

# Myeloma/ Monoclonal gammopathy

Non-Malignant Cancers, Precision Medicine  
& Genome Mapping – Parliamentary &  
Scientific Committee

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# Background – Myeloma is a model cancer illness for today's discussion

- Improving outcomes in myeloma, but remains an incurable cancer
- Cancer with the most number of delayed diagnosis cases
- Monoclonal gammopathy: Precursor state defined – but no agreed management pathway, and remains an under researched area
- Plethora of high cost new therapeutics ( up to £400 million per annum chemo costs for myeloma in England)
- Genomically well characterised, but lacks a precision medicine approach

# Improving outcomes in myeloma

Problem	Strategy	Intervention	Deliverables
Delayed diagnosis			
Precursor state management			
Precision Medicine			
NHS long term plan for cancer			



How do we solve  
these problems?

# Delayed diagnosis



# Over 50%

of myeloma patients visit their GP at least **3 times** prior to a referral to hospital to confirm diagnosis\*



\* Findings from the 2010 National Cancer Patient Experience Survey in England.  
[www.ncbi.nlm.nih.gov/pubmed/22365494](http://www.ncbi.nlm.nih.gov/pubmed/22365494)

Early diagnosis via GP referral is associated with improved overall survival



## 62%

one year survival for patients diagnosed via emergency route

## 88%

one year survival for patients diagnosed via GP referral



Myeloma patients experience some of the longest delays in diagnosis of all cancer patients

## 163 days

Time to diagnosis

First presentation to GP clinic

Referral to specialist

Secondary care diagnosis

Treatment



## 23.5 days

Primary care interval

# Myeloma UK Early Diagnosis programme

## Active -projects

- Identifying early markers
- AI & flagging systems
- Laboratory Best Practice
- MGUS Working Group
- Primary care data modelling
- Health economics model
- Improving communication



## GP education

- Ten Top Tips (Macmillan)
- Myeloma Diagnosis Pathway
- GP education events
- RCGP online educational module
- PULSE/BMJ
- GP conferences
- C the Signs
- Medical Defence Union article
- GP Myeloma Diagnostic Tool

## HCP education

- Allied healthcare professionals
- Myeloma grand round (hospital-wide education event)

# Improving outcomes in myeloma

Problem	Strategy	Intervention	Deliverables
Delayed diagnosis	Education Dissemination of Best Practice	GP & HCP education Lab and clinical best practice Measure health economic benefits	Reduction in diagnosis through emergency routes Improving 1 year survival rates



# Precursor state/ Monoclonal Gammopathy management

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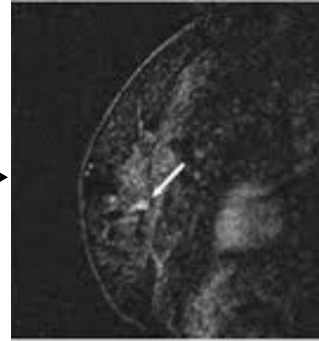
# Treating cancer early: a new paradigm in myeloma?

Screen with mammogram



Detect  
early

Early stage breast cancer



Treat as  
early as  
possible

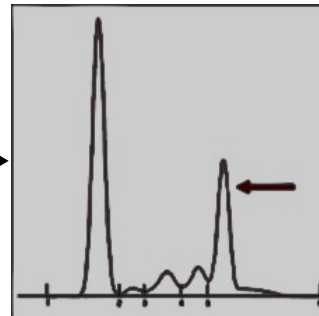
**CURE**

Metastatic breast cancer



Just a blood test! (SPEP)

No  
screening



MGUS and SMM

Watch and  
wait until  
end organ  
damage

**NO CURE**

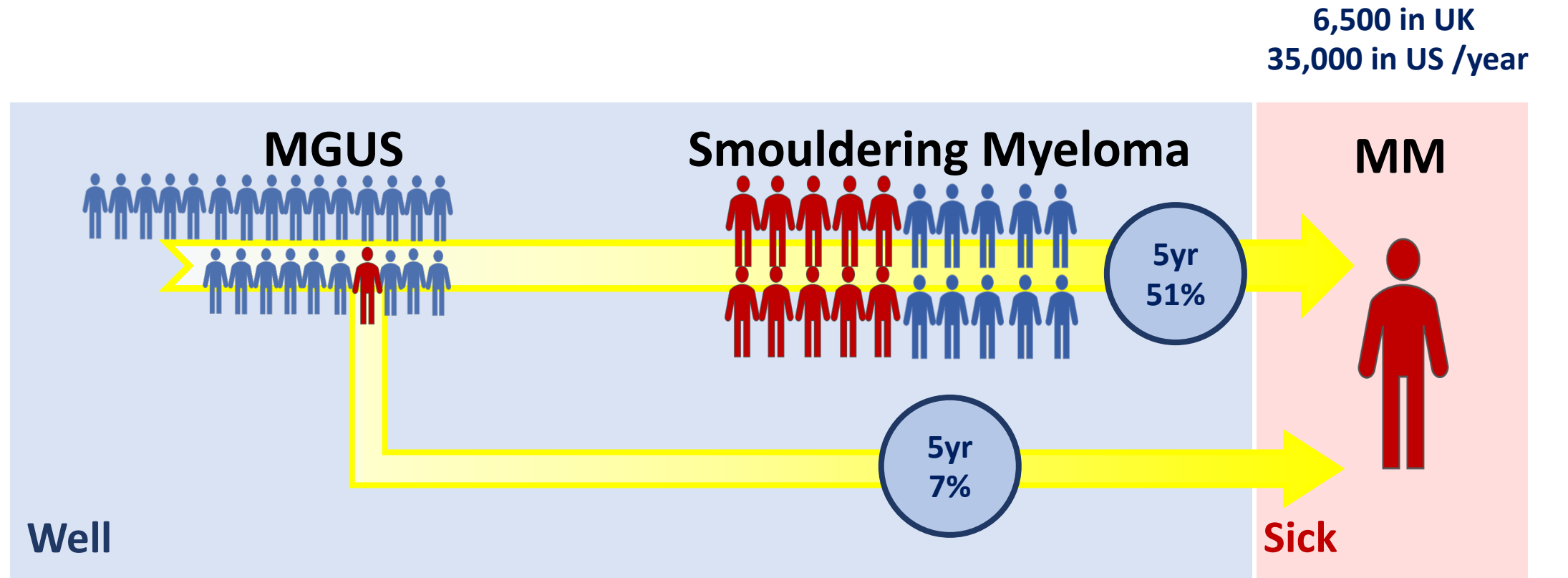


Multiple Myeloma

SPEP – Serum Protein Electrophoresis, MGUS – Monoclonal gammopathy, SMM – Smouldering Myeloma

# Multiple Myeloma: Clinical paradigm for cancer evolution

## Defined precursor states, but not all progress to MM

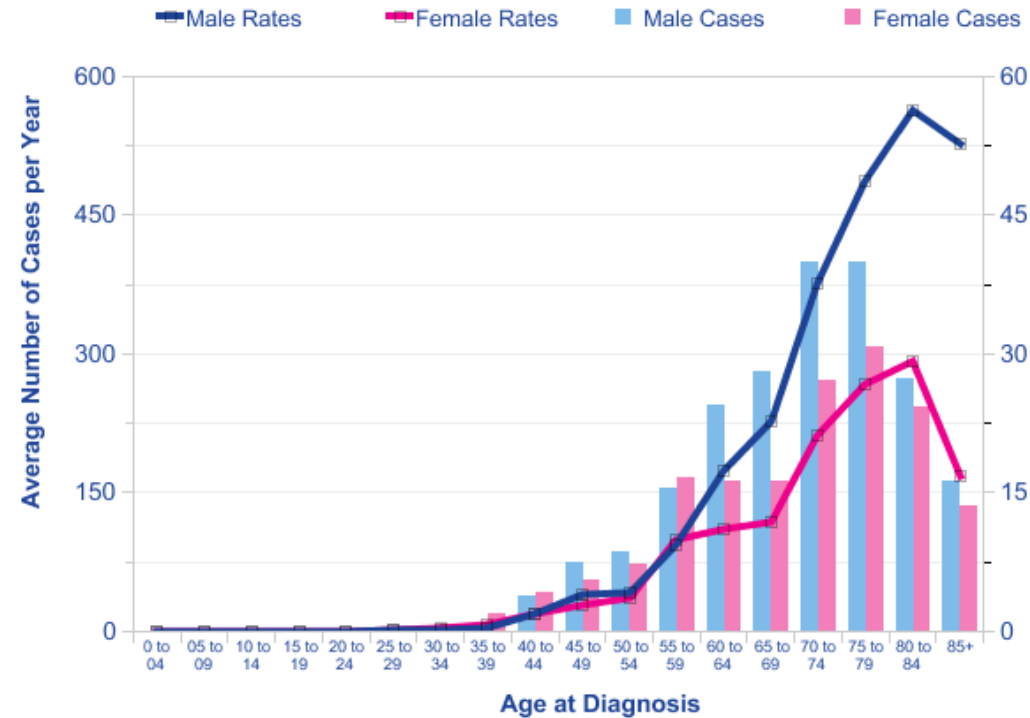


Kyle RA et al., *New England Journal of Medicine* 2007

Kyle RA et al., *New England Journal of Medicine* 2018

MGUS – Monoclonal gammopathy, MM – Multiple myeloma

# Feasibility of a mass screening and monitoring programme for Monoclonal gammopathy



3% of > 50 year olds

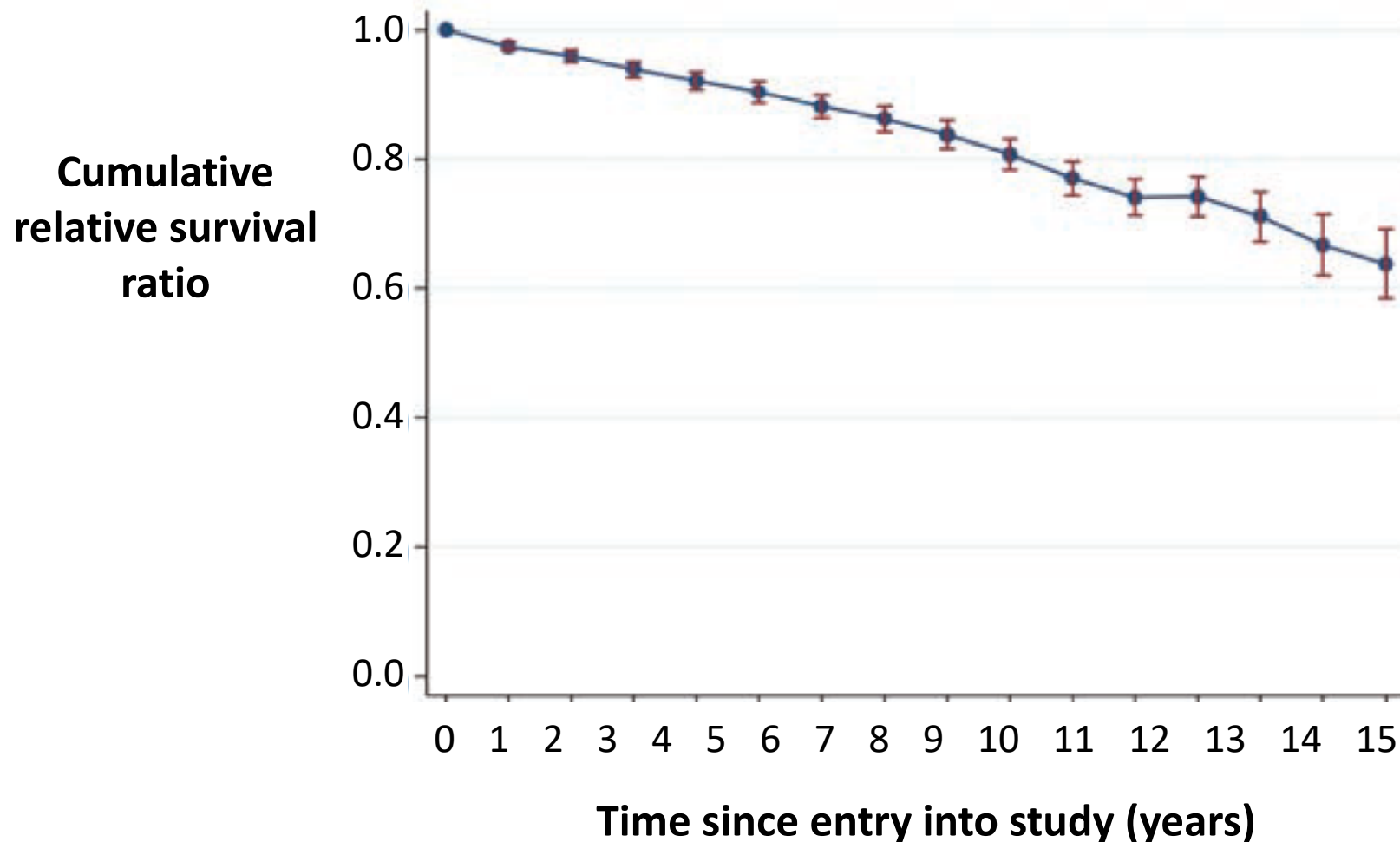
have a monoclonal gammopathy

> 500,000 individuals !

Average Number of New Cases per Year and Age-Specific Incidence Rates, UK estimates based on data from HMRN region

Monoclonal Gammopathy of Undetermined Significance (MGUS, ICD-O-3 9765/1): 2004-2010

# Monoclonal gammopathy is not necessarily benign!



7% (5 years)

**Monoclonal gammopathy of  
unknown significance (MGUS)**

*Precancer*

**Smouldering  
myeloma (SM)**

51%  
(5 years)

**Multiple  
myeloma**

*Cancer*

**Problem 2:** monitoring of higher numbers of MGUS patients puts a huge burden on GPs, increases costs from regular surveillance and adds to patient anxiety

**Strategy 2:** optimise risk stratification for progression to tailor surveillance programmes

**Problem 1:** myeloma is slow to diagnose, leading to worse outcomes

**Strategy 1:** diagnose a higher proportion of people who have MGUS and monitor them for progression to active myeloma

# Improving outcomes in myeloma

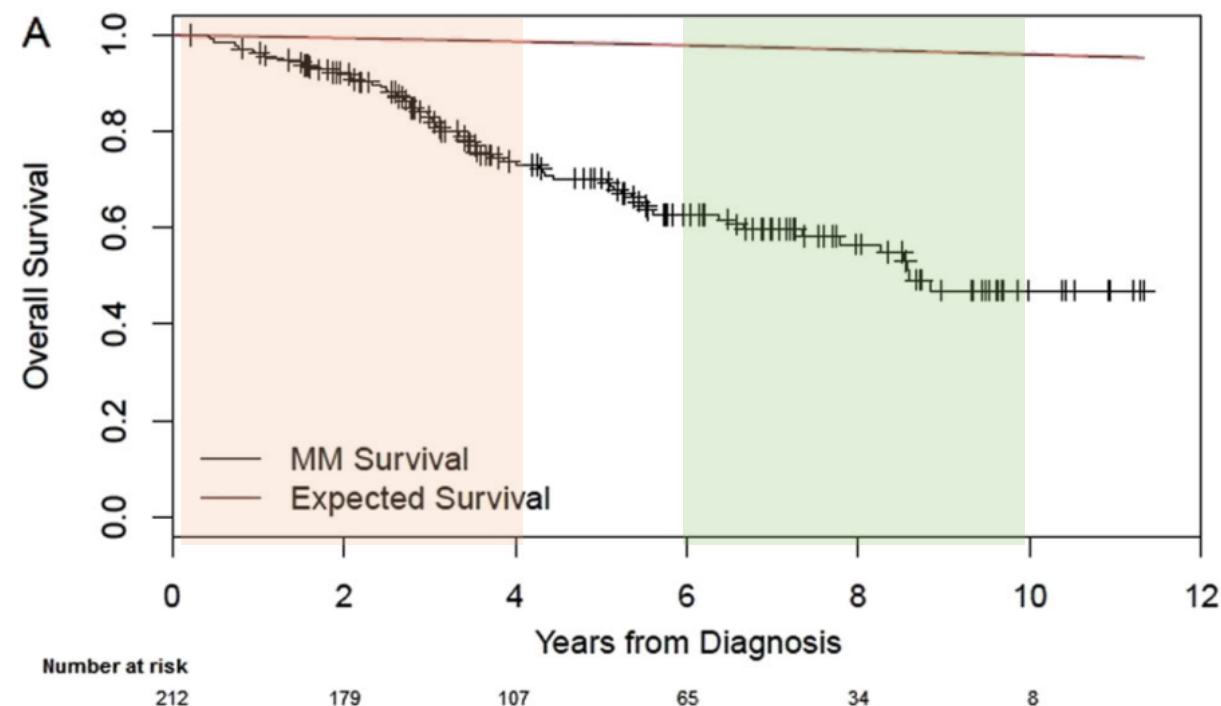
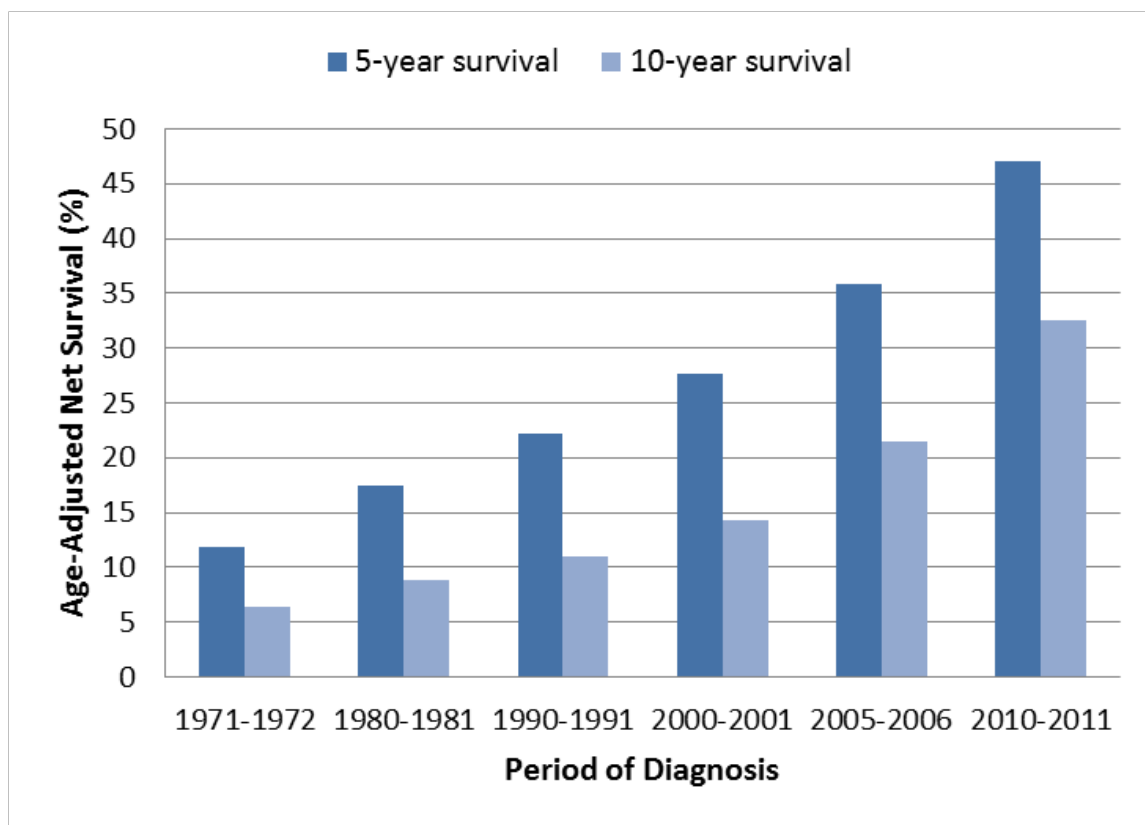
Problem	Strategy	Intervention	Deliverables
Precursor state management	Clinical pathways Research	Commissioned clinical pathways Invest in Monoclonal gammopathy research	Uniform auditable clinical pathways Innovative clinical management

# Precision Medicine for myeloma

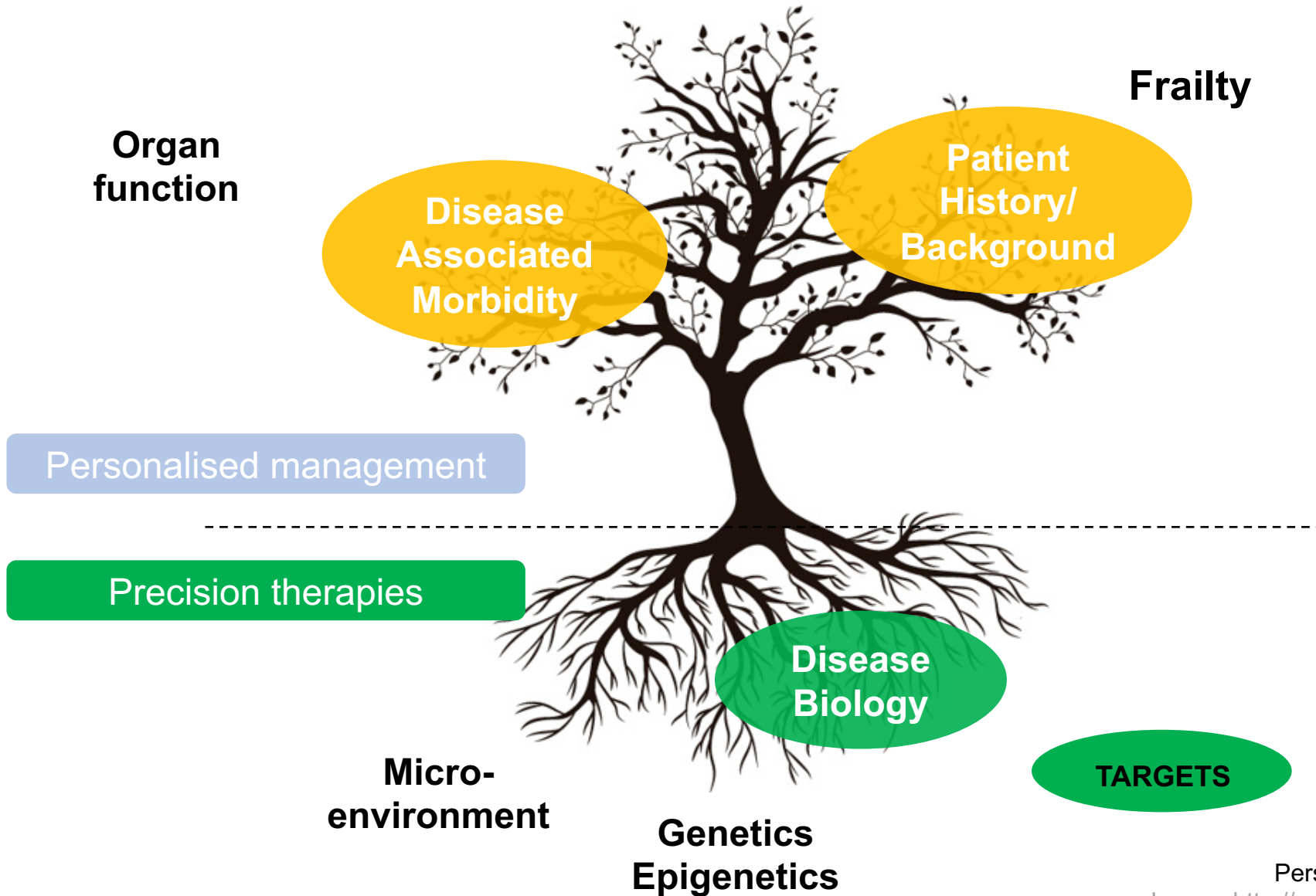




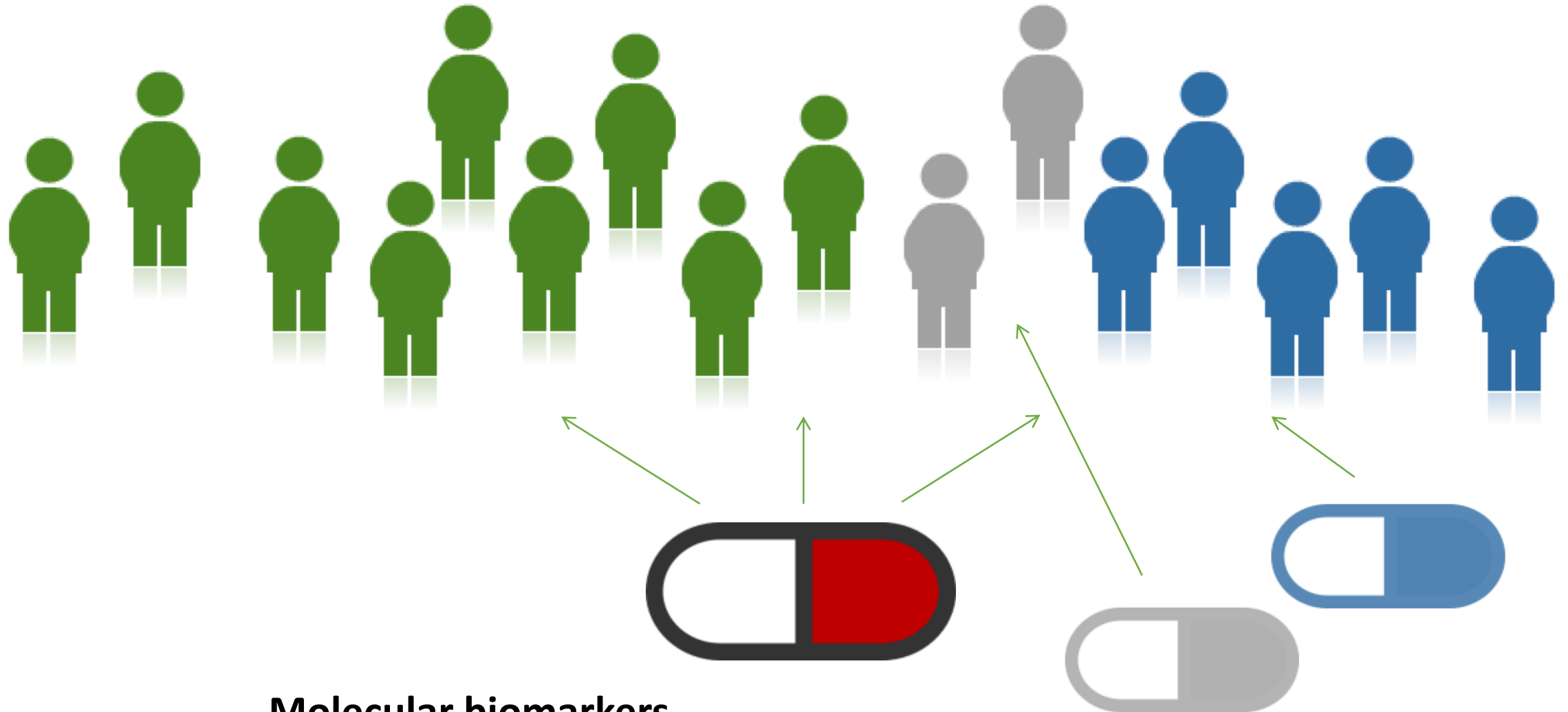
# Survival in myeloma improving – but not for all patients



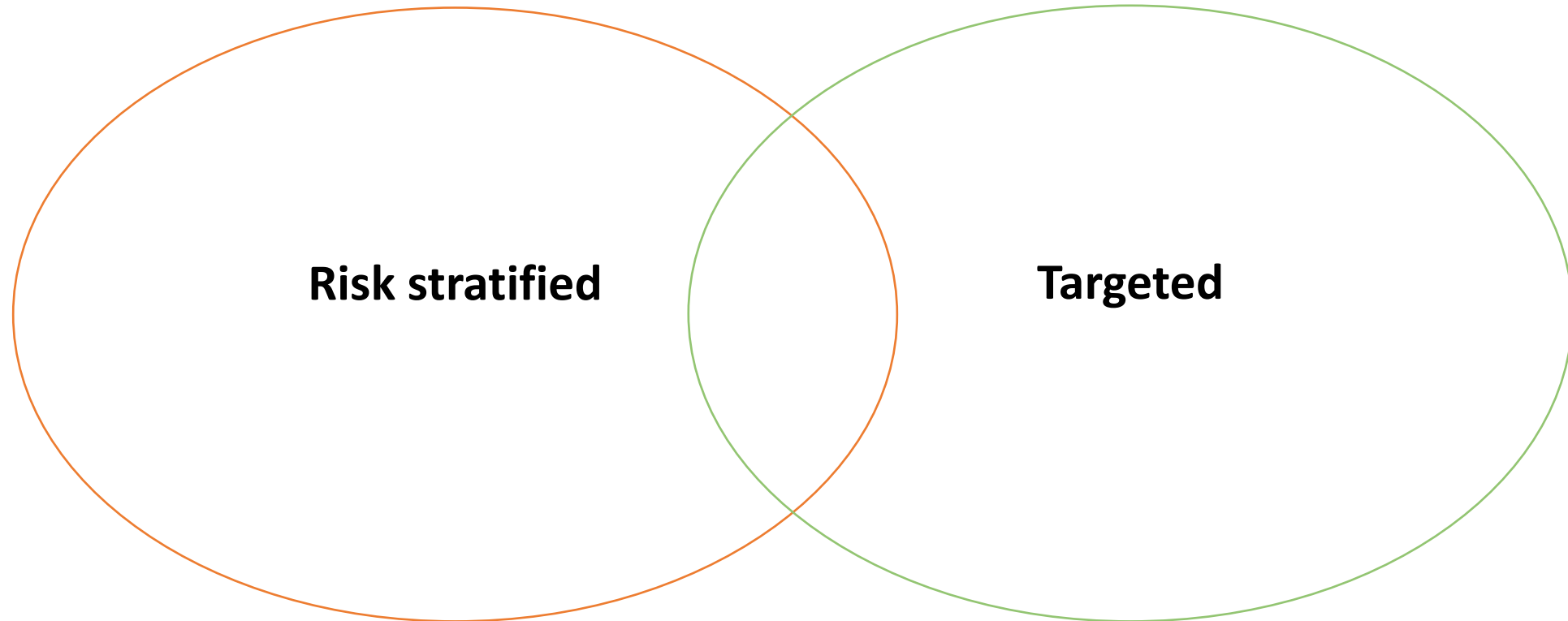
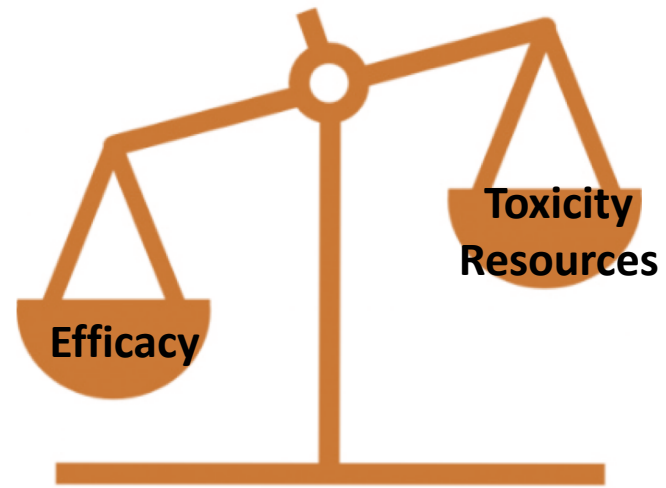
# Challenge: background and disease morbidity



# Potential precision therapy approach?



# Precision therapy



# Improving outcomes in myeloma

Problem	Strategy	Intervention	Deliverables
Precision Medicine for Myeloma	Enhance Genomics testing  Scope for precision medicine approach	Expand Myeloma test directory and genomics provision  Work with Pharma/NICE/NHSE to embed precision Medicine	Higher proportion of patients getting genomic tests Practice Precision Medicine in myeloma care

NHS Long term plan for Cancer  
Care ( but not blood cancers!)

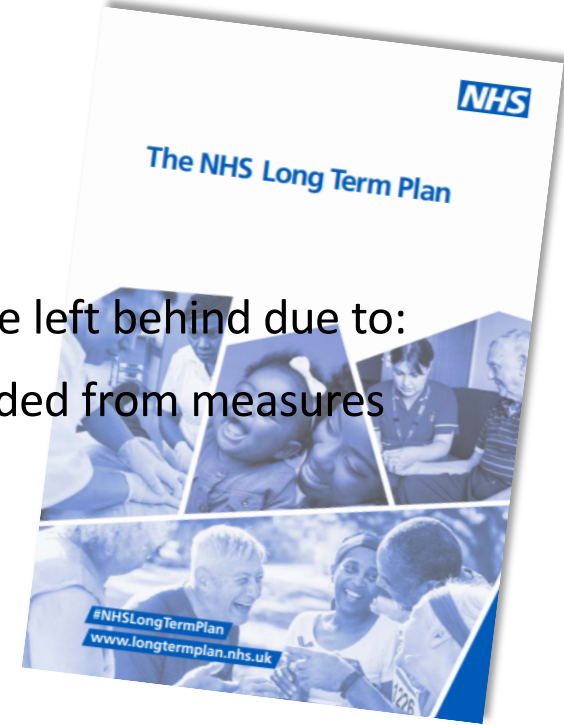
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# NHS Long Term Plan (England)

- Prioritises cancer diagnoses (**75% early diagnosis ambition**) but blood cancer patients could be left behind due to:
- Lack of comprehensive blood cancer data (inc. staging) – fear that blood cancers will be excluded from measures of progress for 75% target
- Recognition of blood cancer signs and symptoms among HCPs and GPs

- **What's needed?**

- New ways to measure improvements in blood cancer diagnosis rates
  - Reduction in the % of diagnoses requiring three or more GP appointments
  - A fall in the percentage of blood cancers diagnosed via emergency routes
- Education to help GPs recognise blood cancer symptoms, the use of blood tests and the interpretation of results
- Review of the Rapid Diagnostic Centres to ensure that they are reducing delays to diagnosis of blood cancer.



# Improving outcomes in myeloma

Problem	Strategy	Intervention	Deliverables
NHS long term plan for cancer	Bring blood cancers into focus	RDC's to review blood cancer diagnostic pathways	Metrics for Myeloma care Early diagnosis



# Improving outcomes in myeloma

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Dr Karthik Ramasamy, personal communication.

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