

HOW TO APPLY THE MULTIPHASE OPTIMIZATION STRATEGY (MOST) IN YOUR INTERVENTION DEVELOPMENT RESEARCH

Module 5

**Rigorous and responsible conduct of
intervention optimization research**

**Lesson 3: What to do if the primary outcome is
years in the future**



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In the previous lesson you learned how to:

- Ensure that all participants are provided at least the standard of care by including a constant component in a factorial experiment



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In this lesson you will learn how to:

- Plan an optimization trial when the outcome of interest is far in the future



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Sometimes the outcome is defined years in the future

- Examples:
 - School-based drug abuse prevention: Program is delivered in 5th grade, outcome is behavior in 11th grade
 - Prevention of Alzheimer's disease: Intervention delivered to adults in their late 30s and early 40s, outcome is onset of Alzheimer's before age 90

The problem

- It would take a long time to conduct any experiment because of the need to wait for the outcome
- Following it with an RCT would double the length of time

Sometimes it is necessary to take the time to accumulate instances of a rare event

- Prevention of cardiac events: Lifestyle intervention delivered when people are in their 50s, outcome is number of heart attacks over the next 20 years
- Prevention of suicide: Intervention delivered to 13 year olds, outcome is number of deaths by suicide by age 30

The problem

- It would take a long time to conduct any experiment because of the need to wait for the outcome
- In this case, need to wait for enough rare events to occur
- Following optimization trial with an RCT would double the length of time

Is it possible to use MOST under these circumstances?

- Yes, if you have a well-specified conceptual model
- In these circumstances you must rely heavily on the conceptual model

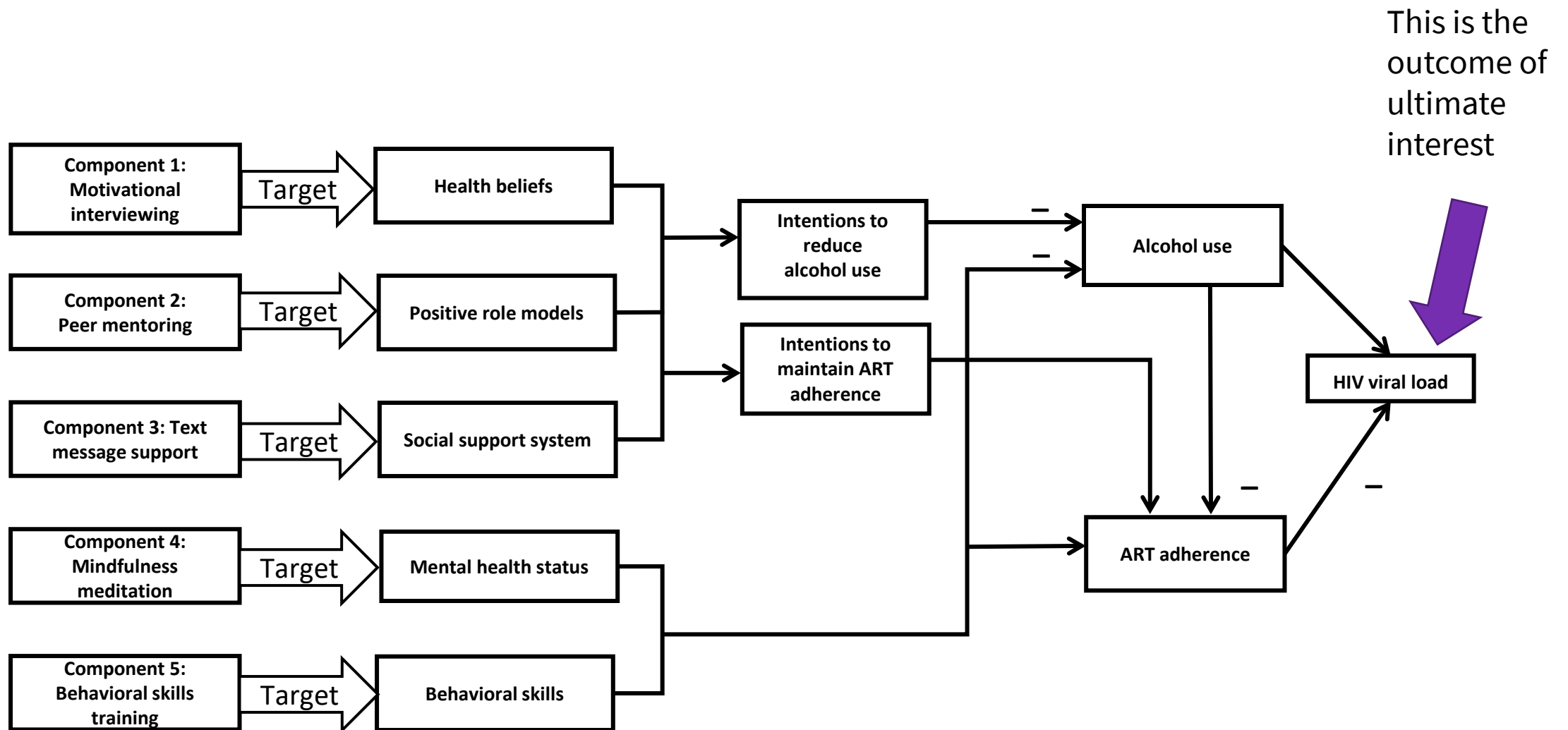


Figure adapted from Collins, L.M., Kugler, K.C., & Gwadz, M.V. (2016)

Suppose we needed to speed up the optimization process

- Instead of using HIV viral load as the outcome variable for the optimization trial, you could use measures of one or more mediators
- In this example, alcohol use and ART adherence are hypothesized to be proximal causes of HIV viral load
- So measures of these variables could be proxy outcomes

Suppose we needed to speed up the optimization process

- Measures of alcohol use and ART adherence could be proxy outcomes
- Logic:
 - According to the conceptual model, the intervention has to change alcohol use and ART adherence to change HIV viral load
 - These variables are likely to show change sooner

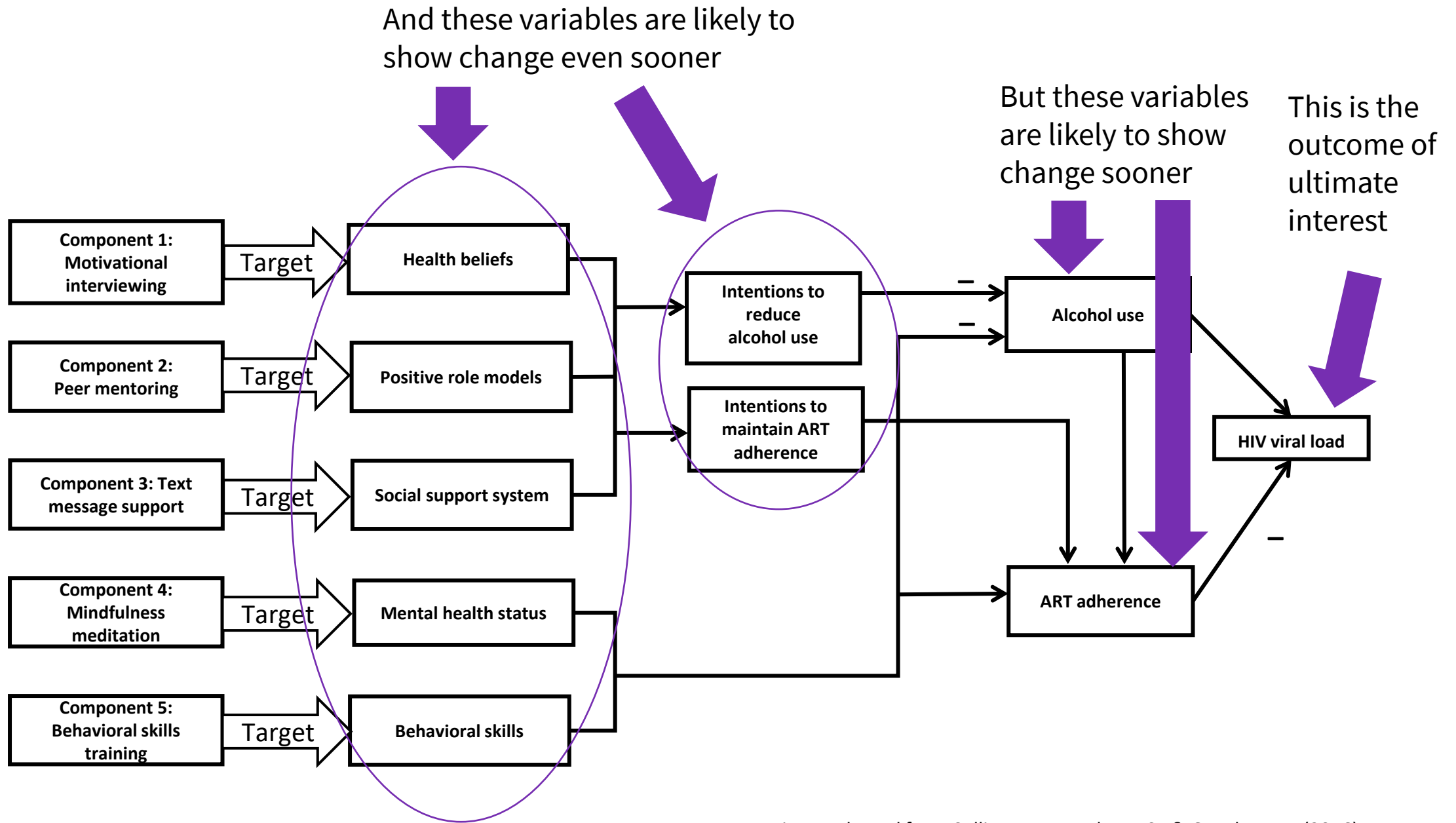


Figure adapted from Collins, L.M., Kugler, K.C., & Gwadz, M.V. (2016)

Why not always optimize using measures of mediators as outcomes? Reason 1

- If you have measures of the mediators and the outcome, you can test the fit of your entire conceptual model to observed data
- This is extremely valuable for making subsequent improvements

Why not always optimize using measures of mediators as outcomes? Reason 2

- Your conceptual model could be incorrect
- You could successfully change a mediator that will not change the outcome
- Without data on the outcome you cannot test this

Why not always optimize using measures of mediators as outcomes? Reason 3

- Ultimately you are interested in effects on the outcome
- It is likely the effect on mediators will be greater in magnitude than the effect on the outcome!

Why not always optimize using measures of mediators as outcomes?

- If effect on mediators is small, little hope of effect on outcome
- If effect on mediators is large, effect on outcome likely to be smaller to an unknown degree

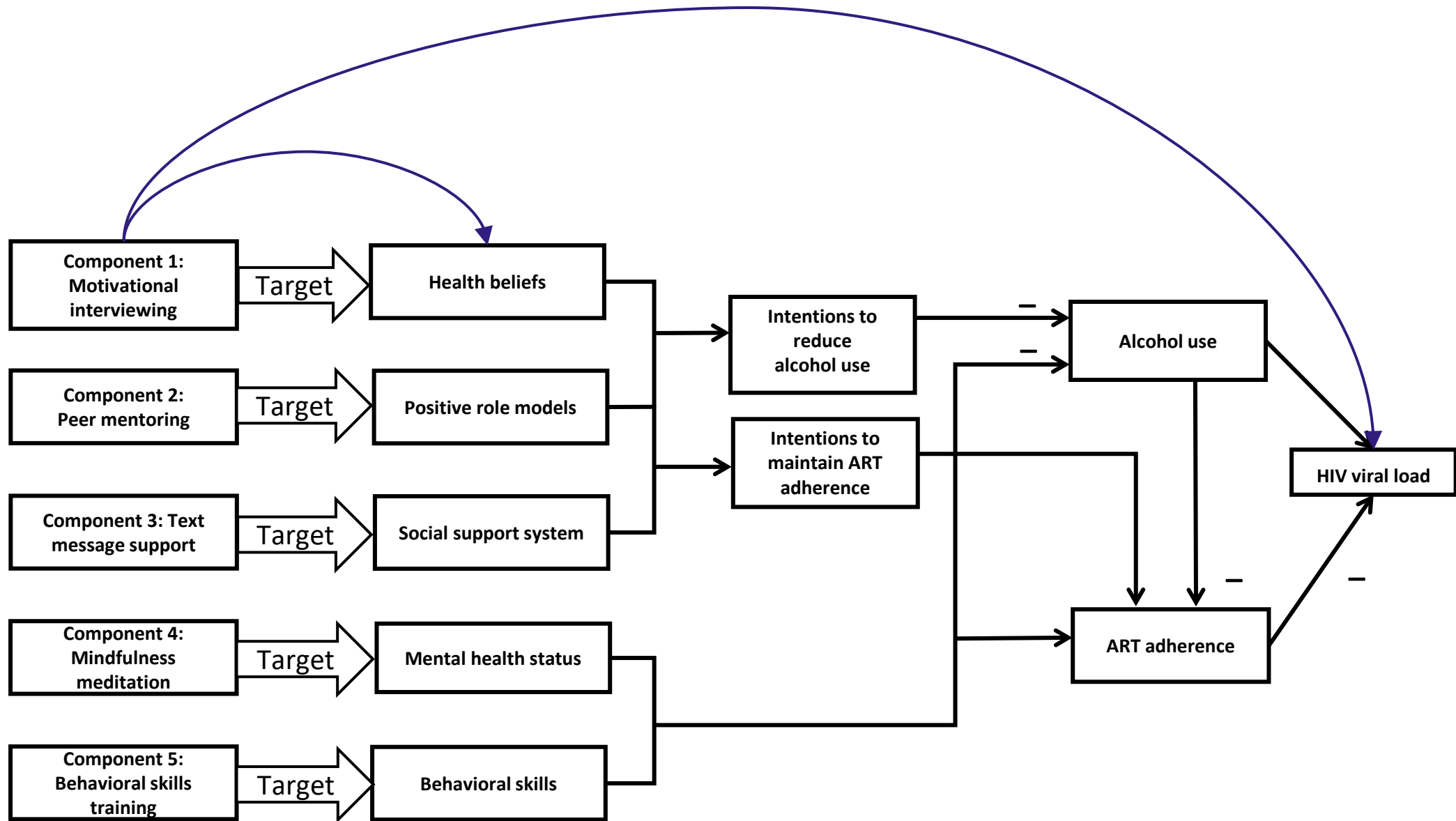


Figure adapted from Collins, L.M., Kugler, K.C., & Gwadz, M.V. (2016)

Keep in mind...

- The conceptual model is always critical
- It's always preferable to optimize based on the outcome
- When you can't, the conceptual model becomes even more critical
- So, develop the conceptual model carefully

Keep in mind...

- It is likely the effect on mediators will be greater in magnitude than the effect on the outcome!
- So take this into account in interpreting the results of the experiment

In this lesson you learned how to:

- Plan an optimization trial when the outcome of interest is far in the future



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In the next lesson you will learn how to:

- Develop appropriate informed consent procedures for a factorial optimization trial



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References cited

- Collins, L.M., Kugler, K.C., & Gwadz, M.V. (2016). Optimization of multicomponent behavioral and biobehavioral interventions for the prevention and treatment of HIV/AIDS. *AIDS and Behavior*, 20, 197-214.