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The impact of treatment line matching on covariates balance and cost effectiveness results: A case study in oncology

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The case (1/2)

- Population: Metastatic breast cancer patients (after 2 or more previous chemotherapies)
- Intervention: Treatment X
- Comparator: Usual care
- Outcome: Costs per quality-adjusted life years (QALYs)

- Main data source: clinical practice data
  - No randomisation
  - Confounding by indication

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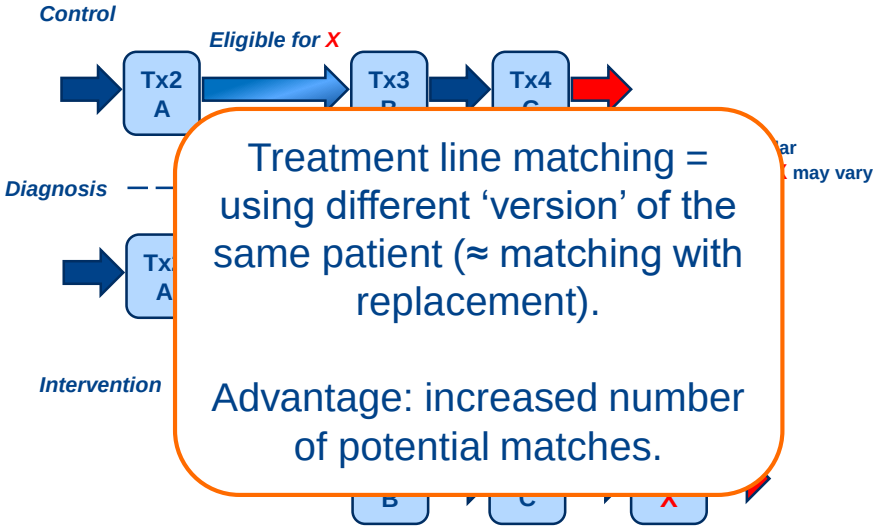
The case (2/2)



Research question

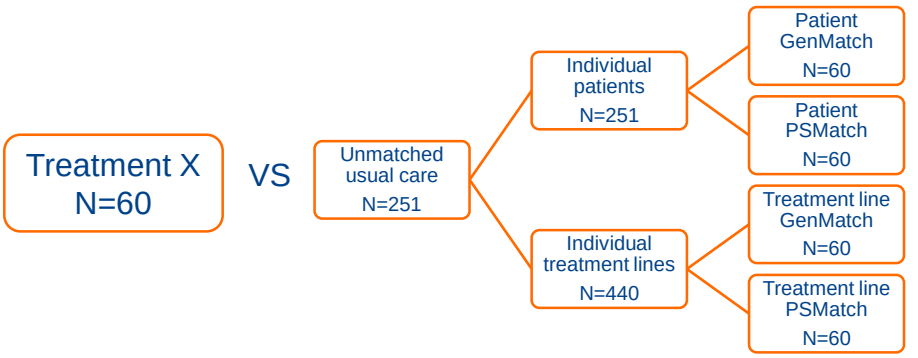
When using propensity score matching or genetic matching, what is the influence of using different treatment lines instead of patients on the covariates balance and ultimately the cost effectiveness of treatment X versus usual care?

Methods – Matching procedure

Matching Levels	Unmatched usual care	Genetic Matching	Propensity score Matching
Not applicable	✓	X	X
Patient level matching	X	✓	✓
Treatment line level matching	X	✓	✓

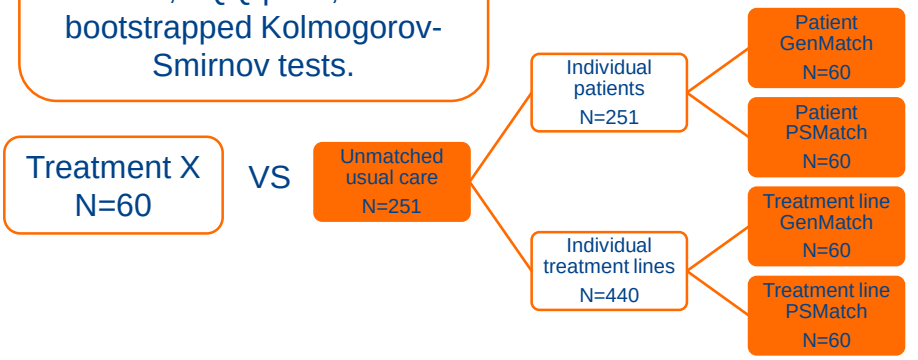
- Matching 1:1 with replacement ('Matching' R package)

Methods - Matching procedure



Methods - Matching procedure

Covariate balance assessed based on median, variance ratio, eQQ plots, and bootstrapped Kolmogorov-Smirnov tests.



Methods – Treatment effectiveness input

- Parametric time-to-event models
  - Progression-free survival (PFS)
  - Overall survival (OS)
- 7 distributions, selection for base-case based on NICE DSU TSD 14.
- Same distribution for PFS and OS in all groups.

Methods – Cost effectiveness analysis

- Health states: Progression-free, progressed, dead
- Perspective: Dutch Health care
- Cycle length: 1 week
- Utility values: Literature
- Health care resources: Treatments, outpatients, hospitalisations
- Outcomes: Incremental cost effectiveness ratio
  Incremental net monetary benefits

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Results – Covariate balance comparison

	Treatment X		Unmatched usual care	
Number of patients	60		251	
Number of previous hormonal therapy				
0-1	28	47%	141	56%
2-3	15	25%	90	36%
4+	17	28%	20	8%
Median				
KS boot				
p-value				
Number				
Median	3		2	
KS bootstrap p-value	N.A.		0.004	

In general, GenMatch performed better than PSMatch, and covariates balance were improved in the treatment line matched groups compared to the patient level matched groups.

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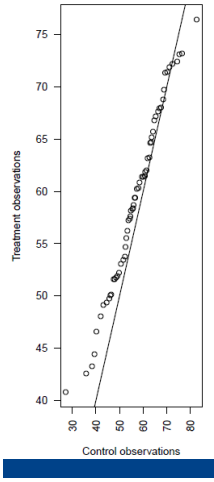
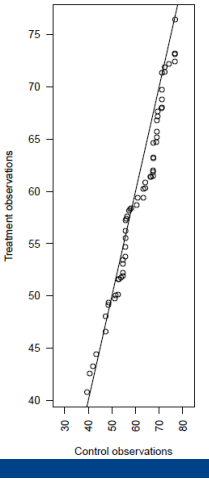
Results – Matching (start age, GenMatch)

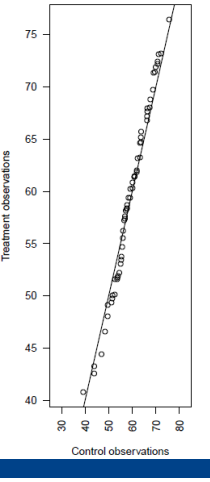
Unmatched



Patient



Treatment line



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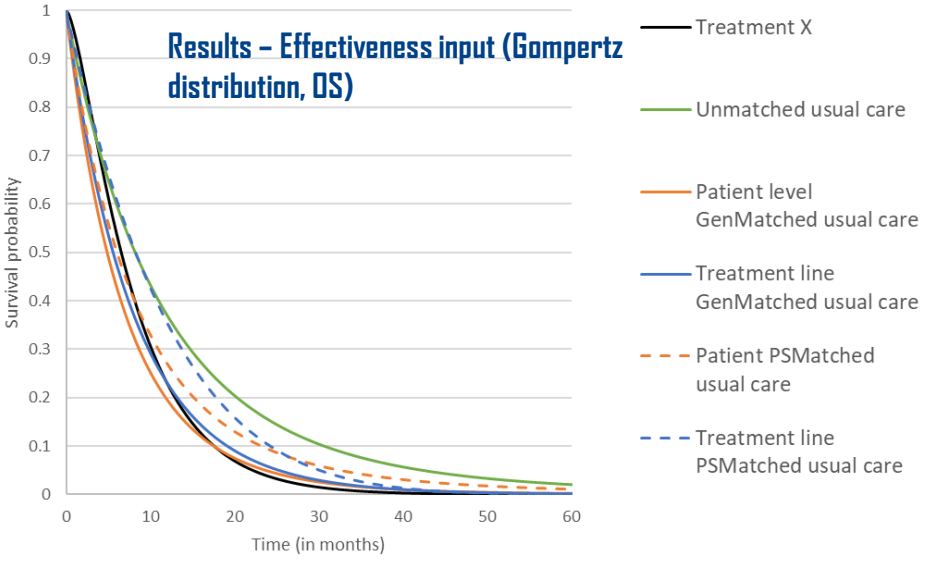
Results – Effectiveness input (Gompertz distribution, OS)



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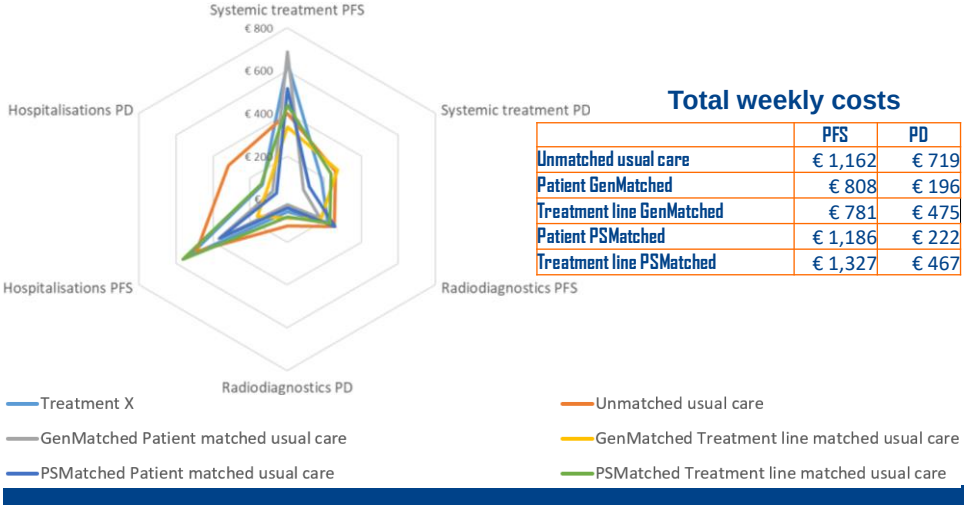
Results – Resource use and costs inputs

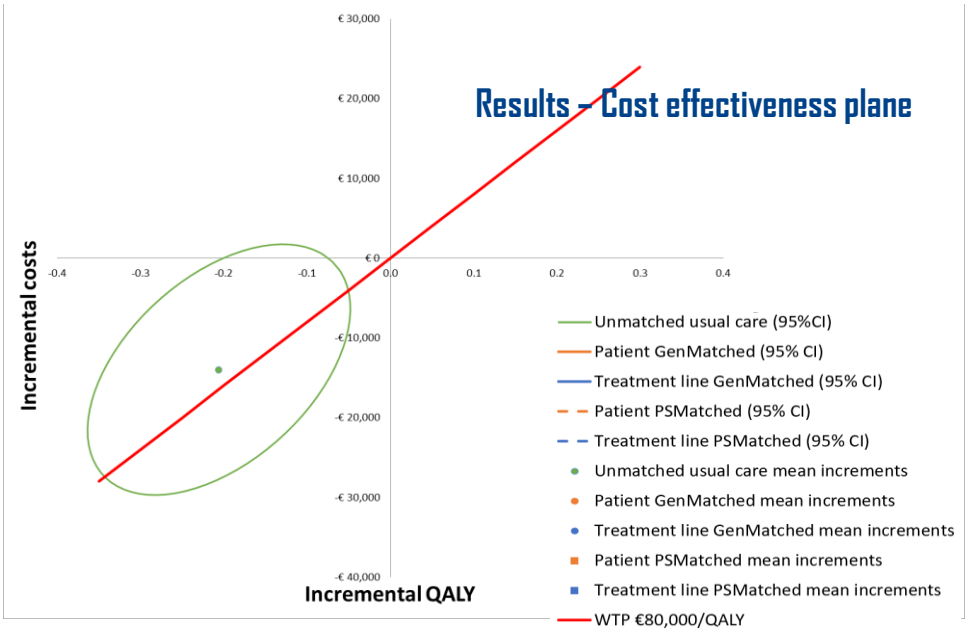


Total weekly costs

	PFS	PD
Unmatched usual care	€ 1,162	€ 719
Patient GenMatched	€ 808	€ 196
Treatment line GenMatched	€ 781	€ 475
Patient PSMatched	€ 1,186	€ 222
Treatment line PSMatched	€ 1,327	€ 467

Results – costs effectiveness (probabilistic)

	Life years	Quality adjusted life years	Costs
Treatment X	0.699	0.424	€ 33,019
Unmatched usual care	1.052	0.630	€ 47,005
GenMatched Patient usual care	0.642	0.393	€ 24,462
GenMatched Treatment line usual care	0.695	0.421	€ 19,755
PSMatched Patient usual care	0.828	0.494	€ 26,320
PSMatched Treatment line usual care	0.915	0.550	€ 38,697



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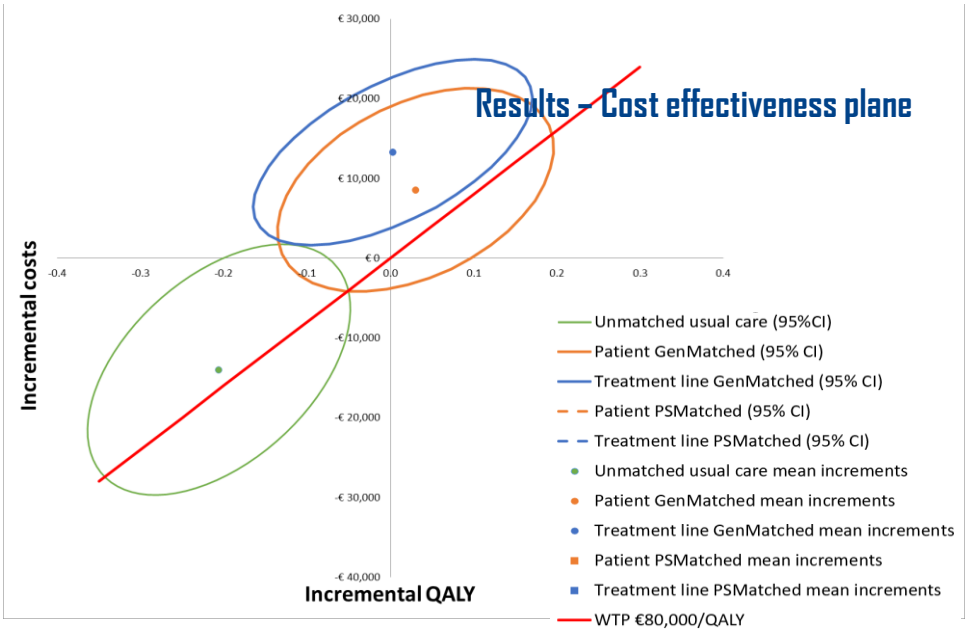

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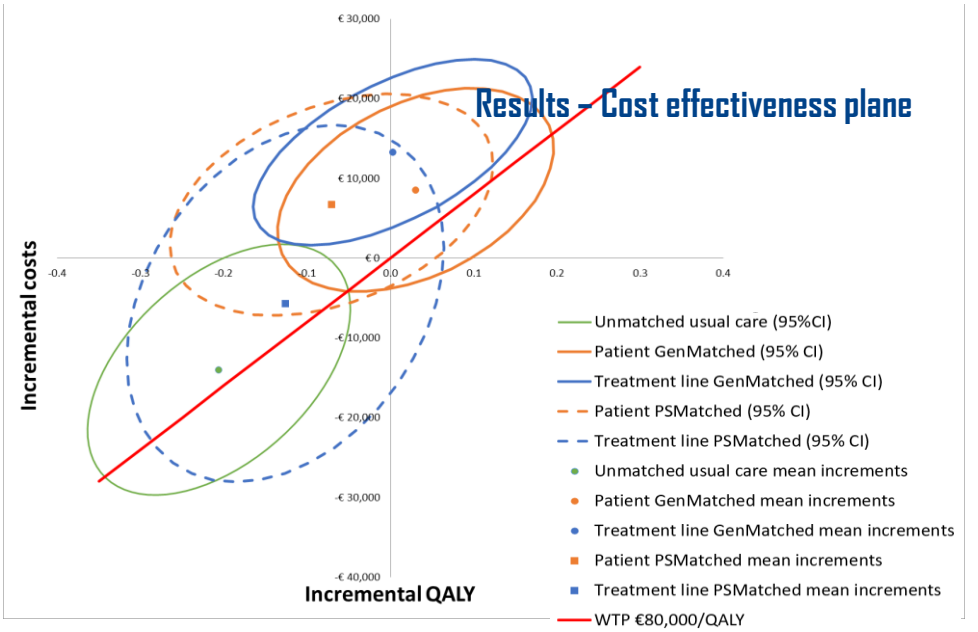
Results – Cost effectiveness plane



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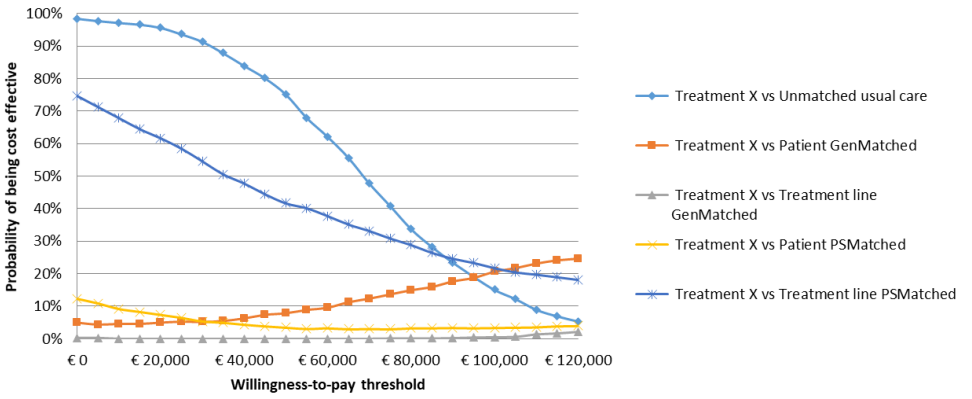
Results – Cost effectiveness acceptability curves



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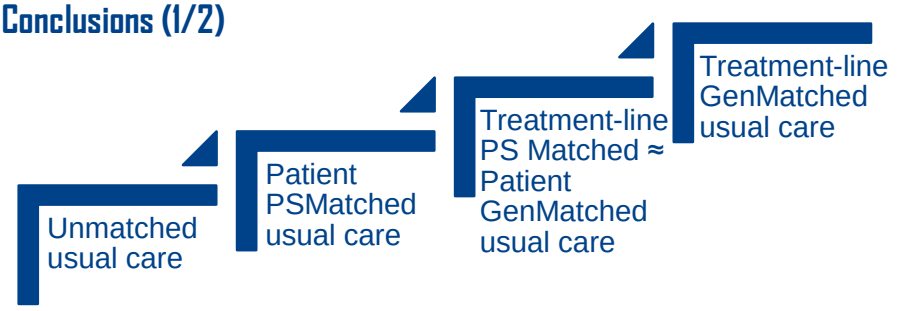
Conclusions (1/2)



- Matching procedures can have substantial impact on model inputs and results.
  - Uncertainty
  - Decision making

Conclusions (2/2)

- Generalisability?

- Treatment line matching seems to be a viable option to increase the number of potential matches when the number of patients in the comparator group is small.

Thank you for your attention!

Acknowledgement: E. Koffijberg

Statements (Richard Grieve)

Non-randomised studies should consider several approaches as part of structural sensitivity analyses.

Statements (Wietske Kievit)

We should rely more on observational comparisons in guideline development and health technology assessment.

Statements (Xavier Pouwels)

Treatment line matching should always be considered when non-randomised comparative evidence is used to inform cost effectiveness analysis.

Statements (Richard Grieve)

Genetic matching is an attractive approach for balancing observed confounders.

Statements (Wietske Kievit)

Residual confounding may be substantial even when good prognostic data are available and is an RCT always necessary for comparative effectiveness questions.

Statements (Xavier Pouwels)

Since comparisons to an unmatched usual care group are biased, as much as a complete case analysis could be, these analyses are uninformative and should not be performed.

Statements (Richard Grieve)

Move to large e-health data offers opportunity for IV methods that fully recognise heterogeneity.