

Risk Factors for Prostate Cancer (CaP)
Incidence and Progression in the
Health Professionals Follow-up Study

Edward Giovannucci

Yan Liu

Elizabeth A. Platz

Meir J. Stampfer

Walter C. Willett

- Heterogeneity in CaP renders it a difficult cancer to study epidemiologically
- Endpoints that have been used
 - incidence (“prevalence”)
 - mortality
 - high-grade
 - advanced stage
 - “aggressive” (combination of stage / grade)
 - recurrence / progression

Further PSA screening has complicated study of CaP epidemiology by:

- increasing the pool of diagnosed cancers
- pushing the diagnosis to earlier stages
- focusing on "prevalence" rather than incidence (i.e. an event)

We assessed 9 risk factors for CaP in the Health Professionals Follow-Up Study on various CaP endpoints, defined by incidence, mortality, stage and grade.

We further assessed:

- various definitions of advanced stage
- pre-PSA era versus PSA era

Health Professional Follow-Up Study

- Prospective study of 51,529 men
- Repeated measures every two years
- Analysis from 1986-2002
- Prostate cancer endpoints:

Incident	n = 3,544
Fatal	n = 312
Advanced stage	n = 523
Non-advanced stage	n = 2,161
High grade (≥ 7)	n = 1,110
Low grade	n = 1,601

Summary of Results for Risk Factors for Prostate Cancer Endpoints in HPFS (1986-2002)

	Incident	Non-advanced	Low-grade	Fatal	Advanced	High-grade
Vigorous activity		↑	↑	↓	↓	
Body mass index				↑	↑	
Calorie intake				↑	↑	
Height				↑	↑	↑
Tobacco (last 10y)			↓	↑		
Tomato sauce	↓	↓	↓	↓		
α -linolenic acid	↑	↑	↑	↑	↑	
Calcium	↑			↑	↑	↑
Family hx of CaP	↑	↑	↑	↑	↑	↑

We found 4 patterns
whereby risk factors of CaP
may influence mortality

(1) Increase Incidence

	Incident	Non-advanced	Low-grade	Fatal	Advanced	High-grade
α -linolenic acid	↑	↑	↑	↑	↑	
Tomato sauce	↓	↓	↓	↓		
Family history CaP	↑	↑	↑	↑	↑	↑

(2) Increase Likelihood of Poor Differentiation

	Incident	Non-advanced	Low-grade	Fatal	Advanced	High-grade
Calcium	↑			↑		↑
Height				↑	↑	↑

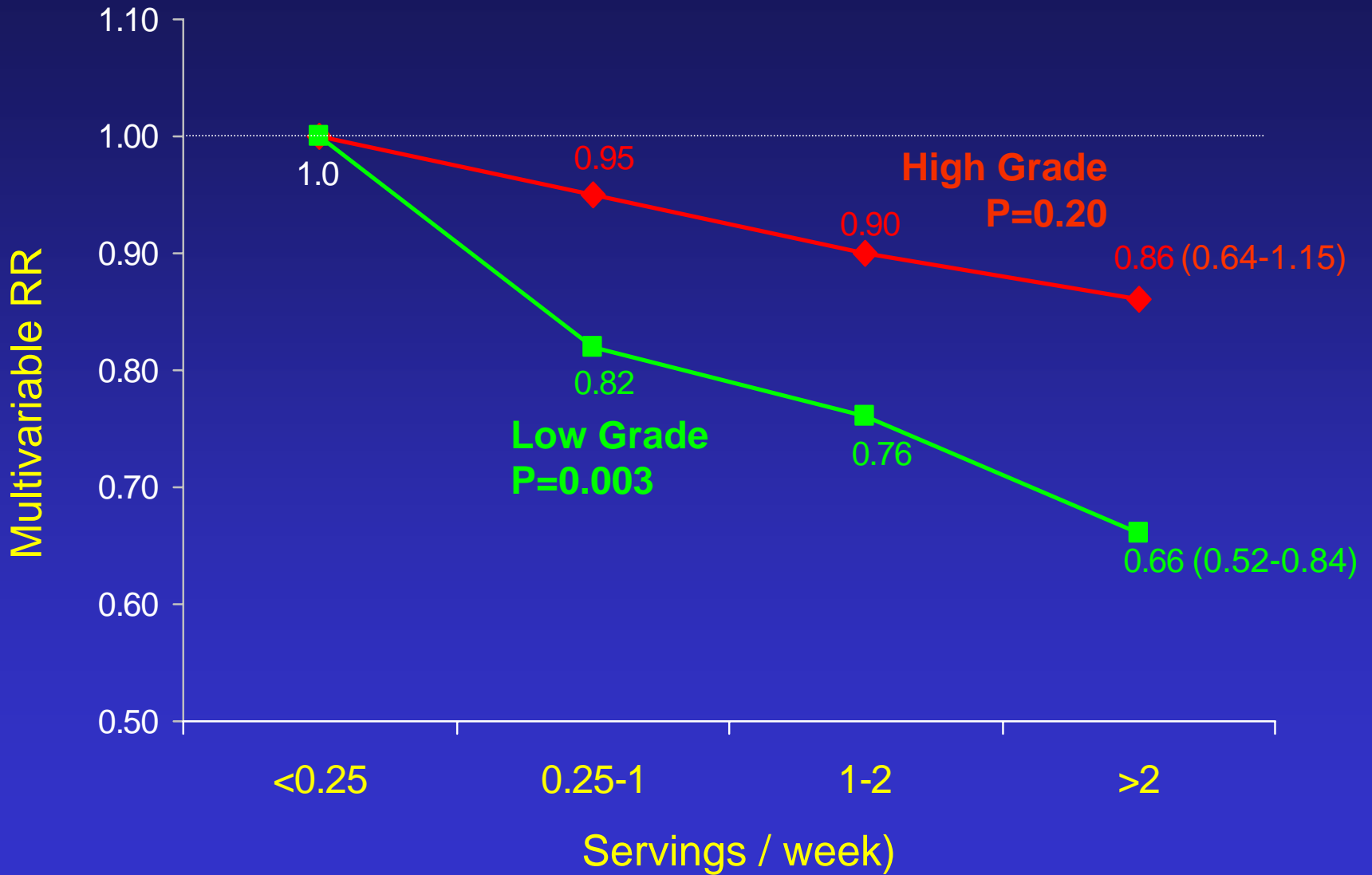
(3) Increase Mortality Independently of Incidence and Grade

	Incident	Non-advanced	Low-grade	Fatal	Advanced	High-grade
BMI				↑	↑	
Physical activity		↑	↑	↓	↓	
Tobacco (last 10y)			↓	↑		

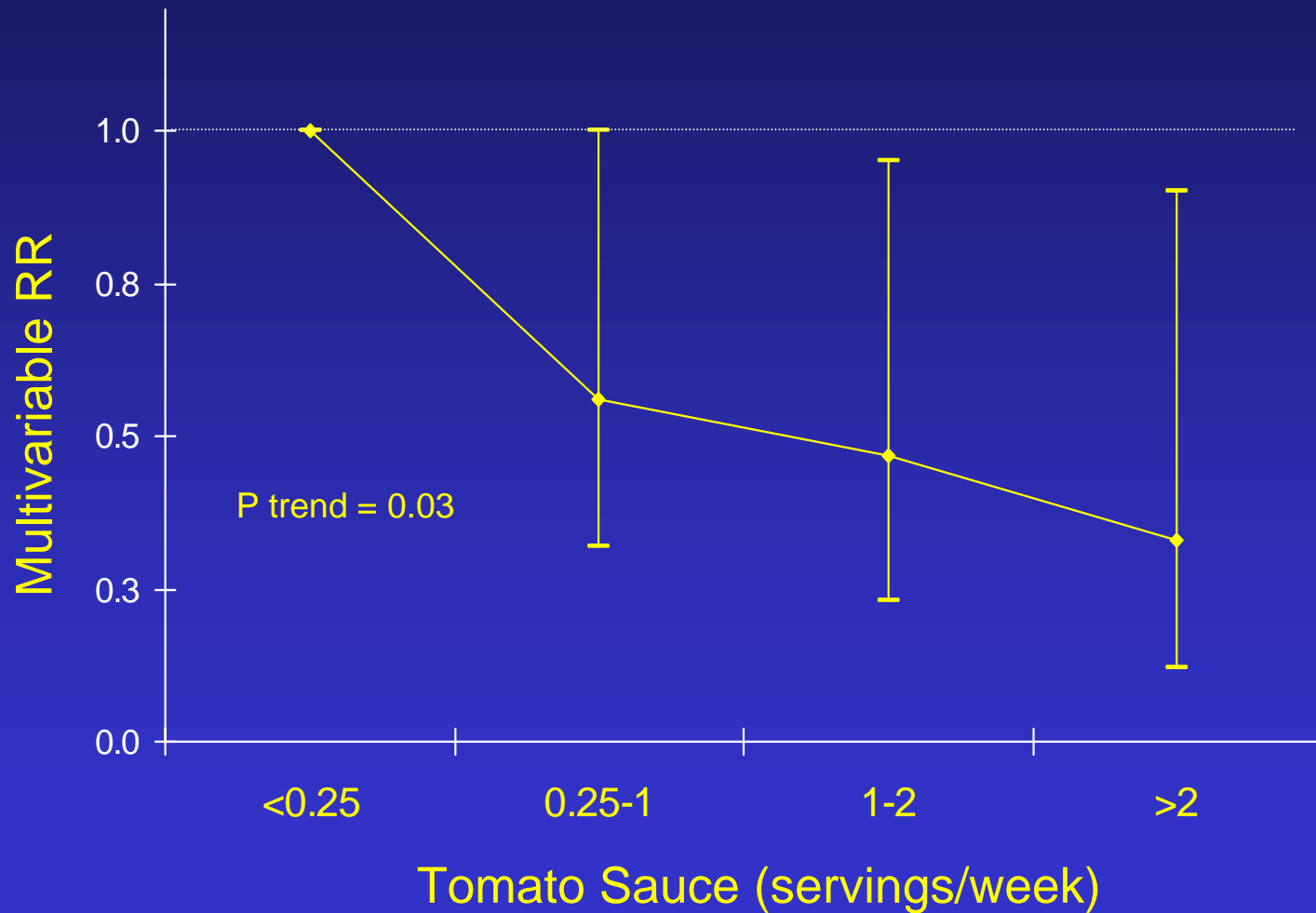
(4) Increase Promotion or Progression Preferentially of Better Differentiated CaPs

	Incident	Non-advanced	Low-grade	Fatal	Advanced	High-grade
Tomato sauce	↓	↓	↓	↓		
α -linolenic acid	↑	↑	↑	↑	↑	

Tomato Sauce



Low-Grade, Advanced CaP (n=83 cases)



Summary

Prostate cancer mortality can be increased by increasing:

- 1) incidence
- 2) likelihood of poor differentiation
- 3) mortality independent of incidence and grade
- 4) preferential progression of better-differentiated CaPs

Examine Two Levels of Advanced Stage

	Organ- Confined	Minimally Extraprostatic	Advanced
	T1 or T2 and N0M0	T3a and N0M0	T3b or T4 or N1 or M1
	n = 2161	n = 345	n = 523
Height			↑
Physical activity			↓
BMI			↑
Energy intake			↑
Calcium intake			↑
α -linolenic intake	↑		↑
Family history of CaP	↑	↑	↑

Many risk factors influence advanced stage,
but only when strictly defined
(seminal vesicle involvement or metastasis)

	Total CaP		Advanced CaP	
	Pre-PSA*	PSA Era	Pre-PSA*	PSA Era
Height			↑	↑
Body mass index			↑	↑
Energy intake			↑	↑
Calcium	↑		↑	↑
α -linolenic acid			↑	↑
Vigorous activity			↓	↓
Tomato sauce	↓	↓	↓	↓

* Before 1/92

Using strict definition of
advanced stage prostate cancer,
associations are similar in
the pre- and post-PSA eras.

Implications

- Most risk factors for CaP mortality do not influence incidence
- High-grade CaP is not a generally appropriate surrogate for CaP progression
- Advanced stage is a good surrogate for fatal CaP, but only when strict definition is used
- Risk factors for pre-PSA and PSA-era converge for advanced CaP (strictly defined)