

Adaptive Treatment Strategies

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Adaptive Treatment Strategies

- ■ “...are individually *tailored sequences* of treatments, with treatment type and dosage adapted to the patient.”
- ■ “Adaptive”
 - ■ Decisions are tailored to individual patients *at the time of treatment*
- ■ “Strategy”
 - ■ A *sequence* of treatment decisions unfolding over time



Adaptive Treatment Strategies?

- Sounds like “Clinical Practice”
 - Doctors tailor treatments to individual patients, and often have a long-range strategy in mind.
- We want to operationalize this
 - We can then construct adaptive treatment strategies from data.

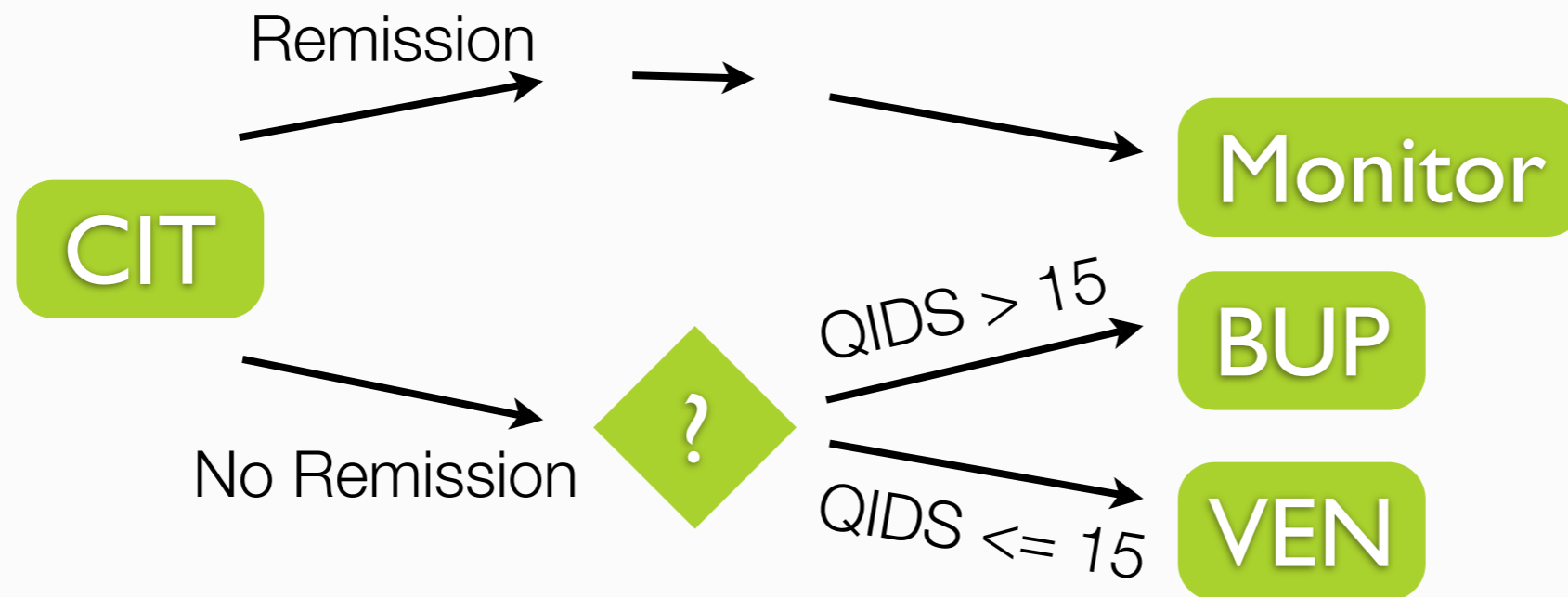
Why Adaptive Treatment Strategies?

- ■ When do doctors use them? Chronic illness.
- ■ Adaptive (tailoring)
 - ■ What works for one patient may not work for another.
- ■ Strategy (sequencing)
 - ■ What works now may not work later.
 - ■ There may be cycles of remission/relapse.
 - ■ **Treatments provide both therapeutic and diagnostic benefit.**

Example: Depression*

- Provide Citalopram for up to 12 weeks.
 - If the patient **remits**, defined by a QIDS-SR depression rating score ≤ 5 , continue to provide Citalopram and **monitor**.
 - Otherwise if the patient **does not remit**,
 - If the patient's QIDS-SR score is > 15 , switch treatment to **Bupropion**.
 - If the patient's QIDS-SR score is ≤ 15 , switch treatment to **Venlafaxine**.
- Here, treatments are *adapted* using QIDS-SR as a tailoring variable, and the *strategy* has up to two treatments

*I am not a psychiatrist! This is a made-up example. Don't try this at home.



- Provide **CIT**alopram for up to 12 weeks.
- If the patient **remits**, defined by a QIDS-SR depression rating score ≤ 5 , continue to provide **CIT**alopram and **monitor**.
- Otherwise if the patient **does not remit**,
 - If the patient's QIDS-SR score is > 15 , switch treatment to **BUP**ropion.
 - If the patient's QIDS-SR score is ≤ 15 , switch treatment to **VEN**lafaxine.

How would we develop such a treatment strategy?

- ■ From Data


- ■ Longitudinal data collected from patients as they follow different paths through a proposed set of possible treatment strategies

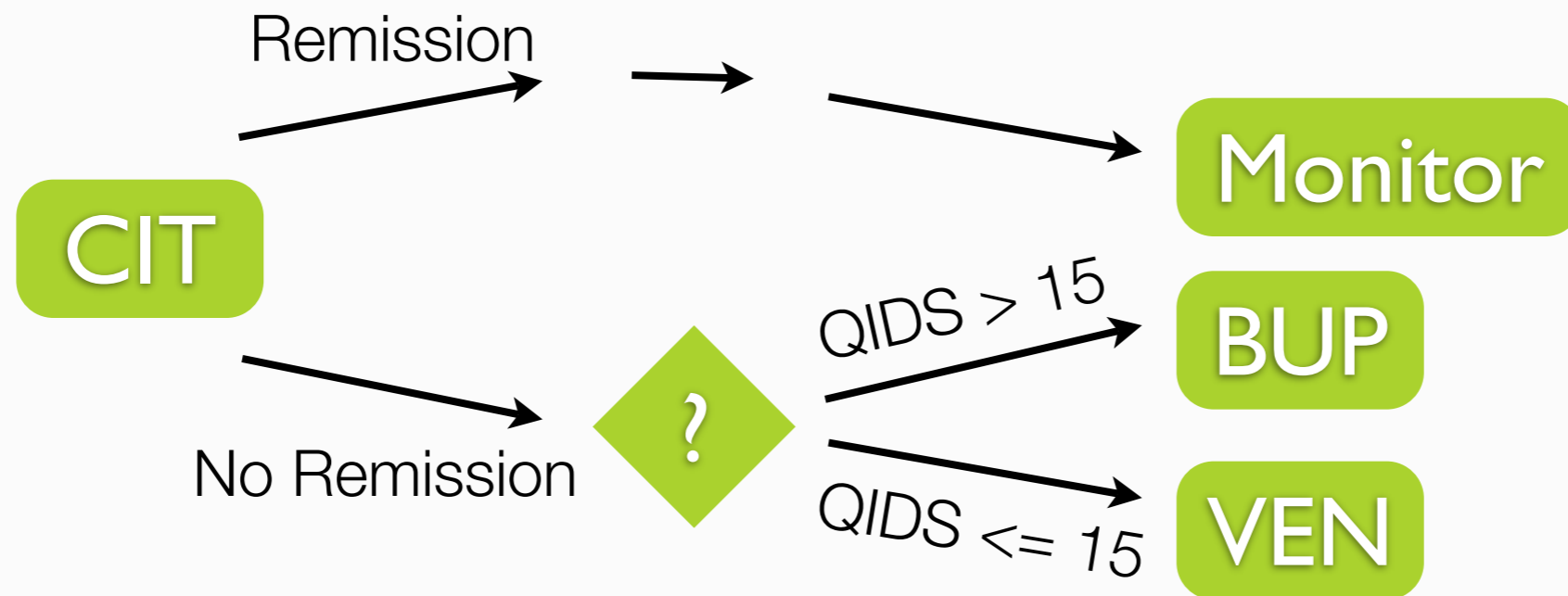
- ■ **Sequenced Multiple Assignment Randomized Trials**

- ■ Pinpoint a *small number* of critical decisions per patient to investigate
- ■ A randomization takes place at each critical decision (multiple randomizations for each patient)
- ■ Goal is to inform the construction of an adaptive treatment strategy.

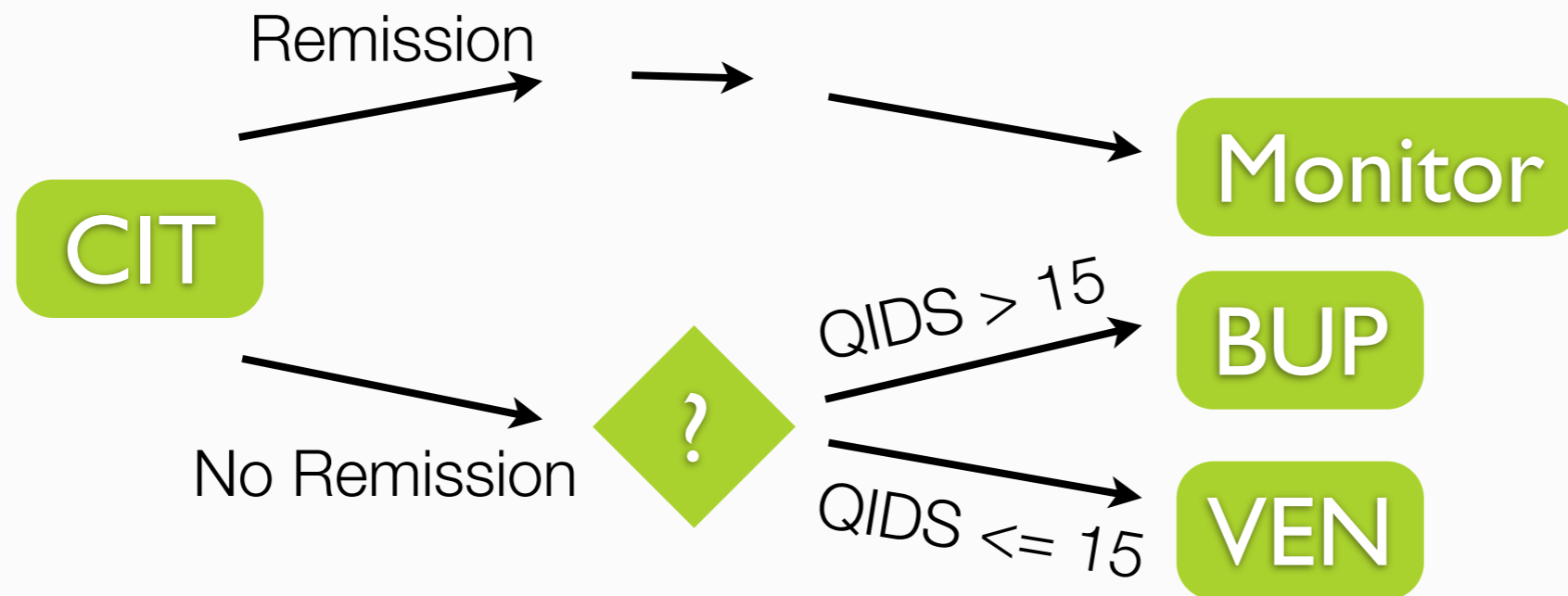


SMART Design Principles

- At each stage, restrict class of treatments only by ethical, feasibility or strong scientific considerations. **Use a summary instead of complicated intermediate outcomes** to restrict class of next treatments.
 - **But collect intermediate outcomes** that might be useful in ascertaining for whom each treatment works best. This information might enter into the adaptive treatment strategy.
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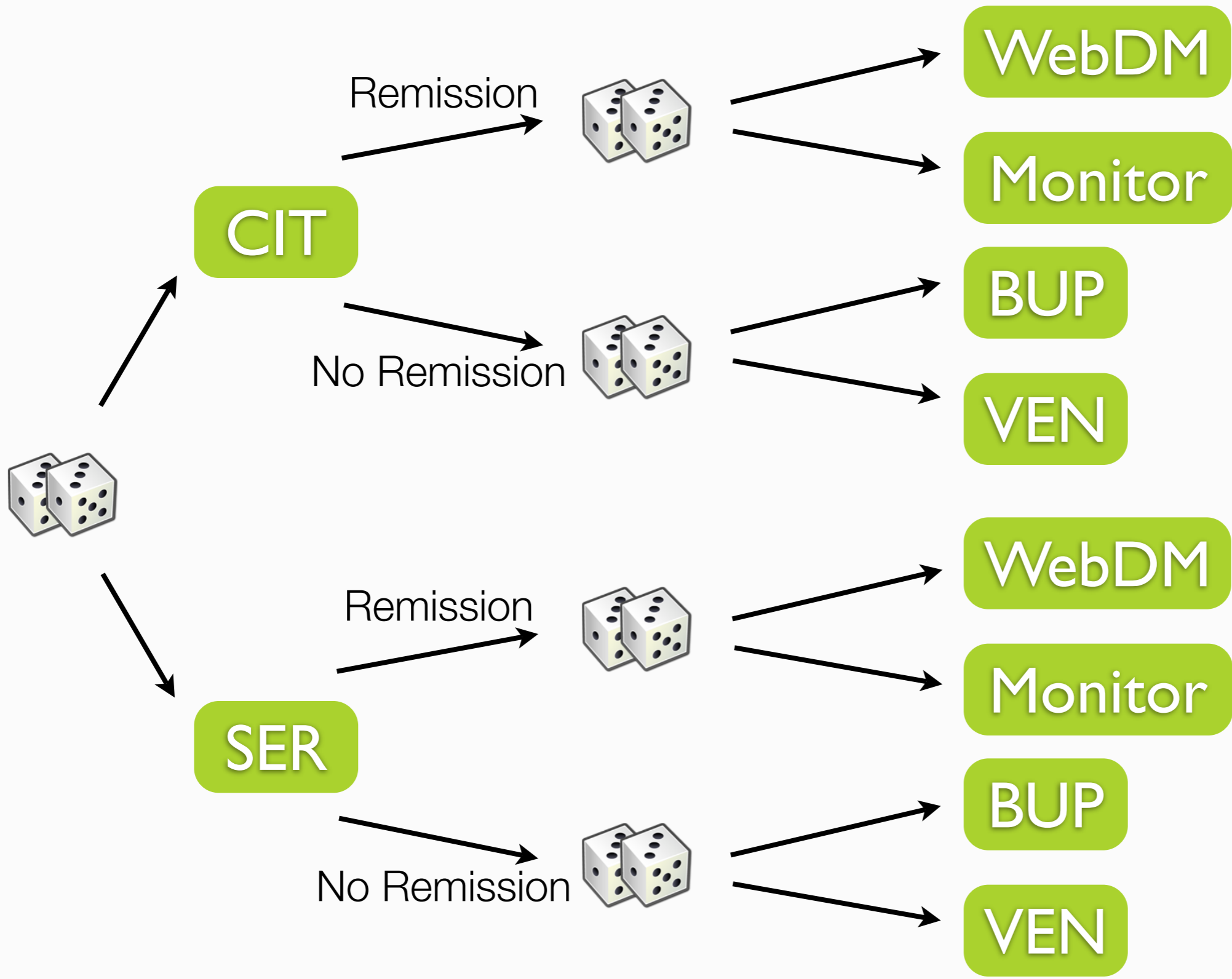


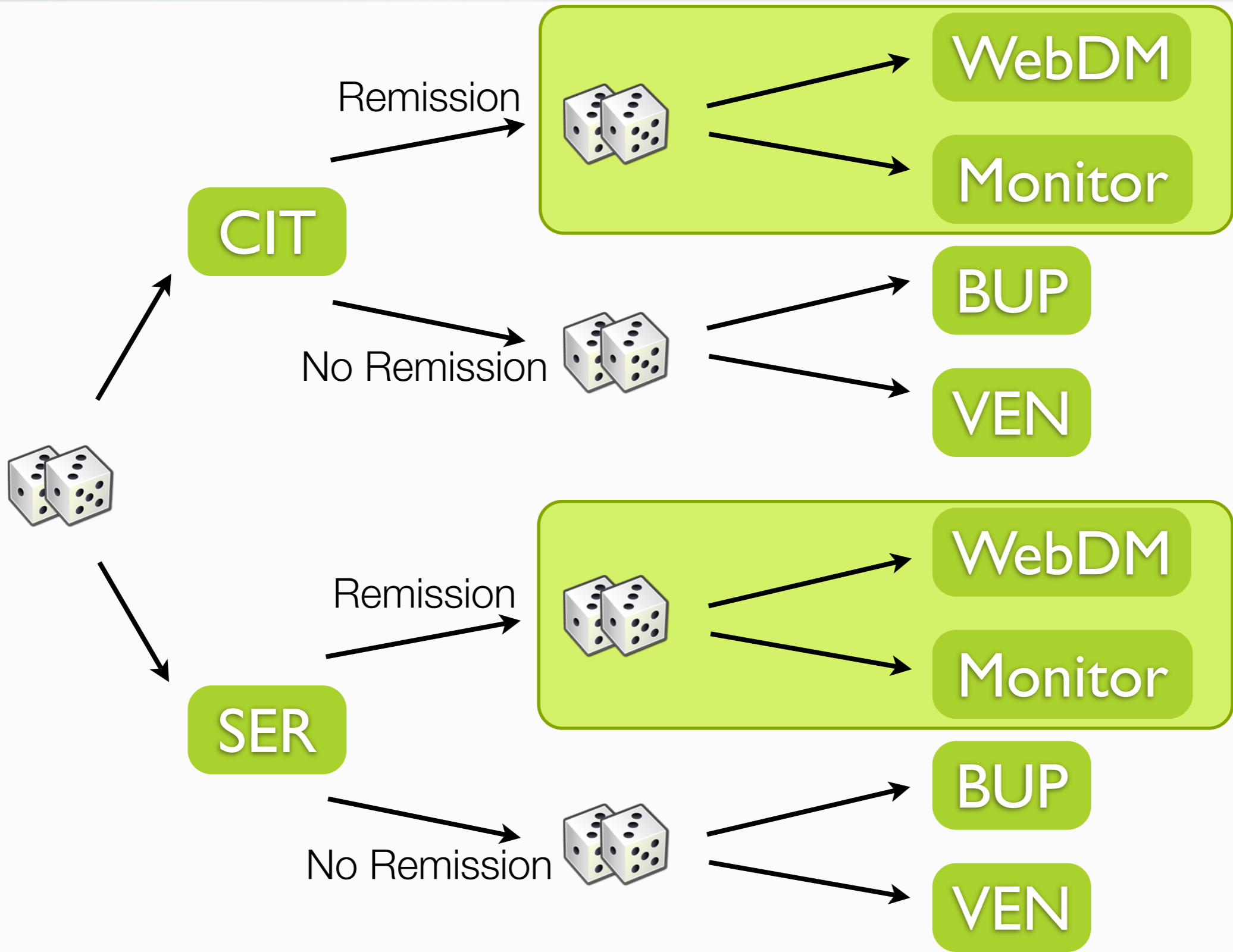
How might we arrive at this strategy?

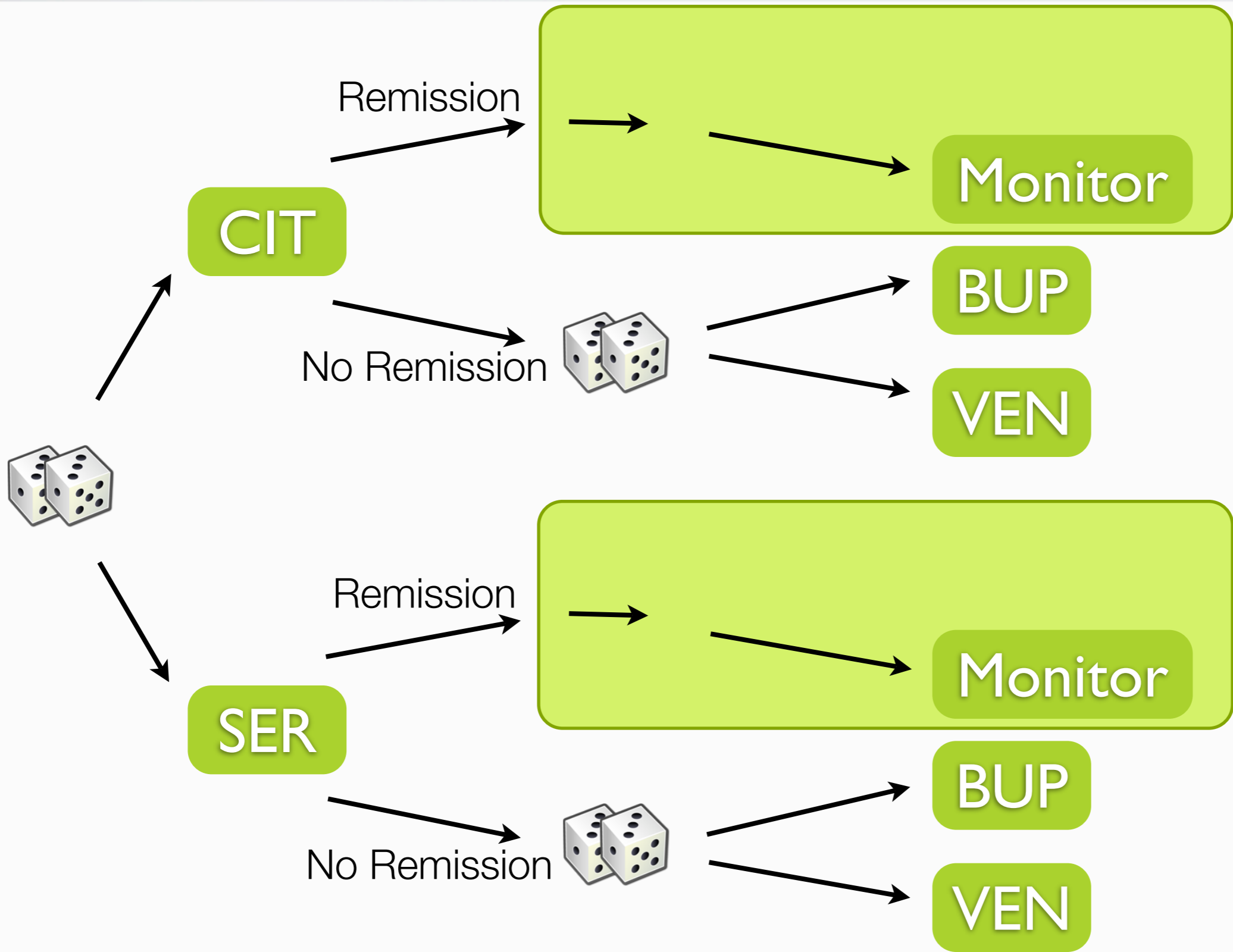


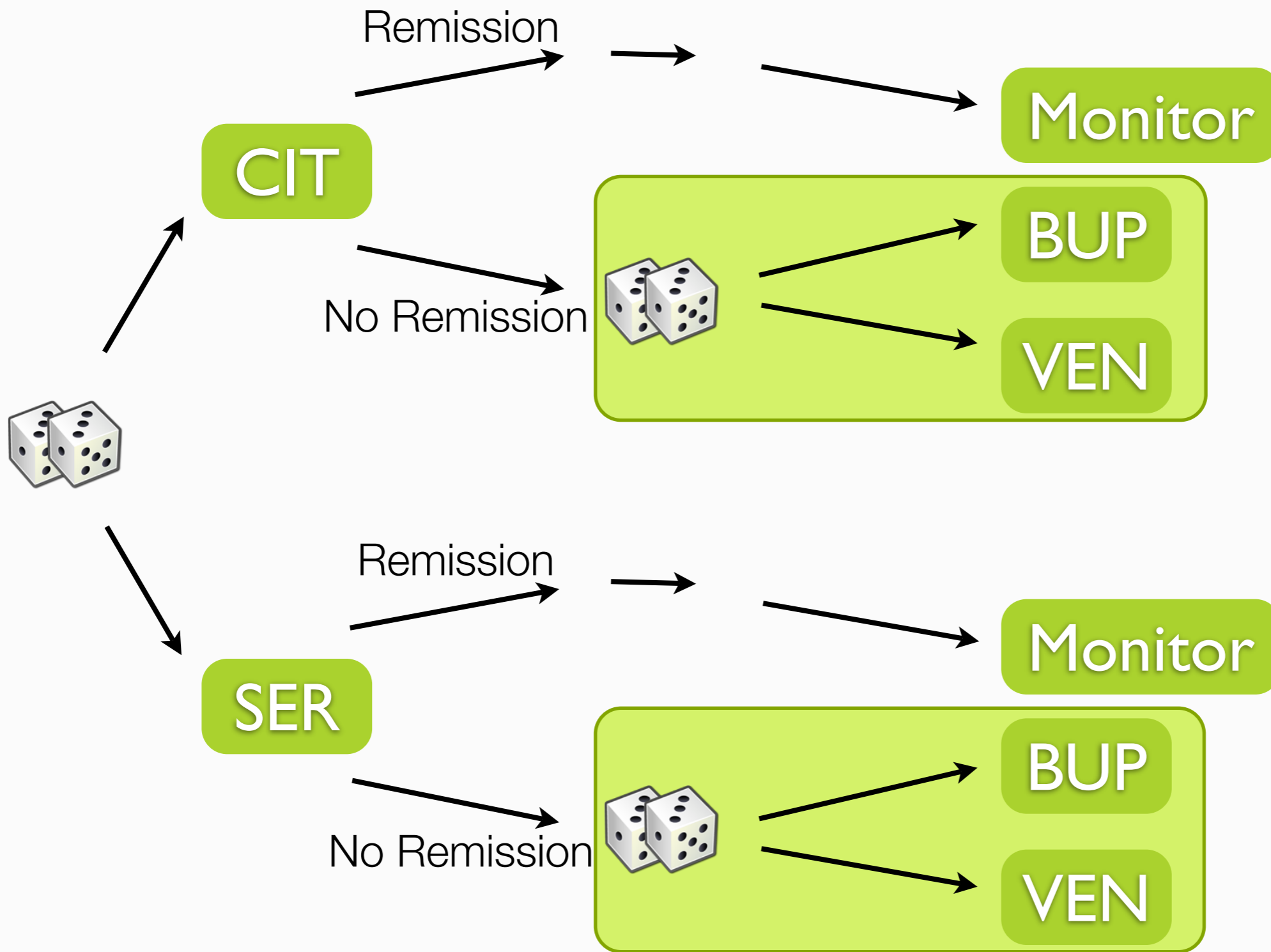
- Run a randomized trial
- Start at the end of the study
- Identify the best final treatment
- Work backwards in time toward the beginning of the study
- Analyses can use patient characteristics/outcomes to provide evidence for a more sophisticated adaptive treatment strategy.

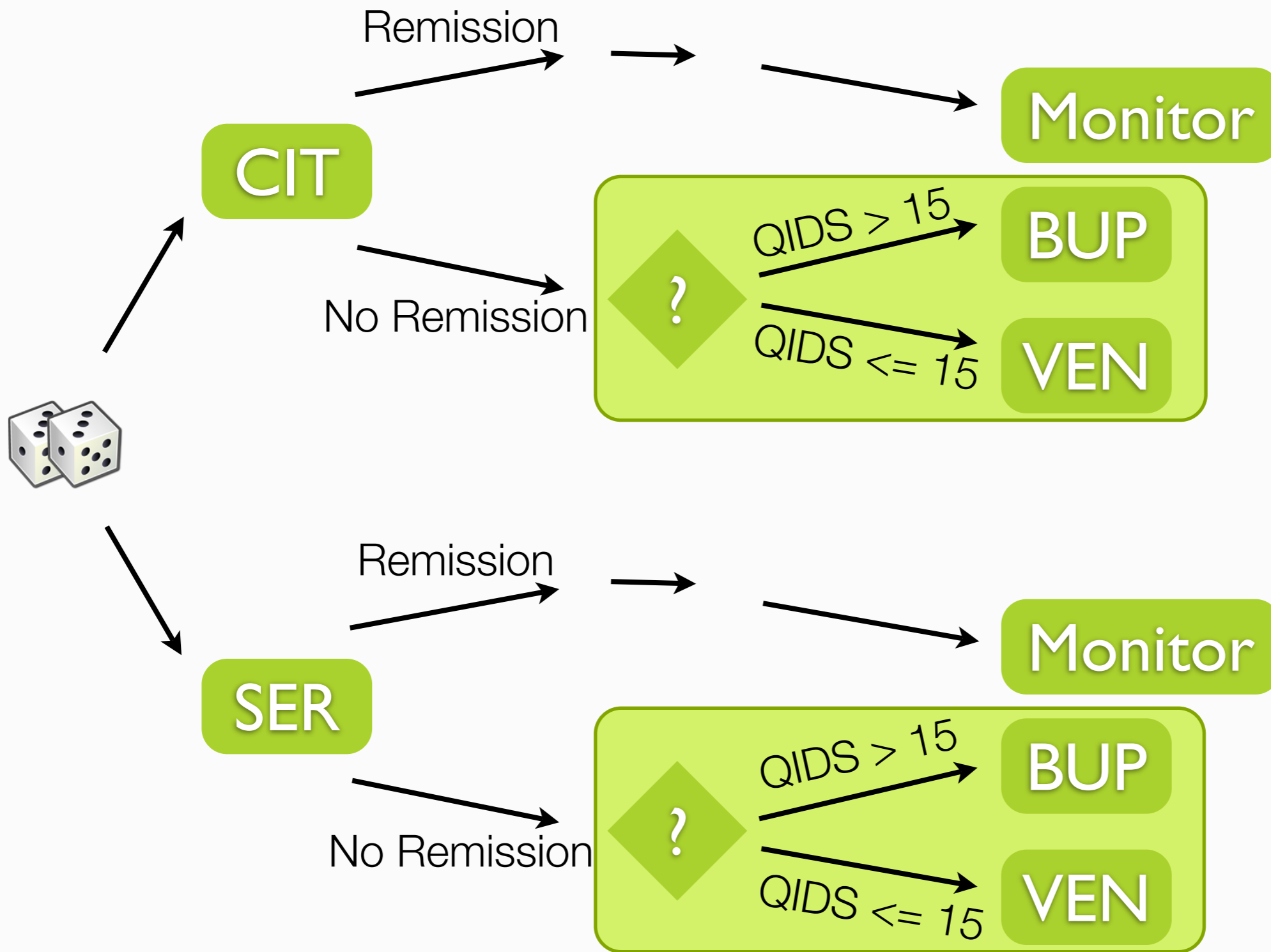
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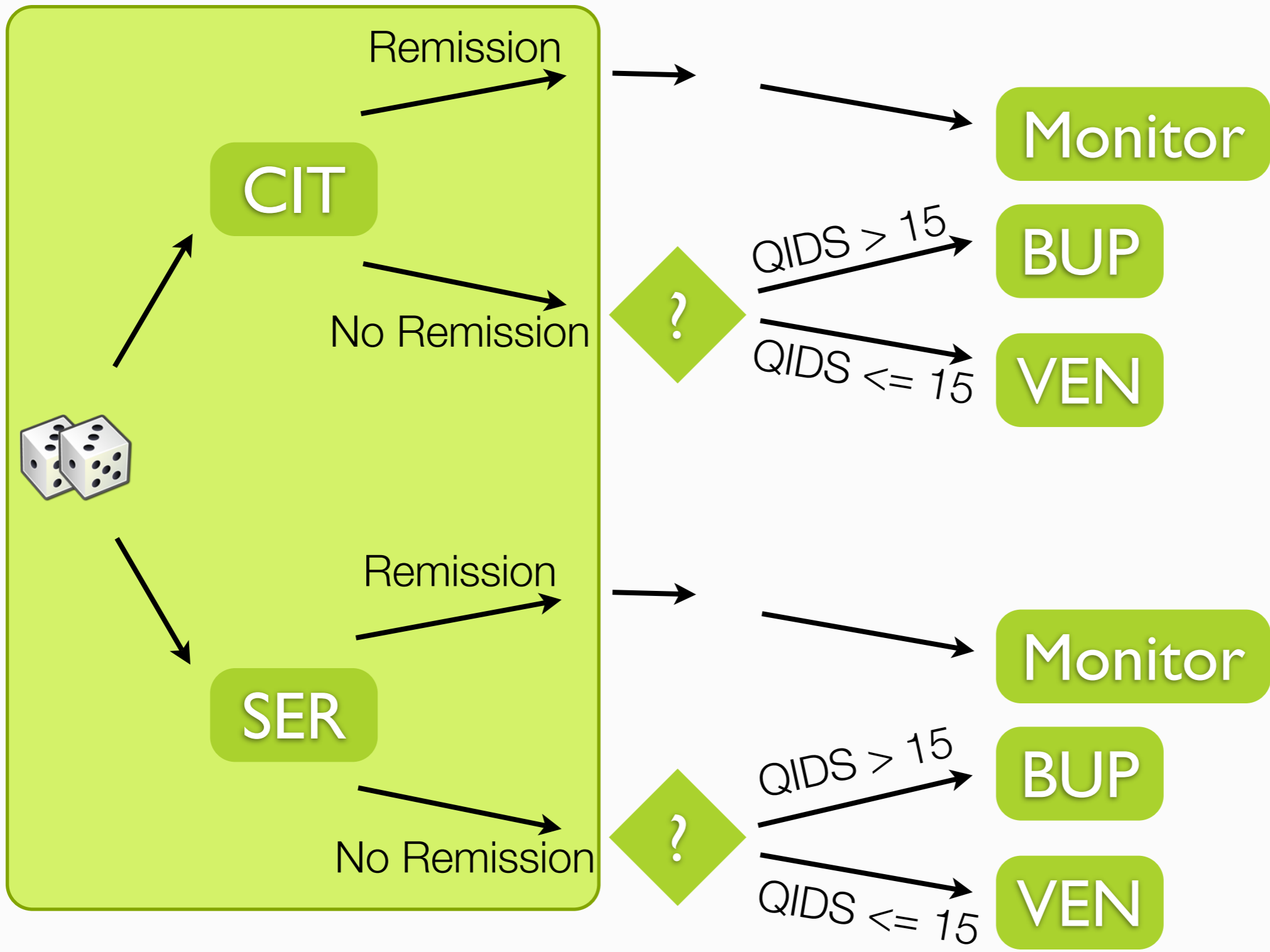


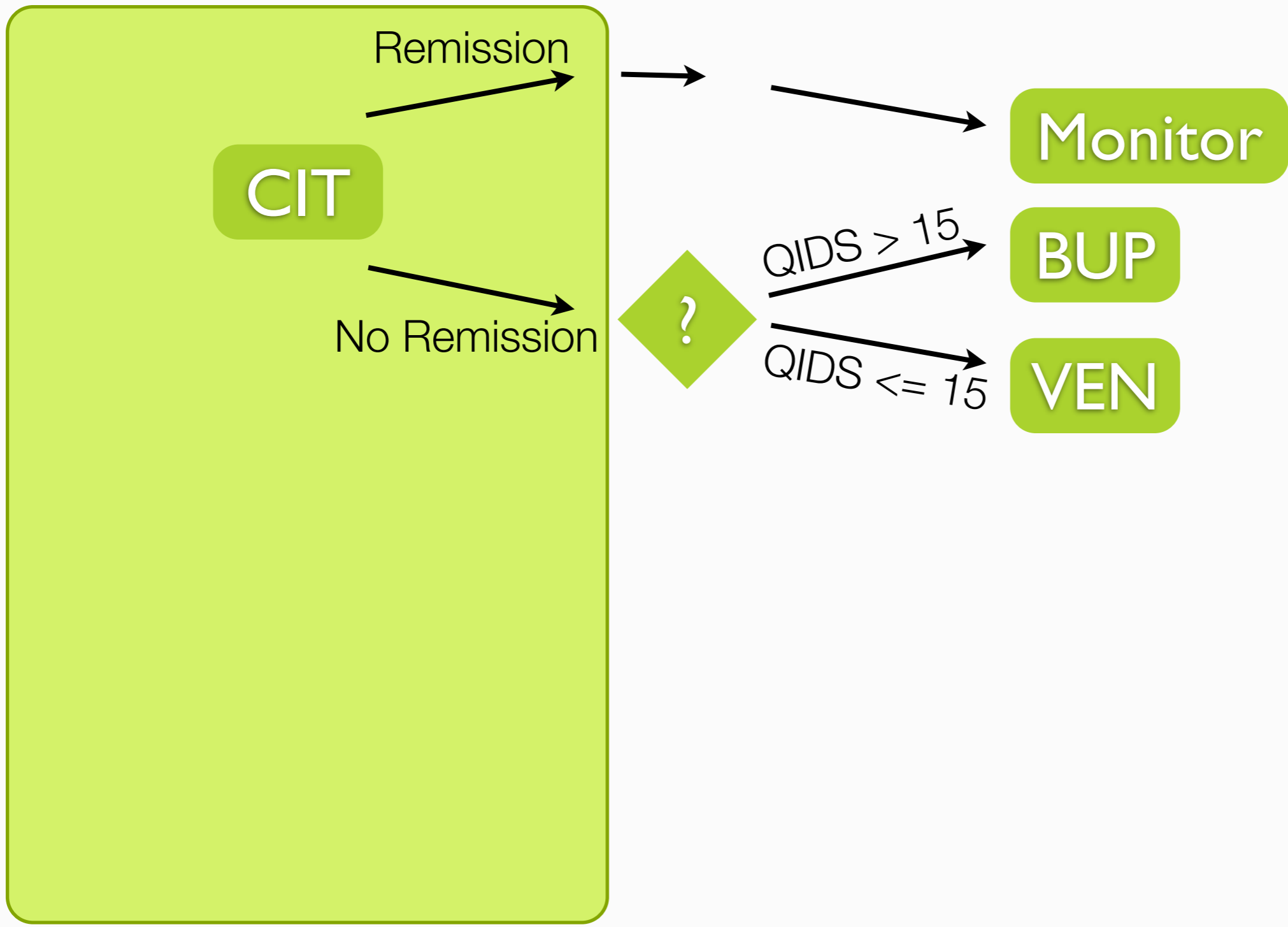


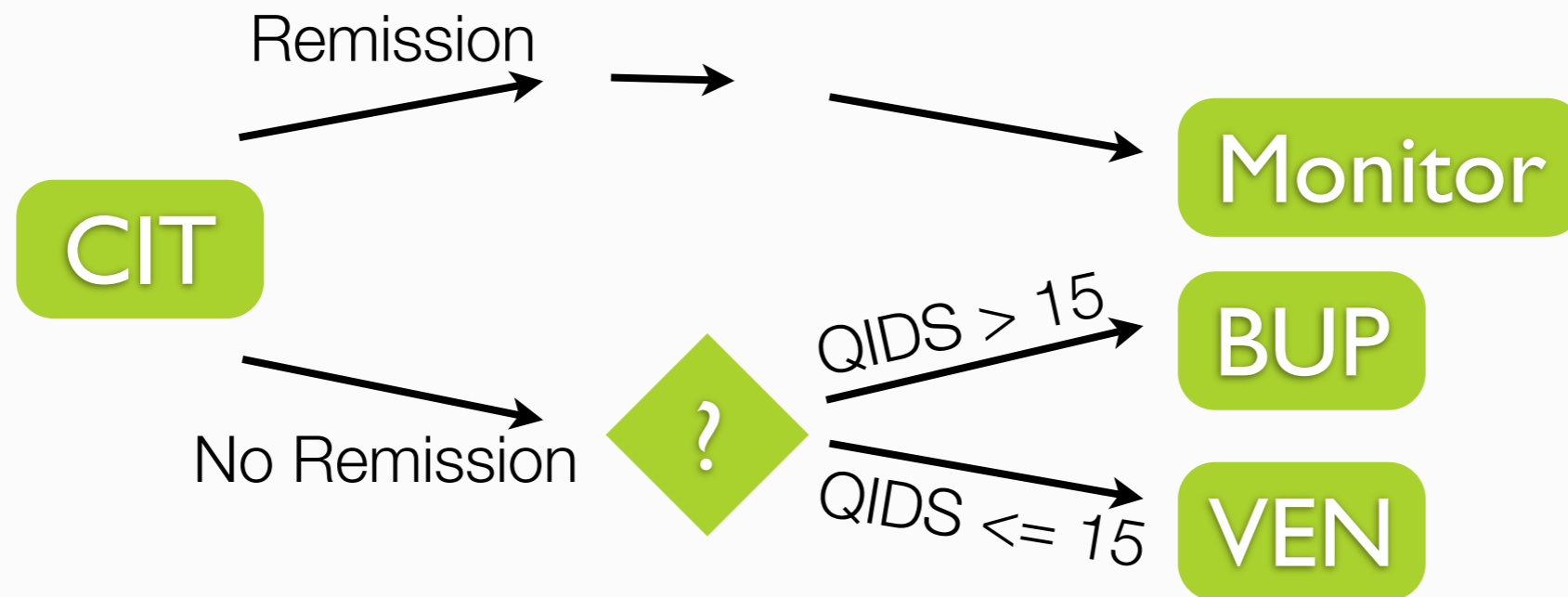












- Run a randomized trial
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Analyses To Date

- ■ STAR*D: Sequenced Treatment Alternatives to Relieve Depression
 - ■ NIMH-funded, ~4000 patients, ~4 stages of treatment
- ■ CATIE: Clinical Antipsychotic Trials of Intervention Effectiveness
 - ■ NIMH-funded, ~1600 patients, ~3 phases of treatment
- ■ Both of these predate SMART, and are quite complicated.
- ■ We have done preliminary analyses of these studies.



Ongoing Research

- ■ How do we know if we've really constructed a good strategy?
 - ■ Eric Laber and I are working on measures of confidence for strategy quality.
- ■ Can the data inform us about which quantities are useful for selecting treatments?
 - ■ Peng Zhang is working on selecting covariates for decision points.
- ■ What if we are interested in an objective that is censored?
 - ■ Zhiguo Li is working on incorporating survival analysis techniques.



Thank You

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