Capsule Commentary on Min et al., Comparative Effectiveness of Insulin versus Combination Sulfonylurea and Insulin: a Cohort Study of Veterans with Type 2 Diabetes: How to Escalate Therapy for Patients who Fail Sulfonylureas

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Using VA administrative data, Min et al.¹ examined outcomes among diabetic patients who had failed sulfonylurea (SU) monotherapy and escalated therapy by transitioning to or adding insulin. With a median follow-up of 1.1 years, they found no differences between the groups for the outcomes of hypoglycemia, CKD, or cardiovascular events. Patients transitioned to insulin alone had slightly lower glycated hemoglobin compared to those transitioned to sulfonylurea and insulin (A1c reduced 0.2 % and 0.4 % at 24 and 36 months, respectively).

While metformin is the most common first-line therapy, many patients are treated with sulfonylureas, either because of intolerance to metformin or contraindications to metformin use. When a patient fails first-line therapy with any agent, there is no accepted guideline on escalating treatment. This study suggests that in patients failing monotherapy with sulfonylureas, clinicians should switch to insulin rather than add it to sulfonylureas, as this may lead to improvements in overall sugar control. Prospective data with longer follow-up would be needed to confirm this and to determine if this improvement in glycemia results in improvement in long-term outcomes; however, clinical trial data for this particular treatment comparison is unlikely, given that most current studies assume metformin to be the first-line therapy.^{2,3}

Long-term comparative effectiveness trials are needed to assess outcomes in patients treated with sulfonylureas, metformin, newer diabetes medications, and their combinations. Sub-group analyses of these clinical trials or analyses of cohort data using advanced statistical methods may be needed to determine effects of specific

treatment comparisons, including the one described in this study, on long-term outcomes;⁴ though these post-hoc analyses are not as valid as well-designed comparative trials. Moreover, what is also needed to guide treatment decisions, in addition to high-quality evidence, is a tailoring of therapy with regards to patients' comorbidities and preferences.⁵

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Conflict of Interest: The authors have no conflicts of interest with any of the material in this manuscript.

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