

**Prostate Cancer- Progress through research**


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 Queen's University Belfast  
 Consultant Oncologist,  
 Northern Ireland Cancer Centre, Belfast



QUEEN'S UNIVERSITY BELFAST CCRCB CENTRE FOR CANCER RESEARCH AND CELL BIOLOGY

**Career to date**


- 1970, Born, County Wexford, Ireland
- 1993 – graduated University College Dublin, Medicine
- 1995-2000 – Radiotherapy Trainee, St. Luke's Hospital, Dublin
- 2000 – 2003- Academic Urology Unit, Royal Marsden, London
- MD 2003
- 2004- present, consultant in clinical oncology, Northern Ireland Cancer Centre
- 2011 – Appointed as Professor
- 2014-2017 – Clinical Director, Northern Ireland Cancer Centre



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**Men you will hear about tonight...**


1. Doug
2. Phillip
3. David
4. Allister

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**Doug**

- 50-55 year old from Russia
- Soldier
- Prostate cancer spread to bone
- PSA?
- Gleason?
- Treatment?

**Oldest known case of prostate cancer**



Died – 700BC

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**Belfast Prostate Cancer Centre of Excellence**



- 4 consultants
- 2 Research Nurses
- 4 Research Radiographers
- 2 Clinical Nurse Specialists
- 2 Clinical Fellows
- 20 open clinical trials

Darren Mitchell, Aidan Cole, Sunil Jain

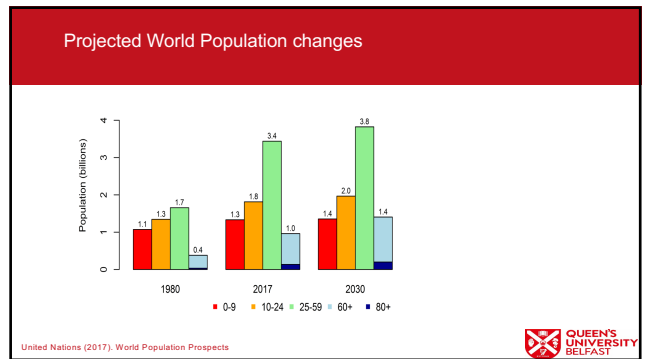
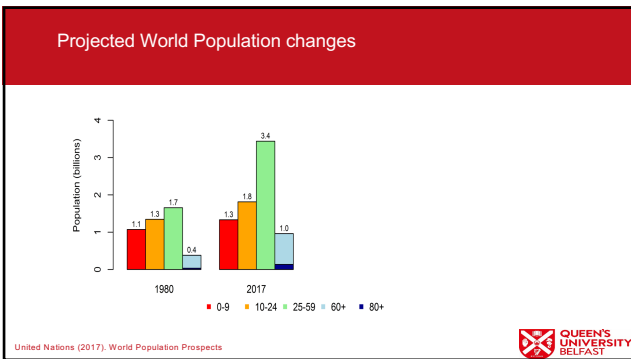
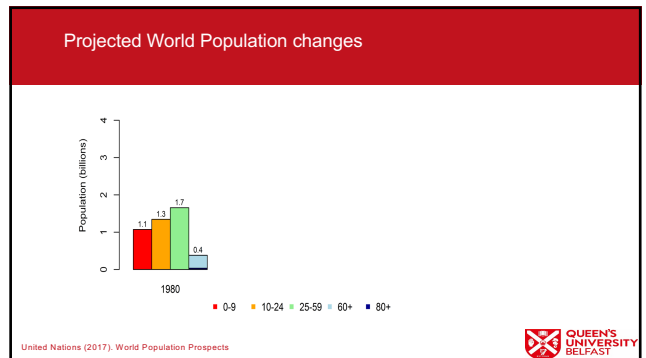
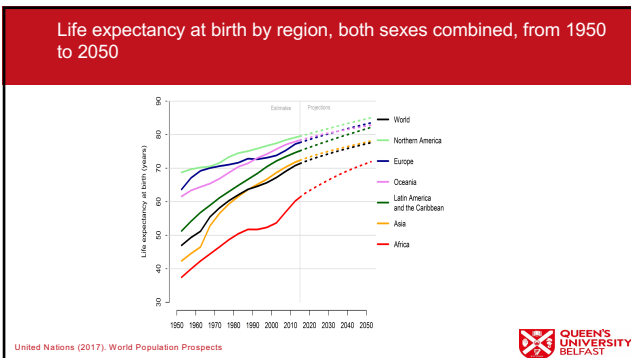
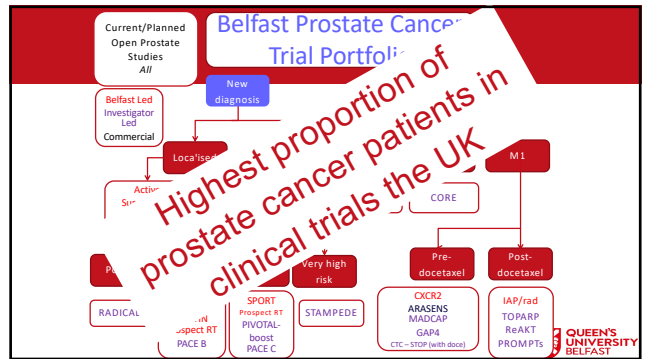
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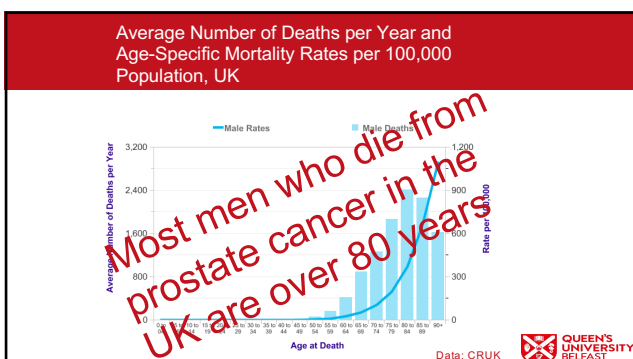
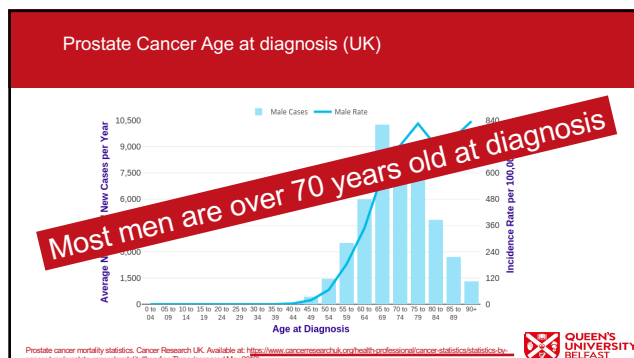
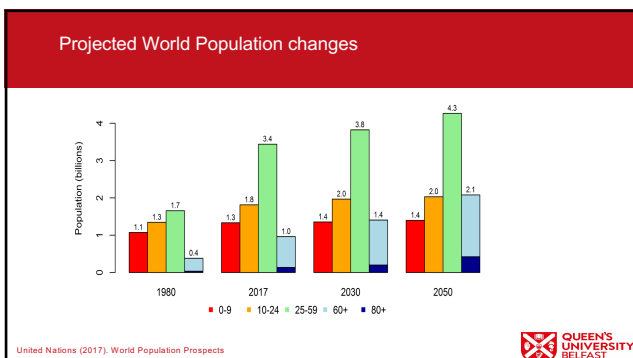
**BELFASTMANCHESTER**  
Centre of Excellence for Prostate Cancer Research



**£7 million grant** To improve radiotherapy in prostate cancer

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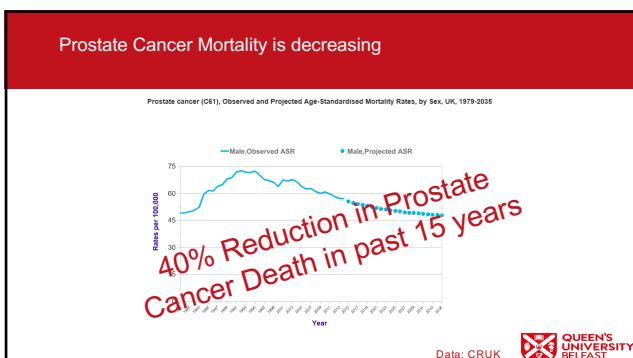
### 'Old age' has changed

Mick Jagger, Rolling Stones world tour 2016, age 76  
*Time is on my side*  
The Rolling Stones

Paul McCartney, headlining Glastonbury 2019 age 77  
*Will you still need me when I'm 64?*  
The Beatles

*I hope I die before I get old*  
My Generation,  
The Who


The Who world Tour 2016, Roger - 76, Pete - 76




### Better treatment of non-metastatic disease

### Metastatic Castration Resistant Prostate Cancer (mCRPC)



- Average of 12 months response to Androgen Deprivation Therapy (ADT)
- Biochemical progression usually first indication of resistance
- Metastatic CRPC is an incurable condition- median survival in modern era- 22 months



Clarke et al. J Clin Oncol 31, 2013 (suppl; abstr 9012)



### 2004–2019 New treatments for advanced prostate cancer

### Phillip

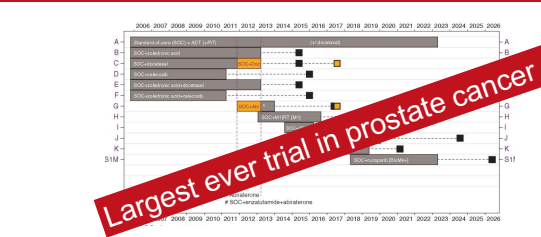

- November 2011
- Aged 53
- IT specialist
- Gleason 4+5
- PSA 550ng/ml
- Widespread bone mets

**Randomised to STAMPEDE Trial (Arm C)**

November 2011




### STAMPEDE Trial

### STAMPEDE Trial

- Most practice changing trial ever in prostate cancer
- Among the many discoveries:
  - 18 month improvement in survival by using Docetaxel or Abiraterone along with hormone therapy in metastatic prostate cancer
  - 4 month improved survival by treating the prostate gland with radiotherapy




### Can local radiotherapy influence outcomes in metastatic prostate cancer?

#### STAMPEDE Arm H - Study design

```

    graph TD
      A[Men with newly diagnosed metastatic prostate cancer] --> B[ADT +/- docetaxel (SOC)]
      A --> C[ADT +/- docetaxel (SOC) + prostate radiotherapy]
      B --- D[1:1]
      C --- D
      D --- E[36Gy/6 fractions/6 weeks or 55Gy/20 fractions/4 weeks]
      E --- F[Schedule nominated before randomisation]
    
```

Stratification variable  
 (<70 vs ≥70 years), nodal involvement (N0 vs N1 vs Nx), randomising site, WHO performance status (0 vs 1 or 2), type of ADT, aspirin or NSAID use, docetaxel use



### Radiotherapy to the prostate in metastatic disease setting

-Results of STAMPEDE Arm H

Low burden

**Radiation - Improving survival in (low volume) metastatic castration sensitive prostate cancer**

Parker C et al. Radiotherapy to the primary tumour for newly diagnosed, metastatic prostate cancer (STAMPEDE): a randomised controlled phase 3 trial. *Lancet* 2018, 392: 2353-66

### Philip

November 2011  
Gleason 4+5  
PSA 550ng/ml  
Widespread bone mets  
STAMPEDE (Arm C)

June 2019  
PSA 0.04ng/ml

### Targeting bone metastases really matters in metastatic castration resistant prostate cancer (mCRPC)

- ~90% of patients with advanced prostate cancer have bone metastases
- Bone metastases are the main cause of death and symptoms in advanced prostate cancer

### The phenotype of prostate cancer in bone facilitates imaging and therapy

Images courtesy of Neil Clarke

### The phenotype of prostate cancer in bone facilitates imaging and therapy

Images courtesy Chris Parker

EDTMP, ethylenediamine tetra(methylene phosphonic acid); HEDP, hydroxyethylidene diphosphonate

### Radium-223 (Xofigo)

Median OS, months: 14.9

HR: 0.75

95% CI: 0.58, 0.98

p value: 0.03

**Improved survival by about 3.5 months**


**More than 50,000 patients have now been treated**

Month	Radium 223	Placebo
0	614	307
3	578	288
6	504	228
9	369	157
12	274	103
15	178	67
18	105	39
21	60	24
24	41	14
27	18	7
30	7	4
33	1	2
36	1	1
39	0	0

**David**

- 67 years old, retired motorcycle police officer
- Back pain for 2 months
- PSA 3300ng/ml
- Alkaline phosphatase- 2000
- Widespread bone metastases

**Joined the ADRRAD Trial**



**ADRRAD Trial (Belfast)**

- Phase 1/2
- T1-4 NO-1 M1b

**Primary Endpoints**

- Toxicity
- Quality of Life

**Secondary end points**

- WBMRI response
- PSA/ALP
- CTCs


Docetaxel x 6

Androgen Deprivation Therapy


Androgen Receptor Signaling Inhibitor (ARSI) (MDM2)

Radium-223

30/30 patients now recruited  
No unexpected toxicity  
No dose limiting toxicity




**David**  
Whole body MRI response assessment



**At diagnosis**  
PSA 3300ng/ml  
ALP 2000

**Post ADT + 6 x Docetaxel**  
PSA 24ng/ml  
ALP 160


**Post RT + 6 x Radium-223**  
PSA <0.03ng/ml  
ALP 70



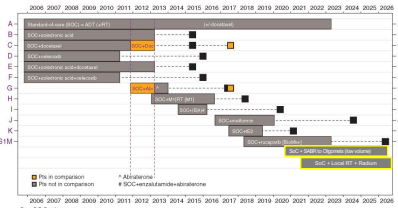

**David**

David's daughter abseiling down Belfast City Hospital Tower for Friends of the Cancer Centre

August 2019 (3 years after diagnosis), PSA 0.03 ng/ml




**STAMPEDE – next steps – More Radiotherapy!**


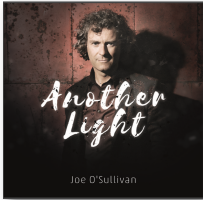
**Allister**

Allister, presented aged 52 in 2008  
Engineer  
PSA 500  
Bone mets  
STAMPEDE, ARM B + Multiple clinical trials  
Died 2016

Inspiration for the song 'Still the Warrior'




**Music**





Take a Deep Breath (2015)      Another Light (2017)


All proceeds to Friends of the Cancer Centre  
Available on iTunes, Amazon, Spotify,  
[FriendsOfTheCancerCentre.com](http://FriendsOfTheCancerCentre.com)



**New Music**



New Album recording October 2019  
World premier of new song:  
'You saw With Your loving Eyes'  
**Tonight, here in Edinburgh!**



**Future for Prostate Cancer**


- Improved imaging (PSMA PET, Whole body MRI)
- Improved understanding of biology (especially genetics)
- Better individualisation of treatment
- PSMA targeted therapies
- Exercise and lifestyle
- ...

**Castration free prostate cancer**

... are making progress but must continue to develop innovative clinical trials



**APCC PANEL MEMBERS**



APCC 2019  
29-31 AUGUST 2019

**Thank you to all the patients (and their families) who have taken part in prostate cancer trials**

Belfast Cancer Patient and Public Involvement Group

[@profjoesullivan](https://twitter.com/profjoesullivan)

