# Learner Questions and Faculty Responses

1. **Since insulin resistance is a central metabolic process, why is pioglitazone, the only agent to directly improve total body insulin sensitivity, not mentioned in prevention?**

   **Response:** *This is a great question. Pioglitazone is probably the best medication to address insulin resistance— however, its effect on fluid retention makes it a much more complicated medicine. If we are looking only at insulin resistance, dyslipidemia, secondary CVA risk reduction and liver— this is a great choice. For the heart (specifically heart failure) and kidney, it is less of a focus.*

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2. **Lifestyle? Nutritional recommendations? Your thoughts**

   **Response:** *The DCRM guidelines reinforce the central role therapeutic lifestyle changes have on this condition. Elements include mental health, nutrition, physical activity, sleep, alcohol use, and smoking.*

   **DCRM guidelines:** Handelsman Y, et al. *J Diabetes Complications*. 2022;36(2):108101. doi:10.1016/j.jdiacomp.2021.108101

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3. **Rank the 4 pillars by the absolute risk reduction for MACE.**

   **Response:** *This is a million-dollar question. No simple answer, as each of these was built on the back of standard of care. The relative contribution is affected by this and by the comorbidities in a given patient. All are needed— order may be based on problems and resources the patient has.*

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4. **What is the role of aldosterone?**

   **Response:** *It is a hormone produced by the adrenal gland to maintain blood volume through the stimulation of sodium reabsorption in the distal nephron. It also helps to excrete potassium in the urine. It raises blood pressure and can cause vascular fibrosis and scarring. It can facilitate more proteinuria and LVH. In this way, it can be counterproductive for vascular health.*

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5. **Please discuss pre-diabetes and the need to start treatments earlier.**

   **Response:** *We all agree this [intervention] would be best applied to people earlier in the pathophysiology— however, there need is great for people with both diabetes and prediabetes, and system barriers have even challenged metformin for prediabetes. So, meds have a heavy lift to get included.*

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6. **Would you use ASIs in combination with SGLT2s or by themselves?**

   **Response:** *It mechanistically makes sense to use ASIs in combination with SLGT2s as they have synergistic mechanisms. There is currently a phase III clinical trial called PREVENT HF that is examining the efficacy at the combo of ASI +SGLT2i in preventing HF. If observational data from the completed trials of finerenone (another drug which works through the aldosterone/MRA pathway) are accurate, we may also find that use of the combination of SGLT2i plus ASi results in less hyperkalemia than with ASi use alone.*

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7. **Opinion on steroidal vs non-steroidal MRAs in CKD, especially given price issue with finerenone.**

   **Response**: *The main issue with steroidal MRAs is an increase in adverse events— while they might be ok interchangeably in very experienced clinicians- this may amplify problems in less experienced clinicians —we have seen this with the GLP-1RAs*.

8. **With a UACR of 30, the hazard ratio is 1.5. So why have the guidelines not changed to reflect lower values?**

   **Response:** *There is a continuous relationship between UACR and the risk of CVD events. The UACR cutoffs of 30 for microalbuminuria and 300 for macroalbuminuria are arbitrary and only help with population definitions. Higher levels of UACR (typically over 300) are associated with greater risk of CKD progression. Therapies which reduce UACR are associated with improved cardiorenal outcomes.*

9. **GFR in the range >60 fail to show those patients with hyperfiltration, a GFR >125 has the same CVD risk as a patient with GFR of 45. Why is not accounted for?**

   **Response**: *It is taught but lost in translation in the masses. Thank you for your passion and diligence!*