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NHS Patient selection for Proton Beam Therapy



Disclaimer

- I am not Adrian Crellin
- I do not work for NHS England (Oversight)
- Observations & opinions are my own



Overview

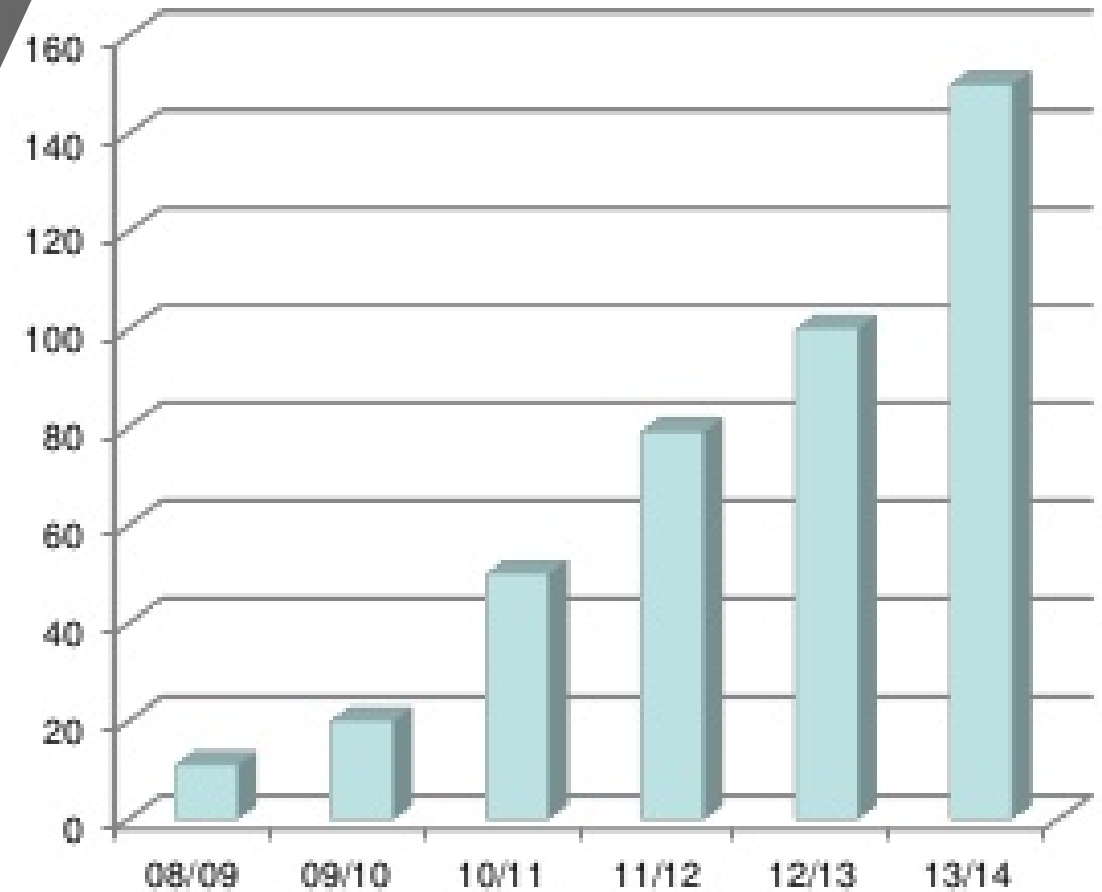
- Proton overseas programme 2008-2018+
- National programme patient selection
 - QALY & Markov chain modelling
- Discrete event simulation & capacity loading
- Observations

10 years of access to proton beam
therapy

PROTON OVERSEAS PROGRAMME

NHS HSC POP

- Started in 2008, with envisaged throughput of 400 patients per year
- Virtual MDT panel
- Numbers small initially, gradually increasing
- Paeds numbers increasing rapidly since 2012



POP indications

Adults & Children

- Chordoma (skull base & paraspinal)
- Chondrosarcoma (skull base)
- Spinal & paraspinal bone / STS (not Ewing's)

Children Only

- Orbital, Parameningeal, H&N rhabdomyosarcoma
- Ependymoma
- Ewing sarcoma
- Retinoblastoma
- Pelvic sarcoma
- Optic pathway and selected glioma
- Craniopharyngioma
- PPNET
- ENB
- *2016: Medulloblastoma*

Overseas Programme casemix

- 1144 accepted patients as of Feb 2018
- Mostly paediatric and TYA indications (integral dose driven)
- Chordoma and Chondrosarcoma make up 87% of treated adult patients (TCP driven)

| Diagnosis | Adult | Teenage and young adult | Paediatric |
|--|-------|-------------------------|------------|
| Chordoma | 147 | 18 | 15 |
| Chondrosarcoma | 86 | 12 | 5 |
| Low grade glioma | - | 16 | 138 |
| Ependymoma | - | 11 | 140 |
| Craniopharyngioma | - | 11 | 87 |
| Rhabdomyosarcoma | - | 8 | 176 |
| Peripheral primitive neuroectodermal tumours | 6 | 8 | 105 |
| Soft tissue sarcoma | 11 | 10 | 15 |
| Other | 17 | 40 | 62 |
| Total | 267 | 134 | 743 |



- UF Jacksonville (Paeds)
- PSI Villingen (Adults)
- Procure Oklahoma
- WPE Essen (TYA & Paeds)

- Mean NHS excess treatment cost over Photon IMRT = **£103,660** per patient
- POP cost to date ~**£120 Million**

Treatment centres

Two centres for England and the
devolved nations

NHS PROTON BEAM THERAPY PROGRAMME

High priority indications

Adults & Children (272)

- Chordoma (skull base & paraspinal)
- Chondrosarcoma (skull base)
- Spinal & paraspinal bone / STS (not Ewing's)

Children Only (128)

- Orbital, Parameningeal, H&N rhabdomyosarcoma
- Ependymoma
- Ewing sarcoma
- Retinoblastoma
- Pelvic sarcoma
- Optic pathway and selected glioma
- Craniopharyngioma
- PPNET
- ENB
- *Medulloblastoma?*

Full list of indications

Adults & Children (1285)

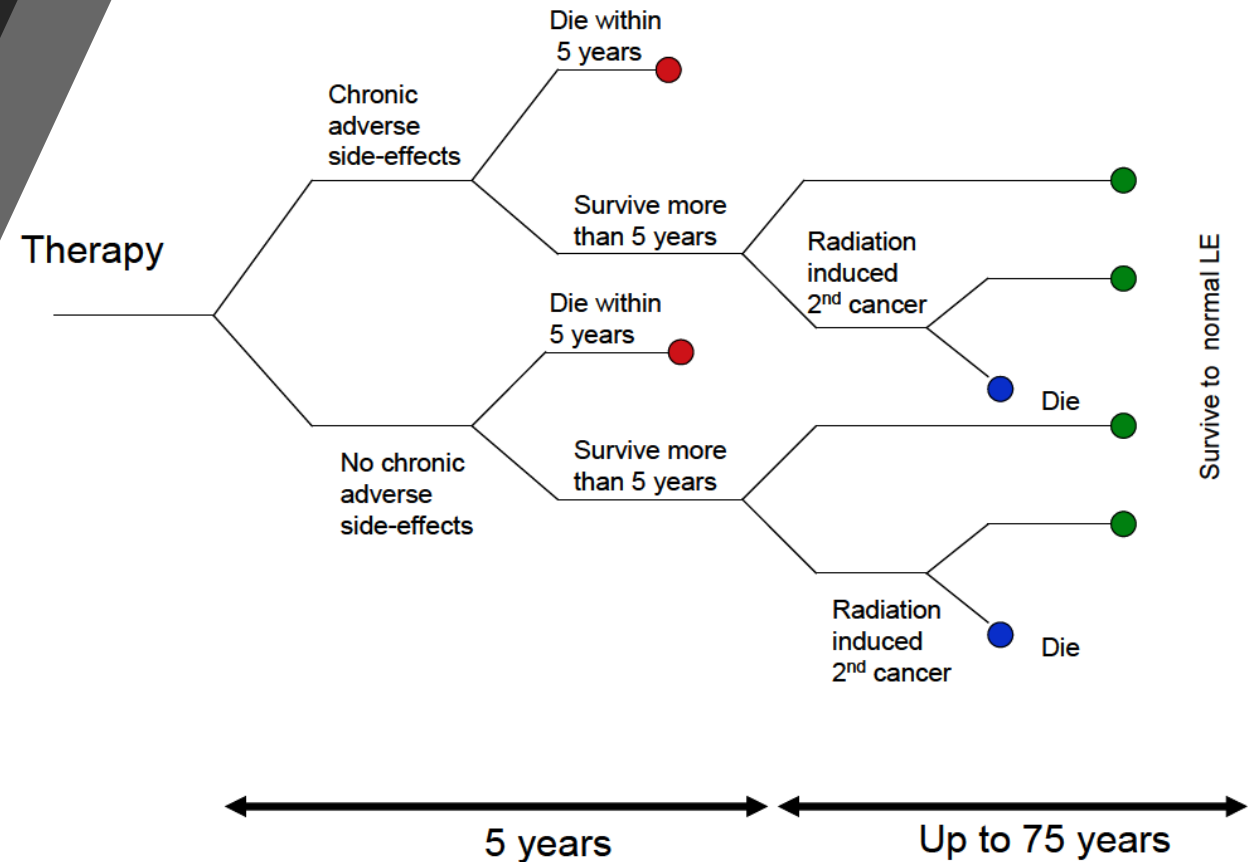
- Chordoma (skull base & paraspinal)
- Chondrosarcoma (skull base)
- Spinal & paraspinal bone / STS (not Ewing's)
- Choroidal melanoma - 100
- Ocular tumours - 25
- Sacral chordoma - 60
- Meningioma - 100
- Acoustic neuroma – 100
- Craniospinal NOS (Pineal) - 10
- Head & Neck, Paranasal tumours - 300
- Intracranial medulloblastoma - 30
- Difficult cases - 300

Children Only (202)

- Orbital, Parameningeal, H&N rhabdomyosarcoma
- Ependymoma
- Ewing sarcoma
- Retinoblastoma
- Pelvic sarcoma
- Optic pathway and selected glioma
- Craniopharyngioma
- PPNET
- ENB
- Medulloblastoma (70)
- Hodgkin's (5)
- Meningioma (3)
- Intracranial germinoma (10)
- Nasopharynx (15)
- Difficult CNS and liver cases (5)
- Very young age (20)

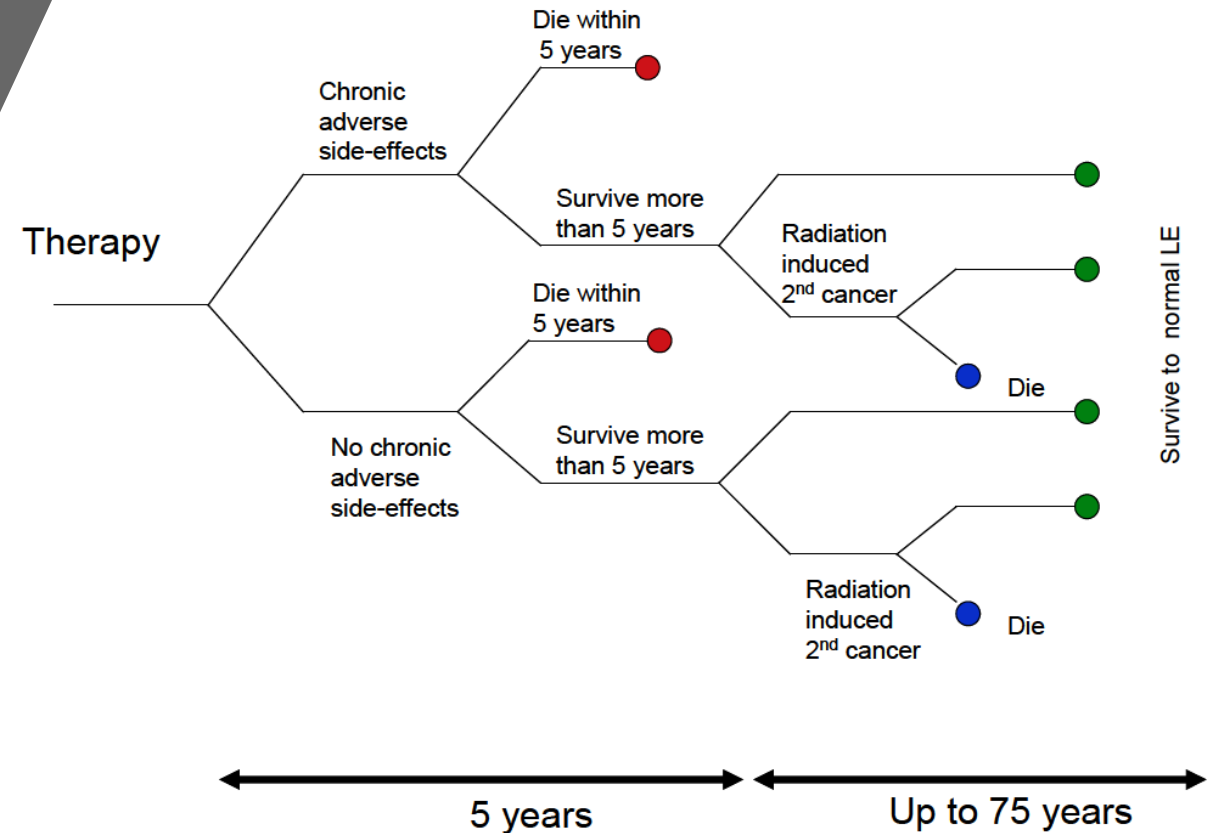
Quality analysis

- In absence of RCT evidence, used Swedish Markov chain simulation approach, with 3 health state endpoints over 80 years of life
- QALY assumes toxicity reduction from 53% for x-ray radiotherapy to 6% for Proton therapy in established indications
- For new indications, toxicity reduction from ~11% to 7%
- No PBT re-treatment in model



Quality analysis

- Survival benefit for PBT over IMRT modest – up to 10% higher 5 year survival
- **No difference** in risk of death from second cancer between PBT and IMRT for adult indications
- **~50% reduction** in risk of death from second cancer for childhood indications



Quality analysis

- Average QALY gains per patient calculated
- Considered high priority indications separately from standard indications
- QALY discount rate applied
 - People prefer to have good quality of life up front at time of diagnosis rather than later in life
- QALY benefit for High priority PBT = 2.5 years
- QALY benefit for all comers = 1.8 years

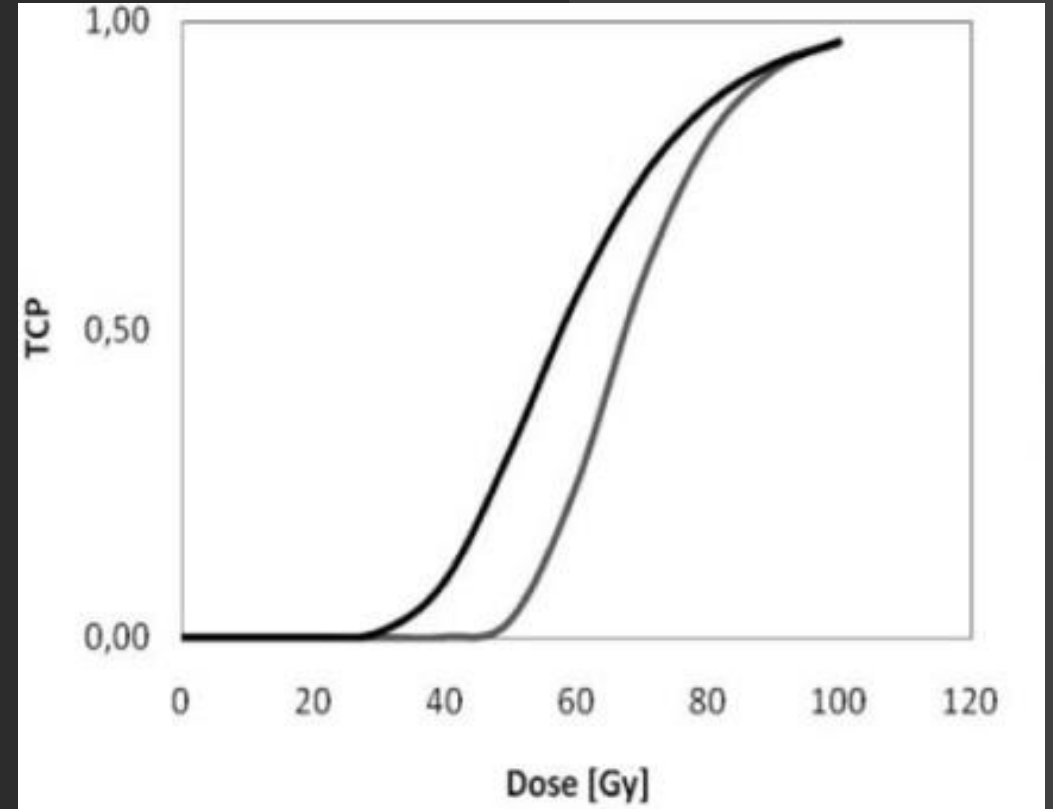
| QALY/ patient | Radiotherapy | | PBT | | Difference (Gain from PBT) | |
|------------------|---------------------------|-----------------|---------------------------|-----------------|----------------------------|-----------------|
| | High priority indications | All indications | High priority indications | All indications | High priority indications | All indications |
| Undiscounted | 22.9 | 14.2 | 27.2 | 17.1 | 4.4 | 2.8 |
| Discounted | 14 | 9.4 | 16.5 | 11.2 | 2.5 | 1.8 |

Quality to Health Economics

- Created Cost model based on 0,1, 2 or 3 centres, treating 1487 patients per year
- Capital cost per site £150.7 Million, annual cost £25.5 Million
- 2 Centre model 750 patients per year
 - Cost per QALY = £19,167
- POP undiscounted cost = £41,464
- NICE threshold £20,000 per QALY
 - £30,000 for high cost (non-curative) systemic therapies

MCMC to TCP / NTCP models

- Is γ_{50} applicable?
 - Ewings / PPNET, High risk Medullo, Chordoma, Chondrosarcoma, ocular melanoma
- Absolute NTCP rate $> 10\%$ with x-rays
 - ALL tumours on ALL indication list 2012
 - Still applicable in era of IMRT 2018?

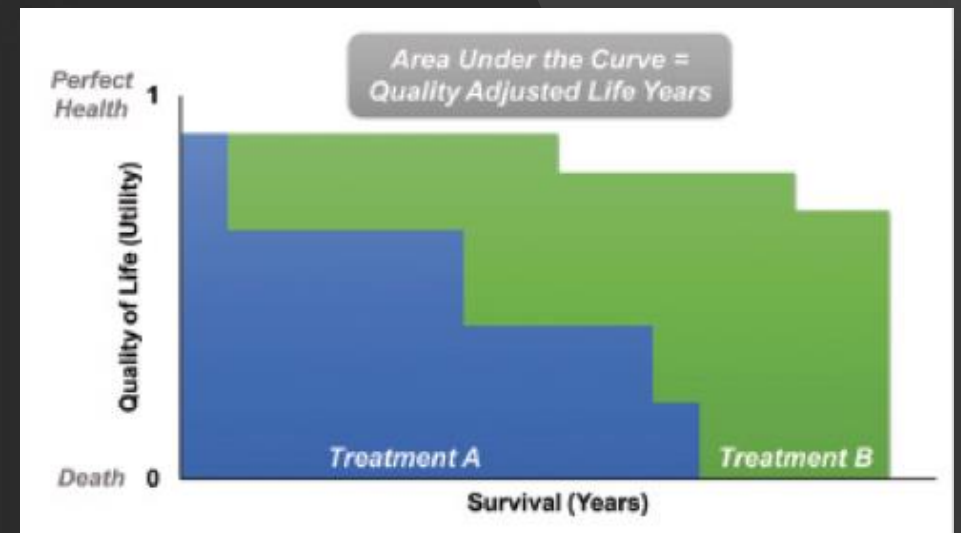


Issues with MCMC approach

- Single therapy intervention
- Toxicity comparators unrealistic for IMRT
- Expansion cohorts poorly defined
- **Static population and case-mix for a 30 year simulation**

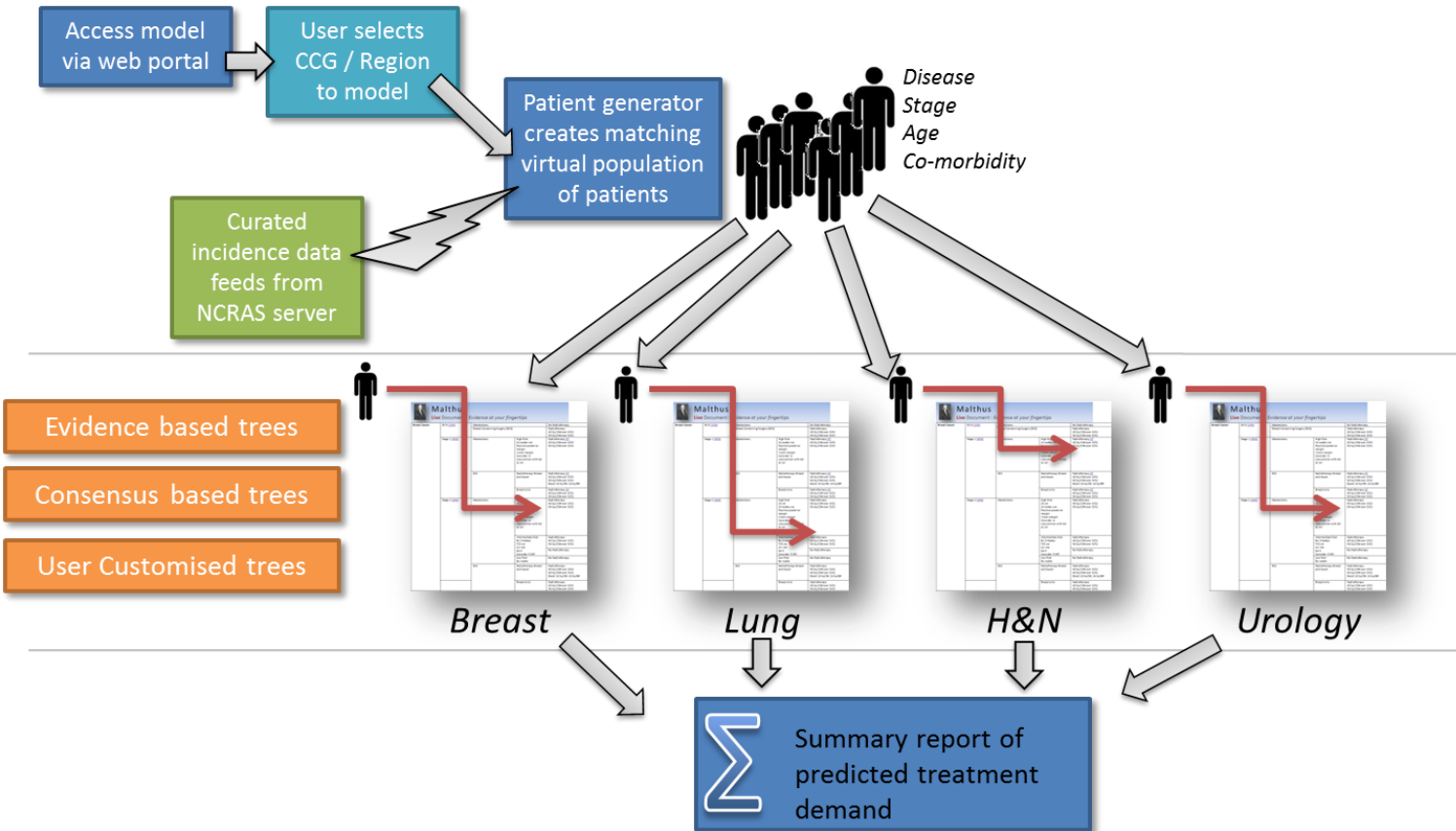
But

- Does give an estimate of cost per QALY that works for the NHS

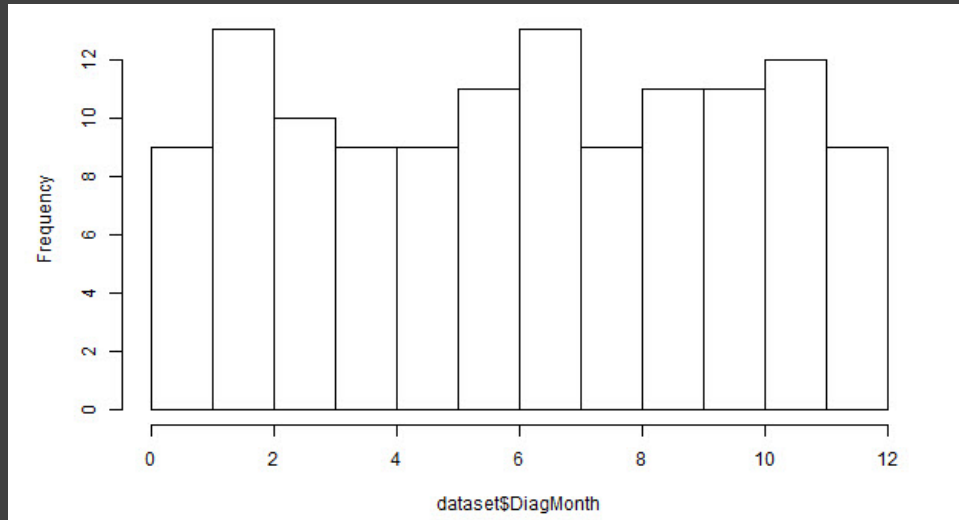


Discrete event simulation

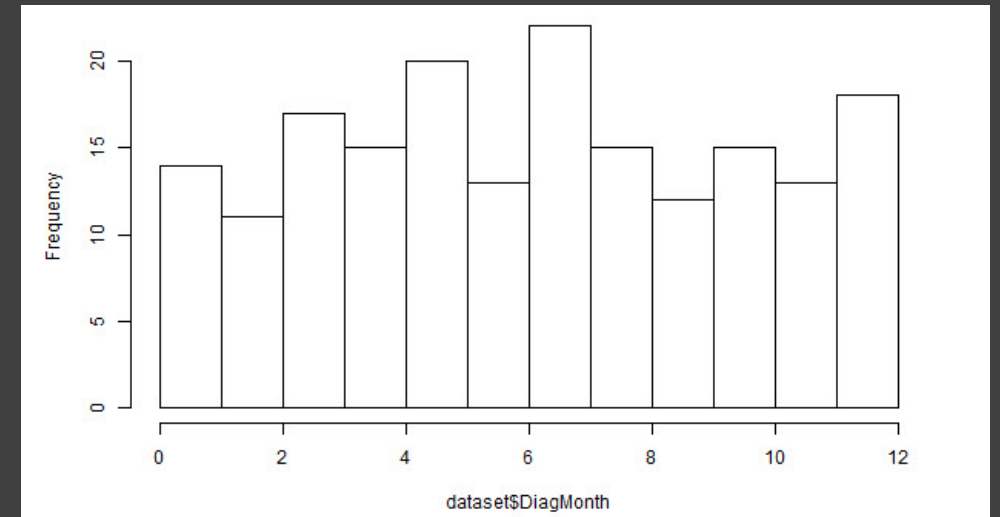
Malthus model



Demand Variation in Paediatric Cases



North of England



South of England

Generating high quality evidence for
PBT

PROTON BEAM THERAPY RESEARCH

Paradoxical landscape

Specialised commissioning

- Clinical services
- Commissioning through evaluation (CtE)
- No commissioning of research

NIHR commissions

- Wide range of preclinical & clinical research
- No funding of excess treatment costs

NCRI CTRAD (Phil & Maria's talk)

1

Coalition of multiple funding bodies (charities and research councils)

2

Mature disease specific networks

3

CTRAD PBT clinical strategy group convened August 2017

Concluding thoughts

Next 3 years will see significant increase in capacity for adult PBT compared to last 10 years

Criteria for expanded access unclear – modelling indicates expected **uncomplicated cure** benefits

Coordinated disease specific trials and data driven (central) evaluation mandated

Information Sources & disclaimers

- National PBT Service Development programme – Strategic Outline Case (2012)
- Lundkist J., Ekman M., Erucsson S. R., Jonsson B. & Giimelius B., 2005, Proton therapy of cancer: Potential clinical advantages and cos-effectiveness, *Acta Oncologia*, 44, pp 850-861
- Crellin, A. The Road Map for National Health Service Proton Beam Therapy. *Clinical Oncology* , Volume 30 , Issue 5 , 277 - 279
- Malthus ODR : "This project involves data derived from patient-level information collected by the NHS, as part of the care and support of cancer patients. The data is collated, maintained and quality assured by the National Cancer Registration and Analysis Service, which is part of Public Health England (PHE). Access to the data was facilitated by the PHE Office for Data Release."

Gratuitous plug!

- Special issue timed to coincide with NHS PBT service start
- Great commentaries and podcasts from ENLIGHT members
- Key articles currently free to download



SPECIAL ISSUE

Clinical Oncology
Proton Beam and Particle
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