Comment

Open-source Automated Insulin Delivery in Type 1 Diabetes – the evidence is out there

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Recent years have seen significant advances in the development of automated insulin delivery (AID) systems, which can improve glycaemic outcomes and burden of treatment for people with diabetes (PwD)[1,2]. AID systems use algorithms to adjust insulin delivery based in part on continuous glucose monitor data. The first broadly available AID algorithms, OpenAPS, is open-source, designed and developed by a community of PwD and their loved ones before commercial AID systems were widely available. Whilst the number of approved commercial AID systems has increased, there are still constraints in their functionality, efficacy, access and worldwide availability[1]. The development and dissemination of open-source AID (OS-AID) systems, behind the hashtag #WeAreNotWaiting, have been held as exemplars of user-led innovation which has paved the way for an impactful form of treatment for a complex disease[3,4]. The body of evidence supporting the safety and efficacy of OS-AID and ethical implications for healthcare practitioners to support the right of PwD and their caregivers to make informed decisions on their treatment was recently highlighted by an international consensus statement endorsed by several professional diabetes organisations[1]. Despite this and growing uptake globally, widespread support from healthcare systems and academics has been lacking. A potential critique of OS-AID has been the lack of RCT evidence[5,6], which has been difficult to generate owing to regulatory and funding barriers, as the algorithm is not owned by academic research or for-profit companies. It must be noted that several commercial AID systems have received regulatory approval based on pivotal clinical trials without control groups or randomisation.

In September's New England Journal of Medicine issue, Burnside and colleagues report findings of the CREATE trial, a landmark multicentre, open-label, RCT using a modified version

of the OS-AID system AndroidAPS with the OpenAPS 0.7.0 algorithm[7]. The 24-week study included 48 children and 49 adults with limited experience of using AID who were randomised to OS-AID and control group, which used sensor-augmented pump therapy. The primary end-point was time-in-range glucose (3.9-10.0 mmol/L/70-180mg/dL) during the final 2 weeks of the trial. This was significantly increased in the AID group (71.2±12.1%) as compared to the control group (54.5±16.0%) ($p<0.001$), with those using OS-AID spending 3 hours and 21 minutes more within range per day and greatest benefit being noted overnight. No severe adverse events were noted with pump hardware malfunction being the main burden for participants.

The findings are in keeping with real-world data, and the effect sizes were comparable to other studies on commercial AID. The study provides reassurance on the safety of this system, in-line with real-world data and international consensus from healthcare professionals[1,4]. Preliminary data from the follow-up study of users who continued using the AID system beyond the trial supports these findings[8]. 18% of the participants were from non-White ethnic groups and 28% were from the lower 2 quintiles of New Zealand's deprivation index. Limitations include lower baseline HbA1c (58.4±8.5 mmol/mol) compared to the general population of PwD, although this is similar to all commercial pivotal studies.

So where does the CREATE trial take OS-AID systems? With support from prior robust data[4], a widely endorsed international consensus[1] and now a high-quality RCT [7], there is ample evidence that all AID, including OS-AID, is beneficial for PwD. However, when it comes to open-source options, barriers to adoption still exist.

There has been resistance from the academic community in recognising user-led approaches as an established form of treatment for PwD. Prior publications have given critical subjective views that were not in keeping with objective evidence or widespread consensus[6]. Similarly, a recent general consensus statement on AID affords very little support or detail for open-source systems[2]. If support from key opinion leaders in the field takes a different tone to the published data, it begs the question of what might be influencing their recommendations for clinical practice and policy-making? Amongst healthcare professionals, there have been concerns regarding understanding the technicalities of open-source systems[9]. Open-source systems rely on a user-led model of learning that disrupts the traditional hierarchy of doctor-patient education. It does not feature an industry supported program of professional or patient education, which has been integral for the implementation of commercial systems. Until these dissonances are resolved, it will be difficult for patient-led approaches that do not have the backing of independent funding or large capital by the medical device industry to support and execute their ideas, run trials, lobby for their regulatory approval, or deliver professional training programs to be given the status they deserve.

Open-source systems are an example of rapid innovation, where real-world data often precedes expensive and time-consuming pivotal studies. Despite the prior absence of an RCT, the OpenAPS algorithm has been used successfully for years. The reproducibility of results from previous real-world studies on OS-AID and the CREATE trial as an RCT reaffirms the views presented in the international consensus on OS-AID[1], which supports the use of real-world evidence in regulatory decisions. It is worthwhile noting that the real-world data showing evidence of benefit was felt to be sufficient by the consensus group, and that the U.S. Food and Drug Administration is evaluating "Loop" as an OS-AID system based on this data[10]. There are significant cost benefits to the health industry ecosystem from using an open-source algorithm that was free and went through exhaustive development, user testing with millions of hours of real-world experience prior to the point of the trial. With lowering environmental and financial impact of treatments being of priority in today's modern world, using a cost-effective approach to advance science and generate technological solutions transparent to users and providers, and validate their safety and effectiveness by using user-driven approaches and real-world data needs to be upheld, rather than demoted.

Along with the open-source community, and in keeping with professional consensus, Burnside and colleagues now firmly demonstrate that OS-AID systems have a place in the management of diabetes. Indeed, the evidence is out there. It now urgently requires the scientific community, healthcare systems and regulatory bodies to understand the potential of user-led innovation and re-think future approaches for the benefit of society.

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