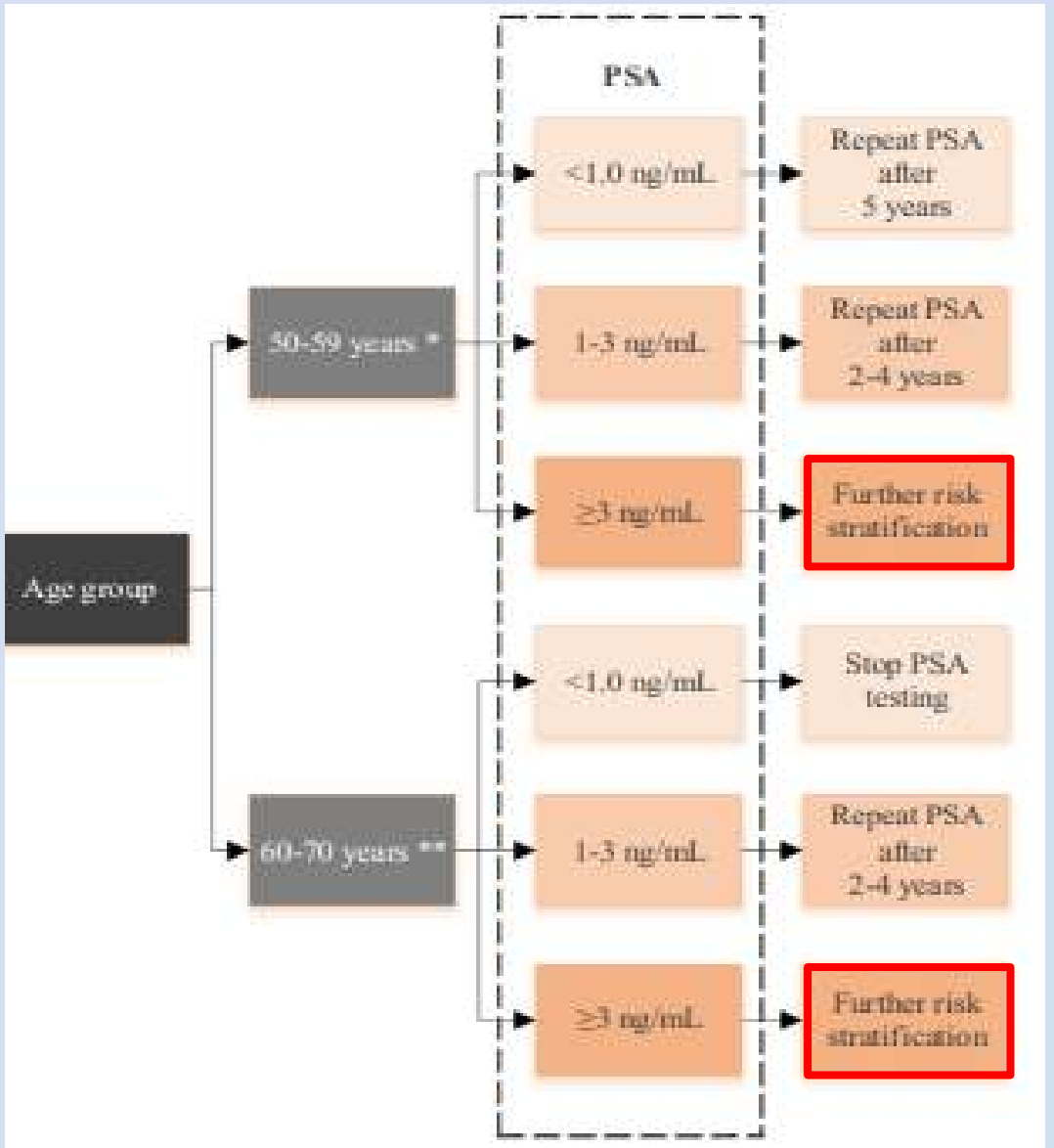
Early Detection of Prostate Cancer in 2020 and Beyond: Facts and Recommendations for the European Union and the European Commission

Hendrik Van Poppel[a,†,*], *Renée Hogenhout*[b,†], *Peter Albers*[c,d], *Roderick C.N. van den Bergh*[e], *Jelle O. Barentsz*[f,‡], *Monique J. Roobol*[b,‡]

Détection Précoce pour l'homme bien informé



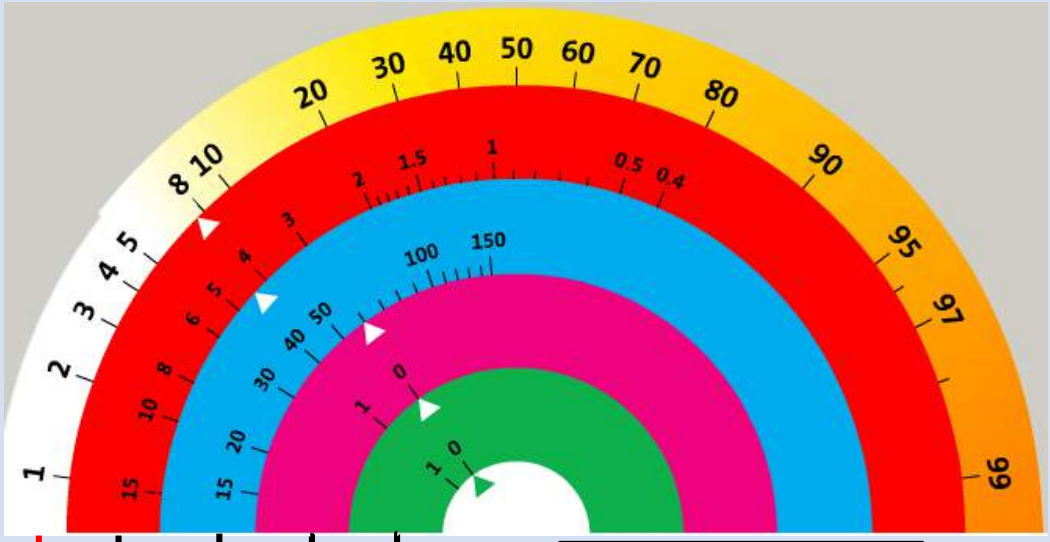
https://patients.uroweb.org/tests/psa-testing/2020



Calculateur de Risque ERSPC (Autres : PCPT, UK, CN…)

- **Risk Calculator 1 – general health calculator** est un point de départ, on regarde les antécédents familiaux, l'âge et tout problème médical lié à la miction.
- **Risk Calculator 2 – the PSA risk calculator:** De futurs investigations sont-elles requises ?
- **Risk Calculator 3 and 4 with TRUS or DRE**: Information sur le volume de la prostate par TRUS ou DRE (25, 40 ou 60 cc). Aide à estimer l'indication d'avoir une biopsie (pour tumeur potentiellement agressive)
- **Risk calculator 3 and 4 with TRUS or DRE and the result of the Phi test**: Augmente légèrement la capacité prédictive.
- **Risk calculator 5** calcule la chance d'avoir un cancer indolent
- **Risk Calculator 6** calcule le risque potentiel d'un homme pour les 4 prochaines années, en prenant en compte l'âge, le PSA, le TR, les antécédents familiaux, le volume de la prostate et les résultats des biopsies antérieures.

The Rotterdam ERSPC risk calculators



Previous biopsy?

Digital rectal examination

Prostate volume

PSA

Risk of (high-grade) PCa)

Advice on whether or not to perform a biopsy

www.prostatecancer-riskcalculator.com

20 – 33% reduction of unnecessary biopsy procedures

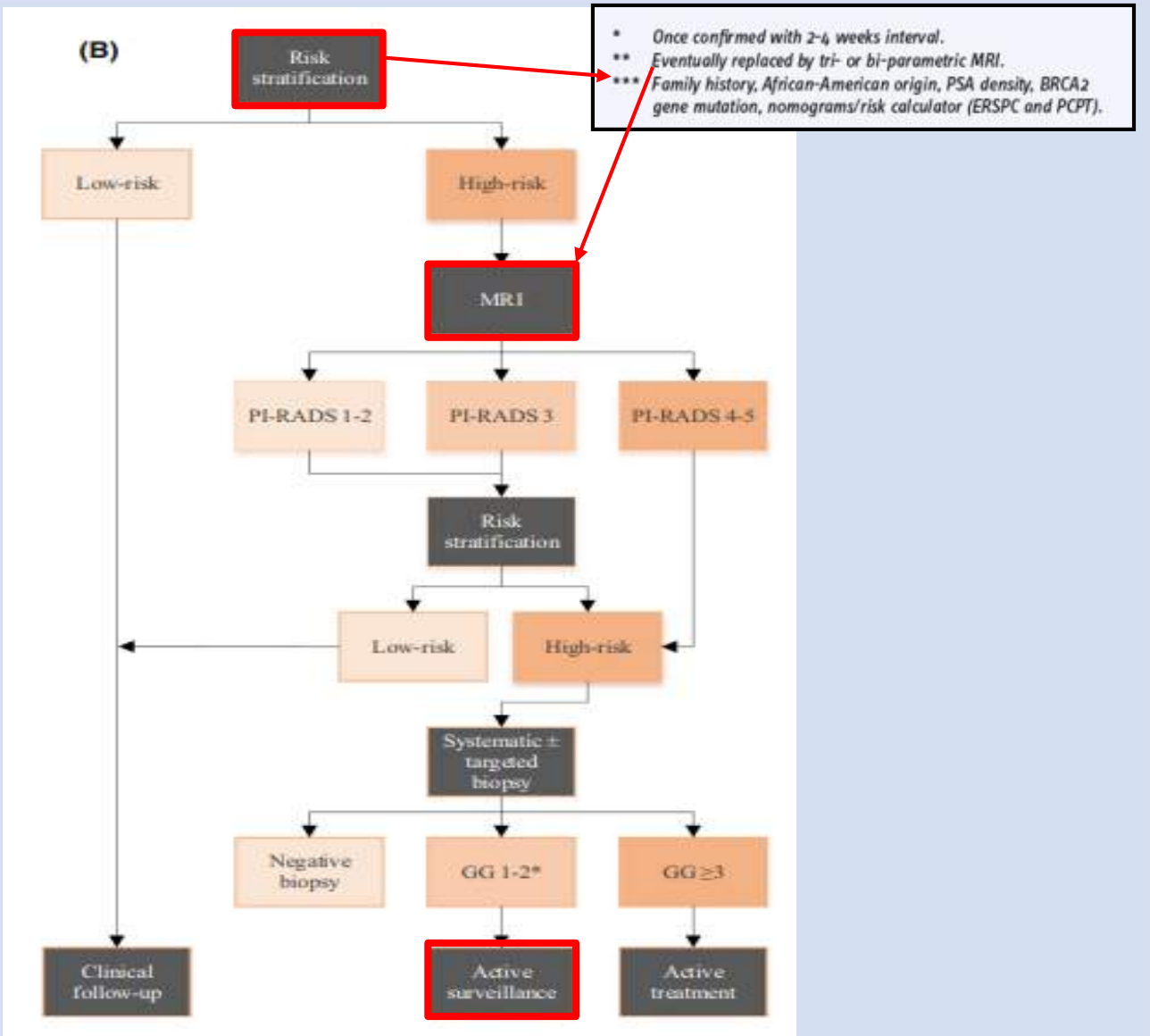
Risk of positive biopsy	Action
< 12.5%	No biopsy
12.5 – 20.0%	Consider biopsy
> 20.0%	Biopsy

PSA élevé ≠ Biopsie

Calculateurs de risque: ERSPC and PCPT …

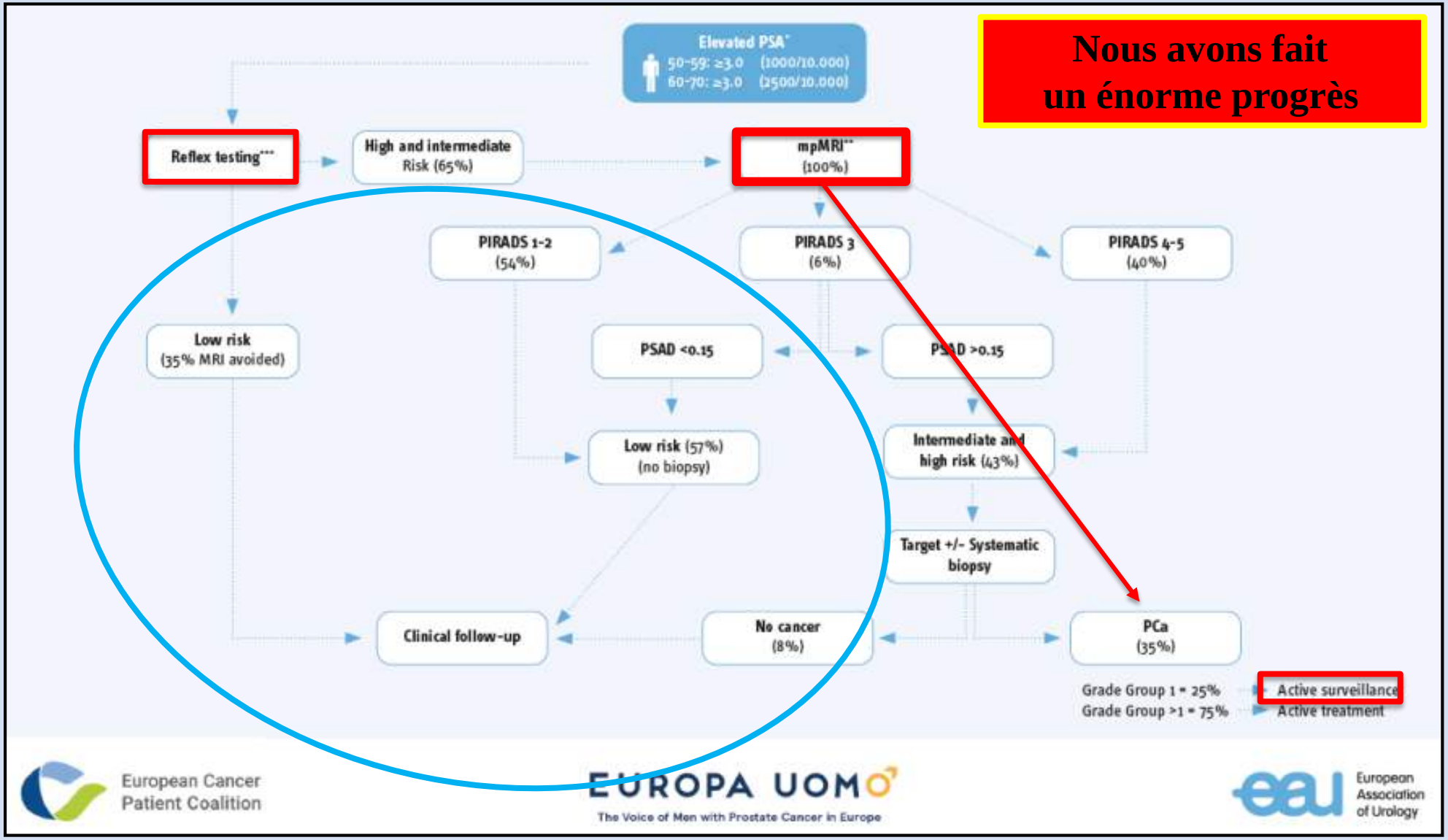
Free, quality controlled Risk Calculators available online:

- ERSPC: www.prostatecancer-riskcalculator.com
- PCPT: Myprostatecancerrisk.com
- Canada: www.prostaterisk.ca



H. Van Poppel et al.,
https///doi.org/10.1016/j.eururo.2020.12.010

Nous avons fait un énorme progrès



S. Collen and H. Van Poppel, BJMO 2020

Coût de la détection tardive du CaP

Le coût total de cet homme avec un CaP était proche de 300.000€ sur 18 ans.

€240,000
pour les médicaments et les soins qui prolongent une vie misérable de 2 à 4 ans

Chirurgie
€5,000

Rechute:
Radiothérapie
€5,000

Castration médicale
€ 11,000

Radium 223, Lu*

Cabazitaxel

Enzalutamide

Docetaxel

Abiraterone

Denosumab

Radiothérapie Palliative

age 62								age 70									age 79
1999	2000	2001	2002	2003	2004	2005	2006	2007	2008	2009	2010	**2011**	2012	2013	2014	2016	**2017**

Nous avons une nouvelle stratégie de détection précoce

Coût versus Economies

1. Calculateur de risque: 0 €
2. PSA: €10/x
3. mpMRI: 150 € (bp aussi bon)
4. Traitement d'un CaP: 10,000 €

1. Moins de biopsies, moins de complications
2. Moins de surdiagnostic/surtraitement
3. Moins de traitements coûteux pour les patients résistants à la castration (€240.000)
4. Moins de décès par CaP -> augmentation du temps de vie professionnelle
5. Bien meilleure Qualité de Vie

Comment éliminer le second cancer mortel de l'homme?

- **Arrêter le screening sauvage qui coûte et ne rapporte rien à la population**
  - **hommes bien informés de 45-50j jusqu'à une expectance de vie >10ans**
  - **risk-calculators, PSA-age, volume et MRI**
- **Biopsie réservée aux hommes à risque**
- **Traiter activement (RPr ou RT) uniquement ceux qui pourraient en mourir**
- **Surveillance Active des CaP à risque bas et intermédiaire**

⟹ **Diminuer la mortalité, améliorer la Qualité de vie, …et économiser**

romania2019.eu
Romanian Presidency of the Council of the European Union

Prostate Cancer Screening
Bucharest, Romania 4-6-2019

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

Early Detection WP5 conference
Budapest, Hungary 20-5-2019

EPAD
European Prostate Cancer Awareness Day

2017
2019-
2020

2016
2017
2018
2019
2020

iPAAC
INNOVATIVE PARTNERSHIP
FOR ACTION AGAINST CANCER

EU2019.FI

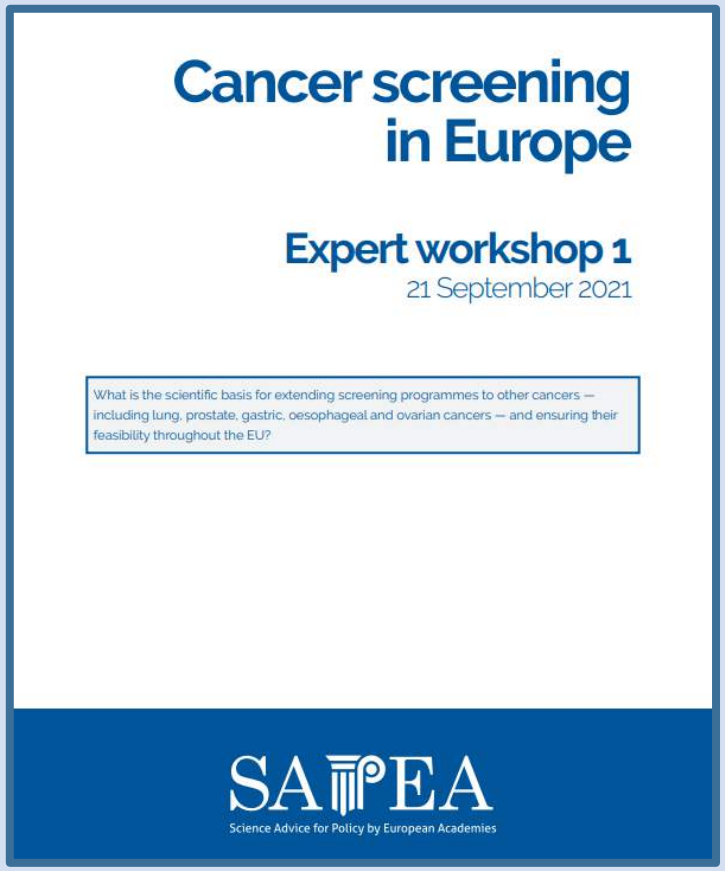
New openings of cancer screening in Europe
iPAAC WP5 conference, side event of Finland's Presidency of the Council of the European Union
5 December, 2019 - 8.30-16:00
Hosted by Finnish Institute for Health and Welfare THL, Cancer Society of Finland
THL main building, Mannerheimintie 166

European Alliance for
Personalised Medicine

24-03-2020
Croatian Presidency of the
Council of the European Union
PARLIAMENTARY DIMENSION

European
Association
of Urology

EAU, EU, and PCa screening



"The experts find the scientific basis for organised prostate cancer screening strong provided that the age criteria are appropriate. It is likely that MRI will become part of prostate screening in the future. We strongly recommend that we need to address the high levels of opportunistic PSA testing in order to reduce overdiagnosis and harm."

The EU4Health program currently has a funding call that will open the way to initiate population-based PCa screening pilot studies, which will lead to a state-of-the-art population-based program suitable for Europe and the rest of the world.

MRI, magnetic resonance imaging ; PCa, prostate cancer; PSA, prostate-specific antigen.

Cancer screening in Europe: Expert Workshop 1. https://sapea.info/wp-content/uploads/cancer-screening-workshop-report-01.pdf.

From 4 2 3

The stakeholders envisioned in this project are:

- **Patients** (Europa Uomo, represented by André Dechamps; Wij Ook, represented by Erik Briers; Think Blue, represented by Fernand Fonteyne)
- **Nurses** (UROBEL, represented by Ronny Pieters; VVUVZ, represented by Luc De Laere)
- **General practitioners** (Domus Medica, represented by Bram Spinnewijn; CEBAM, represented by Patrick Vankrunkelsven)
- **Urologists** (BVU, represented by the board; BBVU, represented by Filip Ameye and Christophe Ghysel; SBU, represented by Christophe Assenmacher)
- **Radiation oncologists** (BRAVO, represented by Gert De Meerleer; BESTRO, represented by ***)
- **Medical oncologists** (BSMO, represented by ***)
- **Radiologists** (BSR, represented by Geert Villeirs)
- **Belgian Cancer Registry**, represented by Liesbet Van Eycken
- **Mutualities**, represented by ***
- **EAU**, represented by Hein Van Poppel
- **Cancer Centre – OD Public Health and Surveillance**, represented by Mieke Goossens

https://www.collegeoncologie.be/fr

College of Oncology

NATIONAL EXPERT–BASED PRACTICE GUIDELINES

PROSTATE CANCER

Guidelines V1.2021

European Association of Urology

EXPERT PANEL

These guidelines have been developed by a national multi-institutional and multidisciplinary expert working party, based on international guidelines.

COLLEGE OF ONCOLOGY

Prof. Dr. Marc Peeters – *Chairman College of Oncology*

Prof. Dr. Jacques De Grève – *Chair of the guidelines working party*

Ms. Isolde Van der Massen, MSc – *Scientific coordinator*

LEADER EXPERT PANEL

Prof. Dr. Thierry Roumeguère – *Belgian Society of Urology (SBU)*

EXPERT PANEL

Prof. Dr. Sylvie Rottey – *Belgian Society of Medical Oncology (BSMO)*

Dr. Daan De Maeseneer – *Belgian Society of Medical Oncology (BSMO)*

Prof. Dr. Raymond Oyen – *Belgian Society of Radiology (BSR)*

Prof. Dr. Olivier De Hertogh – *Belgian Society for Radiotherapy & Oncology (BeSTRO)*

Prof. Dr. Gert De Meerleer – *Belgian Society for Radiotherapy & Oncology (BeSTRO)*

Prof. Dr. Sandrine Rorive – *Belgian Society of Pathology*

Prof. Dr. Sofie Verbeke – *Belgian Society of Pathology*

Prof. Dr. Karolien Goffin – *Belgian Society of Nuclear Medicine* (*BELNUC)*

Prof. Dr. Karel Decaestecker – *Belgian Association of Urology (BVU)*

Dr. Julien Van Damme – *Belgian Society of Urology (SBU)*

Prof. Dr. Hein Van Poppel – *European Association Urology (EAU)*

DIAGNOSTIC EVALUATION

SCREENING AND EARLY DETECTION

- Early prostate-specific antigen (PSA) testing can be offered to (EAU + consensus working group (WG); strong recommendation):
  - Men > 50 years
  - Men > 45 years with a family history of prostate cancer
  - Men with African origin > 45 years
  - BRCA2 carriers > 45 years
- The healthy male population and the general practitioners need to be informed that, although getting prostate cancer cannot (probably not) be prevented, dying from prostate cancer can be prevented. The first step is always PSA testing. Following the age and the value, PSA testing should be repeated, stopped or further risk stratification needs to be done. The decision tree in the Appendix should be used (Figure 1) (Van Poppel, Hogenhout, et al., 2021; Van Poppel, Roobol, et al., 2021). (Consensus WG, strong recommendation)
- Testing for prostate cancer in men should not be done in men with a life expectancy less than 10 years. (ESMO + consensus WG, strong recommendation)
- Life expectancy can be calculated by using the following link: https://www.mdcalc.com/charlson-comorbidity-index-cci. (Consensus WG, strong recommendation)
- Risk calculators are useful to determine (on an individual basis) what the potential risk of cancer may be, thereby reducing the number of unnecessary biopsies. It is recommended to use the European Study Randomized of Screening for Prostate Cancer (ERSPC) risk calculator (http://www.prostatecancer-riskcalculator.com/seven-prostate-cancer-risk-calculators). When patients are categorized for low-risk, they will go for clinical follow-up. If patients are categorized for high-risk, they will go for multiparametric MRI (mpMRI) that will allow further risk stratification depending on the prostate imaging – reporting and data system (PI-RADS-v2) score. There has been a comparative study between the ERSPC and the prostate cancer prevention trial (PCPT) risk calculators were the ERSPC proved to be superior (Schumm, 2020). (Consensus WG, strong recommendation)

CLINICAL DIAGNOSIS

- MpMRI or biparametric MRI (bpMRI) must be performed before prostate biopsy and a standardized/structured report must be provided. (ESMO + consensus WG, strong recommendation)
- Clinicians should provide radiologists a request with relevant and obligatory information needed for performance of the optimal MRI-procedure (clinical information, serum PSA, previous biopsy, previous therapy). (Consensus WG, strong recommendation)
- Adhere to PI-RADS guidelines for mpMRI acquisition and interpretation and evaluate mpMRI results in multidisciplinary meetings with pathological feedback. (EAU, strong recommendation)

Conclusions

1. Le dépistage précoce sauve des vies
2. Il est possible de diminuer drastiquement les décès par CaP (asssez facilement)
3. Informer la population des hommes adultes et les médecins généralistes

   - “Si vous ne voulez pas mourir du CaP …”

   - Pas de dépistage de masse à un public non-averti, non-informé

Tout homme en bonne santé et bien informé devrait se voir proposer un dépistage précoce