



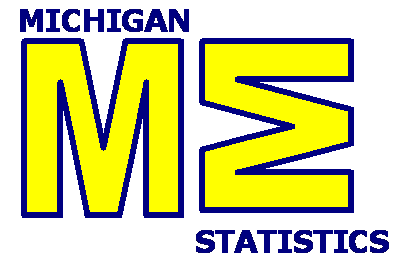
# ***SMART Case Studies***

## **Module 3**

**Getting SMART About Developing Individualized,  
Adaptive Health Interventions**

**VA MIRECC & Univ of Maryland Medical Ctr  
Baltimore, Maryland, Feb 25**

**Daniel Almirall & Susan A. Murphy**

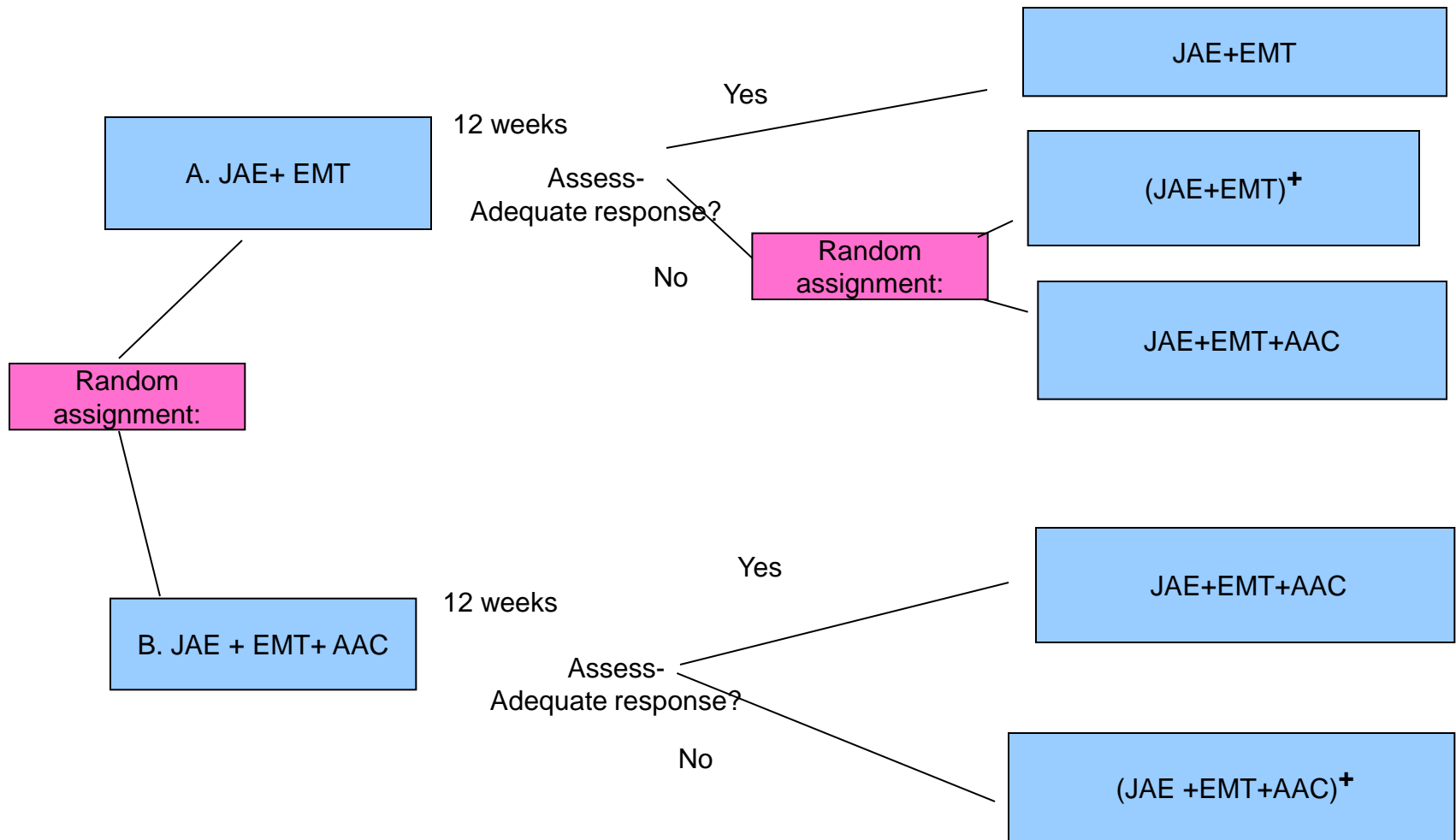




# Outline

- Adaptive ASD Developmental and Augmented Intervention (Kasari, PI)
- Adaptive Pharmacological and Behavioral Treatments for Children with ADHD Trial (Pelham, PI)
- Adaptive Reinforcement-Based Treatment for Pregnant Drug Abusers (Jones, PI)
- Extending Treatment Effectiveness of Naltrexone (Oslin, PI)
- Comparison of SMARTs

# Kasari ASD Study





# Kasari ASD SMART

- Population & Rationale:
  - Non-verbal children with ASD who have not made satisfactory progress by age 5 even though they have received traditional intensive interventions
  - These children experience poor outcomes yet represent 25-30% of children with ASD.
  - Planning for a “rescue” if the first treatment does not go well is crucial.
  - AAC are expensive and not clear if needed.



# Kasari ASD SMART

- Critical Decisions:
  - Which treatment to provide first? Which treatment to provide non-responders?
- Treatments:
  - JAE, EMT, AAC, (JAE+EMT)<sup>+</sup>, (JAE+EMT+AAC)<sup>+</sup>

# Kasari ASD SMART

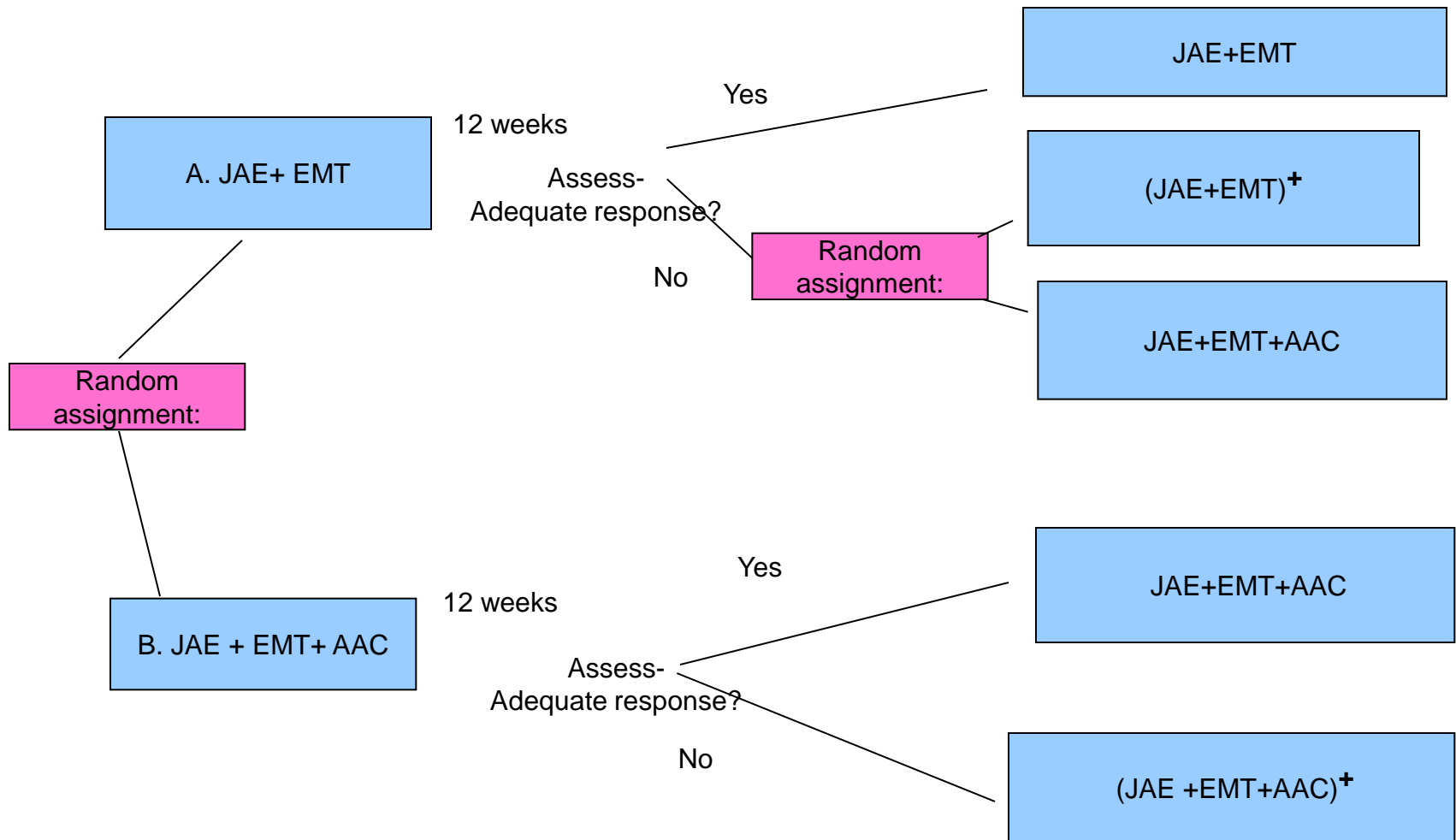
- Embedded Tailoring Variables: (*a*) total social communicative utterances, (*b*) percentage communicative utterances, (*c*) number different word roots, (*d*) mean length of utterance in words, (*e*) number of utterances where the function is to comment (rather than request), (*f*) words per minute, and (*g*) unique word combinations (included only if the child's target talk consists of more than two words).



# Kasari ASD SMART

- How are the embedded tailoring variables used?
  - Two differences for each of the 7 variables is calculated. This yields 14 measures.
- How and when is (non) response assessed?
  - At 12 weeks
  - The criterion for response is 25% or more improvement on at least 50% of the 14 measures.

# Kasari ASD Study





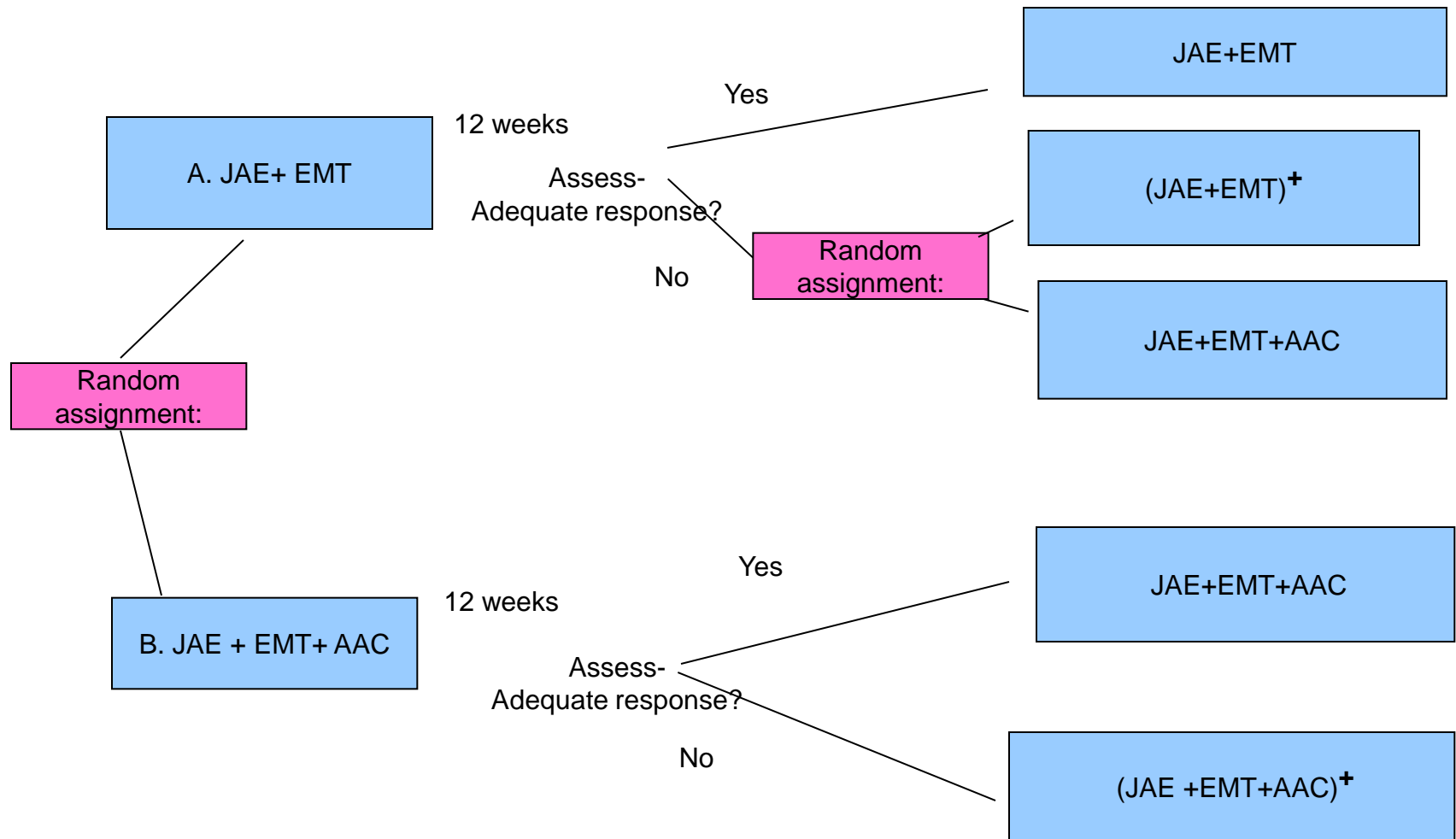


# Kasari ASD SMART

## 3 Embedded Adaptive Health Interventions

- 1) Start with JAE+EMT; if non-responder  
JAE+AAC, else JAE+EMT
- 2) Start with JAE+EMT; if non-responder  
(JAE+EMT)<sup>+</sup>, else JAE+EMT
- 3) Start with JAE+AAC; if non-responder  
(JAE+AAC)<sup>+</sup>, else JAE+AAC

# Kasari ASD Study

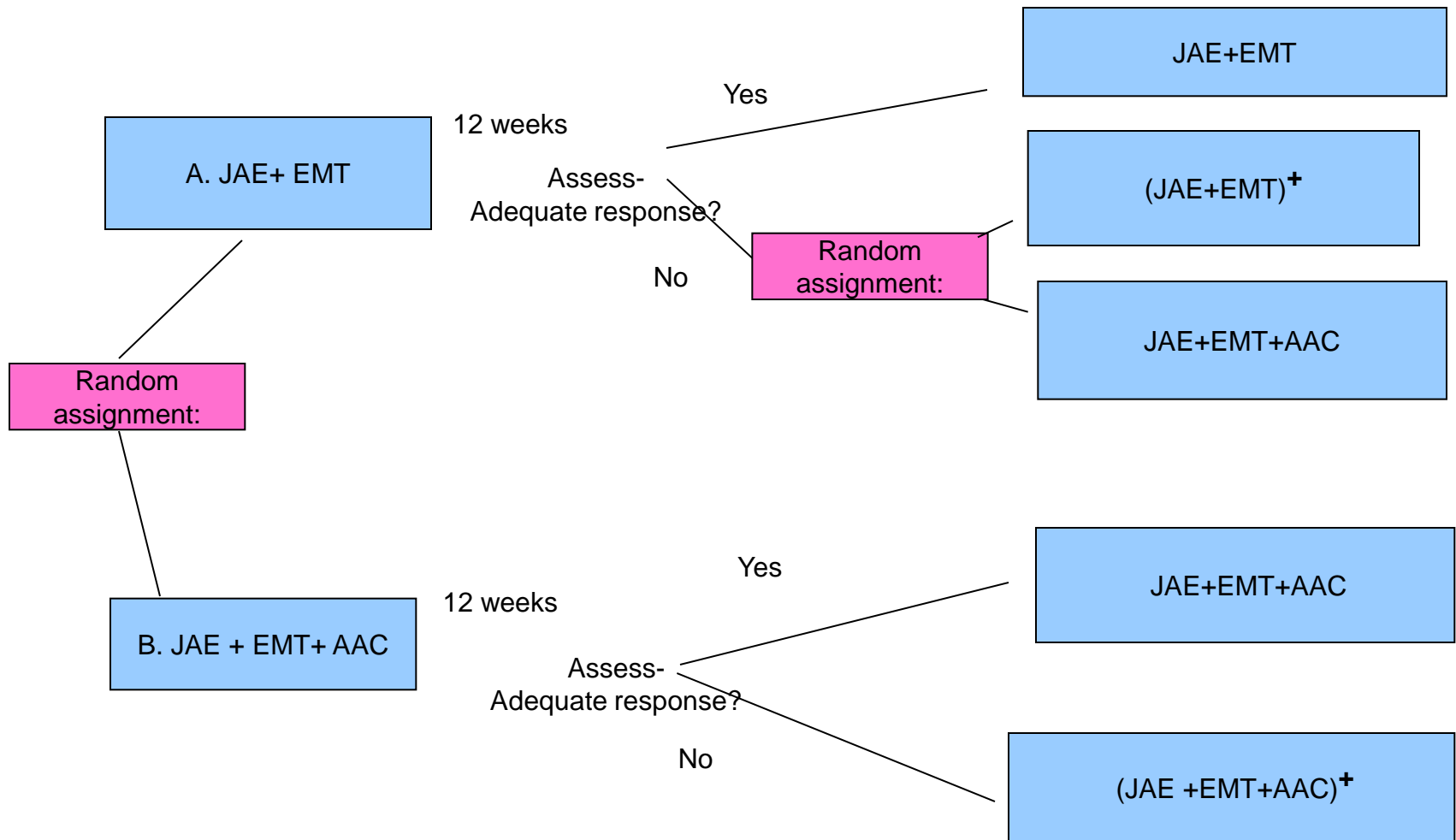




# Kasari ASD SMART

- Primary Analysis
  - To compare the slopes in outcome measures of communication and language over 6 months for the two treatments: JAE +AAC strategy vs enhanced JAE strategy
- Secondary Analyses
  - Investigate moderation by baseline variables, investigate if other variables might be used to tailor treatment.

# Kasari ASD Study

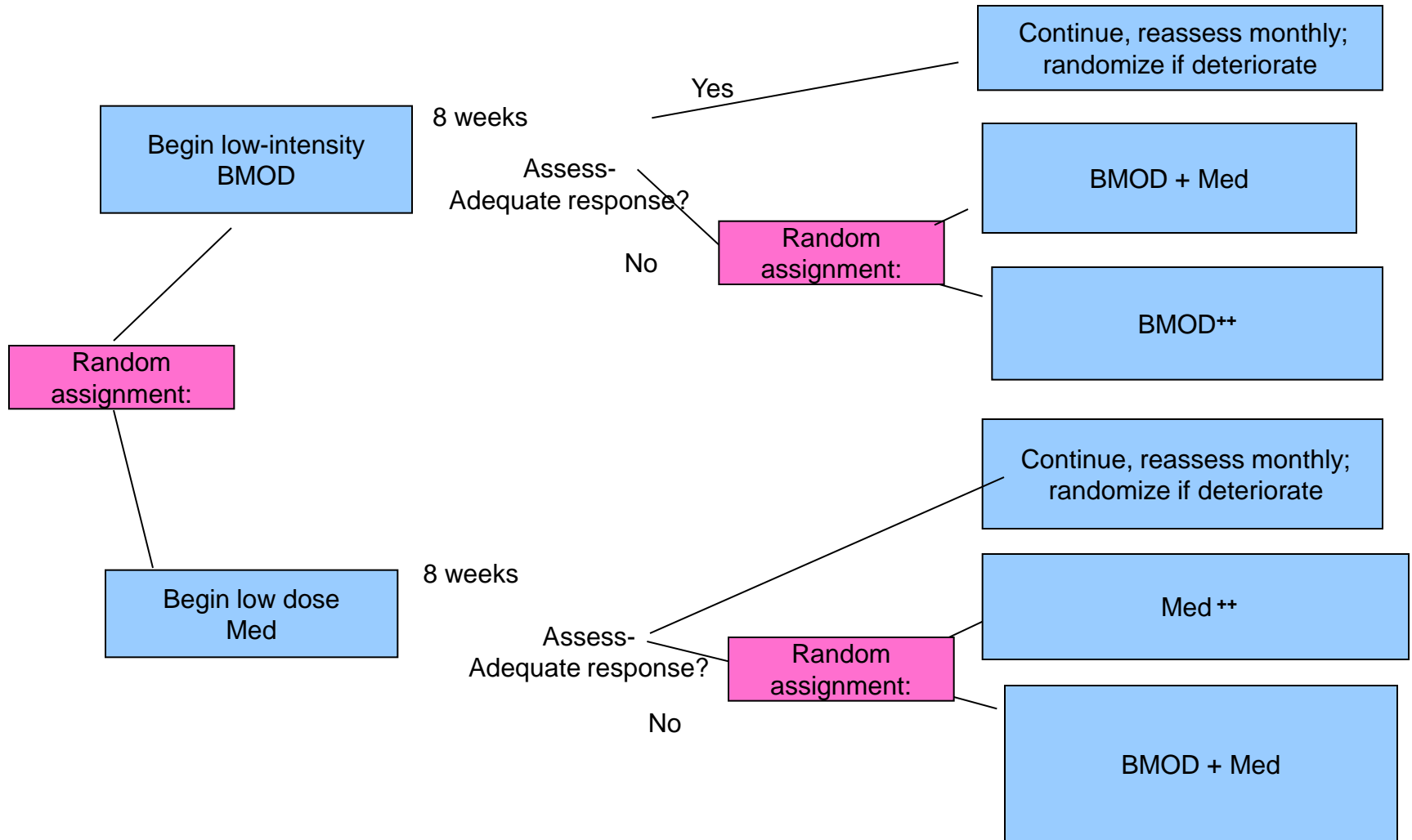




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# Pelham ADHD Study





# Pelham ADHD SMART

## Population & Rationale:

- Children with ADHD, ages 6-12
- **Much debate** on whether the first-line intervention should be pharmacological or behavioral especially for younger children.
- Planning for a “rescue” if the first treatment does not go well is crucial because 20-50% do not substantially improve on first treatment.



# Pelham ADHD SMART

- Critical Decisions:
  - Which treatment to provide first? Which treatment to provide non-responders?
- Treatments:
  - Med, Med<sup>++</sup>, BMOD, BMOD<sup>++</sup>

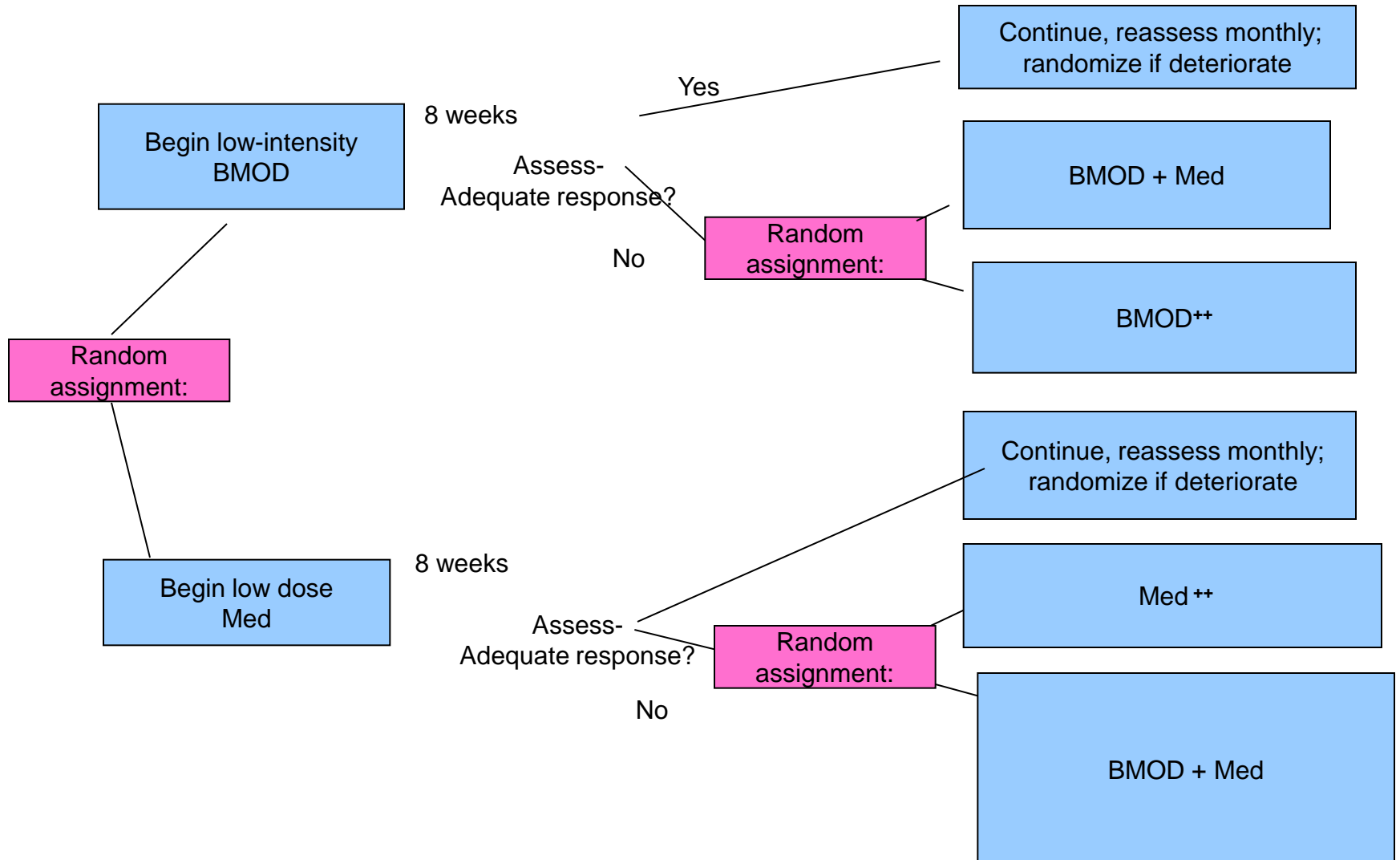




# Pelham ADHD SMART

- Embedded Tailoring Variables: (*a*) Teacher reported Impairment Scale (IRS), (*b*) Teacher reported individualized list of target behaviors (ITB)
- How and when is (non) response assessed?
  - At 8 weeks and every 4 weeks thereafter
  - The criterion for non-response is an average performance of less than 75% on the ITB and a rating of impairment in at least one domain on the IRS.

# Pelham ADHD Study





# Pelham ADHD SMART

## 4 Embedded Adaptive Health Interventions

- 1) Start with BMOD; if non-responder BMOD<sup>++</sup>, else BMOD
- 2) Start with BMOD; if non-responder BMOD +Med, else BMOD
- 3) Start with Med; if non-responder Med<sup>++</sup>, else Med
- 4) Start with Med; if non-responder BMOD+Med, else Med.



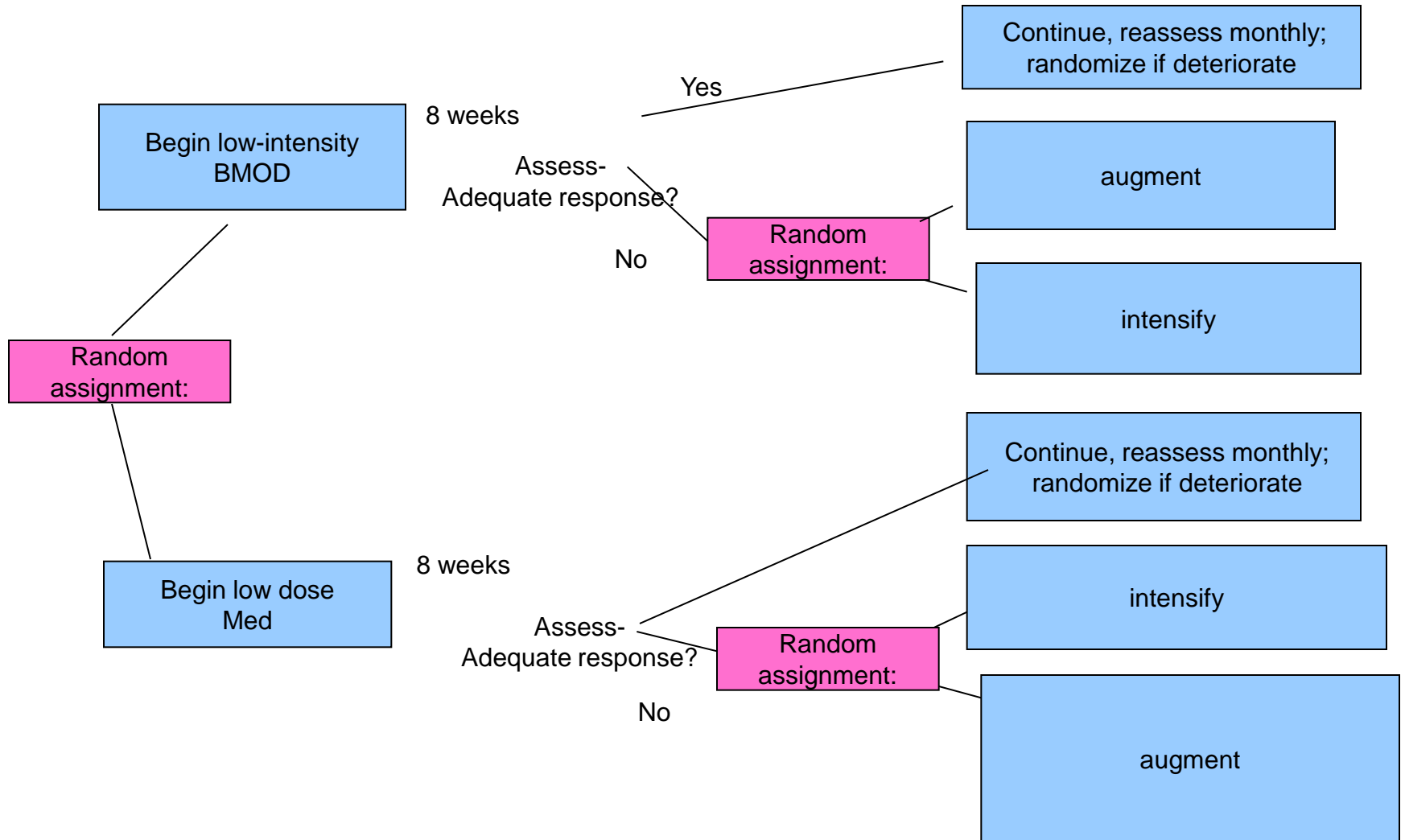
# Pelham ADHD SMART

## 4 Embedded Adaptive Health Interventions

**\*\*conceptualized in terms of *tactics*\*\***

- 1) Start with BMOD; if non-responder intensify, else continue same
- 2) Start with BMOD; if non-responder augment with other treatment, else continue same
- 3) Start with Med; if non-responder intensify, else continue same
- 4) Start with Med; if non-responder augment with other treatment, else continue same.

# Pelham ADHD Study

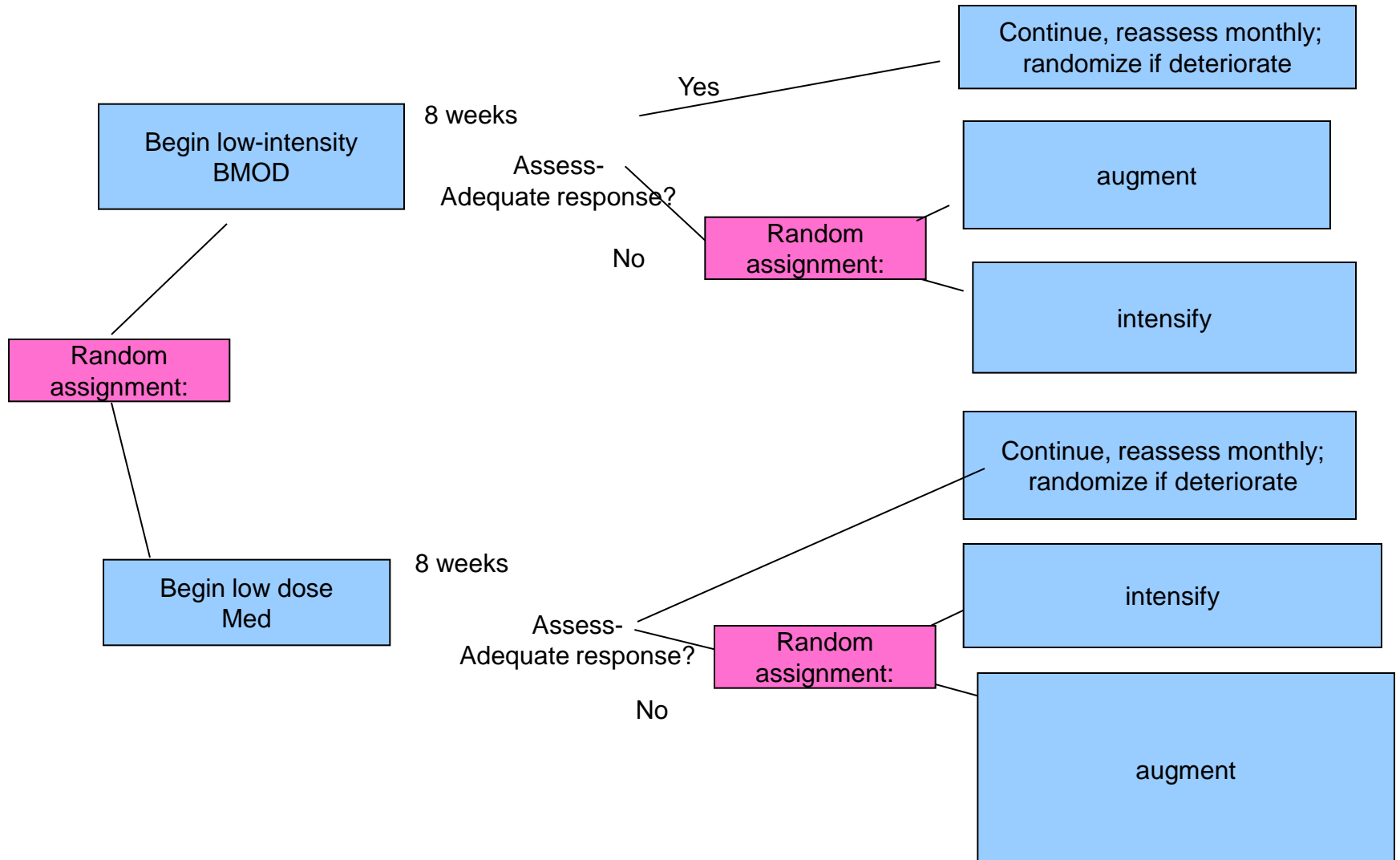




# Pelham ADHD SMART

- Primary Analysis
  - To compare the change in teacher ratings of child behavior across 8 months for the two treatments: Med first strategies vs BMOD first strategies
- Secondary Analyses
  - Investigate moderation of the effect of initial treatment/secondary treatment/adaptive health interventions by baseline variables; investigate if other variables might be used to tailor treatment.

# Pelham ADHD Study



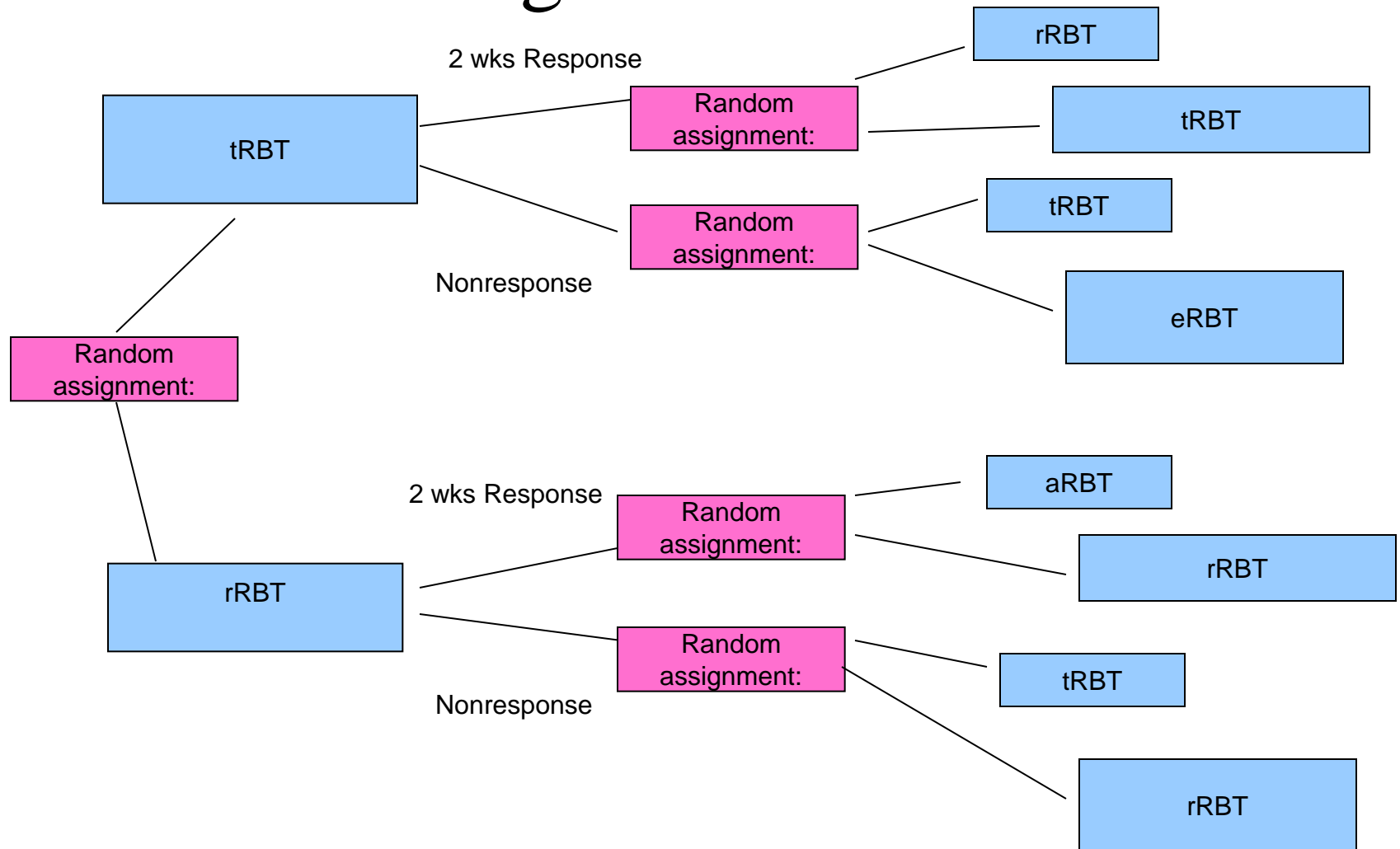


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# Jones' Study for Drug-Abusing Pregnant Women





# Jones Drug Abuse SMART

## Population & Rationale:

- Drug Abusing (Opioid/Cocaine) Pregnant Women
- Reinforcement based treatment (RBT) is an efficacious intervention but,
  - RBT is costly to administer and time-consuming on the part of the participant,
  - About 40% of participants do not respond as well as desired

# Jones Drug Abuse SMART

## Critical Decisions:

- (a) Whether the frontline version of RBT can be reduced in intensity and scope;
- (b) whether a woman who does not respond quickly should continue on the same version or be moved to a more-intensive, larger-scope version of RBT; and
- (c) whether the intensity and scope of RBT can be reduced if a woman responds quickly.

# Jones Drug Abuse SMART

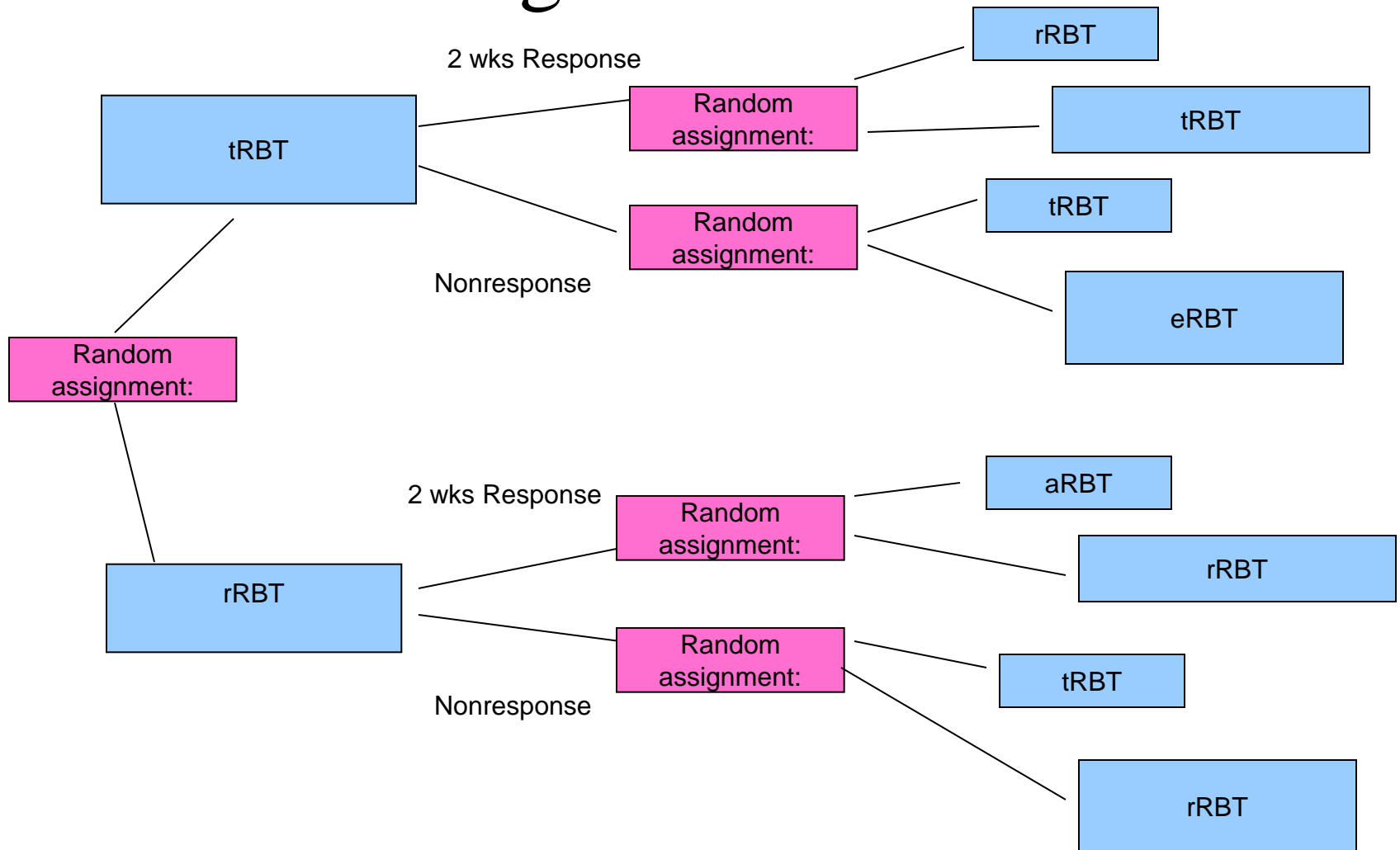
- Treatments:
  - aRBT < rRBT < tRBT < eRBT (increasing order in intensity/scope)
- Embedded Tailoring Variables:
  - a) self-reported drug use, b) results of urine tests, and c) attendance on intervention days



# Jones Drug Abuse SMART

- How and when is (non) response assessed?
  - At 2 weeks
  - The criterion for nonresponse is missing an intervention day with no excuse, or a positive opioid/cocaine urine specimen, or self-report use of either drug.

# Jones' Study for Drug-Abusing Pregnant Women





# Jones Drug Abuse SMART

## 8 Embedded Adaptive Health Interventions

- 1) Always tRBT
- 2) Start with tRBT; if non-responder tRBT, if responder rRBT
- 3) Start with tRBT; if non-responder eRBT, if responder tRBT
- 4) Start with tRBT; if non-responder eRBT, if responder rRBT



# Jones Drug Abuse SMART

## 8 Embedded Adaptive Health Interventions

- 5) Always rRBT
- 6) Start with rRBT; if non-responder tRBT, if responder rRBT
- 7) Start with rRBT; if non-responder rRBT, if responder aRBT
- 8) Start with rRBT; if non-responder tRBT, if responder aRBT

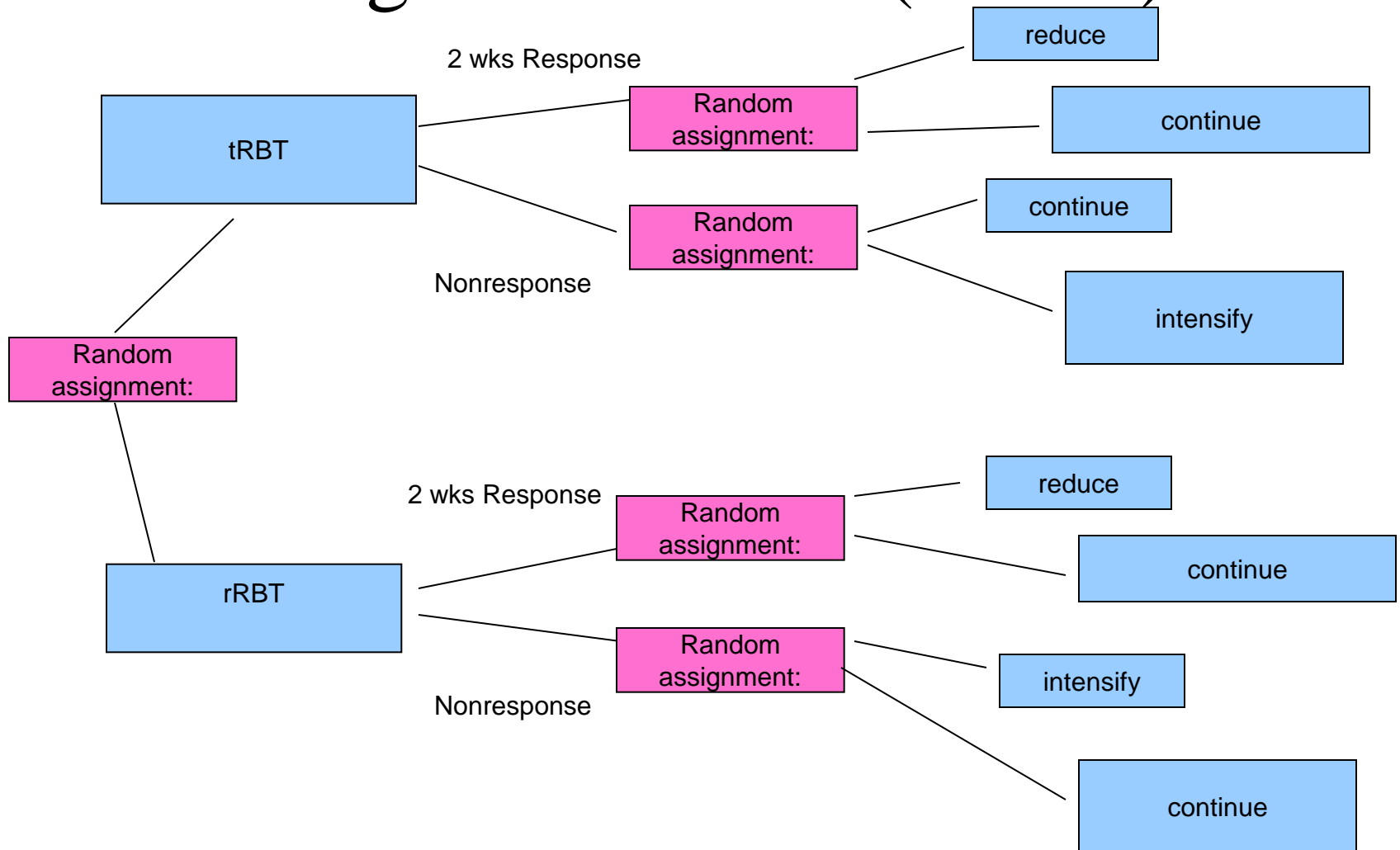




# Jones Drug Abuse SMART

- Primary Analysis
  - To compare program completion (delivery of child while in treatment) of the always tRBT arm versus the always rRBT arm (two non-adaptive strategies!)
- Secondary Analyses
  - Investigate moderation by baseline variables, investigate if other variables might be used to tailor treatment.

# Jones' Study for Drug-Abusing Pregnant Women (tactics)

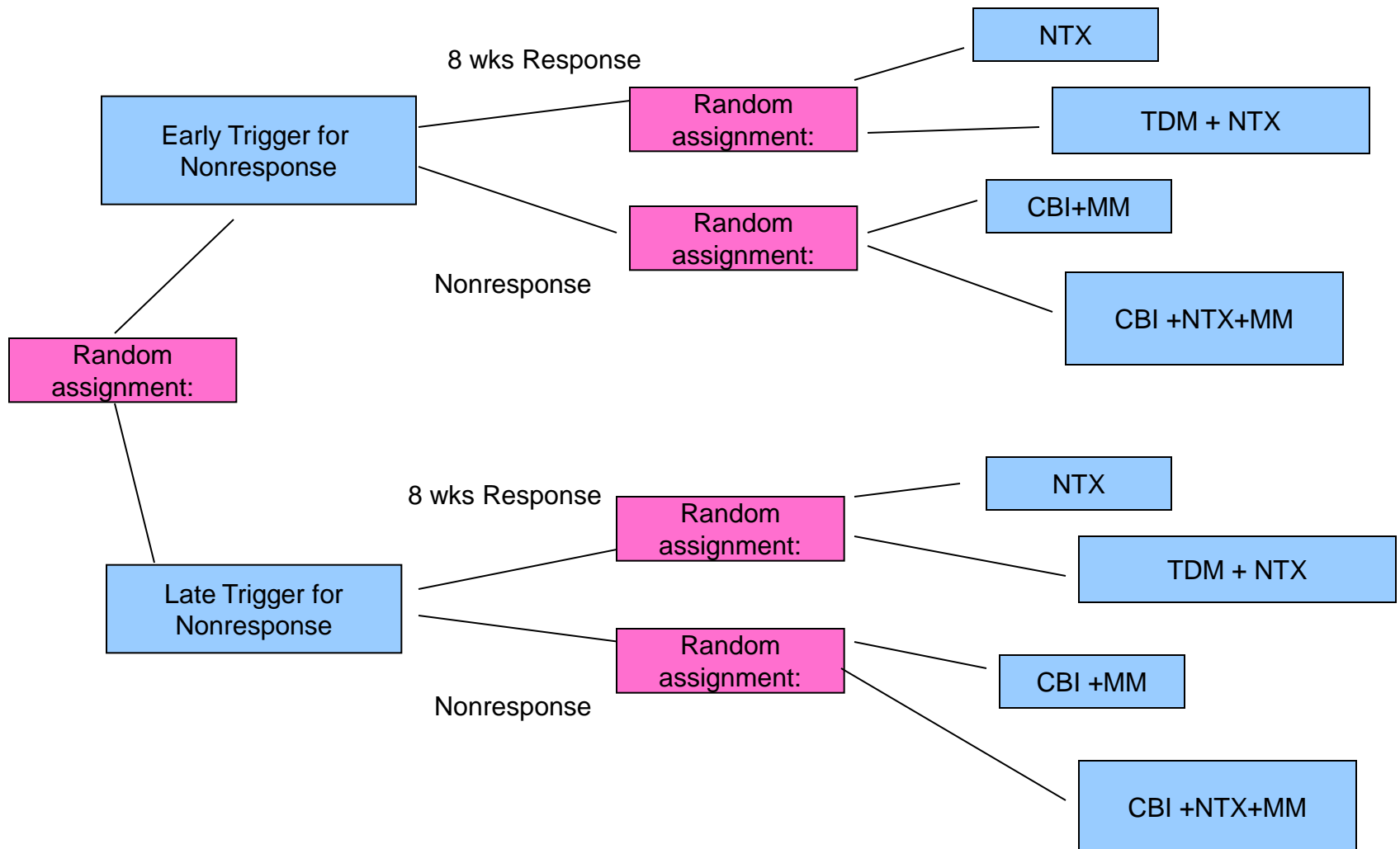




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# Oslin Alcoholism SMART





# Oslin Alcoholism SMART

## Population & Rationale:

- Alcohol Dependent Adults who completed an Intensive Outpatient Program
- Naltrexone (NTX, an opiate antagonist) is efficacious but clinical use is limited.
  - Around 1/3 of patients relapse while on NTX.
  - Would like to inform longer term management based on NTX
  - Non-adherence is common

# Oslin Alcoholism SMART

## Critical Decisions:

- (a) What extent of drinking behavior best reflects nonresponse to NTX?
- (b) What type of treatment would be useful for participants who do not respond adequately to NTX?
- (c) What type of treatment would be useful in reducing the chance of relapse among participants who respond adequately to NTX?



# Oslin Alcoholism SMART

- Treatments:
  - NTX, MM, CBI, TDM
- Embedded Tailoring Variable:
  - Weekly self report of heavy drinking days.



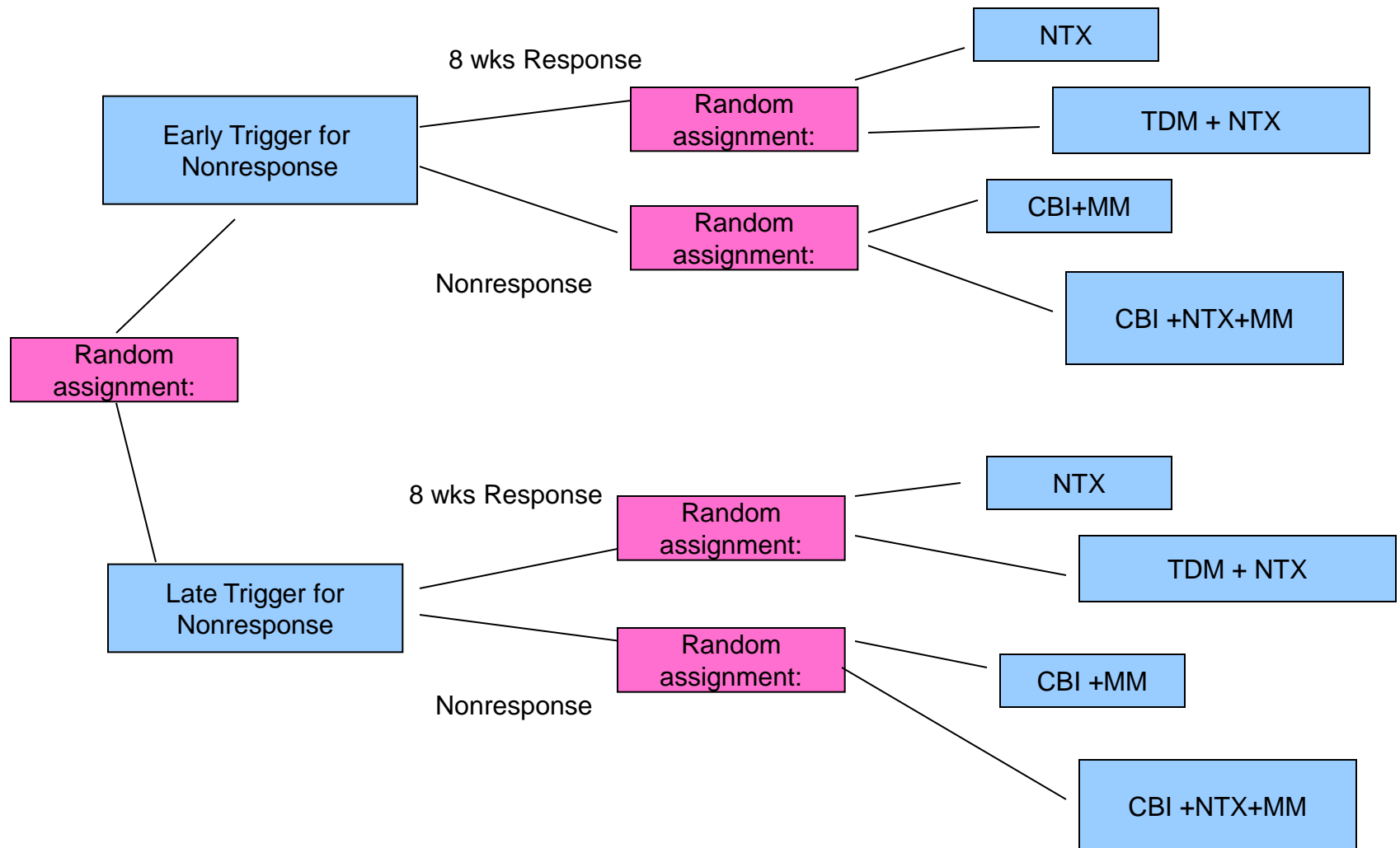
# Oslin Alcoholism SMART

How and when is (non) response assessed?

- Initially, each week, for 8 weeks
  - Early trigger criterion for non-response: 2 or more heavy drinking days since beginning NTX
  - Late trigger criterion for non-response : 5 or more heavy drinking days since beginning NTX
- If, after 8 weeks, the non-response criterion is not met then the participant is a responder.



# Oslin Alcoholism SMART





# Oslin Alcoholism SMART

## 8 Embedded Adaptive Health Interventions

- 1) Start with NTX+MM; if 2 HDD occurs prior to 8 weeks, augment to CBI+NTX+MM, else at 8 weeks continue on NTX
- 2) Start with NTX+MM; if 2 HDD occurs prior to 8 weeks, switch to CBI +MM, else at 8 weeks continue on NTX
- 3) Start with NTX+MM; if 2 HDD occurs prior to 8 weeks, augment to CBI+NTX+MM, else at 8 weeks continue on NTX and add TDM



# Oslin Alcoholism SMART

## 8 Embedded Adaptive Health Interventions

- 4) Start with NTX+MM; if 2 HDD occurs prior to 8 weeks, switch to CBI+MM, else at 8 weeks continue on NTX and add TDM
- 5) ..
- 6) ..
- 7) ..
- 8) ..



# Oslin Alcoholism SMART

- Primary Analysis
  - Focus on non-responders to NTX+MM.  
Compare drinking outcomes (e.g. percent days abstinent) on CBI+NTX+MM versus to CBI+MM.
- Secondary Analyses
  - Test effectiveness of TDM for responders; test two criteria for non-response; assess moderation (psychosocial distress, severity of alcohol dependence, adherence in first stage)



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# Comparison of SMART Studies

## Dimensions

- 1) Which participants are multiply randomized?
- 2) When are participants re-randomized?
- 3) The types of the critical decisions
- 4) What are the primary research questions?



# Comparison of SMART Studies

Which participants are multiply randomized?

- A subset of non-responders: ASD (only nonresponders to JAE+EMT)
- All non-responders: ADHD, Drug Abusing Pregnant Women, Alcohol Dependence
- All responders: Drug Abusing Pregnant Women, Alcohol Dependence



# Comparison of SMART Studies

When are participants randomized for the second time?

- At one fixed point in time only
  - ASD (month 3), Drug Abusing Pregnant Women (week 2), Alcohol Dependence (responders at week 8)
- At any one of several fixed times
  - ADHD (at month 2 and each month thereafter), Alcohol Dependence (non-responders at week 2 and weekly until week 8)



# Comparison of SMART Studies

What kinds of critical decisions are investigated?

- Which treatment first and which second?
  - ASD, ADHD, Drug Abusing Pregnant Women
- How soon to give up on initial treatment and which treatment to provide second?
  - Alcohol Dependence



# Comparison of SMART Studies

What are the primary research questions?

- Comparison of stage 1 treatments, controlling, by design, for stage 2 treatments.
  - ASD, ADHD
- Comparison of stage 2 treatments, controlling, by design, for stage 1 treatment
  - Alcohol Dependence (non-responders)
- Comparison of two embedded treatment strategies.
  - Drug Abusing Pregnant Women

# Questions?

More information:

H. Lei, I. Nahum-Shani, K. Lynch, D. Oslin and S.A. Murphy. A SMART Design for Building Individualized Treatment Sequences, *The Annual Review of Clinical Psychology* (2012), Vol. 8: 21-48