Use of Adjuvant Pharmacotherapy in Type 1 Diabetes: International Comparison of 49,367 Individuals in the Diabetes Prospective Follow-up and T1D Exchange Registries

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The majority of those with type 1 diabetes (T1D) have suboptimal glycemic control (1–4); therefore, use of adjunctive pharmacotherapy to improve control has been of clinical interest. While noninsulin medications approved for type 2 diabetes have been reported in T1D research and clinical practice (5), little is known about their frequency of use. The T1D Exchange (T1DX) registry in the U.S. and the Prospective Diabetes Follow-up (DPV) registry in Germany and Austria are two large consortia of diabetes centers; thus, they provide a rich data set to address this question.

For the analysis, 49,996 pediatric and adult patients with diabetes duration ≥1 year and a registry update from 1 April 2015 to 1 July 2016 were included (19,298 individuals from 73 T1DX sites and 30,698 individuals from 354 DPV sites). Adjuvant medication use (metformin, glucagon-like peptide 1 [GLP-1] receptor agonists, dipeptidyl peptidase 4 [DPP-4] inhibitors, sodium–glucose cotransporter 2 [SGLT2] inhibitors, and other noninsulin diabetes medications including pramlintide) was extracted from participant medical records. The proportion using adjuvant medication was tabulated by registry and overall and stratified by medication class and age range. Logistic regression models to assess factors associated with adjuvant medication use were performed by registry. Linear regression was performed to assess the association between adjuvant medication use and HbA_{1c}, adjusting for age, sex, diabetes duration, ethnic/minority status, BMI, and total daily insulin.

The use of any adjuvant medication was 5.4% in T1DX and 1.6% in DPV ($P < 0.001$). Metformin was the most commonly reported medication in both registries, with 3.5% in the T1DX and 1.3% in the DPV ($P < 0.001$). For the T1DX, GLP-1 agonists were next (0.91%), followed by SGLT2 inhibitors (0.63%) and DPP-4 inhibitors (0.04%). In DPV, DPP-4 inhibitor use frequency was 0.13%, followed by that of SGLT2 inhibitors (0.13%) and GLP-1 agonists (0.07%). "Other" medications, which included pramlintide (T1DX only), sulfonylureas, and incretin therapy of unknown type, were the third most common agents used in T1DX and second in DPV (0.86% and 0.21%, respectively). The frequency of adjuvant medication increased with age for combined registry data. However, when separated by registry, adjuvant use was highest in those aged 26 to <50 years in the T1DX (12.1%) while it was highest in those aged ≥50 years in the DPV (7.0%) (Fig. 1). Use of adjuvant medication was associated with older age, higher BMI, and longer diabetes duration in both registries; female sex in T1DX only; and lower total daily insulin dose in DPV only (all $P < 0.001$). Mean ± SD HbA_{1c} in those using and not using adjuvant medication was 8.4 ± 1.7% (68 ± 18 mmol/mol) vs. 8.5 ± 1.7% (69 ± 18 mmol/mol) in T1DX (adjusted $P = 0.04$) and 8.2 ± 1.7% (66 ± 18 mmol/mol) vs. 7.9 ± 1.5% (63 ± 16 mmol/mol) in DPV (adjusted $P < 0.001$).

Adjunctive agents, whose proposed benefits may include the ability to improve glycemic control, reduce insulin doses, promote weight loss, and suppress

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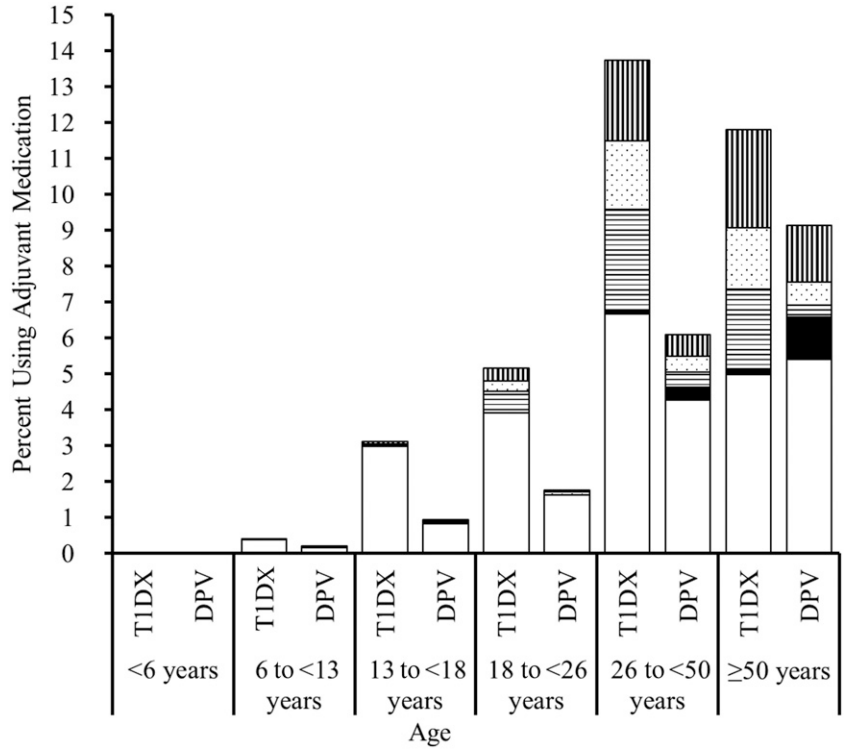

Figure 1—Use of adjuvant noninsulin medication by registry, stratified by age range. Solid white bar, metformin; solid black bar, DPP-4 inhibitor; horizontal striped bar, GLP-1 agonist; dotted bar, SGLT2 inhibitor; vertical striped bar, other.

dysregulated postprandial glucagon secretion, have had little penetrance as part of the daily medical regimen of those in the registries studied. Use of these agents was higher in the T1DX than in the DPV and more common in adults as compared with youth with T1D. Metformin was the most commonly reported medication; however, it is important to note that registry data did not capture the intent of adjuvant medications, which may have been to treat polycystic ovarian syndrome in women. Further prospective study of the patterns of adjuvant pharmacotherapy use and the long-term impact on metabolic control is needed in patients with T1D.

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