

Mapping the patient population through prognostic modeling

Communicating value to decision-makers: What's your prognosis?

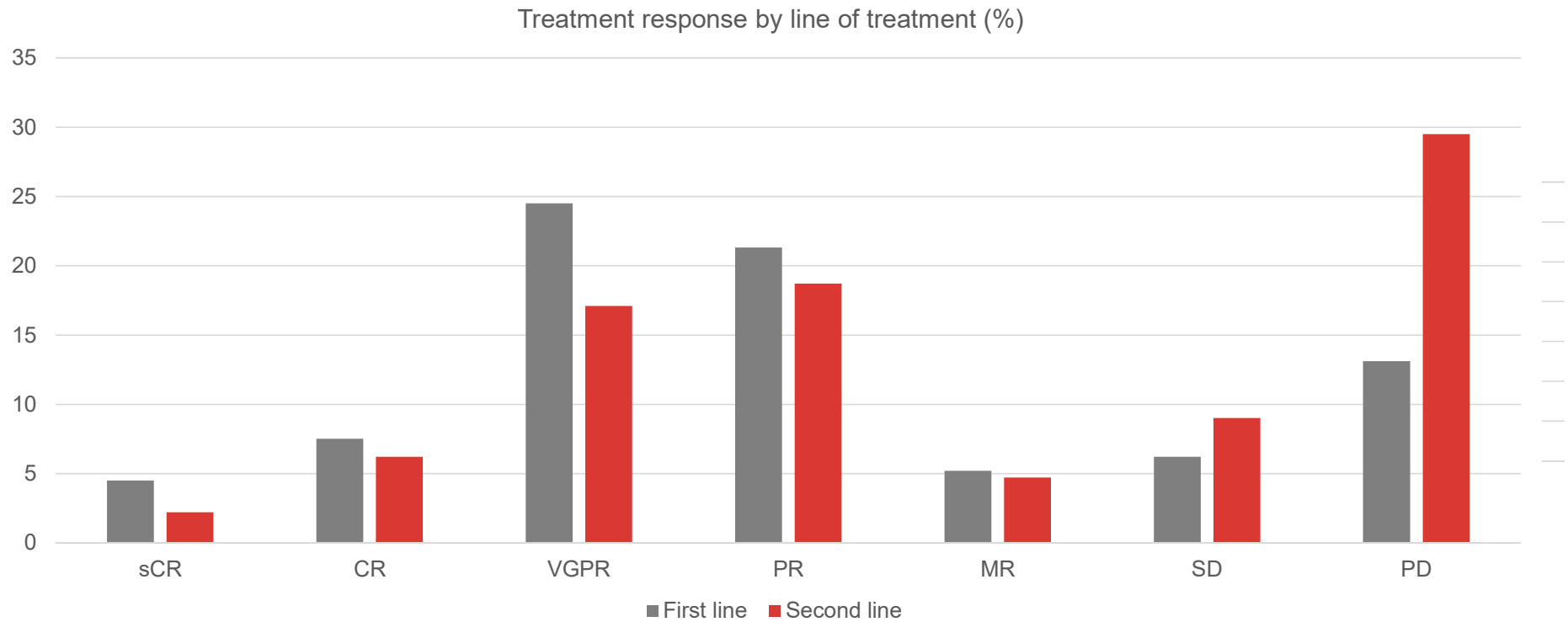
WALTER BOUWMEESTER & ELISABETH FENWICK

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Who will benefit from treatment?

VARIABILITY IN TREATMENT OUTCOMES STANDARD OF CARE



Hajek et al, 2018. RWE study MM



PD=progressive disease, SD=stable disease, MR= minimal response, PR=partial response, VGPR= very good PR, CR=complete response, sCR=stringent CR



The solution

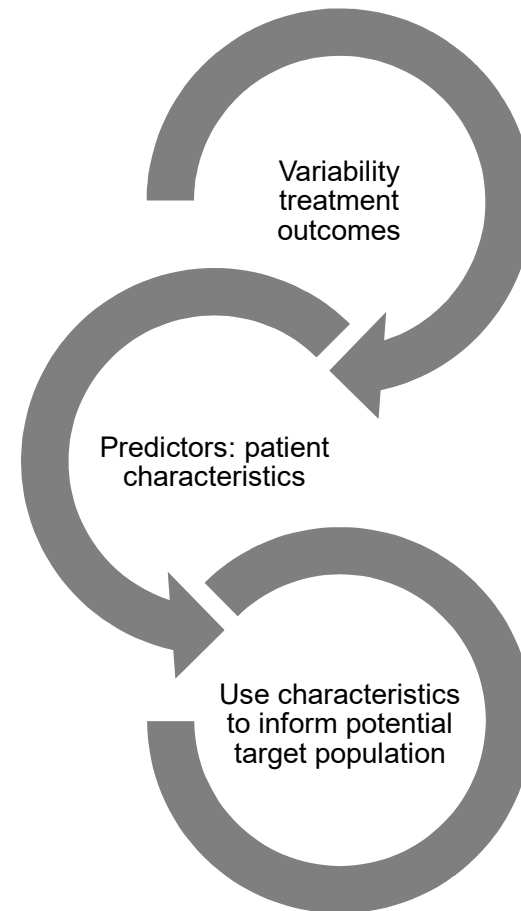


Who will benefit from treatment?

Patients with (future) unmet needs can be identified through a research concept that is called “*prognostic research*”

Synonyms:

- Prediction modelling
- Risk equation modelling

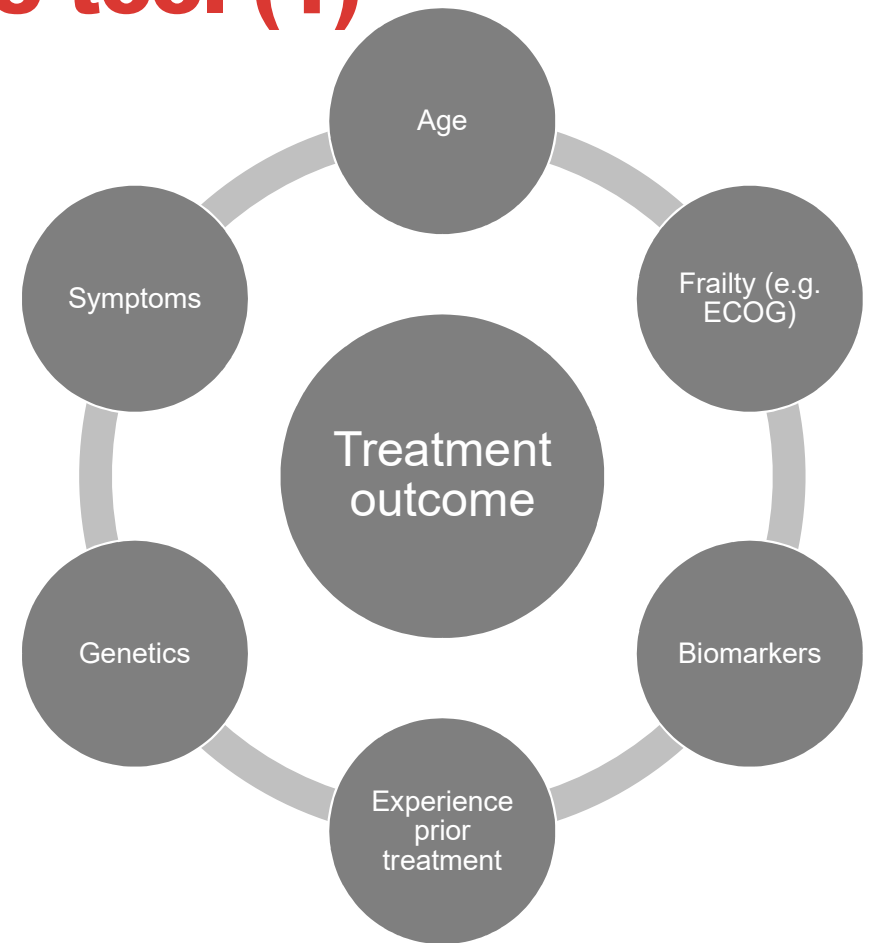


Developing a prognostic tool (1)

REGRESSION

► Typically numerous candidate predictors

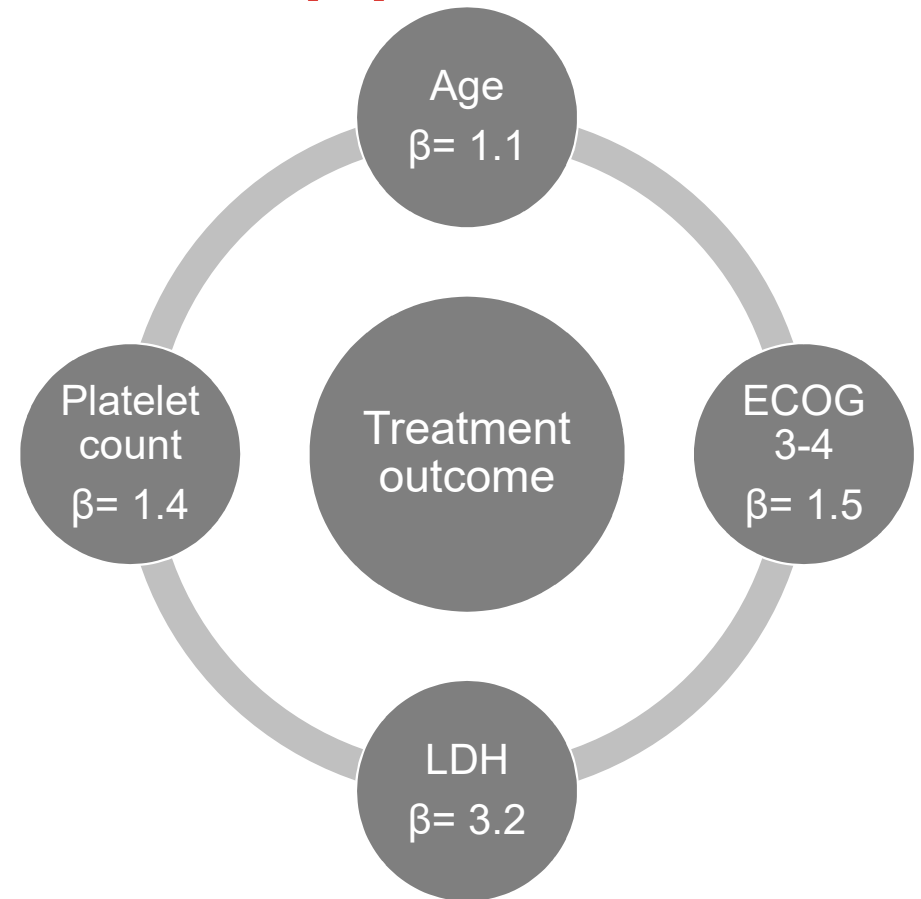
- with an *unknown predictive effect*
- for which it is unknown whether they predict response *independent of other predictors*



Developing a prognostic tool (1)

REGRESSION

- ▶ Regression modelling allows for
 - selection of independent predictors
 - estimating the predictive effect of each characteristic (β or weight)



Developing a prognostic tool (2a)

PROGNOSTIC SCORE AND RISK GROUPS

$$y = 1.1 \cdot \text{age} + 1.6 \cdot \text{LDH} + 0.4 \cdot \text{platelet count} + \dots$$

ID	age	LDH	platelet	Score
1	65	200	203	
2	73	300	153	12
3	50	220	107	
4	81	290	137	

Score patient 2 =

$1.1 \cdot 73$ (age) +

$1.6 \cdot 300$ U/L (LDH) +

$0.4 \cdot 150$ 10E/L (platelet) + ...



Regression



Prognostic score



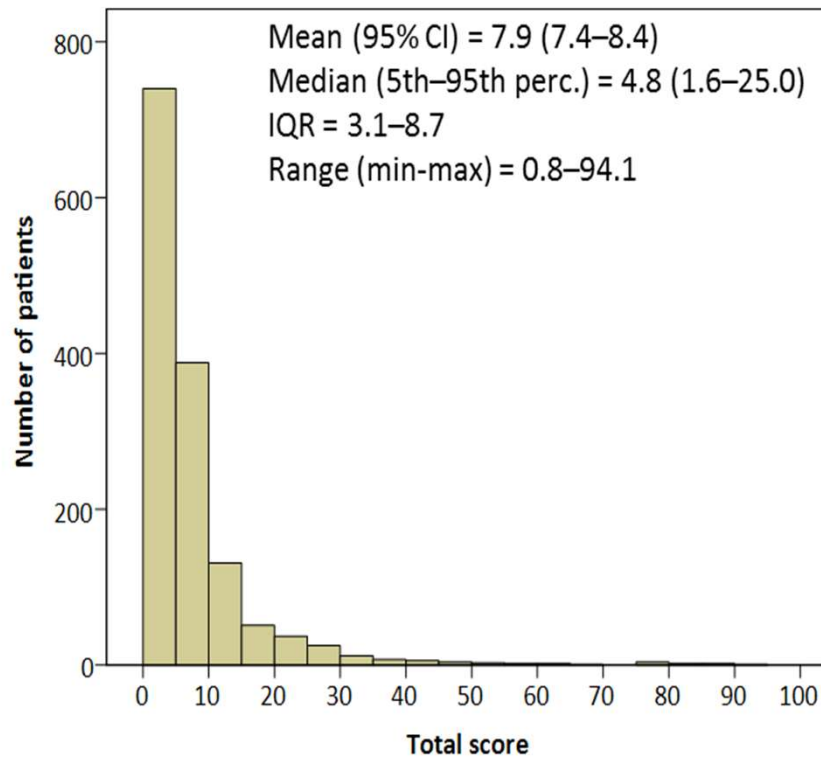
Risk groups



Target population

Developing a prognostic tool (2a)

PROGNOSTIC SCORE AND RISK GROUPS

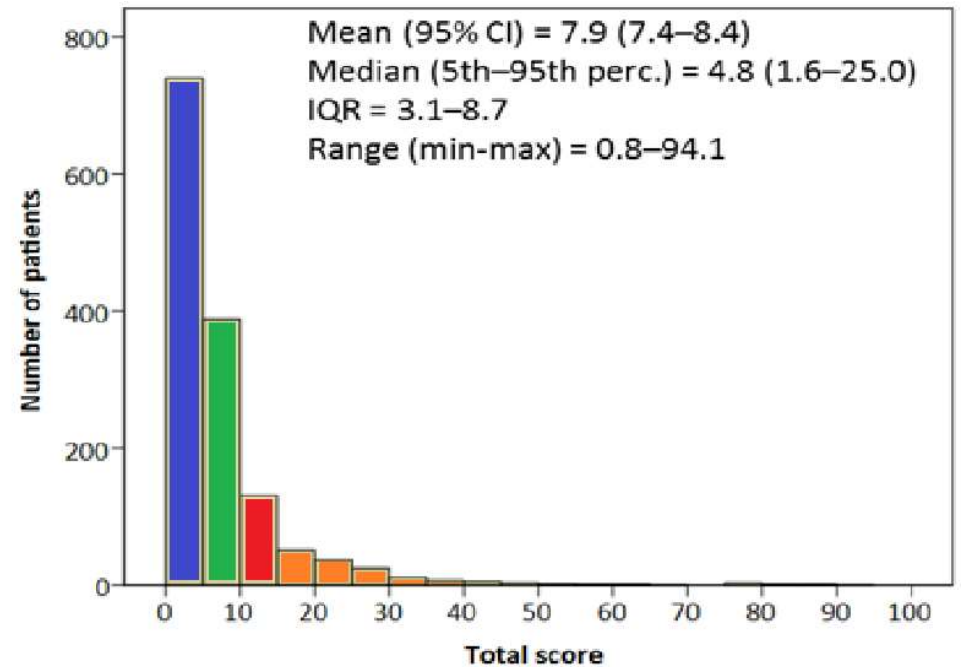


Developing a prognostic tool (3)

RISK GROUPS

➤ Risk groups:

- Based on the prognostic score
 - which is a summary of patient characteristics
- Methodology:
 - Categorization of the score such that groups have a distinct survival
 - K-adaptive survival partitioning



	Risk group 1	Risk group 2	Risk group 3	Risk group 4
Cut-off score	≤3	3 – 7	7-15	>15

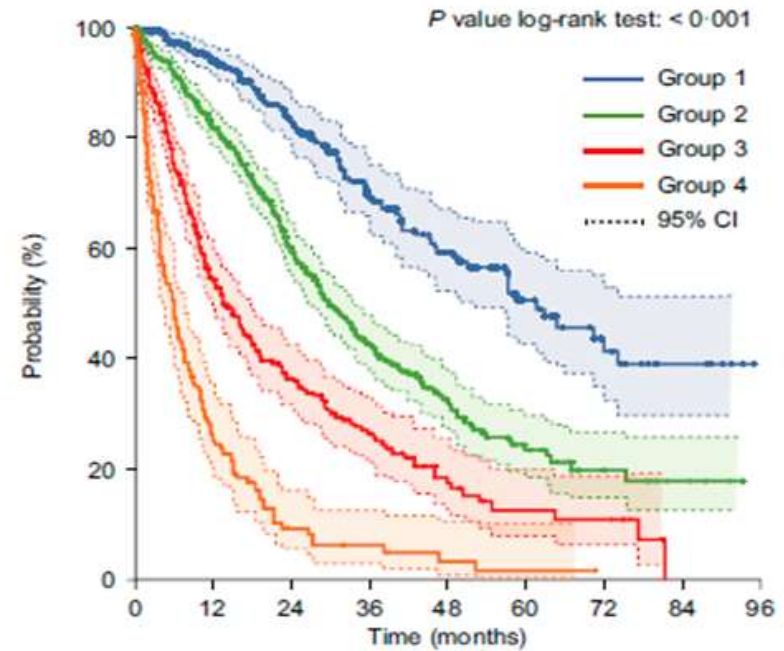


Developing a prognostic tool (3)

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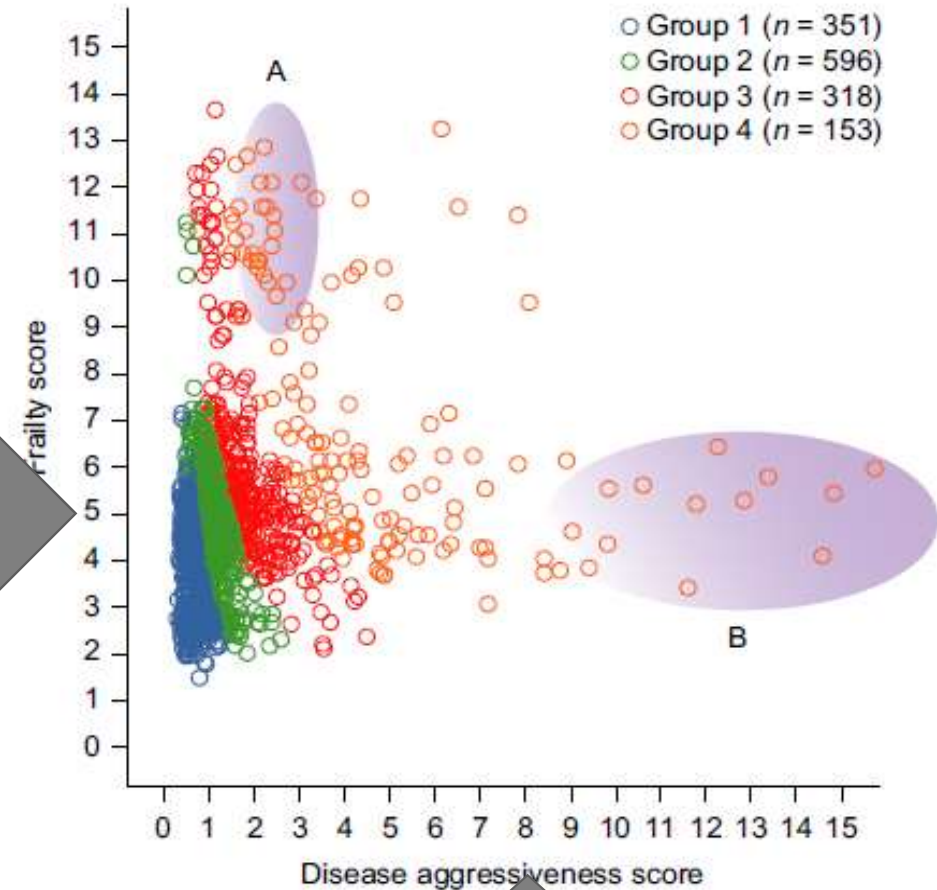
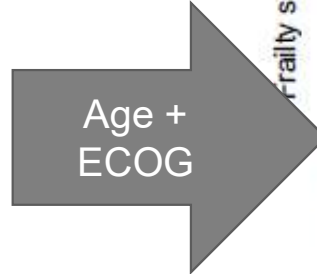
	Risk group 1	Risk group 2	Risk group 3	Risk group 4
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Developing a prognostic tool (4)

MAPPING THE PATIENT POPULATION

- The total prognostic score could be split in clinical relevant sub-domains
- Based on clinical expertise
- e.g. prognostic score = frailty score + aggressiveness score



Developing a prognostic tool (4)

INFORM TARGET POPULATION FOR PRODUCT DEVELOPMENT

➤ Mapping your patient population

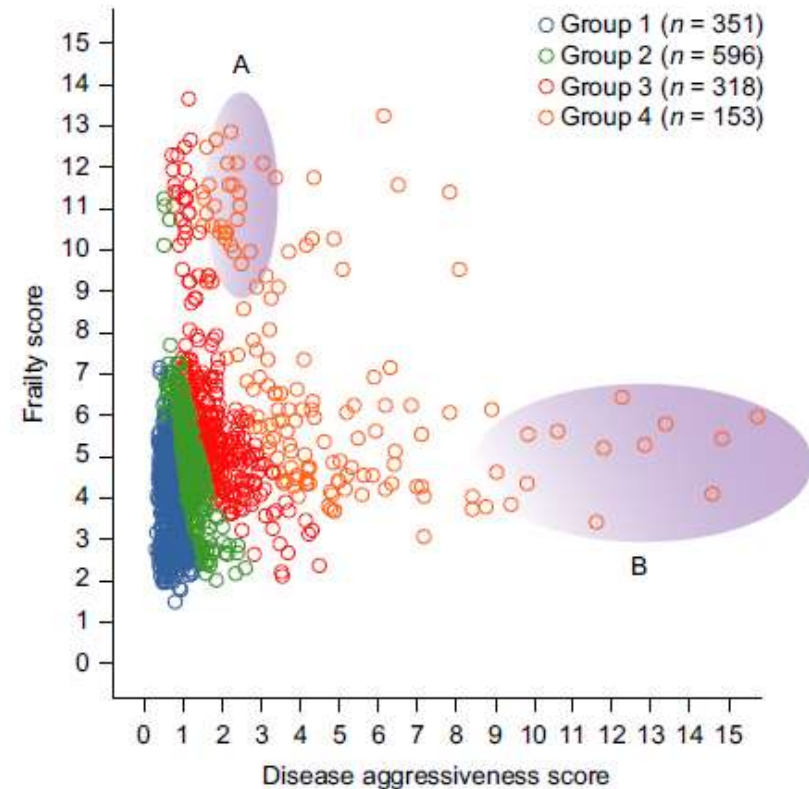
- Risk groups: prognosis
- Domain within the score: driver

➤ Frail patients may be treated differently

- E.g. mono-therapy

➤ Versus fit patients with aggressive disease

- E.g. triplet therapy



Regression



Prognostic score



Risk groups

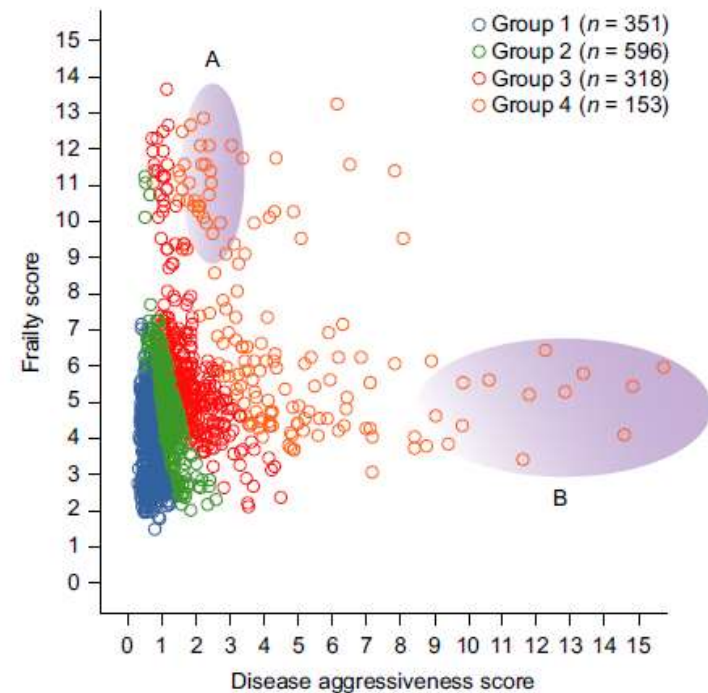


Target population

So, prognostic modeling enables

➤ Characterizing the patient population

- with unmet needs
- that may be included in trials
- facilitating reflection on TPP
 - target product profile



Questions?

► The actors today have been

- Walter Bouwmeester
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- Elisabeth Fenwick
- efenwick@Pharmerit.com

► Pdf of the presentation:

- http://www.pharmerit.com/resources_library/

► Relevant literature:

- Moons KG, de Groot JA, **Bouwmeester W**, Vergouwe Y, Mallett S, Altman DG, Reitsma JB, Collins GS. Critical appraisal and data extraction for systematic reviews of prediction modelling studies: the [CHARMS checklist](#). PLoS Med. 2014 Oct 14;11(10):e1001744.
- Hájek R, Delforge M, Raab MS, Schoen P, DeCosta L, Spicka I, Radocha J, Pour L, Gonzalez-McQuire S, **Bouwmeester W**. [Development and validation of a novel risk stratification algorithm for relapsed multiple myeloma](#). Br J Haematol. 2019 Aug 6.
- Hájek R et al. [A Novel Risk Stratification Algorithm for Relapsed Multiple Myeloma: Assessment of Performance and Validation Using Real-World Patient Data From France, Germany and the United Kingdom](#). EHA 2018.

