



Ethnicity & Prognosis

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Making Cancer History®

The Challenge

Prostate cancer is an emergent international challenge !

- **Are there international differences in reported incidence and mortality? Are the reported differences subject to ascertainment bias?**
- **Are geographically detected prostate cancer biologically *distinct*?**
- **Should differences in Ethnicity be determinates of care for *individual* patients?**

Fig. 1

(a) age-standardized prostate cancer incidence rates

(b) age-standardized prostate cancer mortality rates.

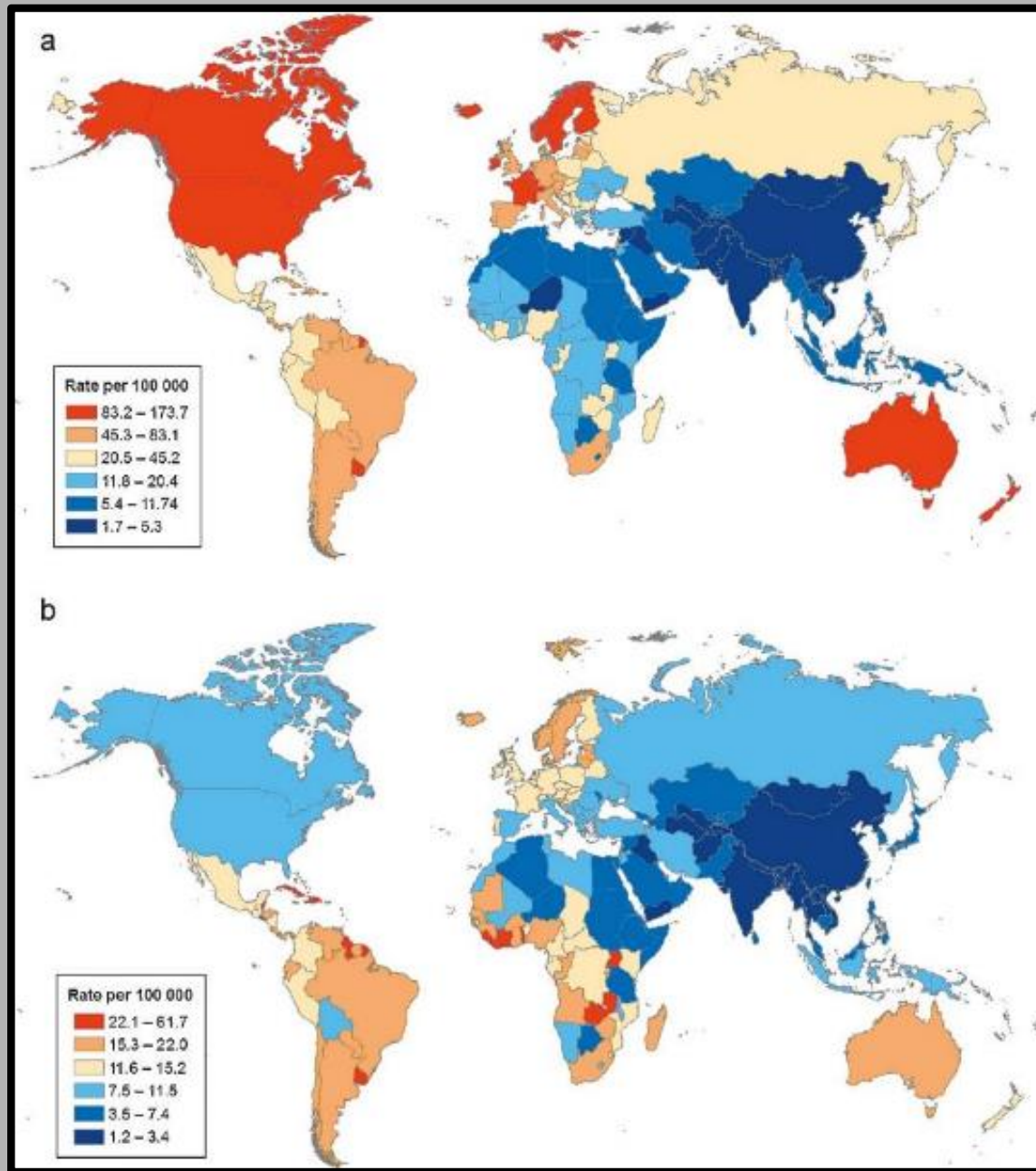
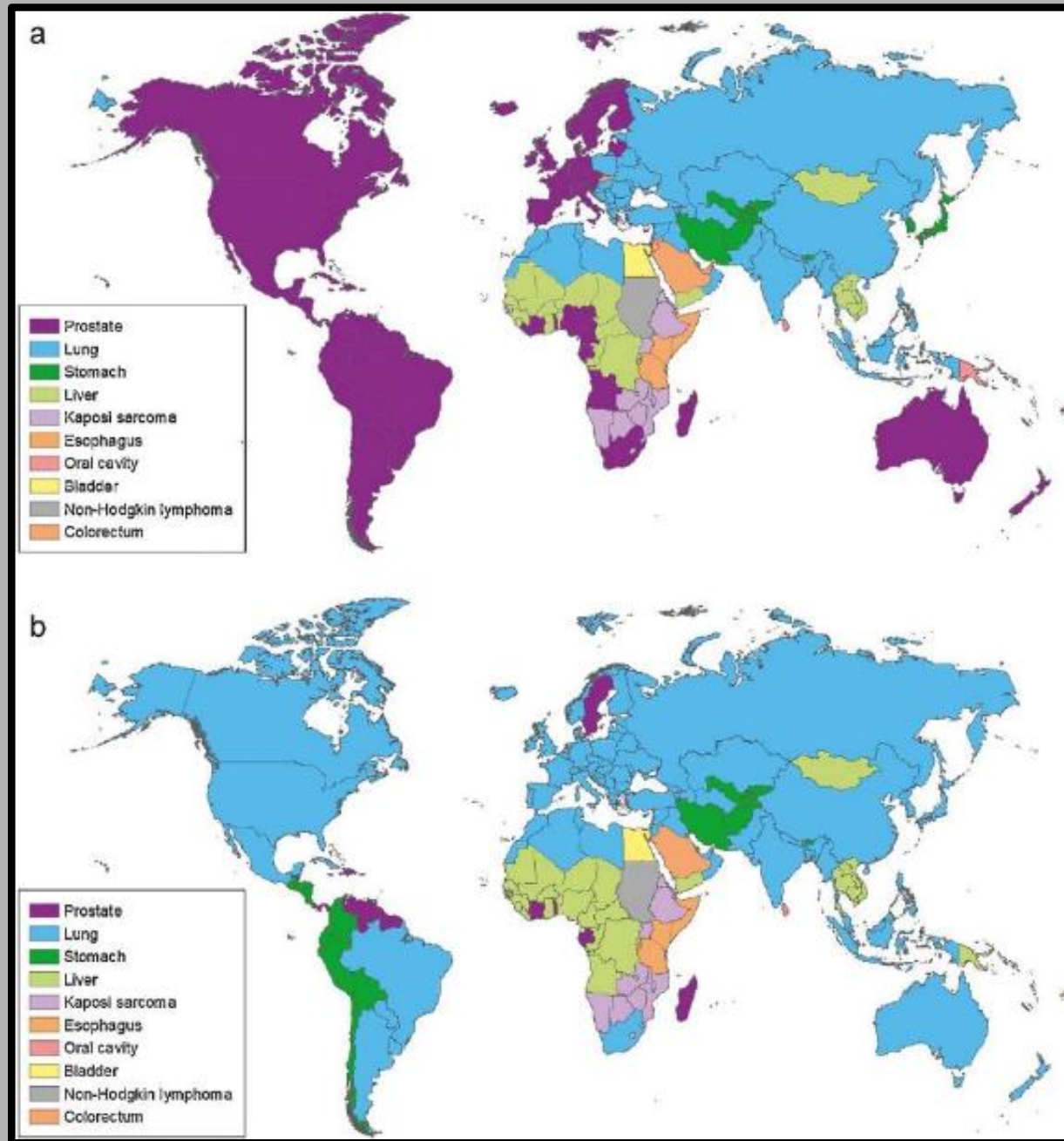


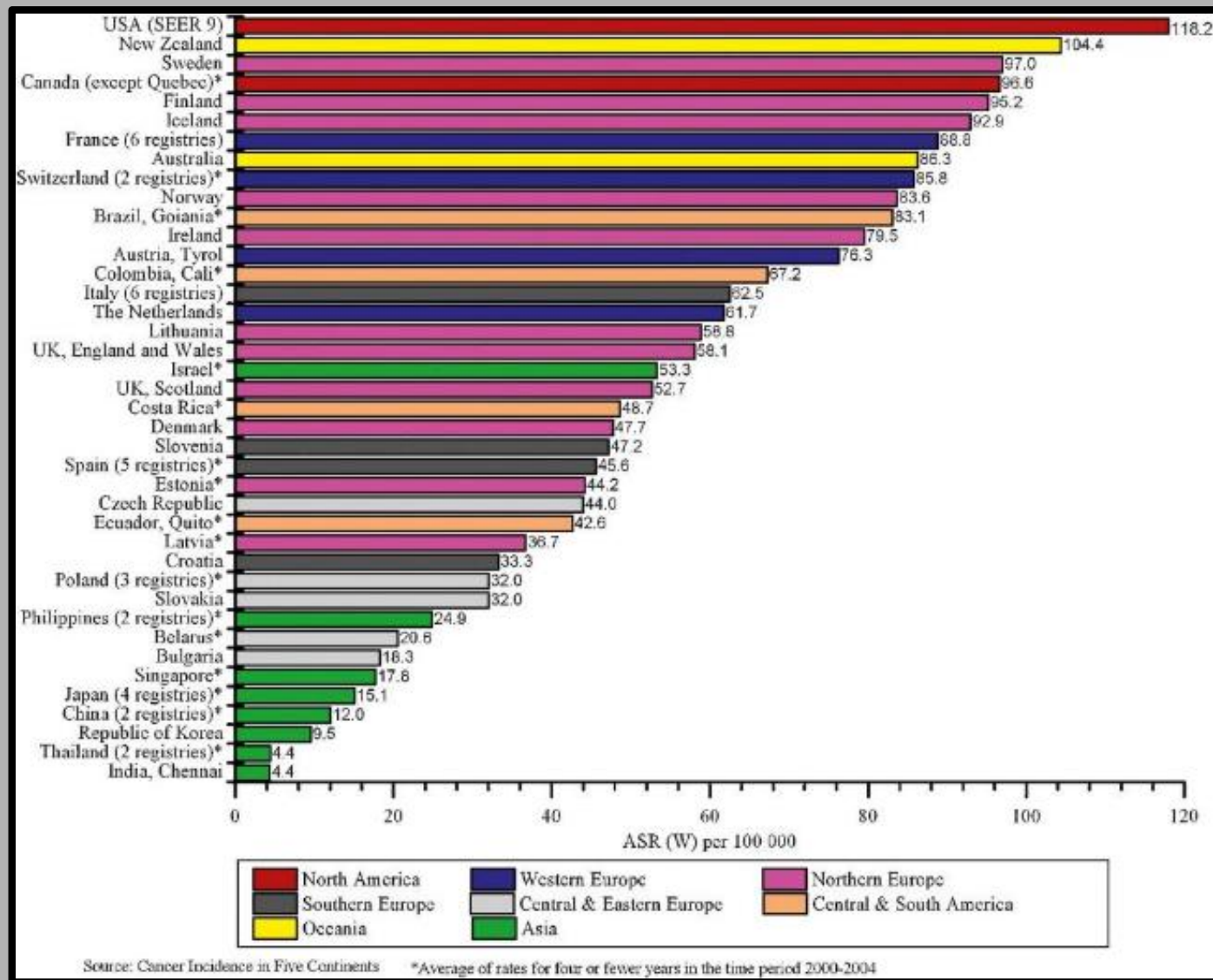
Fig. 2



(a) Most commonly diagnosed cancer among men worldwide, 2008;

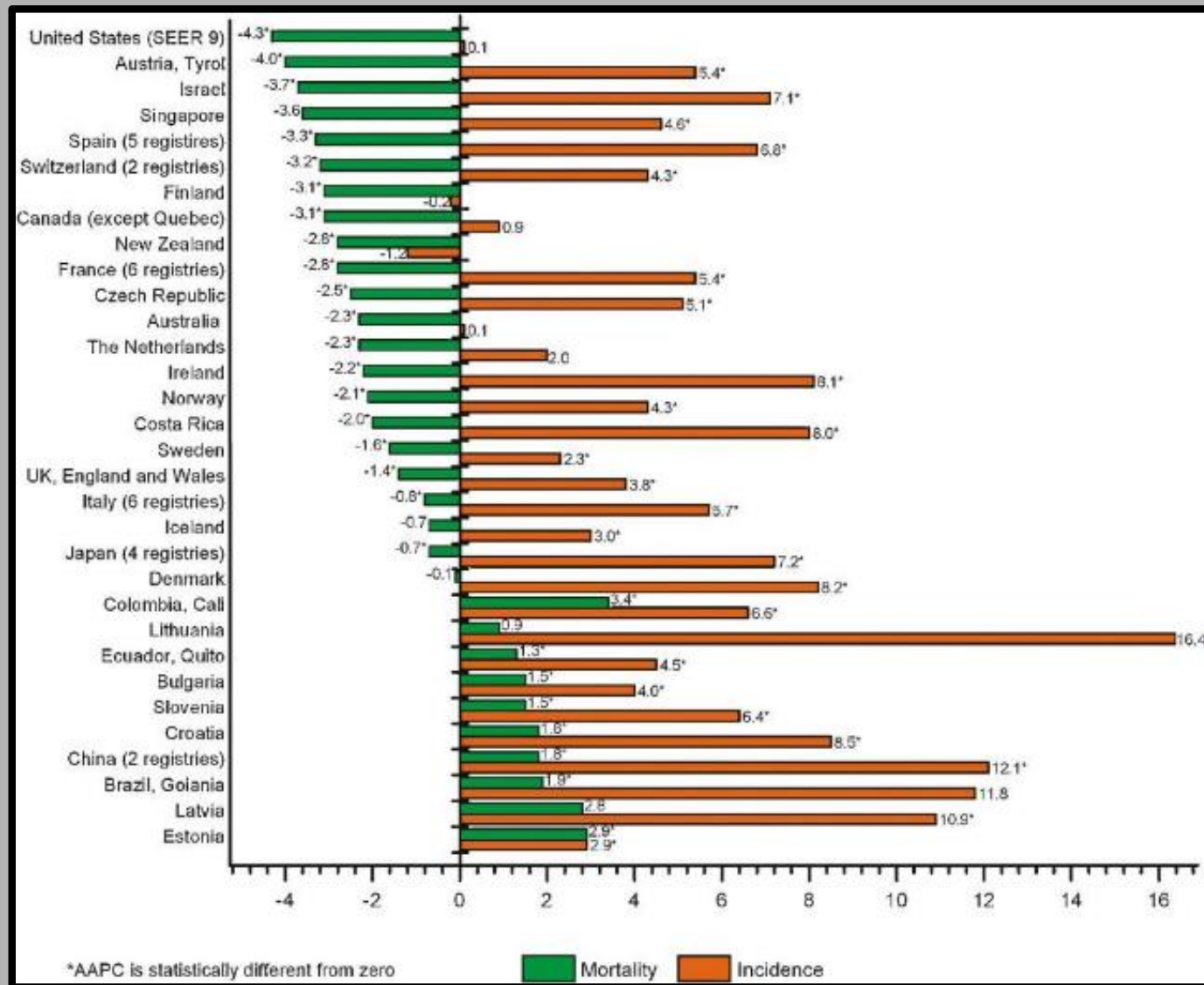
(b) leading cause of cancer deaths among men worldwide, 2008. Source: GLOBOCAN 2008 [1].

Fig. 3



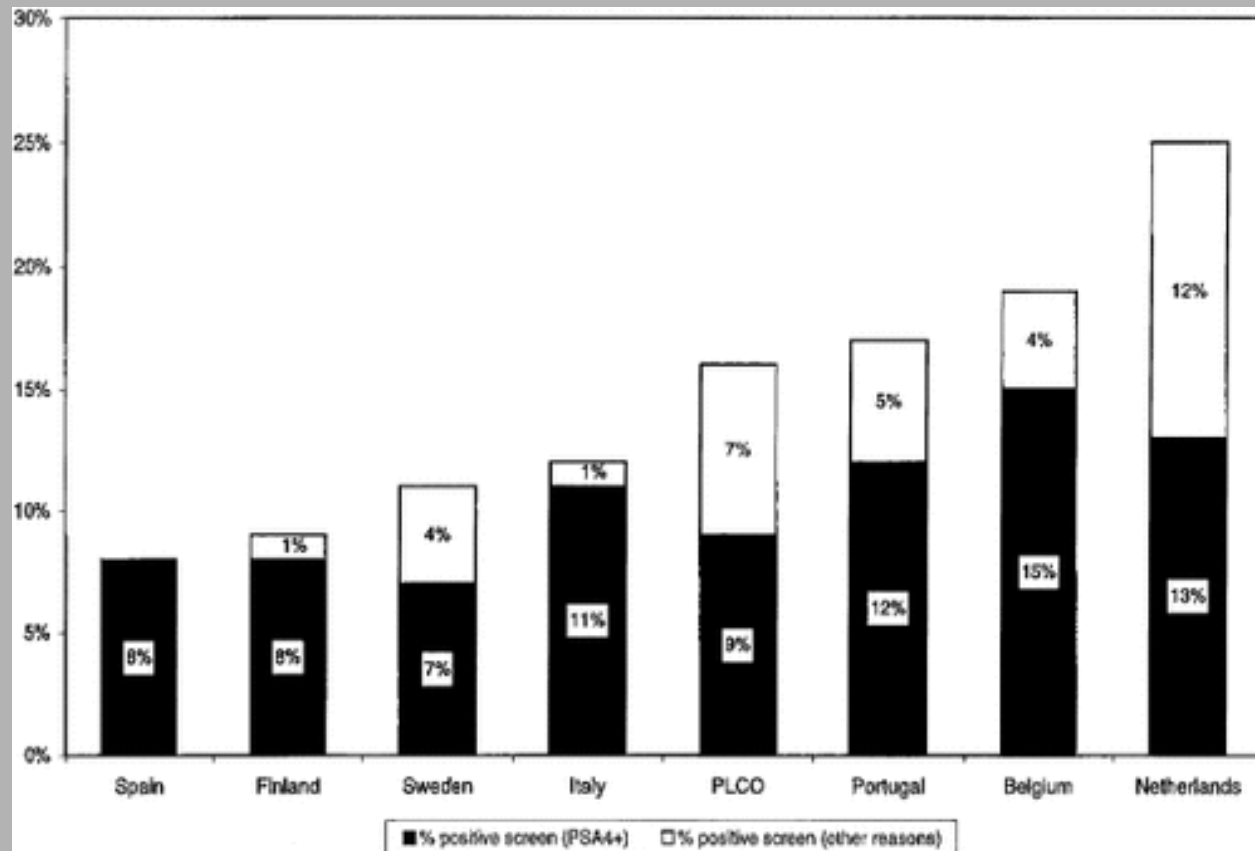
Prostate cancer incidence rates for select registries, 2000–2004. Source: Cancer Incidence in Five Continents [4]. ASR (W)=age-standardized rate (world); SEER=Surveillance Epidemiology and End Results. *Average of rates for ≤ 4 yr in the time period 2000–2004.

Fig. 5



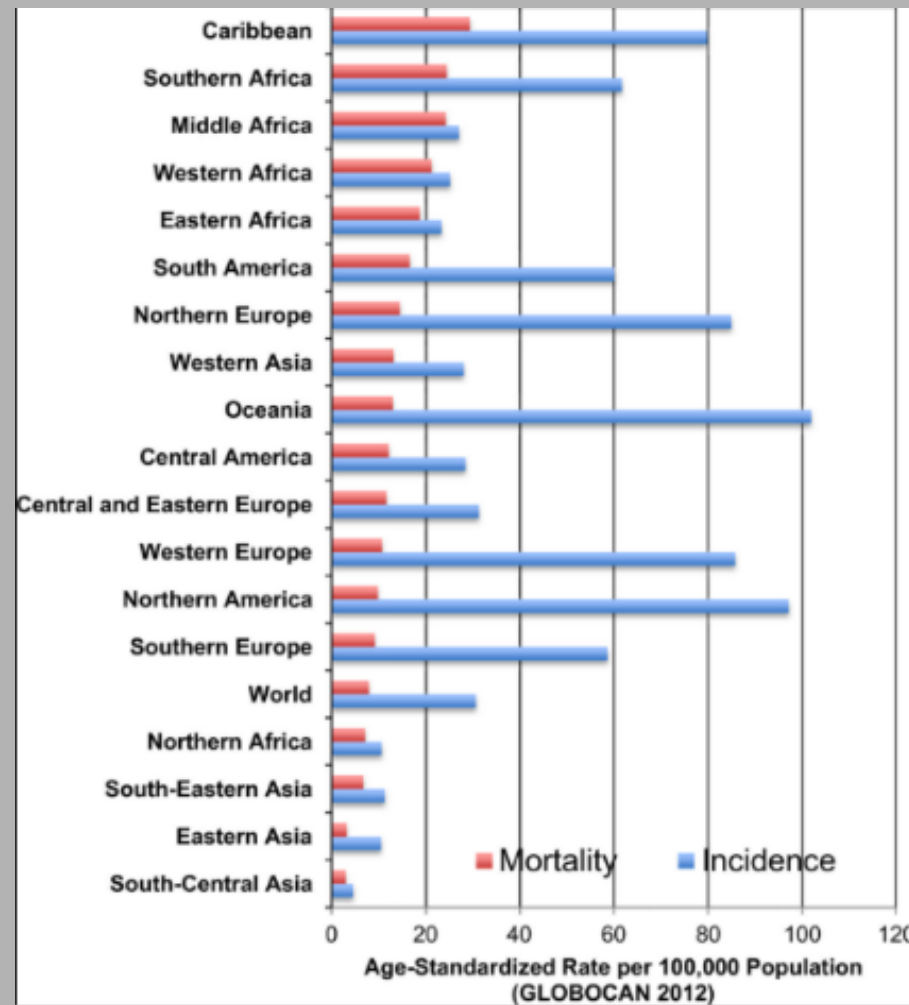
Average annual percent change (AAPC) in incidence and mortality rates for the last 10 yr of available data. SEER=Surveillance Epidemiology and End Results.

Screen Detected Cancer : Europe



Large-scale randomized prostate cancer screening trials: Program performances in the European randomized screening for prostate cancer trial and the prostate, lung, colorectal and ovary cancer trial

International Incidence & Mortality



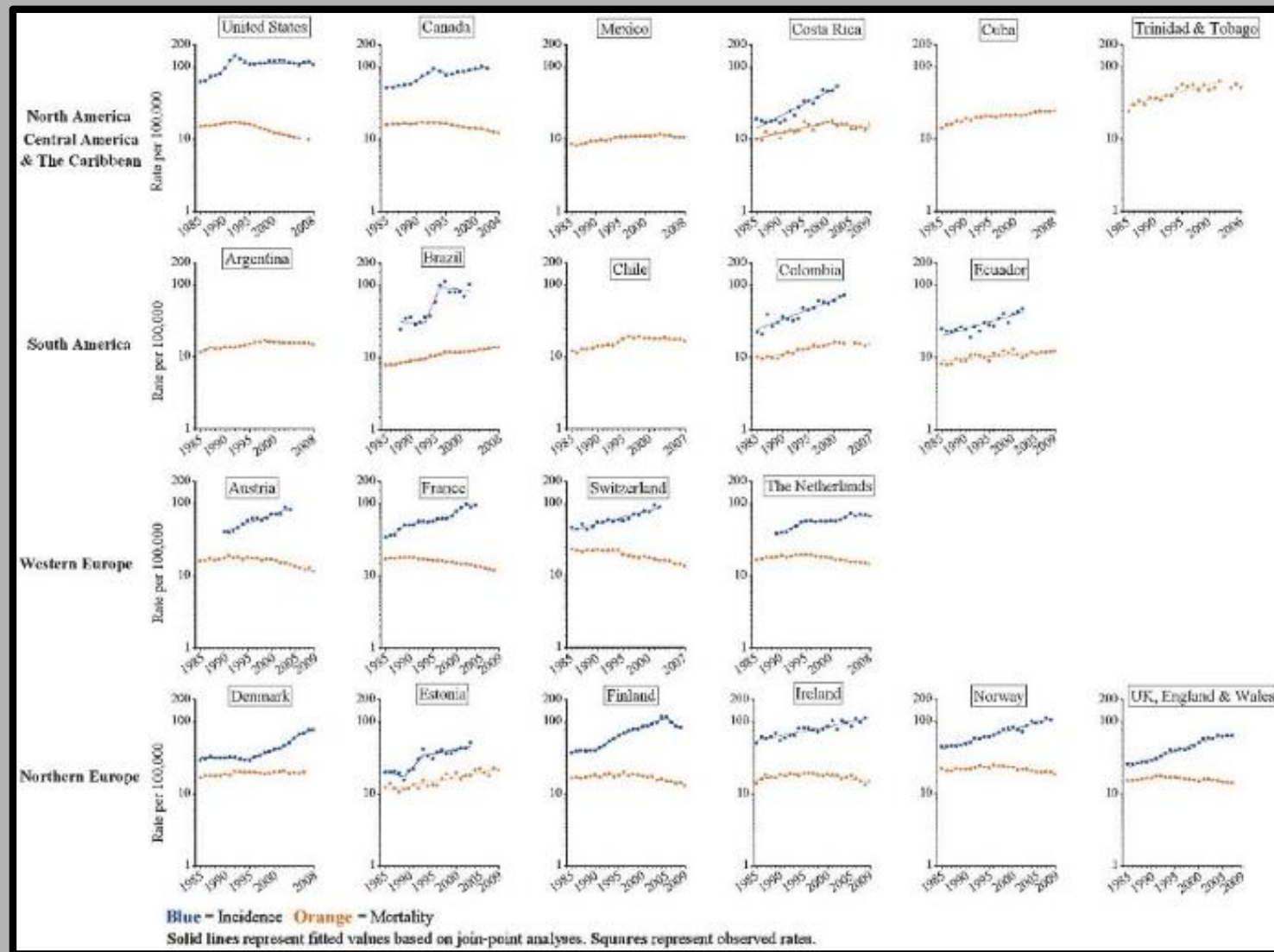
Global Prostate Cancer Incidence and Mortality by World Region

The Challenge

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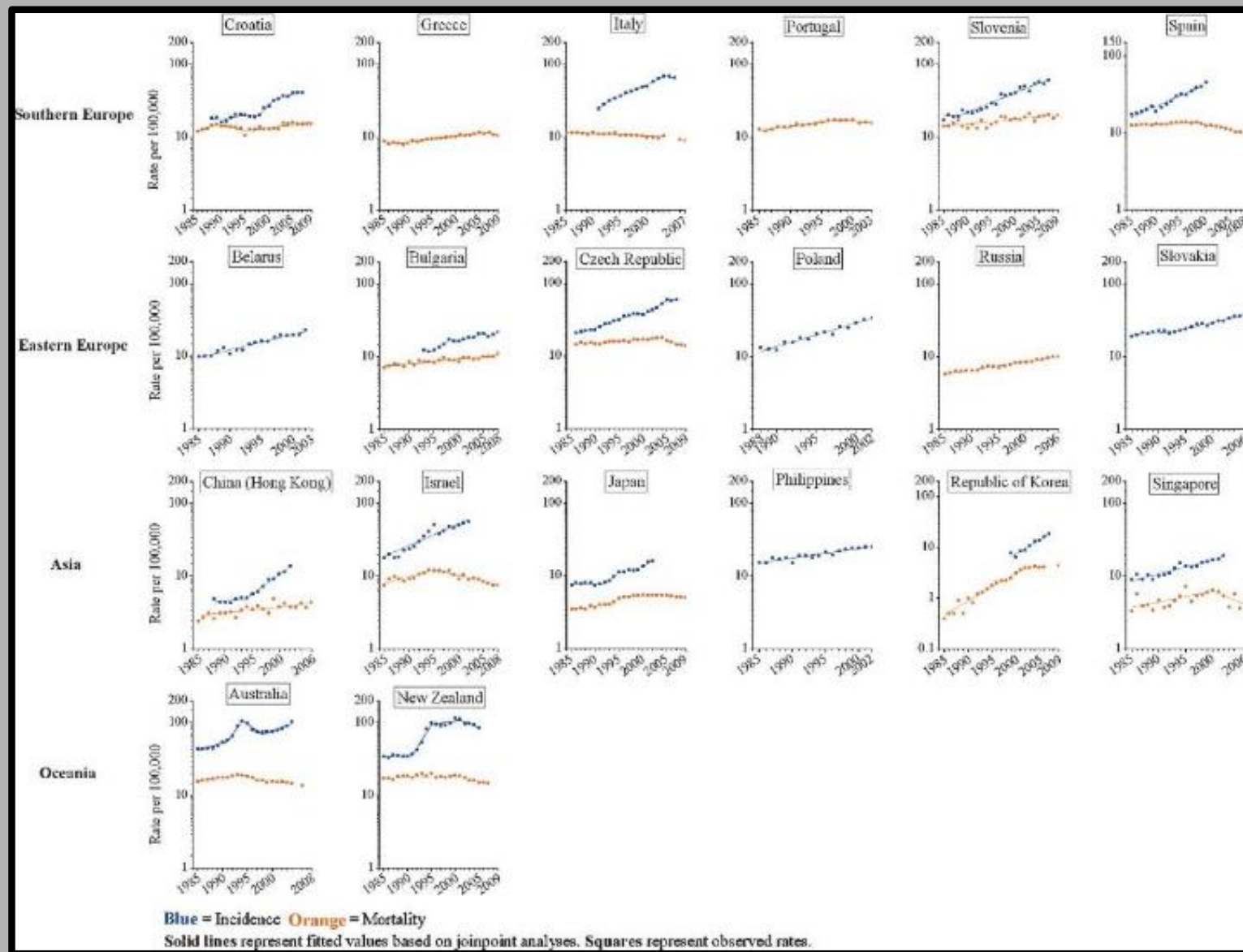
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- **Should Ethnicity be determinant of care for individual patients?**

Fig. 6



World Health Organization (WHO) mortality database [22]

Fig. 6 (Continued)



Trends in prostate cancer incidence and mortality rates, select countries. Sources: incidence: Cancer Incidence in Five Continents [4]; mortality: World Health Organization (WHO) mortality database [22]

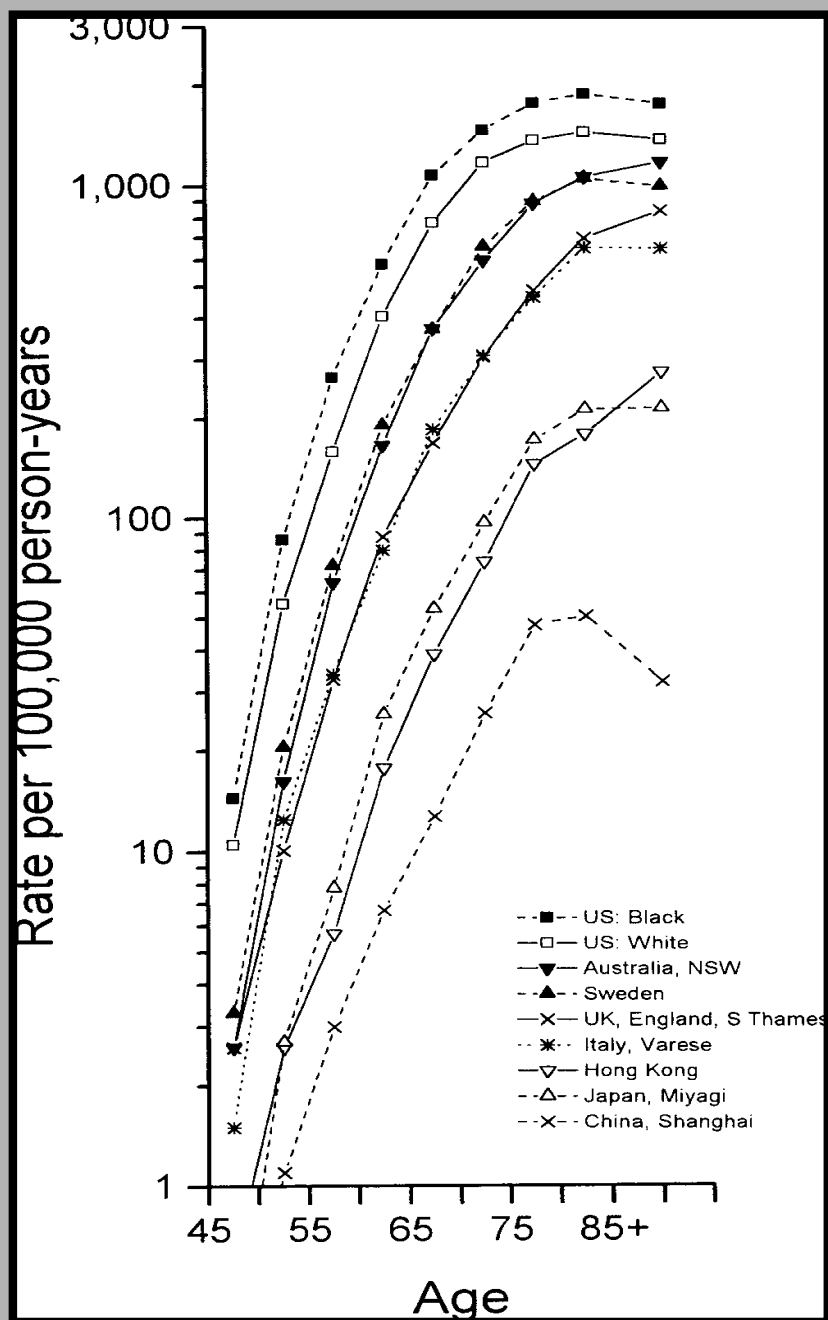


FIGURE 2 – Age-specific incidence curves of prostate cancer in 8 countries, 1988–92

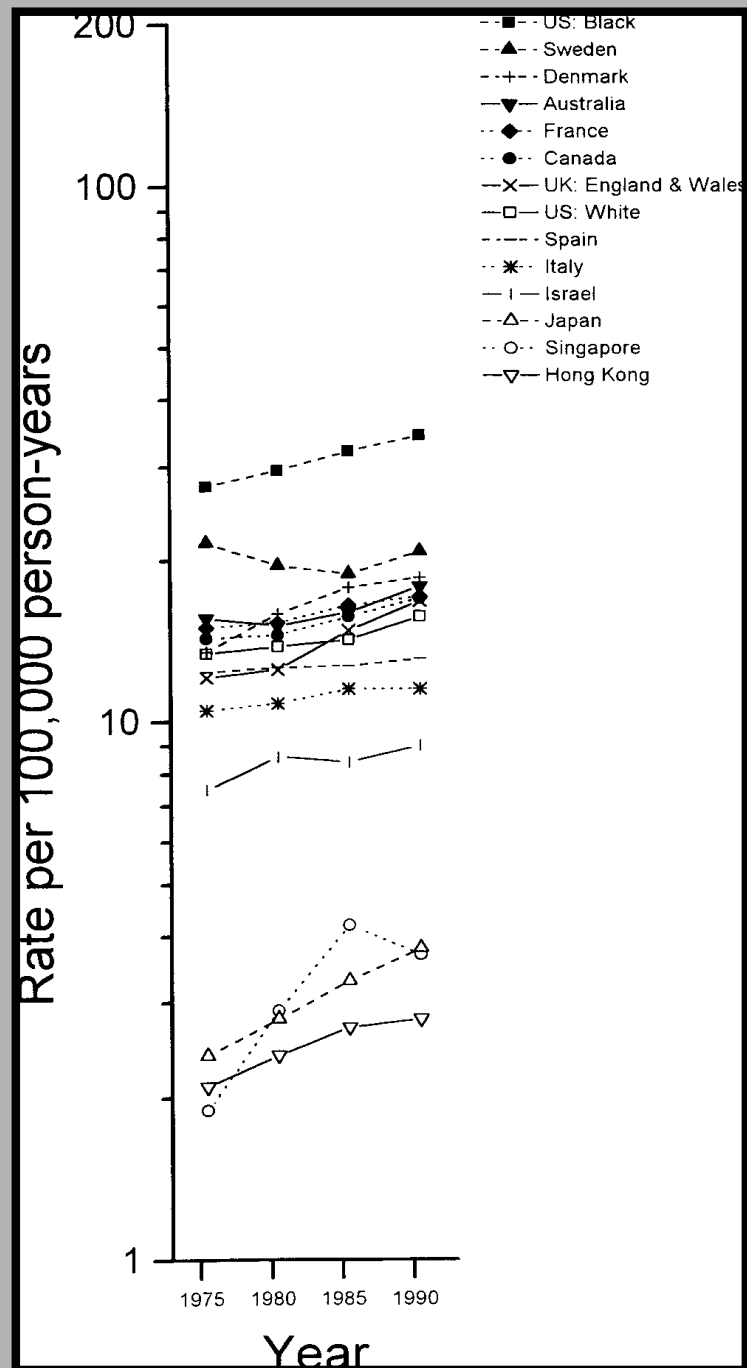


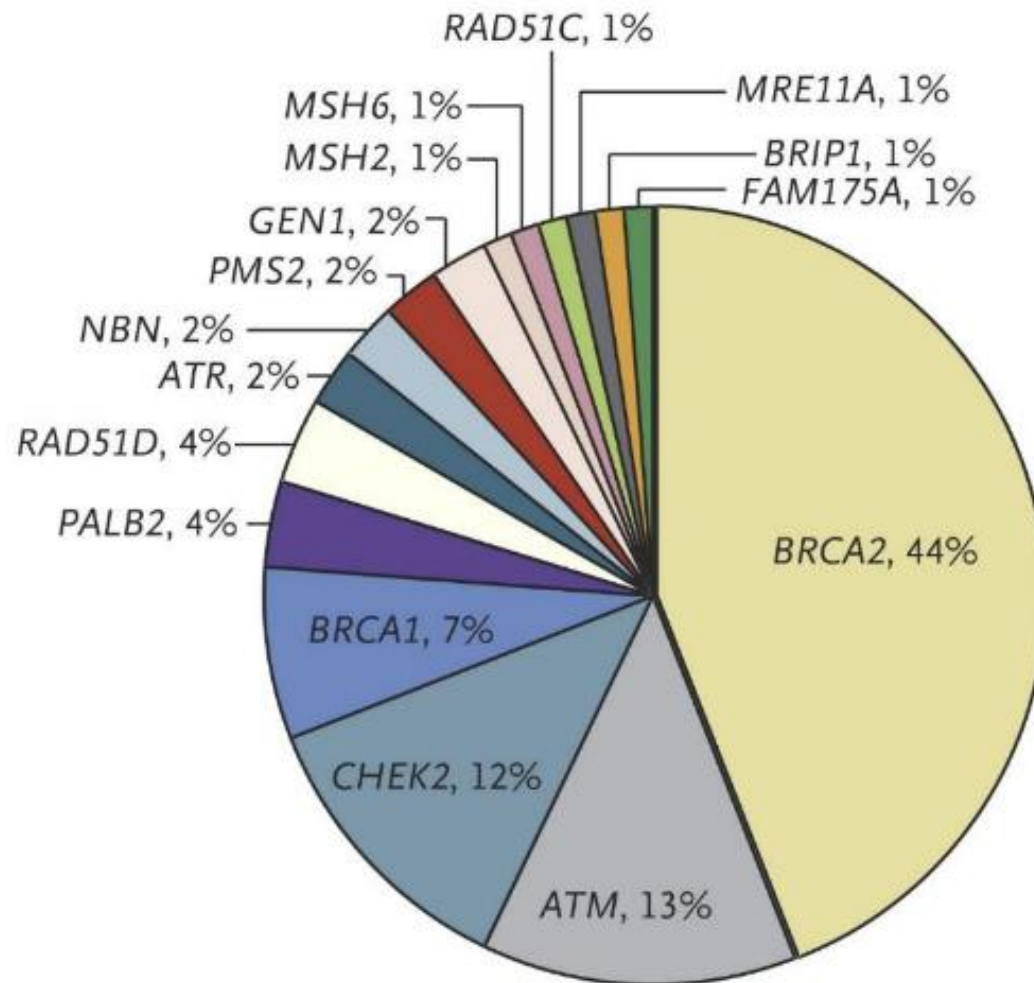
FIGURE 3 – Age-adjusted mortality trends of prostate cancer in 13 countries, 1973–77 to 1988–92

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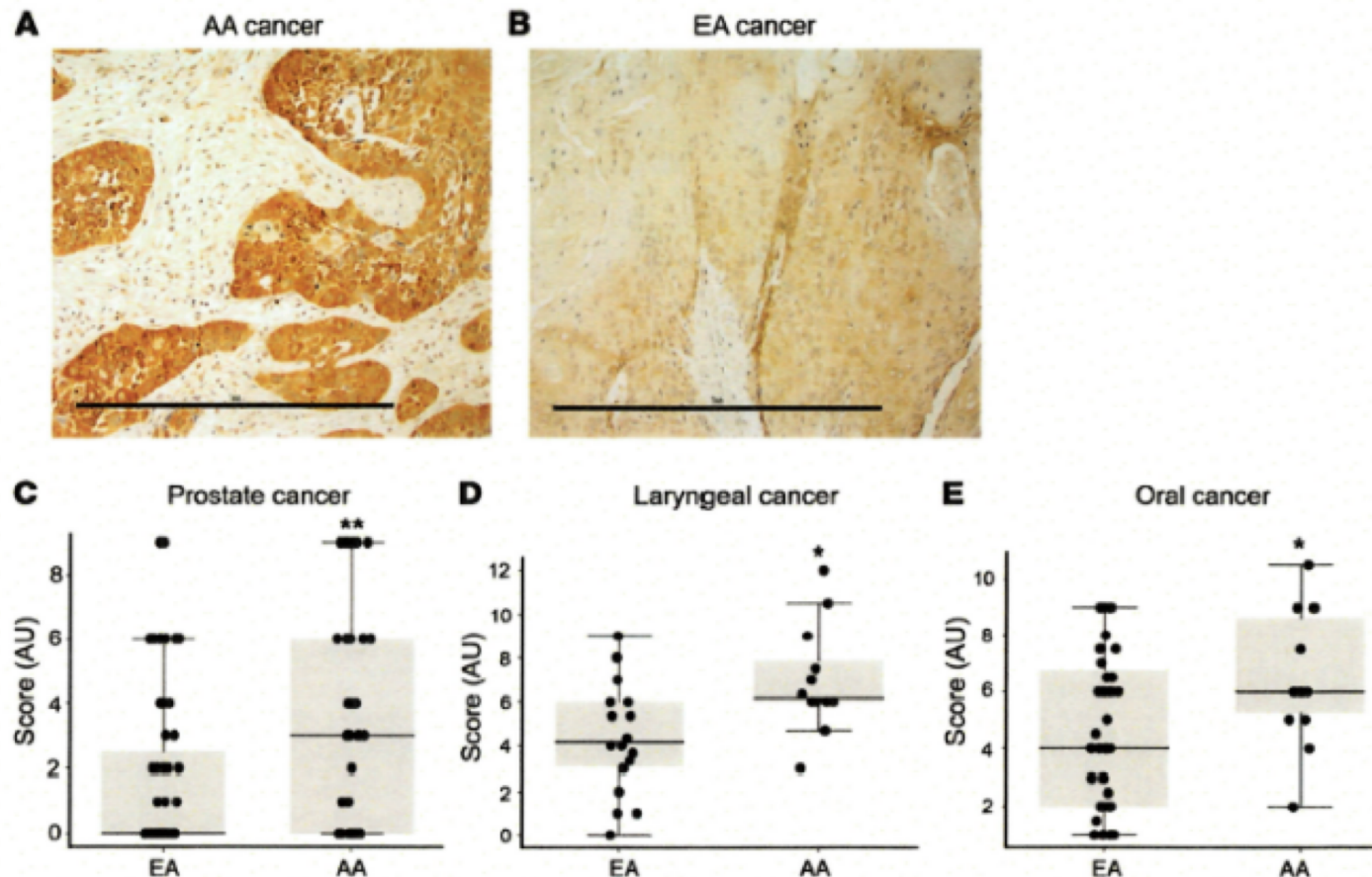
All cancers not created equal: Distribution of Presumed Pathogenic Germline Mutations



Potentially Deleterious Germline & Somatic by Ethnicity ?

Author	Platform	Population	Outcomes
Jaratlerdsiri et al. Cancer Discovery 2018	Whole Genome Sequencing	102 South African + controls	Higher TMB not explained by DDR
Rand et al. Human Molecular Genetics 2016	GWAS (WES of Germline) (platform had limited coverage)	2000 patient case control I study	No increase risk of nonsynonymous variants in African Americans
Huang et al. Cancer Discovery 2017	WES In intermediate to high risk Pca (matched normal & Tumor)	102 discovery 90 validation	Variant of DDR 3.9% in African (interestingly BRCA2) Somatic: FOXA1,SPOP and newly reported ERF SCNA specific to AA
Piyarathna ** JCI 2019	GSEA & Mitochondrial staining (in silico analysis)	Pan Cancer study	Differences Mitochondrial biogenesis

Metabolism & Ethnicity



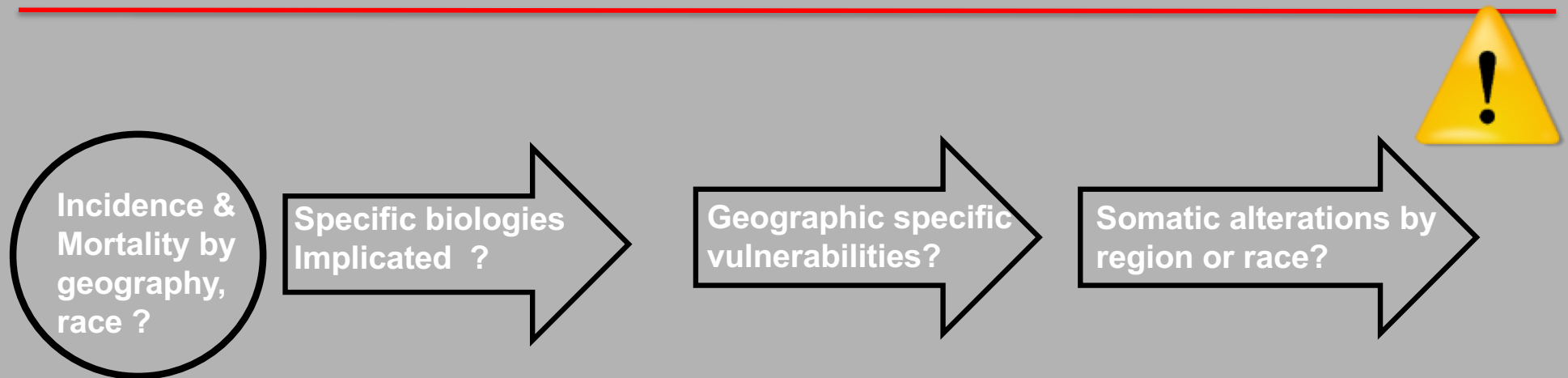
Tissue microarray analysis shows increased mitochondria in samples from African American patients. (A) Tissue microarray analysis (TMA) of samples stained for mitochondria showed increased mitochondrial staining in African American patients compared with (B) European American patients (representative image). Scale bars: 1 mm. (C) TMA data showing increased staining for mitochondria in prostate cancer in African American patients ($n = 53$) compared with prostate cancer in European American patients ($n = 51$). (D) Same as in C, but for laryngeal cancer ($n = 12$ African American patients; $n = 17$ European American patients). (E) Same as in C, but for oral cancer ($n = 14$ African American patients; $n = 43$ European American patients). $**P < 0.01$, $*P < 0.05$; Wilcoxon rank sum test; data are mean \pm SD.

The Challenge

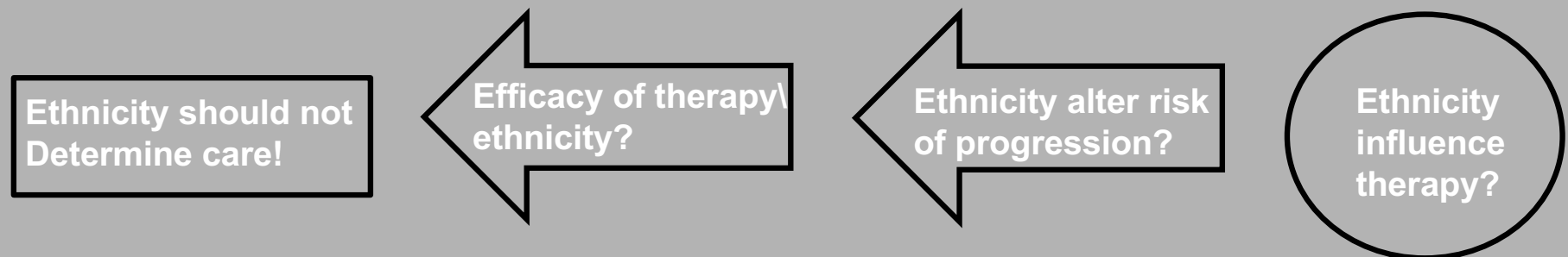
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- **Are geographically detected prostate cancer biologically *distinct*?** Some studies link presence of deleterious alterations (somatic or germ line) with Ethnicity
- **Should difference be determinant of care of individual patients**

Analytic Paths



Mortality rates by region *appear* distinct, frequency of deleterious alterations differ by ethnicity in some studies But etiology uncertain



Therapy & surveillance should be informed by stage & grade, genetics in an Ethnicity agnostic manner

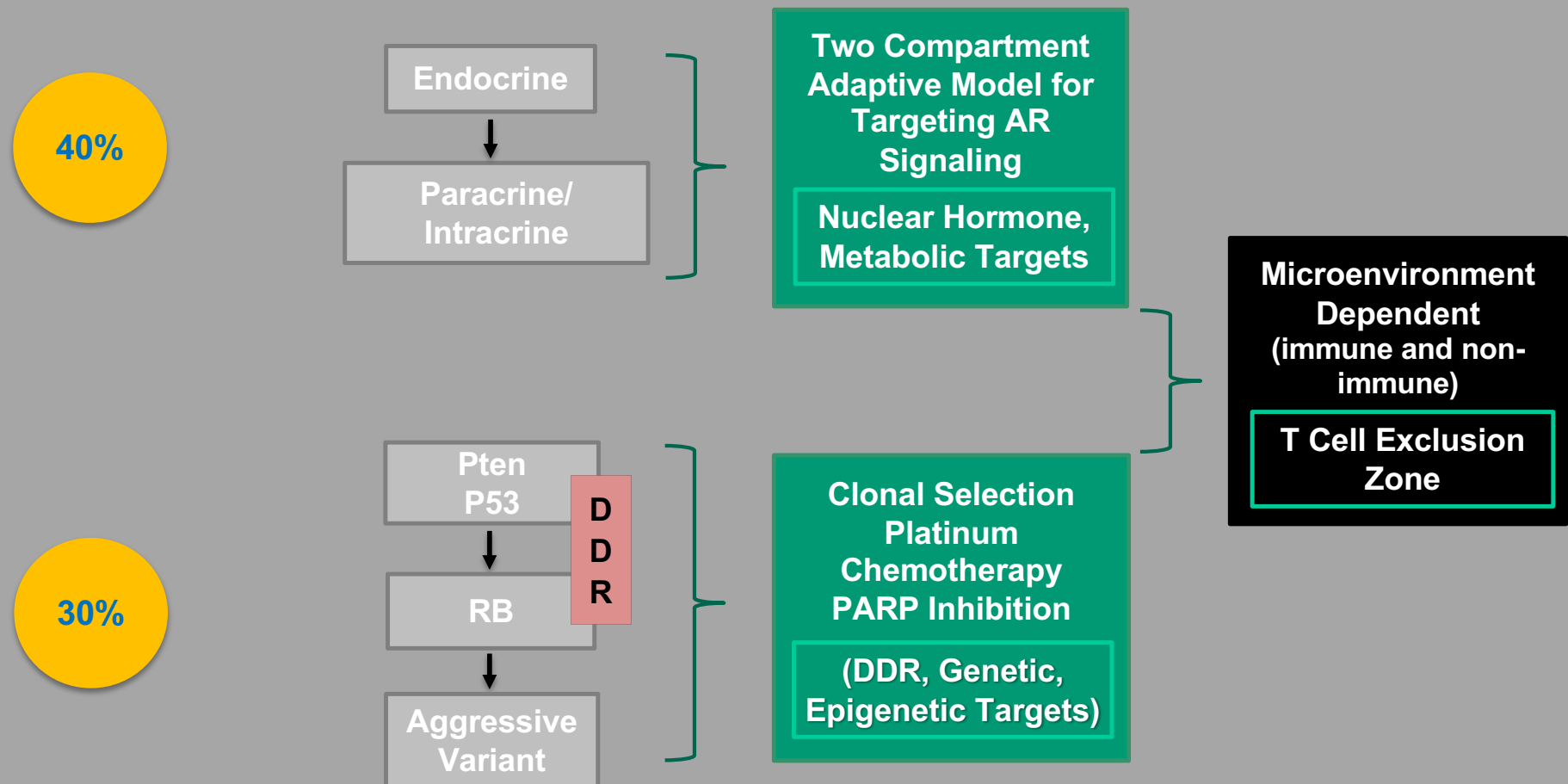
Conclusions

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- **Are geographically detected prostate cancer biologically *distinct*?** Some studies link presence of deleterious alterations (somatic or germ line) with Ethnicity.
- **Should Ethnicity be determinant of care for individual patients?**
No! There is evidence to support ethnicity as an independent determinant of clinical phenotype.

“Domain of Prostate Cancer Progression”

Therapeutically Relevant Modeling Prostate Cancer Progression



Future



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- The role Gene- Environment interaction on Prostate Cancer clinical phenotype outcomes must be understood
 - The “*exo-environment*” must be studied (diet, physical activity, microbiome) .
 - Findings should must benchmarked to known biologic states ?
 - Control for health care and reporting patterns essential!