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**Cc:** Costa, Lauren <Lauren.Costa@va.gov>  
**Subject:** [External] Hypoglycemia GWAS analysis

Hello, all,

Hope you’re well. I chatted with Larry at the CHARGE meeting last week about next steps for moving the hypoglycemia GWAS forward. Now that we’re nearing a comprehensive view of the counts of cases/controls based on a variety of definitions of hypoglycemia (thanks to Brian), I think it would help to have an analysis plan for us to discuss and agree upon – sorry if this has been started already and I’m behind.

Aside from deciding on the study population and case/control definitions, I think we have a few other decisions to make up front:

1. Stratification variables- race and sex?
2. How should diabetes medications be accounted for – as a planned Gene x Drug interaction analysis or as a secondary analysis after the primary GWAS?
3. How should glycemic control be accounted for – as a planned Gene x HbA1c interaction analysis or as a secondary analysis after the primary GWAS?
4. How to handle other predictors of hypoglycemia- e.g, age, renal function, cognitive impairment?

I think #2 in particular would be good to discuss before we start as I think we should have a plan to address Gene x Drug interactions in the context of hypoglycemia. I think #3 and #4 can be addressed in secondary analyses – either stratified by hypoglycemia risk factors or testing whether genetic data add to hypoglycemia prediction models that include known risk factors. That said, any and all input would be helpful at this stage.

If people are open to it, I think it would be great to try to discuss these issues on next Monday’s hypoglycemia “task force” call.

Thanks for any thoughts. Hope you all have a great July 4th.

-Sridharan