

Treating High Risk Prostate Cancer

Surgery Has The Edge!

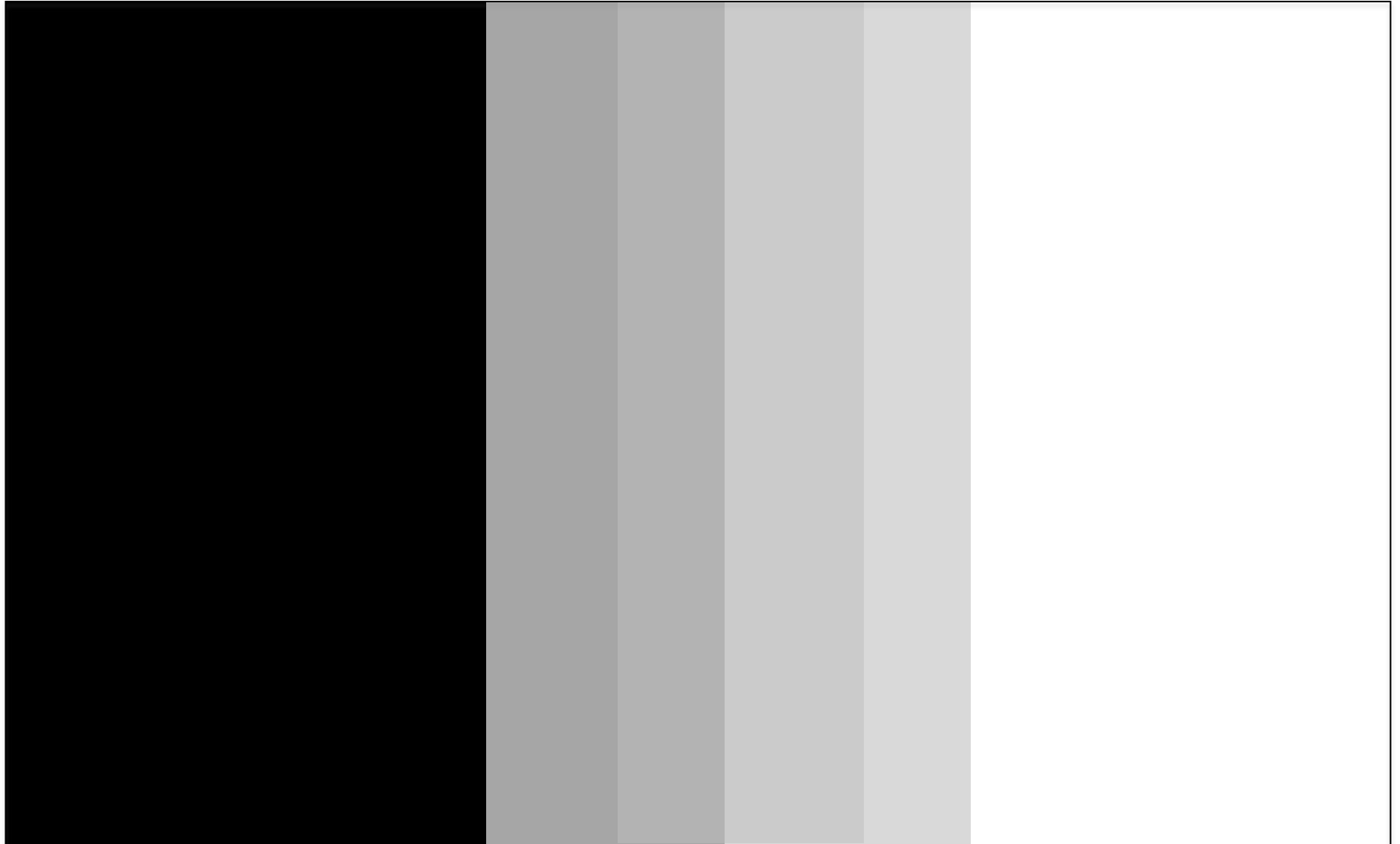
Alan McNeill

Department of Urology
Lothian University Hospitals

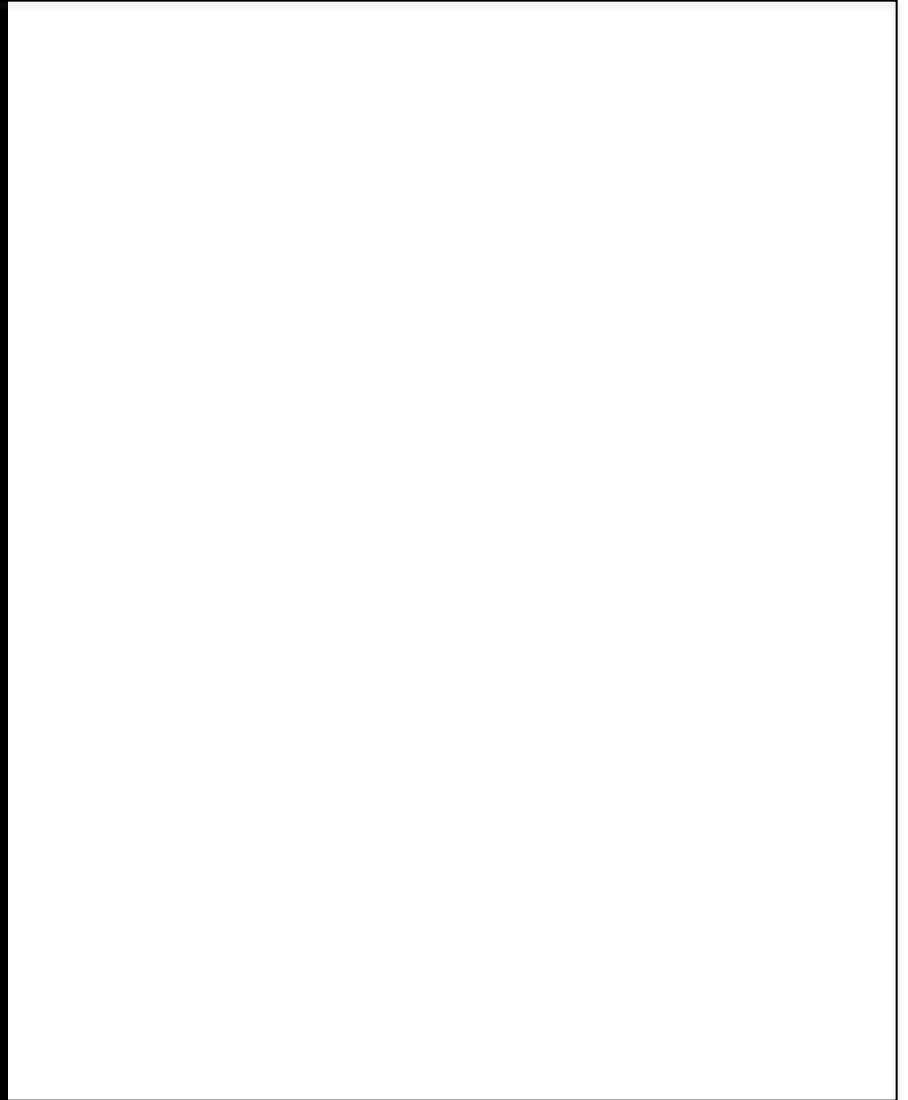
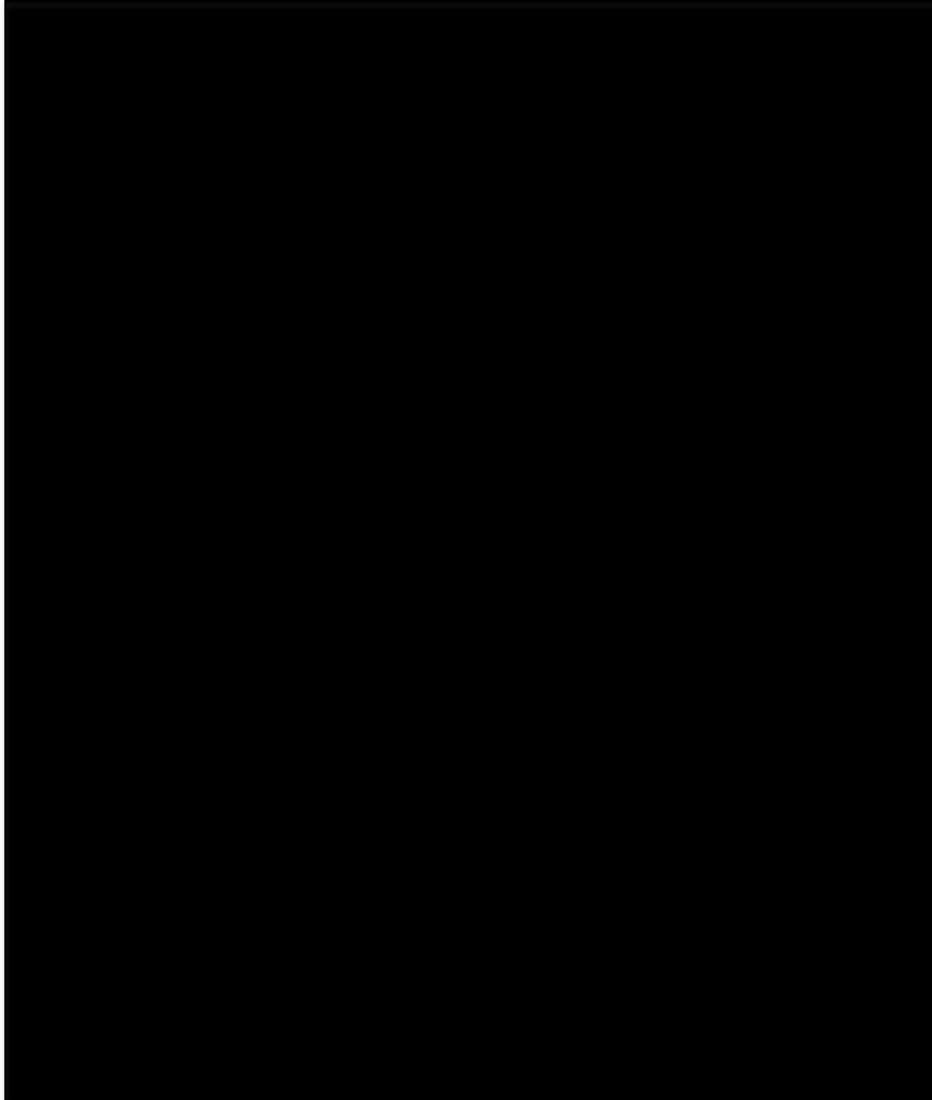


Perspective

Radiologists'



Surgeons'

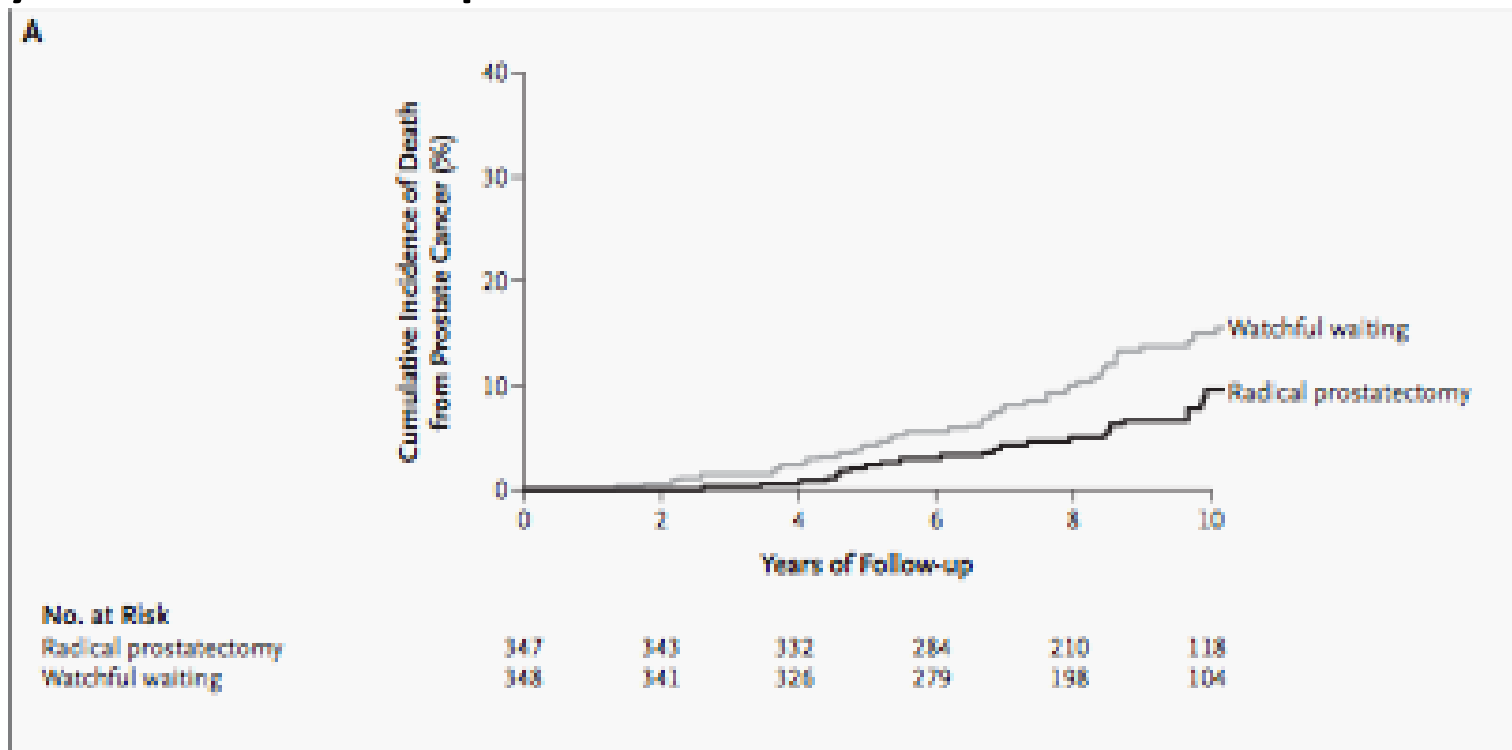


Tony Blair's



Why is there any grey with PCa?

- Natural history of the disease means 10-15 year follow-up needed to assess treatments



(Bill-Axelsson, NEJM 2005)

Radical Prostatectomy

- Good oncological and functional outcomes, particularly with high-volume practice
 - Pathological evaluation of what has been removed
 - Simplicity of follow-up – PSA present or absent
- Complications well recognised and effective remedies are available

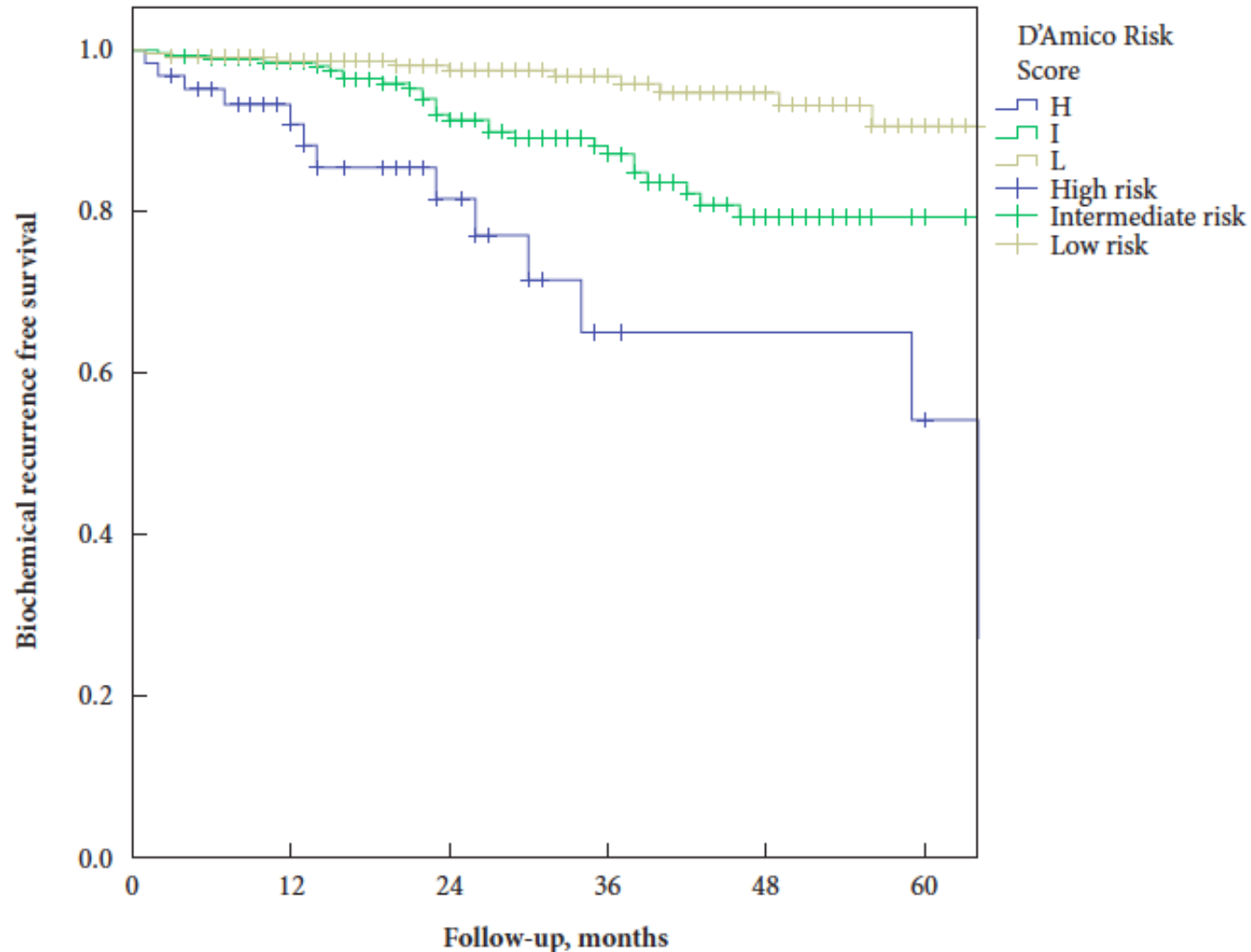
Radical Prostatectomy

- Additional oncological benefits being recognised
 - Improved survival even with LN+ive disease
 - Reduced risk of future metastasis
 - Reduced risk of problems of advanced local disease
- **Offers prospect of multimodal therapy**
 - **with evidence of little impact on QOL**

RALP/LRP Approach Is More Palatable

- Smaller incisions
 - Less pain
 - Faster recovery
- Less blood loss
 - Low transfusion rate
- Fewer complications
- Higher volume centres/surgeons
 - Better outcomes
- Better vision – x 10 magnification
- Reduced blood loss
- More accurate dissection
- Improved outcomes

5 Year Risk of PSA Relapse (>0.2) – Personal Series



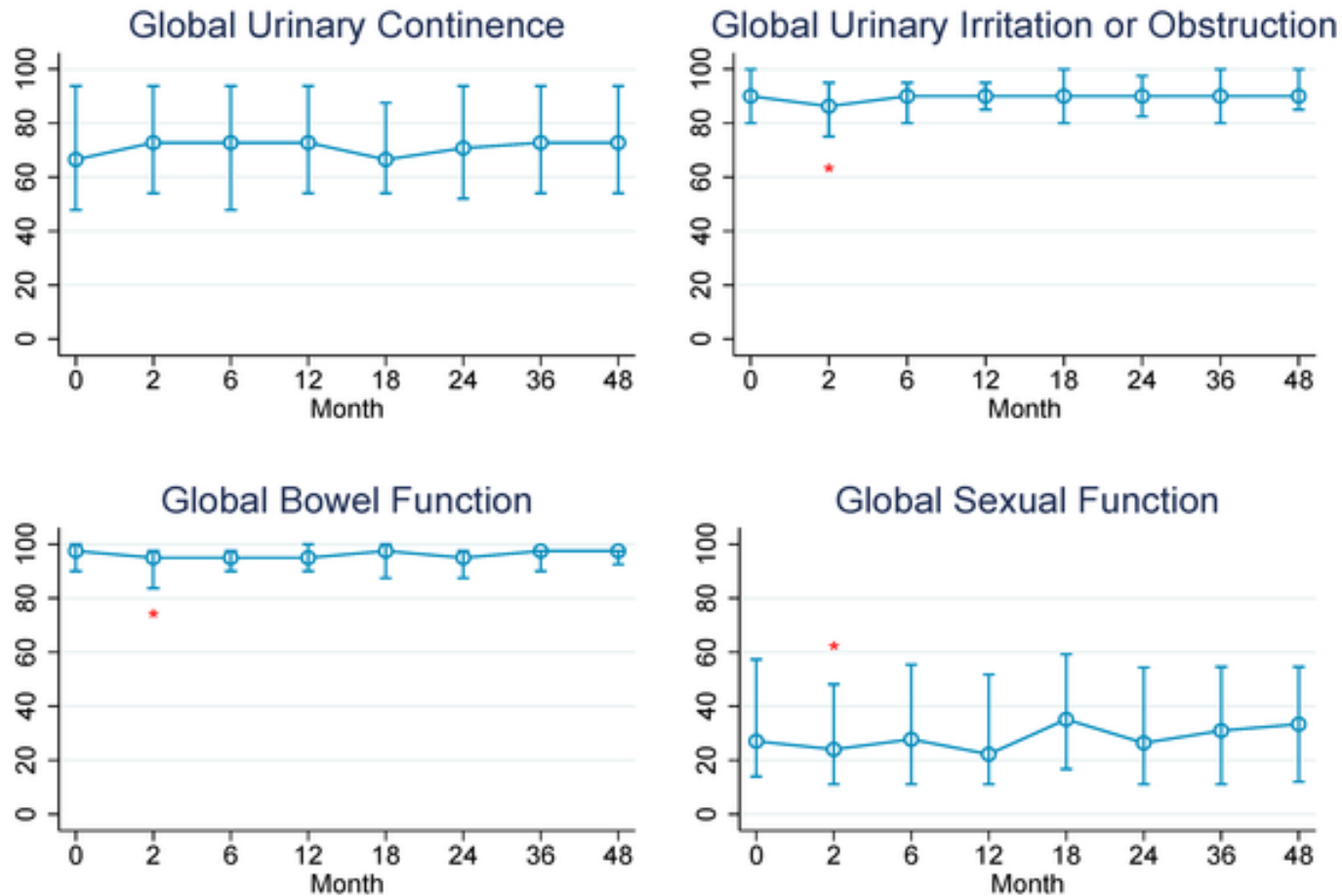
PSA relapse

- PSA relapse due to local or metastatic recurrence
 - Local relapse tends to occur later with slower PSADT
 - Failure to PSA nadir <0.1 or rapid PSA relapse (within 1 year of RP) usually indicates metastatic disease

Salvage RT: Intermediate-Term Quality of Life

- Retrospective analysis of QOL after post-op RT using EPIC survey (n=118)
- RT 68 Gy (pelvis 59%); ADT 56%
- Median FU circa 3 years
- No reduction in GU, GI or sexual QOL
- No worsening in incontinence
- Pelvic nodal RT did not adversely affect QOL
- *Intermediate follow-up single institution study*

Salvage RT: Intermediate-Term Quality of Life



Melotek JM, Liao C, Liauw SL (2015) Quality of Life after Post-Prostatectomy Intensity Modulated Radiation Therapy: Pelvic Nodal Irradiation Is Not Associated with Worse Bladder, Bowel, or Sexual Outcomes. PLoS ONE 10(10): e0141639.

doi:10.1371/journal.pone.0141639

<http://journals.plos.org/plosone/article?id=info:doi/10.1371/journal.pone.0141639>

Dose-escalated salvage RT: acute toxicity

- RCT of 70 Gy vs 64 Gy for post-operative RT (n=344)
- 2nd endpoint: CTCAE acute toxicity
- No differences in toxicity or QOL
- QOL similar, except for urinary sx at 3 mo (44% vs 38%)
 - No worsening in continence
- Urinary QOL affected by: baseline sx, 70 Gy, ↑BMI
- *3 month results only; await trial results regarding impact of dose escalation on disease outcomes*

Acute Grade 2+ toxicity

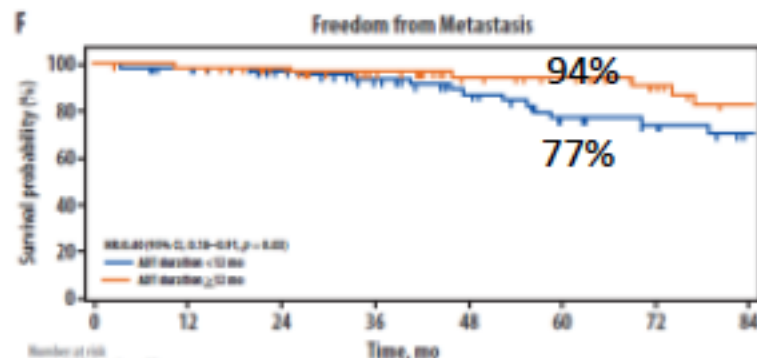
	70 Gy	64 Gy	p
GI tox	17%	13%	0.2
GU tox	15%	16%	0.8

Dose escalated salvage RT results in mild acute toxicity with minor differences in urinary QOL.

Ghadjar, JCO 2015 ID 26527774/Liau

ADT use with post-operative RT

- Retrospective analysis of post-op RT, with varying use of ADT (n=680)
- 3D/IMRT 68.4 Gy
- ADT in 21%, median 12 mo
- Median FU 58 mo
- ↑FFBF with ADT use
- >12 mo ADT, given for aggressive features, resulted in ↓DM (no Δ in PCSM or OM)
- *Congruent with RTOG 9601; heterogeneity in this retrospective report; doesn't assess risks of ADT*



Consider long term ADT with post-op RT in men who have high risk features.

Jackson, Eur Urol 2015 ID 26004800/Liauw

Salvage Prostatectomy Post-RT

- Possible and many centres report good outcomes
- However BAUS RP Registry records that low numbers of salvage prostatectomy are performed (0.4%)
- In my own series of 1100 LRP - 4 salvage LRP (0.36%) following RT (2 BT, 2 post-EBRT), whilst >28 have received salvage EBRT and 9 receiving LHRHa

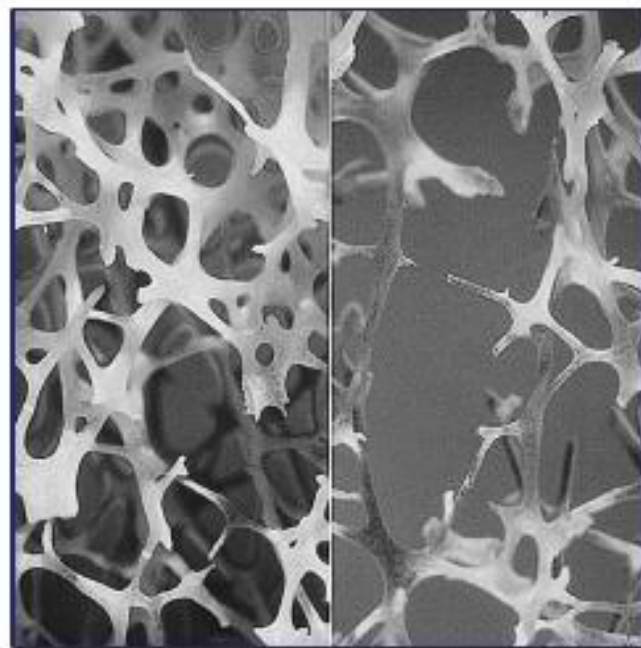
ADT has significant side effects

Long-term side-effects of ADT

Sarcopenic obesity



Bone loss



Androgen Deprivation Therapy and Future Alzheimer's Disease Risk

- Retrospective cohort. Question: Does androgen deprivation therapy (ADT) increase risk of subsequent Alzheimer's disease?
- Text processing software of EMR to review ICD, med lists, disease concepts from clinical notes in 16,888 individuals with PC
- Results:
 - 14.2% received ADT, median follow-up 2.7 y
 - Propensity score matched HR 1.88 (P=0.21), multivariable Cox HR 1.66 (P=0.31) for risk of Alzheimer's and ADT
 - Increased risk associated with increasing duration of ADT- those with at least 12 months ADT had greatest risk (HR 2.12) and significant trends with categorical duration
- Conclusions: ADT associated with risk of Alzheimer's as defined by billing codes, clinical documentation.

Course and Predictors of Cognitive Function in Patients With Prostate Cancer Receiving Androgen-Deprivation Therapy: A Controlled Comparison

- Cohort control study. Question: Does androgen deprivation therapy (ADT) impact cognitive function at 6, 12 mo using Neuropsych battery?
- Results:
 - ADT patients baseline demo: higher Charleston, less educated, “non-white”, higher Gleason score
 - Change in impaired cognitive performance: 6mo OR 1.21, 12mo 2.42
 - More stringent criteria for impairment: OR 1.72, 2.97
 - SNP in rs1047776 associated with impairment on ADT- impairment rate more than doubled in 44% with WT GG allele and did not if AA or AG (OR at 12 months 14.0).
- Conclusions: Impairment higher on ADT and increases over time. SNP in *GNB3* gene associated with risk on ADT

Summary

- RP good treatment for all-comers
 - Stand alone for low/intermediate-risk disease
 - Reduces risk of further metastasis and improved survival with LN+ive disease
 - Avoids risk of understaging/undergrading disease
 - Predictable problems with good remedies
 - **Excellent start to multimodality treatment for high-risk disease, which may reduce the need for ADT**

What patients want?

