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Prediction models: why much of what you've been told is wrong or irrelevant

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Five golden rules

- Don't like a coefficient? Feel free to change it
- What is faster, a road bike or a mountain bike?
- It doesn't matter if the hotel is too expensive
- What happened to Dr. Scardino's patients in Houston in the 1990's is not the sum total of cancer biology
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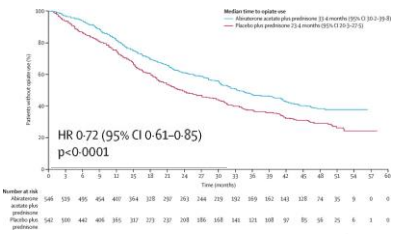
Prediction modeling is unlike other areas of biostatistics

Don't change the data on abiraterone!



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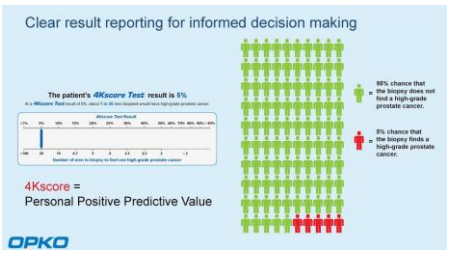
What coefficient should we use for a model?



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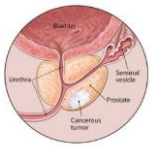
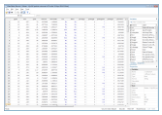
What is the increase in risk of prostate cancer for African Americans?





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What coefficient?

- 0.5: A meta-analysis of our existing data
- 1.0: Reported in the literature from a large definitive study
- 0.8: The most recent of our studies

So we decided ….

0.60

The optimal value would have been … 0.59

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Every guideline for prostate cancer screening and treatment emphasizes life expectancy


GUIDELINE STATEMENTS

Additional Statements


American Urological Association (AUA) Guideline

EARLY DETECTION OF PROSTATE CANCER: AUA GUIDELINE

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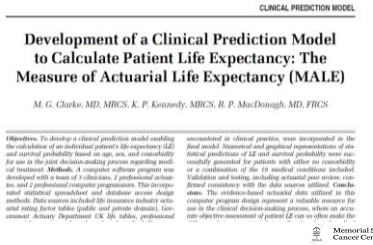
But only one good model, and that not designed for US clinical care



CLINICAL PREDICTION MODEL

Development of a Clinical Prediction Model to Calculate Patient Life Expectancy: The Measure of Actuarial Life Expectancy (MALE)

M. G. Clarke, MD, MRCS, K. P. Kennedy, MRCS, R. P. MacDonagh, MD, FRCS

Objectives. *To develop a clinical prediction model enabling the calculation of an individual patient's life expectancy (LE) and survival probability based on age, sex, and comorbidity for use in the joint decision-making process regarding medical treatment.* **Methods.** *A computer software program was developed with a team of 3 clinicians, 2 professional actuaries, and 2 professional computer programmers. This incorporated statistical spreadsheet and database access design methods. Data sources included life insurance industry actuarial rating factor tables (public and private domain), Government Actuary Department UK life tables, professional encountered in clinical practice, were incorporated in the final model. Numerical and graphical representations of statistical predictions of LE and survival probability were successfully generated for patients with either no comorbidity or a combination of the 10 medical conditions included. Validation and testing, including actuarial peer review, confirmed consistency with the data sources utilized.* **Conclusions.** *The evidence-based actuarial data utilized in this computer program design represent a valuable resource for use in the clinical decision-making process, where an accurate objective assessment of patient LE can so often make the*

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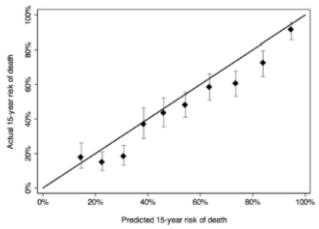
We created a new model based on MALE

- Me: } for hype
- Mat hype
- Me:



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Which is faster?

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Logistic regression isn't up to the task

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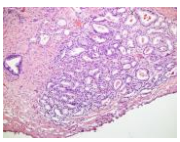
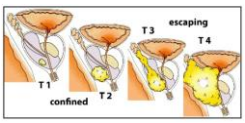
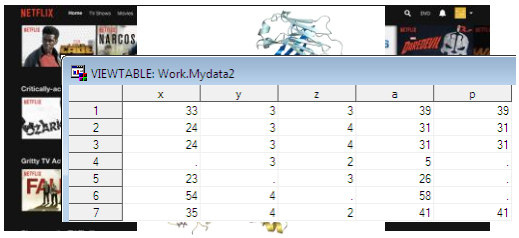
Logistic regression helpful for prostate cancer prognosis





When is machine learning of benefit



	x	y	z	a	p
1	33	3	3	39	39
2	24	3	4	31	31
3	24	3	4	31	31
4	.	3	2	5	.
5	23	.	3	26	.
6	54	4	.	58	.
7	35	4	2	41	41

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Can I afford the holiday?

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So why does it matter if the patient has low albumin?

Patient Characteristics	HR	*p* Value	Prognostic Score
Skin metastasis	4.49	<0.0001	130
Low BMI < 18.5	2.09	0.0003	81
High serum LDH (>ULN)	1.74	<0.0001	48
Adrenal metastasis	1.52	0.0002	52
PS 1 (vs. PS 0)	1.45	<0.0001	35
Low serum albumin (<LLN)	1.45	<0.0001	32

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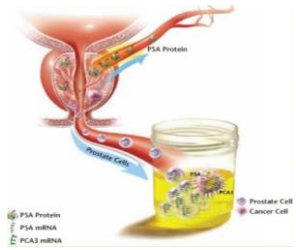
Sophisticated test: but is your score over 35?



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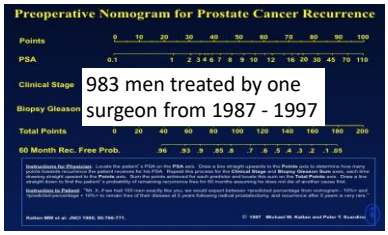
The prediction model that changed everything



983 men treated by one surgeon from 1987 - 1997

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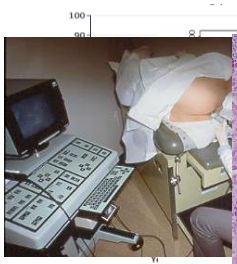
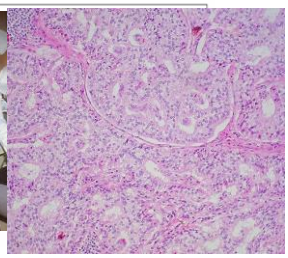
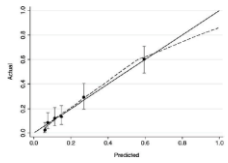
Has anything changed since 1997?



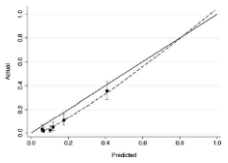


Changes in grading, practice, lead to miscalibration

Applied to 1987 - 1995



Applied to 1996 - 2011



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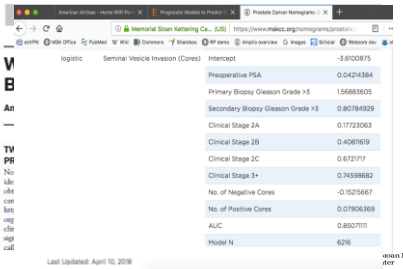
Update prediction models as new data become available



logistic	Seminal Vesicle Invasion (Cores)	Intercept	-3.6100875
		Preoperative PSA	0.04214384
		Primary Biopsy Gleason Grade >3	1.56883605
		Secondary Biopsy Gleason Grade >3	0.80784929
		Clinical Stage 2A	0.17723063
		Clinical Stage 2B	0.40811619
		Clinical Stage 2C	0.672177
		Clinical Stage 3+	0.74598682
		No. of Negative Cores	-0.15215667
		No. of Positive Cores	0.07906369
		AUC	0.8507111
		Model N	6216

Last Updated: April 10, 2018

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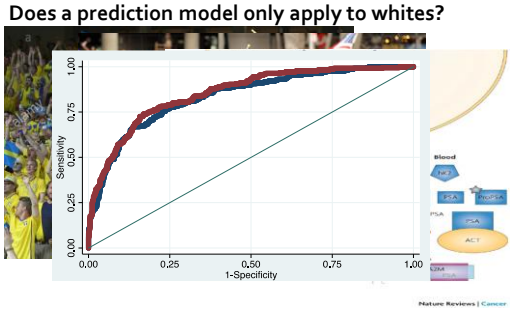
Which chicken is smarter?

Does a prediction model only apply to whites?



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Emergency in the lab!

- AUC 0.98

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A "devil's dilemma"

- AUC 0.55

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Discrimination is robust to coefficients

- True model:
  - Log odds $Y = 2X_1 + X_2 + 0.5X_3 - 4$
- Corrupted model:
  - Log odds $Y = 0.67X_1 + 4X_2 + 0.25X_3 - 4$

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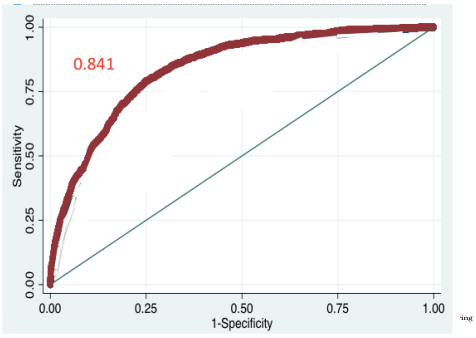
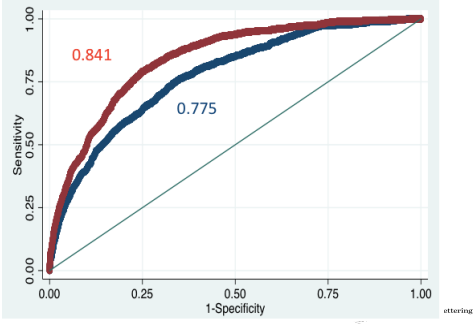
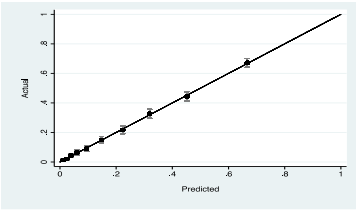




Calibration typically perfect on internal validation



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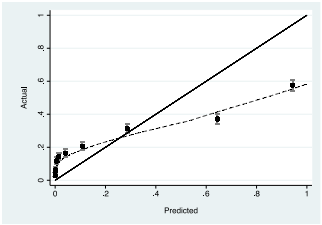
Calibration very sensitive to correct coefficients



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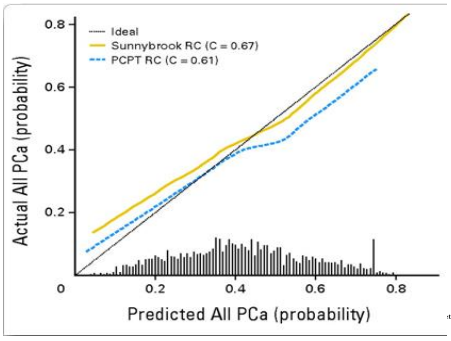

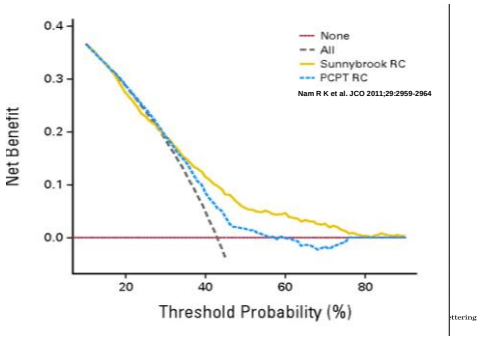

How to evaluate models

- Discrimination:
  - How much information are my predictors giving me?
- Calibration:
  - Do I need to adjust coefficients or intercept?
- Clinical utility:
  - Should we use this model in practice?

Statistician

Doctor or policy maker

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In sum…

- Feel free to change a coefficient
- Use machine learning, logistic regression, tarot cards, whatever

THOUGH I'D ADVISE

- don't throw away data by dichotomizing continuous variables

AND:

- Evaluate clinical utility
- Worry about biological and medical differences between cohorts

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