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Health Solutions

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Common Challenges & Solutions in Analysis & Reporting of PROs in Oncology Clinical Trials

The power of **knowledge.**
The value of **understanding.**

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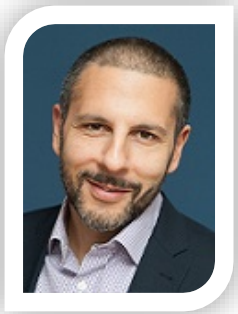

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- Key Learning Objectives:
  - The specific challenges associated with the analysis of data from oncology studies.
  - Why traditional statistical methods for clinical trials can lead to biased results when applied to oncology studies.
  - Possible analytic methods to help account for potential biases and help you better understand your patients.
  - Why safety and patient-reported outcome endpoints may appear contradictory in oncology trials.

Assessment schedule may not be optimal

- Is beginning of cycle the most appropriate time?
- Dose adjustment / interruption may delay treatment cycles.
- How about more assessments during the early cycles while the majority of patients are still in the study?

Imperfect measures may be redundant

- Currently used measures are static.
- Impact of new therapies are missed.
  - Skin rash
  - Vitiligo
  - Photosensitivity
- Summary scores may be misleading.
- Questionable content validity.

Missing Data are just annoying

- Common and rarely random.
- No one cares about exploratory endpoints.
- Suboptimal analytical methods.

PROs are rarely presented in context of efficacy and safety

- Demonstrating Tx-A (PRO) = Tx-B (PRO) is unique to cancer.
- Proving the null hypothesis using imperfect instruments in an underpowered study is nothing to shout about.
- Often this conclusion is not supported by safety data.

Current state of PROs in cancer studies

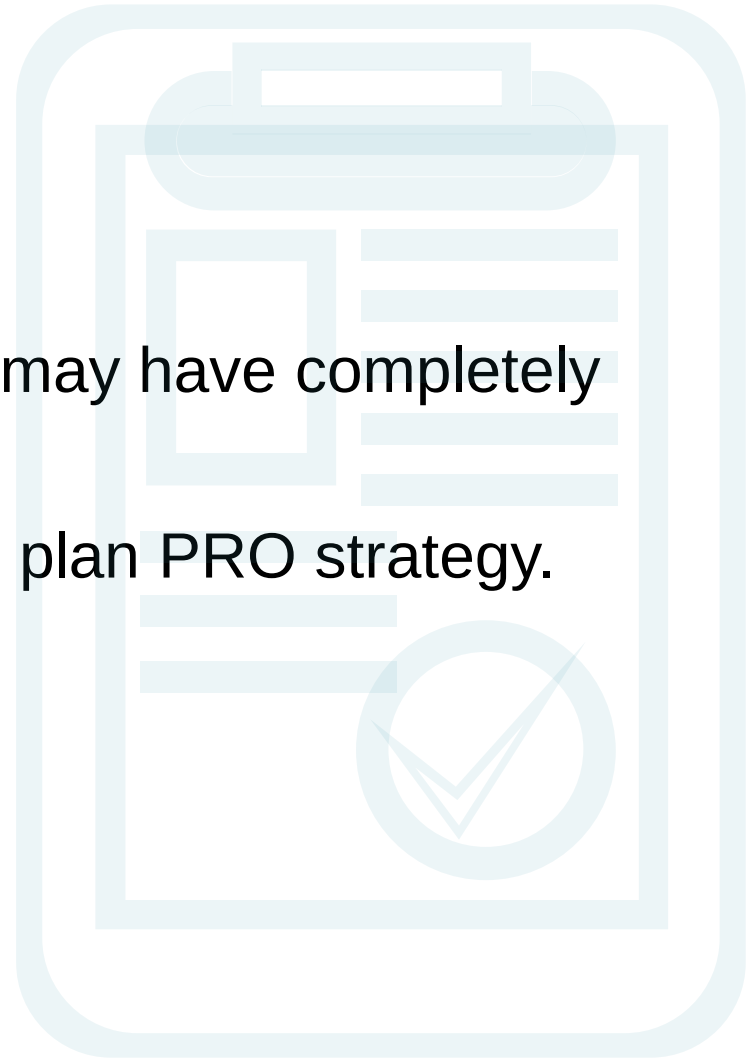
PRO instruments may not be capturing what is needed

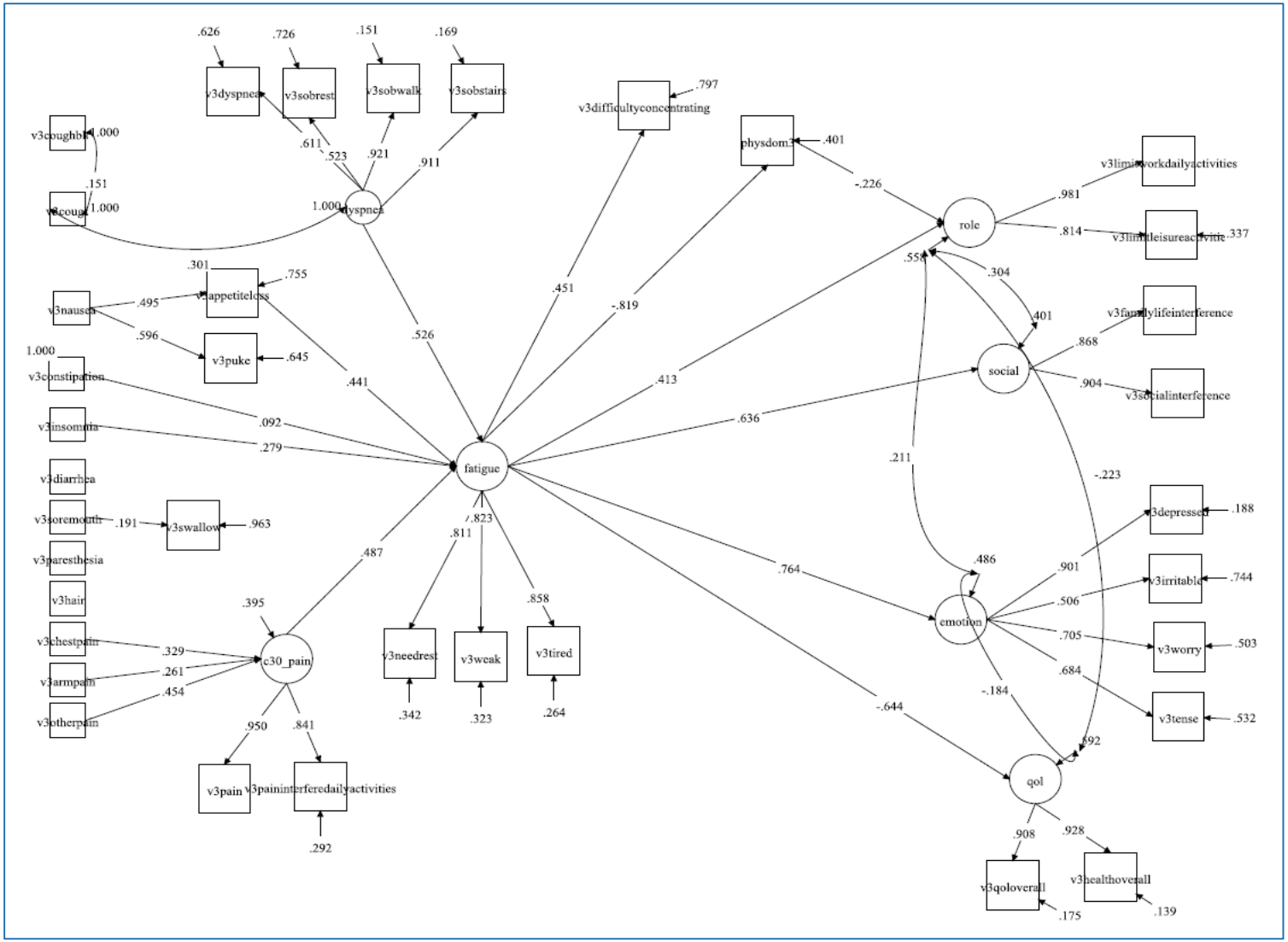
Data capture itself as a process is not ideal

Missing Data

PRO Instruments Are Not Ideal

- PRO instruments should:
  - Measure what is needed
  - Be sensitive enough
- New immuno-oncology therapies may have completely different symptom profile.
- Important to invest time upfront to plan PRO strategy.





Dependent variable	Explanatory variable	Total effects	Direct effects	Total indirect effects
GLBLQOL	Dyspnea	-0.345***	NS	-0.345***
GLBLQOL	Nausea	-0.141***	NS	-0.141***
GLBLQOL	Pain	-0.319***	NS	-0.319***
GLBLQOL	Appetite Loss	-0.284***	NS	-0.284***
GLBLQOL	Insomnia	-0.180***	NS	-0.180***
GLBLQOL	Constipation	-0.059*	NS	-0.059*
PHYSICAL	Dyspnea	-0.431***	NS	-0.431***
PHYSICAL	Nausea	-0.179***	NS	-0.179***
PHYSICAL	Pain	-0.399***	NS	-0.399***
PHYSICAL	Appetite Loss	-0.361***	NS	-0.361***
PHYSICAL	Insomnia	-0.229***	NS	-0.229***
PHYSICAL	Constipation	-0.075*	NS	-0.075*

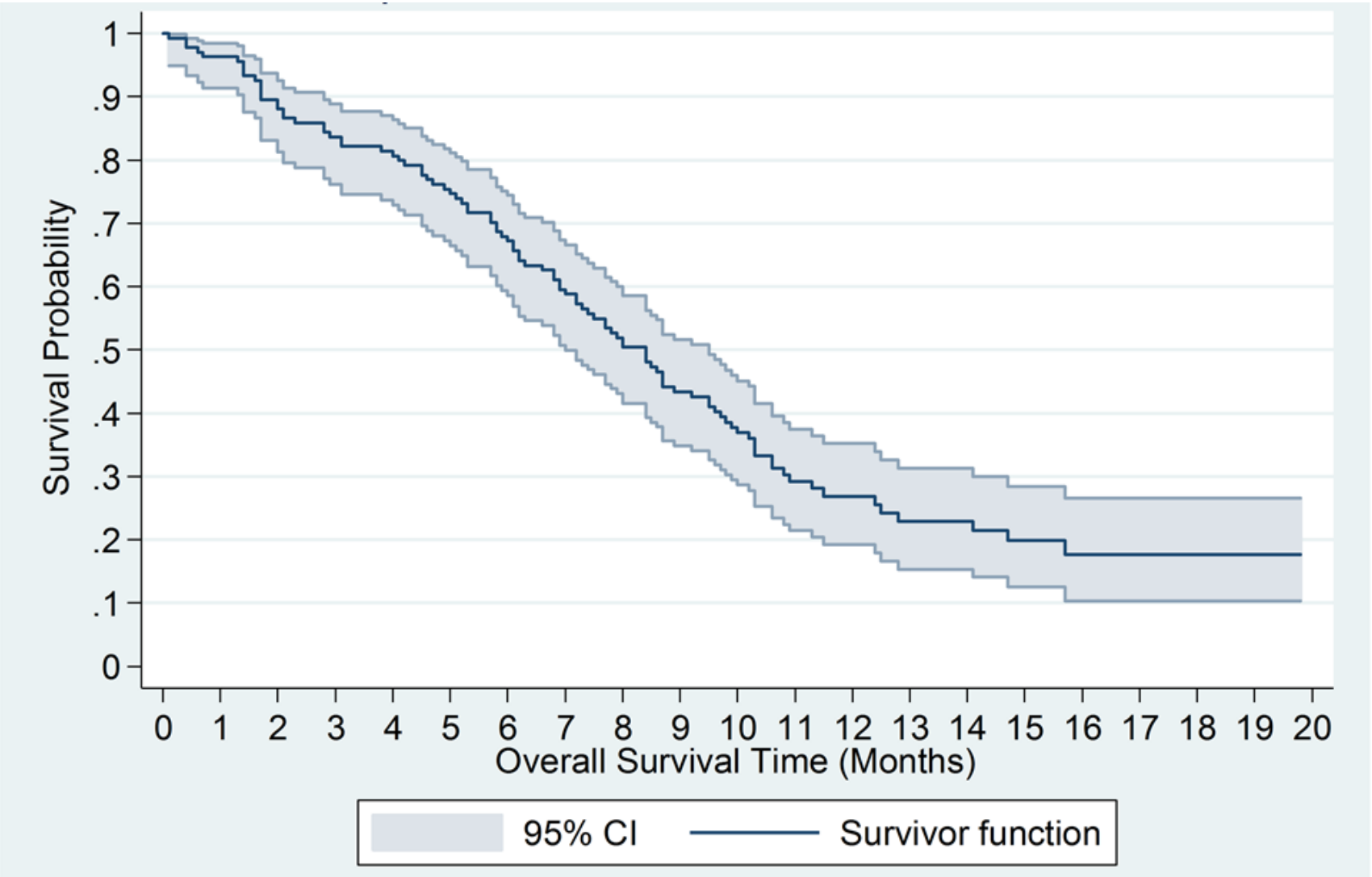
Data Capture Is Not Ideal

- PRO data collection frequency and around events of interest.
- Patient burden
- Analysis: Experimental to observational mindset
  - Fixed visits vs. continuous time
  - Data-driven analytic decisions
  - Importance of sensitivity analyses

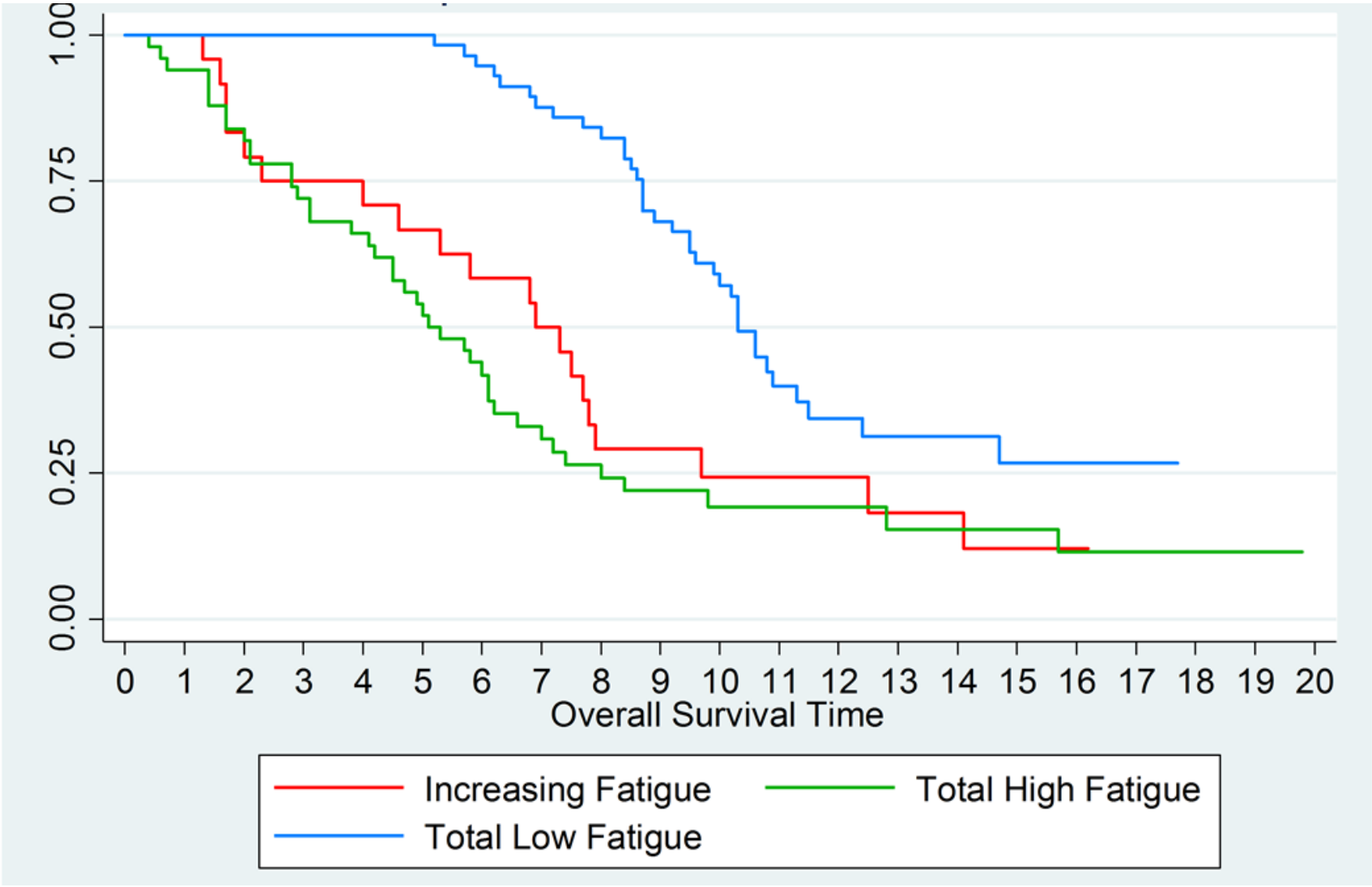
Missing Data

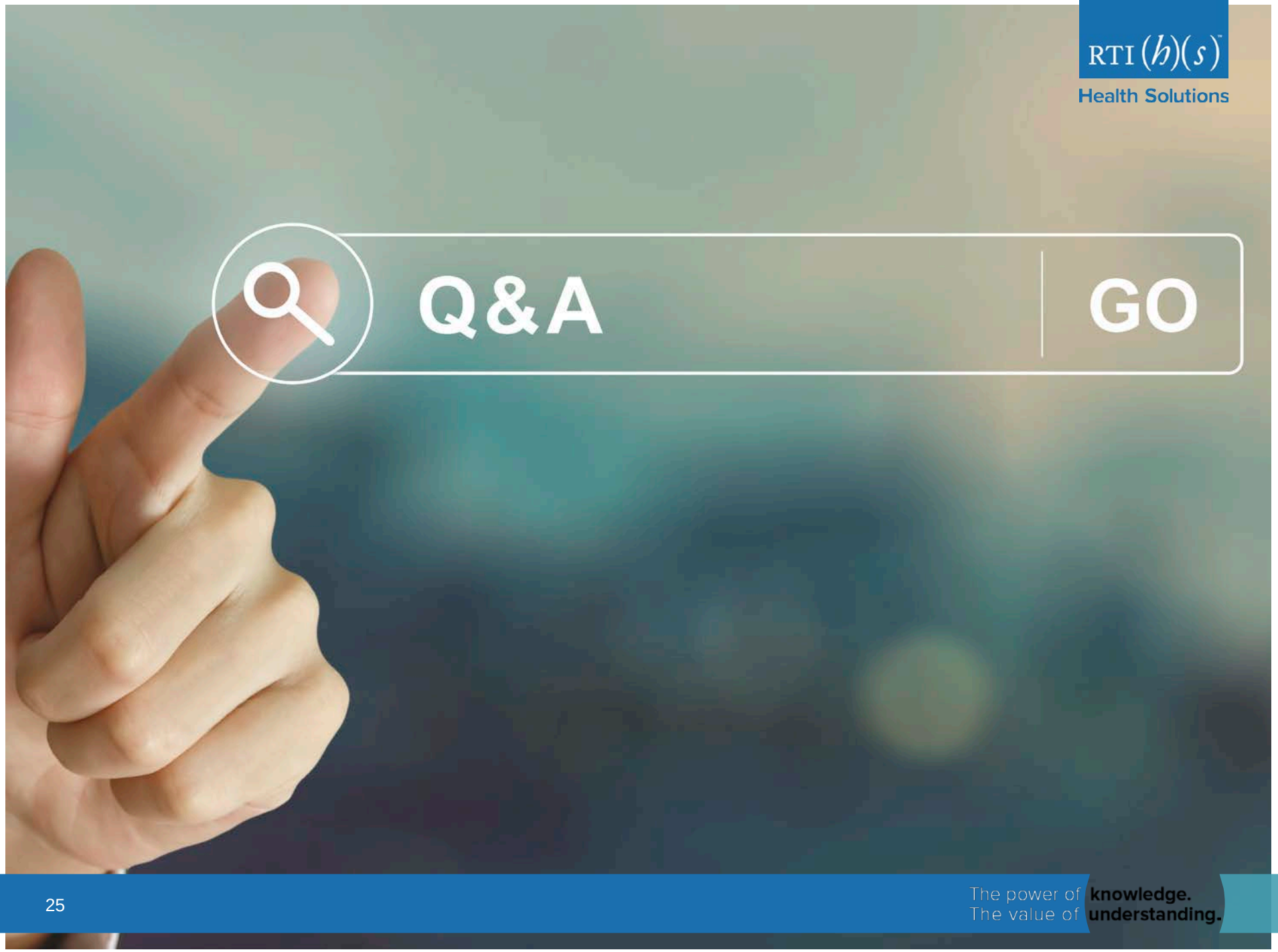
- Very common and usually not at random.
- Traditional mixed effects models and imputation methods do not work well.
- Need to account for the informative nature of missing data.
  - Selection Models / Shared Parameter Models
  - Pattern Mixture Models
  - Extended Pattern Mixture Models

Kaplan-Meier Overall Survival Estimate



Kaplan-Meier Survival Estimates





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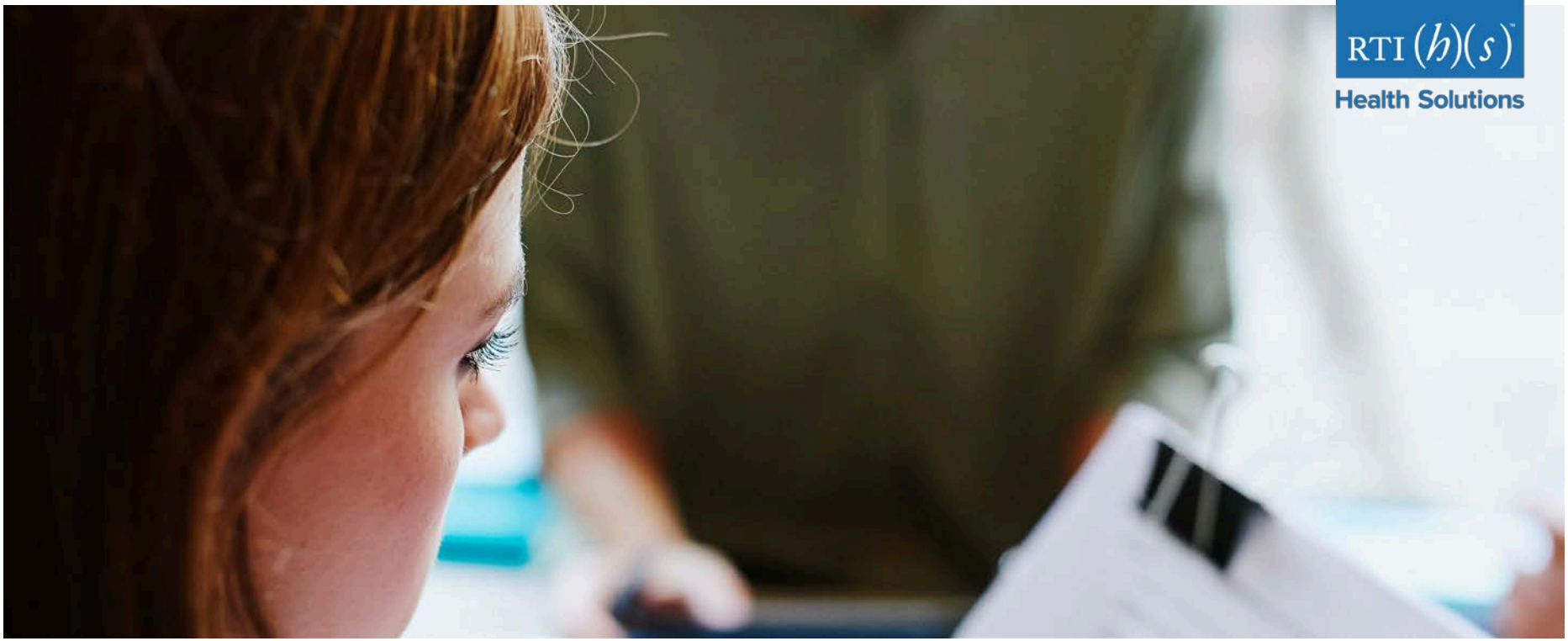

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Generating knowledge and providing greater understanding so that you—and those who regulate, pay for, prescribe, and use your products—can make better decisions.

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RTI-HS Contact Information

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