Benefits & risks of using WDMs for HTA submissions

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Summary from perspective of (commercial) user

Benefits

- **Model is**
  - Validated (hopefully!)
  - Published
  - Accepted (maybe)
- **Much (most?) of the heavy lifting is done**
  - Input structure designed
  - Logic worked out
  - Default inputs included
  - Equations developed
  - Assumptions known and consequences identified
- **More comprehensive look at disease**
- **Lower investment (maybe) & less time required**

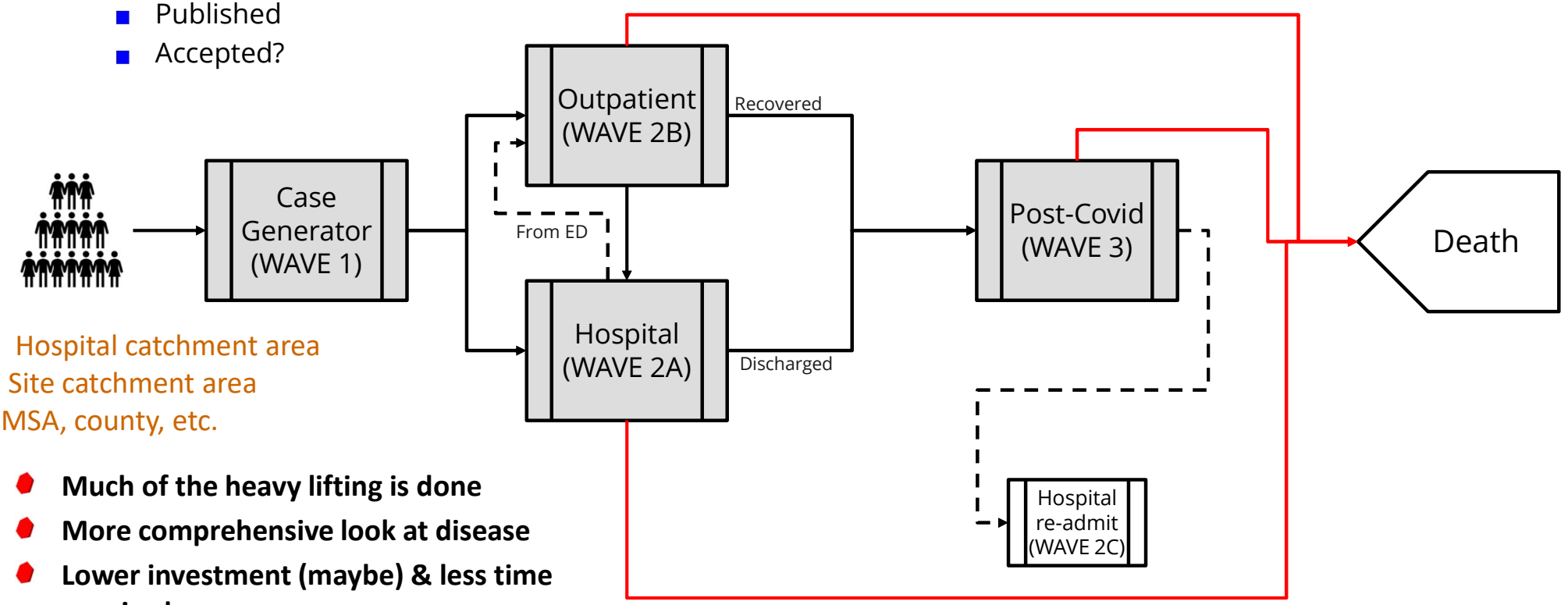
Risks

- **Exceeds what is needed for submission**
  - Complexity
  - Opacity
  - More data required to adapt inputs
  - Longer runtimes
  - More voluminous output (perhaps)
  - Lose focus on intervention's effects
- **Impairs incorporating intervention of interest**
  - May require "translating" RCT measures
  - May not know effects on some model outcomes
  - Modifying equations can be difficult
  - May not address novel MoA or nature of effect (e.g., curative)

- **Provides better, less biased comparability…?**

COVID-19 WDM

- **Model is**
  - Validated
  - Published
  - Accepted?



Hospital catchment area
Site catchment area
MSA, county, etc.

- **Much of the heavy lifting is done**
- **More comprehensive look at disease**
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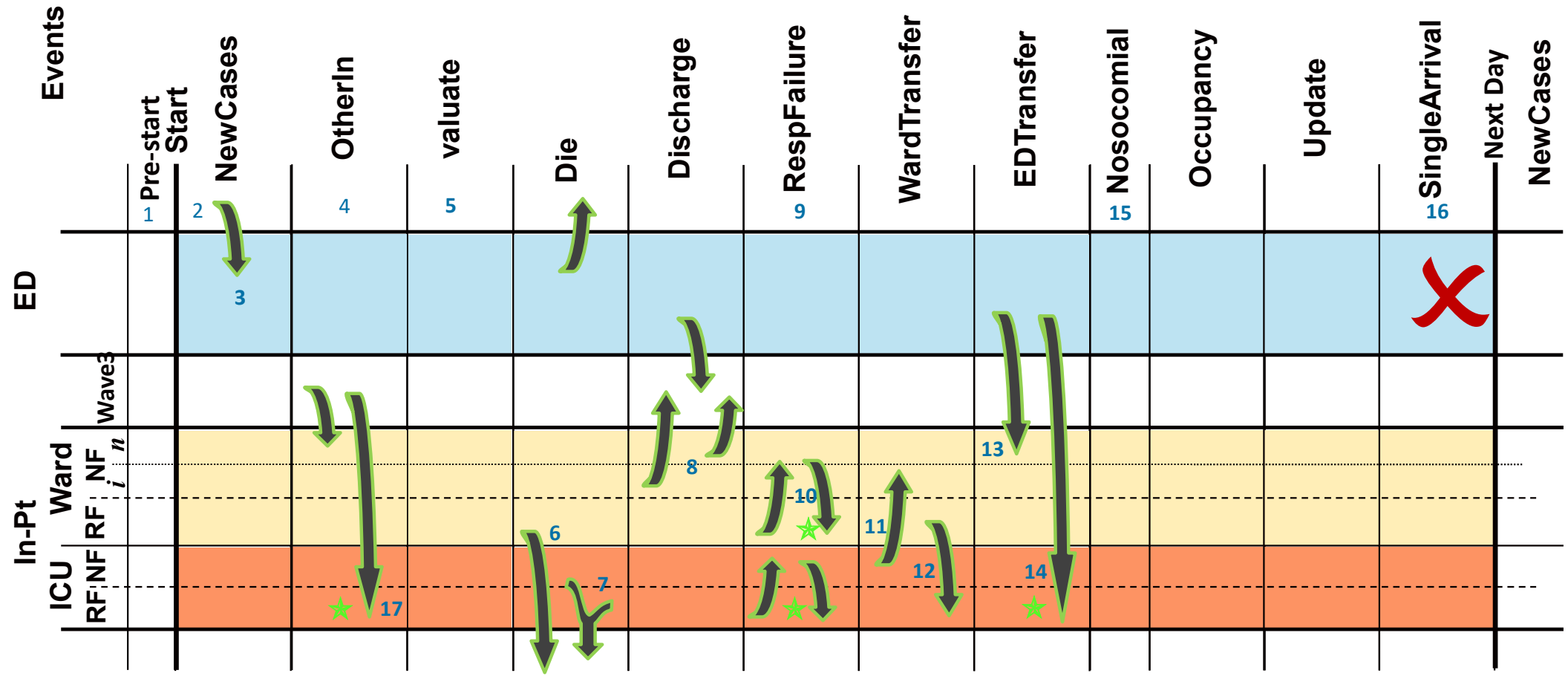
Path diagram – WAVE 2



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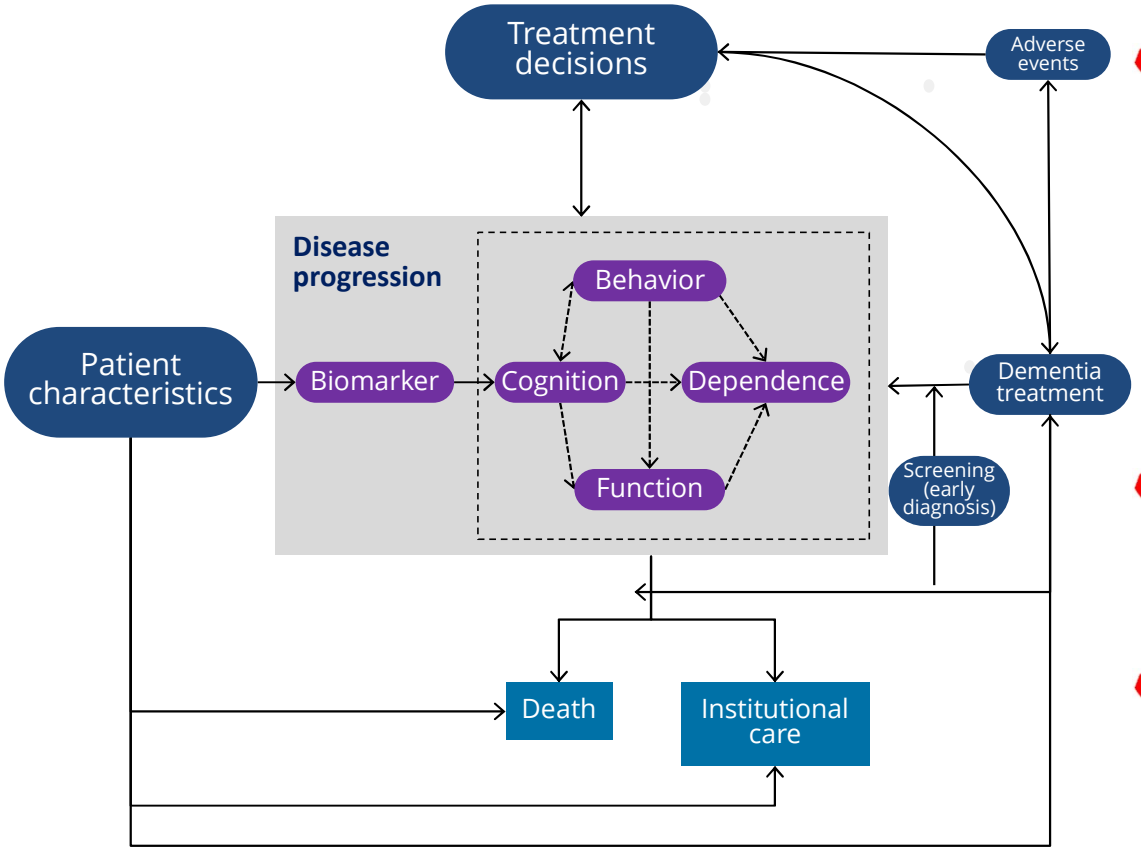
Assumptions (partial list Module 2A)

1. Locations can be pre-populated to reflect a real starting day, or set to specific numbers to create a custom cohort, or set to zero
2. New cases arrive in ED, before valuations, die, D/C so that they can experience these events
3. Distinction by RF doesn't take place in ED
4. Alternative way to generate new cases directly into hospital or to allow for transfers from other hospitals to Ward NF*n* and ICU RF
5. Valuate is by location & by RF; applies to anyone present at start of day + New arrivals + Other in
6. Ward deaths are among those with RF only
7. ICU deaths are in anyone (not by RF)
8. D/C only from Ward NF maintaining *i/n* distinction
9. RF status changes happen before ward transfers
10. RF status changes ignore the *i/n* distinction (implicitly this allows relapse)
11. ICU to Ward transfers are only from NF
12. Ward to ICU transfers are only from RF
13. ED transfers to Ward are to NF*n*
14. ED transfers to ICU are to RF
15. Optional event that adds nosocomial cases
16. Event triggered when Single arrival option is set – empties out the ED so no one continues to next day
17. Treatment may be given at any of the ✯

Alzheimer's Disease (AD) ACE Simulator



- **Simulates outcomes across the full spectrum of AD (preclinical to severe)**
  - Represents the course of AD as a combination of evolving conditions (e.g., characteristics that persist over time) and events (e.g., treatment start/stop, death)
  - Simulates the effects of symptomatic treatment or disease modification
  - Considers patient heterogeneity
- **Has been extensively VALIDATED against published** literature and ongoing trials. It has shown strong predictive validity against external data
- Is coupled with a CLINICAL TRIAL SIMULATION (CTS) engine that allows assessment of clinical trial designs.