DIY artificial pancreas systems: here to stay?

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Abstract
Diabetes technology has been advancing rapidly over recent years. While some of this is driven by medical technology companies, a lot of the driving force for these developments comes from people living with diabetes (#WeAreNotWaiting) who have developed their own 'do-it-yourself' artificial pancreas systems (DIY APS) using continuous glucose monitoring, insulin pumps and smartphone technology to run algorithms shared freely with the intent of improving quality of life and glycaemic control. Existing evidence, although observational, seems promising but more robust data are required to establish the safety and outcomes. This is unregulated technology and the off-label use of interstitial glucose monitors and insulin pumps can be disconcerting for people living with diabetes, health care professionals, organisations, and diabetes technology companies alike.

Here we discuss the principles of DIY APS, the outcomes observed so far and the feedback from users, and debate the ethical issues which arise before looking to the future and newer technologies on the horizon.
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Key words
closed loop; type 1 diabetes; insulin pump; OpenAPS

Introduction
Diabetes care, both historically and at present, is being propelled forwards by advancing technologies. Those living with type 1 diabetes are constantly seeking ways to improve their quality of life and are finding ways to achieve this with newer technologies. Current technology funded through the NHS for those who meet pre-specified criteria includes continuous glucose monitoring (CGM; examples include Dexcom G5 and G6), flash glucose monitoring (Abbott FreeStyle Libre), and continuous subcutaneous insulin infusions (CSII or insulin pumps). Although these are all well recognised to improve outcomes, what many aspire to is an artificial pancreas.

Research and approval for the clinical use of artificial pancreas systems have been slow to develop. Until recently, the most advanced technology available on the NHS (to a limited number and dependent on the availability of local funding) was the Medtronic Minimed 640G sensor augmented pump – a combination of CGM and insulin pump therapy with inbuilt predictive low glucose suspend of insulin delivery. Medtronic has more recently launched the Medtronic Minimed 670G system, the first-to-market hybrid closed-loop system. Hybrid closed-loop systems require the user to 'announce' their meals by inputting their carbohydrate into the system so it can calculate the bolus for meals. In between times, the pump regulates insulin delivery with the aim of keeping the glucose in the target range. This system has shown favourable outcomes in real-world observational data with over 3141 users in the USA with a mean time in range (3.9–10mmol/L) of 73% during automode.[1]

However, at the time of writing, funding for closed-loop systems in the UK is limited to the few who meet both NICE TA151 for insulin pumps and NG17 criteria for CGM, and who also live in the one in five clinical commissioning groups which fund CGM in line with NICE recommendations. Few will be able to afford to self-fund the system.

In view of this, an increasingly encountered cohort of driven and tech-savvy people with diabetes have started a #WeAreNotWaiting movement and have created a community that openly shares knowledge of the necessary algorithms needed to unlock further functionality to build a 'do-it-yourself' artificial pancreas system (DIY APS) – such as 'OpenAPS' or 'Android APS'. The #WeAreNotWaiting movement has evolved and many are now building their own artificial pancreas using existing NHS-funded technology (insulin pumps and CGM/flash glucose monitoring).

The challenge is understanding how this complex system of insulin

delivery works and the impact on outcomes in terms of HbA1c, complications and quality of life. More importantly, we need to understand the potential risks to users, as well as where health care professionals stand ethically and legally in supporting users who adapt and use their licensed devices in an off-label fashion.

What is a do-It-yourself artificial pancreas system?

A do-it-yourself artificial pancreas system (DIY APS) describes the automated insulin delivery closed-loop systems developed by the diabetes community, often referred to as 'OpenAPS', although this term actually only refers to one of many specific types of DIY APS. Figure 1 outlines the basic component parts of any DIY APS, while Table 1 shows combinations of pumps, user interfaces and hardware compatible with the three current APS platforms.

DIY APS is based on: use of CGM (real-time or intermittent converted to real-time with additional hardware, e.g. Miao Miao); an algorithm which calculates insulin doses; a communication device and an insulin pump. These systems work by automatically adjusting basal rates and boluses in response to CGM input based upon four equations (see Figure 2). Essentially, if the glucose goes up, the system delivers more insulin; if the glucose goes down, it delivers less. There are three forms of DIY APS in use and the choice of system is generally driven by insulin pump availability.

OpenAPS

The initial system, by Ben West, Scott Leibrand and Dana Lewis, was developed on a small Raspberry Pi computer and a communication stick to talk to 'old' Medtronic pumps. This system has developed over four years, with increasing functionality, to become 'OpenAPS'. OpenAPS uses the first derivative of the glucose and compares the change in glucose over the last 15 minutes to either increase or decrease insulin delivery (Figure 2). The system can recommend changes in insulin to carbohydrate ratios and insulin sensitivity factor settings through either Autosens (looking back 8–24 hours) or Autotune (which looks back either 24 hours or a user-defined amount of time). Although this system was the first in development, more recently users have been opting for Android APS which offers the advantage of a wider range of compatible, in-warranty pumps and also removes the need for users to carry the communication 'stick' with them.

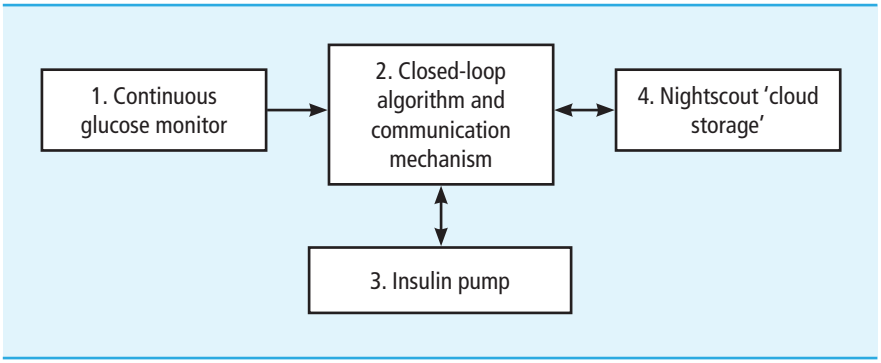

Figure 1. Components of a DIY artificial pancreas system

DIY Loop		
User interface	**Hardware**	**Pump(s)**
iPhone Apple Watch	RileyLink	Medtronic OmniPod (Alpha)
OpenAPS		
User interface	**Hardware**	**Pump(s)**
Pump Pebble watch	Linux microcomputer	Medtronic
Android APS*		
User interface	**Hardware**	**Pump(s)**
Android phone Smart watch	None	Dana R Dana RS Roche Combo Roche Insight Virtual pump

*Work in development with RileyLink to allow Medtronic and OmniPod usage.

Table 1. Three commonly encountered artificial pancreas systems and their compatible component parts. (Based on @AdrianLxM)

Equations governing basic OpenAPS behaviour

```
if (predBG < min) { // low-temp for 30m (to zero or as required to get predBG up to min)
    var rate = Math.max(0, $basal-2*(min-predBG)/isf); // calculate required low-temp rate
    var duration = 30; // always set temps to the minimum duration supported by the pump
    if (! typeof currentTempRate === 'undefined' && rate < currentTempRate) {
        setTemp(rate, duration);
    }
} else if (predBG < target) { //cancel any high-temp; let any low-temp run
    if (! typeof currentTempRate === 'undefined' && currentTempRate > basal) {
        setTemp(0, 0); // cancel temp
    }
} else if (predBG > max) { // high-temp as required to get predBG down to max (up to basal+highTempMax U/hr)
    var rate = $basal + Math.min(highTempMax,2*(predBG-max)/isf)
    if (! typeof currentTempRate === 'undefined' && rate > currentTempRate && iob < maxIOB) {
        setTemp(rate, duration);
    }
} else if (predBG > target) { //cancel any low-temp; let any high-temp run
    if (! typeof currentTempRate === 'undefined' && currentTempRate < basal) {
        setTemp(0, 0); // cancel temp
    }
```

predBG = predicted blood glucose; basal = baseline insulin level; temp = temporary.

Figure 2. Some example equations used by OpenAPS to calculate insulin doses

Loop

Loop runs on the iPhone and is based around an algorithm different from OpenAPS – developed by Nate Racklyeft and Pete Schwamb. In reality, there is little difference between the results achieved, just how it is calculated. Every time Loop makes a prediction it uses the glucose value from 30 minutes ago and includes the between that value and the current glucose to calculate an adjustment in insulin dose and future glucose level accordingly. Loop has the disadvantage of using a communication device (a RileyLink) and the same 'old' out-of-warranty Medtronic pumps[2] used by OpenAPS. It also gives the capability to bolus from within the app or its corresponding Apple Watch app.

Android APS

Android APS takes the functionality from OpenAPS and runs it on an Android smartphone. Android APS was developed in Europe by Milos Kozak and Adrian Tappe. Android APS works with modern in-warranty pumps which have Bluetooth capability such as Dana R(S), Roche Accu-chek Combo and Roche Insight pumps.

These various DIY APS algorithms have only evolved over recent years. The Juvenile Diabetes Research Foundation (JDRF) has developed a maturity model for closed-loop systems. Figure 3 shows the development of DIY APS through that maturity model. The functionality at the base of the columns shows elements of the algorithms within OpenAPS and Android APS and their development over time.

The evidence for DIY APS

Loop, OpenAPS and Android APS are in use globally by over 1000 users with more than 7.3 million hours of use.[3] The published data so far are all observational, but are nonetheless impressive.

Dana Lewis and team at 'OpenAPS' collected and analysed self-reported outcomes in 2016 and again in 2018. The 2016 analysis of 18 users' self-reported glycaemic control outcomes showed a reduction in HbA1c from 7.1% to 6.2%, and an increase in time in range (TIR) from 58% to 81%.[4]

This was mirrored by cross-over analysis from 20 further users who switched to 'OpenAPS' in 2018 which demonstrated a decrease in estimated HbA1c (established from CGM readings) from 6.4% to 6.1% within the first four to six weeks. TIR also improved in this cohort,[5] and it provides support that 'OpenAPS' can improve measures of glycaemic control in those with pre-existing tight glucose control.

Finally, a further analysis was also conducted on outcomes reported via Twitter posts – with 328 users, carers or parents analysed – which demonstrated improved HbA1c and reduced glucose variability.[6]

Observational data from a paediatric cohort in Korea demonstrated similar outcomes in a much younger population, with reduced HbA1c and reduced time in hypoglycaemia.[7] An Italian group have also analysed data from 20 of their adult users which echoed the findings of Dana Lewis as well as that of the Korea cohort, with reductions in HbA1c and reduced time in hypoglycaemia – although changes in TIR and time above range did not reach statistical significance.[8]

Most of the evidence available is limited by being from a small self-selecting population of people who have invested time and effort into managing their diabetes. Objective data are not currently available to describe the clinical outcomes. There are no data describing the impact in those with pre-existing poor control.

These systems are unapproved and, thus far, unregulated. Within the highly selective group of users, in 2016 there were no reported episodes of severe hypo- or hyperglycaemic emergency events (namely diabetic ketoacidosis and hyperglycaemic hyperosmotic state) in over 150 000 hours of use.[4] However, current users tend to represent a cohort of 'experts' in type 1 diabetes, and whether the same outcomes would be achieved in the hands of those who are less tech-savvy remains to be seen.

There are currently no data which assess whether the system directly improves microvascular and macrovascular complication outcomes, but it can be presumed that

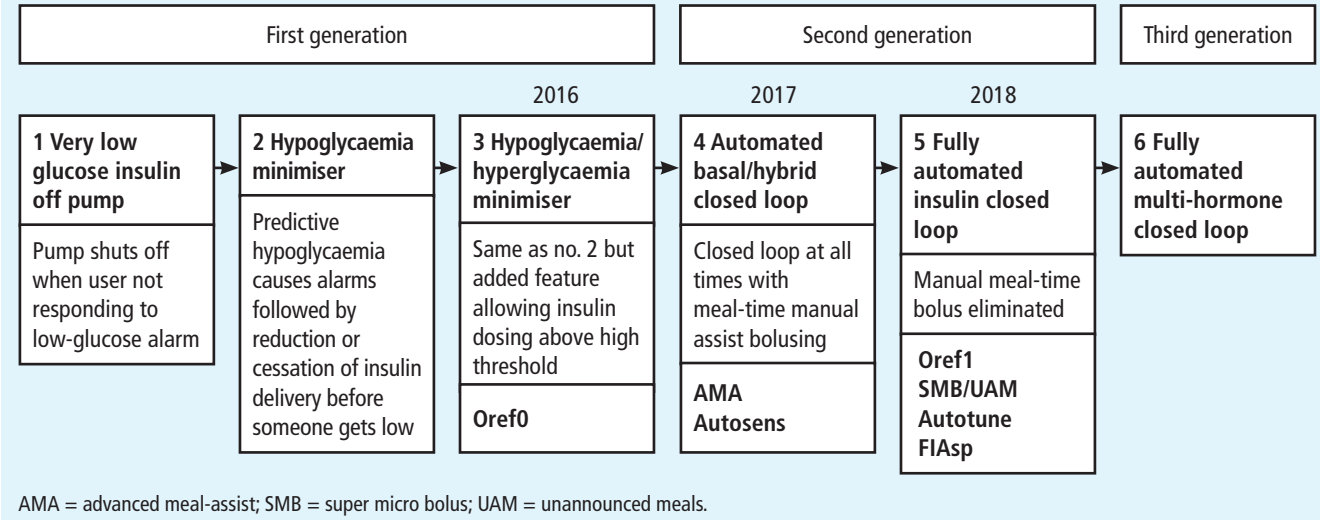

Figure 3. Progression of DIY artificial pancreas system algorithms

the reductions observed in HbA1c will confer benefit.

User feedback and quality of life

Managing type 1 diabetes on a daily basis is a labour-intensive process; it has been estimated that using DIY APS can save up to one day per month in time.[9] A computer making 288 decisions per day (once per 5 minutes on receipt of new glucose data) about whether to increase, sustain or decrease insulin is invariably going to out-perform a human.

Users of DIY APS report the single biggest improvement is the ability to have an uninterrupted night's sleep and to wake up with the glucose level in range.[4,6] Users of the system have describe it as 'life changing'; some quotations from people living with diabetes who use DIY APS can be found in Box 1.

What results do you get from DIY APS?

- 'My HbA1c is 43mmol/mol with 0% hypo – no more worrying about what my glucose is and where it is going, Android APS will take care of it. I feel cured!'
- 'I am not doing anything and I can't even remember the last low I had. This looping is phenomenal! It's changed my life, given me more freedom and much more time free from worry.'
- 'I am not so good at managing T1 when "something else" is happening. It was far smarter at managing a cold than I have ever been.'
- 'The huge psychological benefit this has provided... I felt like I was "failing" so much of the time before – regardless of the effort I made – now I am now longer "failing".'
- 'It's not all about HbA1c. My time in range has gone from 60% to 95% and my involvement time has gone from 5–10mins/hr to 1min/hr with no more disruptions to sleep.'

Box 1. Quotations from users of DIY artificial pancreas systems

Commercially available closed loop: the end of DIY APS?

Commercially available hybrid closed-loop systems are now emerging on the market, with the recent launch of Medtronic MiniMed 670G and more to follow this year and the next (see Table 2). Some may assume this will reduce the uptake of DIY APS. However, this is unlikely to be the case.

Firstly, the lack of dedicated NHS funding for commercially available, safe, regulated and approved closed-loop systems means that the uptake of DIY APS is likely to continue to grow. Indeed, people living with diabetes in the UK can now access the component parts required for a DIY APS system through the NHS; they just need to build the system. Many are now using the FreeStyle Libre flash glucose monitor with a Miao Miao (or similar) to allow the FreeStyle Libre to communicate via Bluetooth to an NHS-funded insulin pump with the closed-loop algorithm on their mobile phone. This is, of course, off-label use.

Secondly, while building a DIY APS is no easy task, there is vast support available from the community for building the system. Across the country, there are 'build' sessions running where the tech-savvy DIY APS expert users support less expert users to build their own artificial pancreas. These events are often advertised on Facebook and Twitter and as such can attract large numbers. Each session typically has ~30 attendees and lasts a full day. Once they have built their system, they are reliant on the online diabetes community for support. What was once a system for a select few is quickly spreading more widely in the diabetes community. We have no idea exactly how many UK users there are, although the Looped UK Facebook page now has over 600 members, suggesting the numbers are growing.

Third, we have the system itself. Commercial companies are in a race to develop a safe, effective system which meets all the regulatory needs and has the evidence to support use. DIY APS has not had such constraints. The systems have been tried, tested and tweaked day-in and day-out by hundreds of people with type 1 diabetes who have persistently fed back information on glitches and suggestions for improvement. What they now have are responsive, effective algorithms built by the diabetes community, for the community. Unlike other options, they are not reliant on frequent blood glucose monitoring or accurate carbohydrate counting. They seem to deliver tight glucose control, in a way people with diabetes want it to.

So, in summary, we have what users describe as an effective system, with support available from the community, potentially through the use of NHS-funded devices (with the exception of the Miao Miao – currently retailing at $199). Until the day the NHS provides dedicated funding for commercially available closed-loop systems, it seems that this diabetes treatment option is here to stay.

Ethical and medicolegal concerns

With an increasing number of people with diabetes accessing and using DIY APS, health care professionals need to consider their position on this. JDRF have recently issued their national position statement.[10] They cannot endorse DIY diabetes technology as it is unregulated, with potential safety concerns. They do, however, highlight an ongoing commitment to respecting patient choice but recognise that health care professionals may need enhanced indemnity, as well as dedicated training, in order to fully assist in the use of these systems.

The algorithms used in DIY APS are currently unregulated and untested in clinical trials. While CGM and insulin pump technology are regulated for use in diabetes care, their use in combination with DIY APS algorithms makes their use off-label.

The risks are unknown, but could relate to:

- The algorithm.
- User interaction with the system and general safe pump use.
- Use of out-of-warranty pumps.
- Use of 'out-of-warranty' older pumps purchased online.

Risks associated with the algorithm are unknown. There is no formal reporting of issues, no way of collating information about errors, and no way of distributing a national (or international) field safety notice. The community does communicate through online platforms, but there is no formal way of alerting all users should a safety issue be identified.

Company	Active trials	Key points of difference
Phase 1		
Xeris	1	Dual hormone Tubeless/patch insulin delivery
Insulet Corporation	1	Tubeless/patch insulin delivery
Beta Bionics iLet dual hormone	3	Dual hormone Rechargeable battery/green Small size Algorithm complexity
Cellnovo Pepper TypeZero	3	Smartphone compatible Tubeless/patch insulin delivery Algorithm complexity
Phase 2		
Tandem	3	Rechargeable battery/green Small size
Roche	2	Smartphone compatible
Beta Bionics iLet glucagon only	3	Rechargeable battery/green Small size Algorithm complexity
Cellnovo Diabeloop	3	Tubeless/patch insulin delivery
Bigfoot	1	Smartphone compatible Insulin pen compatible
Phase 3		
Beta Bionics iLet insulin only	3	Rechargeable battery/green Small size Algorithm complexity
Approved		
Medtronic 670G	16	

Table 2. Upcoming diabetes technologies coming to market on the road to an artificial pancreas. (Data derived from Juvenile Diabetes Cure Alliance pictorial, accessible at http://thejdca.org/artificial-pancreas-projects-2018)

Currently, most DIY APS users are 'experts' in type 1 diabetes, often with very good control before they start DIY APS. The risks of them mismanaging an insulin pump set failure etc are probably low and therefore the risks on DIY APS are also, probably, low. However, as the uptake of DIY APS grows, it is possible less expert individuals will start to use the system and they may not be equipped with a detailed knowledge of how to use insulin pumps, and how to optimise their settings for use with the algorithm etc. Many health care professionals have an extremely limited understanding of DIY APS and will only be able to provide limited technical advice and support in this context. Users of this system do so at their own risk and, as such, health care professionals are limited in the advice they can provide on glucose optimisation using this system.

Some users purchase out-of-warranty older Medtronic pumps online to use with their DIY APS; a black market now exists for such devices that can be sold for approximately £700. There is an undoubted risk associated with this: the history of the pump is unknown, it may have faults, and there is no company support. However, the emergence of Android APS as an option which works with commercially available pumps such as the Dana RS may overcome this issue.

From a medicolegal perspective, DIY APS puts health care professionals and the users in a difficult situation. The components of DIY APS can be provided on the NHS for those who meet pre-specified NICE criteria for insulin pumps, CGM or FreeStyle Libre. The steps required to allow the components to communicate with the algorithm are undertaken by the user. If an individual comes into clinic using the system, it is important to have an informed discussion about the risks of using the system. However, this is challenging, given the relative lack of data. Ultimately, individuals using the system do so at their own risk. The risks are unknown but potentially might include hypoglycaemia, hyperglycaemia, ketoacidosis and potentially death if the system malfunctions and appropriate corrective action is not taken. The health care professional's duty is to ensure that the user understands how to safely manage the component parts: the insulin pump and the CGM or FreeStyle Libre, as well as what to do in an emergency

Finally, there are other potential considerations for the user. With the off-label and unregulated use on the component parts of DIY APS, it is possible that use may invalidate insulin pump insurance, or travel insurance for instance. If a user is admitted to hospital while abroad with a severe hypoglycaemic event, is the individual's insurance valid? Further, the DVLA have recently approved CGM and flash glucose monitoring for driving. Would the use of DIY APS invalidate the user's car insurance? These are challenging scenarios which are certainly worth consideration.

The future

So what does the future hold for these systems? Figure 3 shows that OpenAPS has probably developed as far as it can in terms of functionality.[11] Android APS with the ability to communicate with the widest range of pumps is continuing to add pumps to its capabilities.

However, Loop is developing in a different direction. In October 2018

Tidepool, a not-for-profit diabetes technology organisation in the USA, announced that they intend to deliver Loop as a supported Food and Drug Administration regulated mobile app in the App Store. They are working with pump manufacturers to make Loop available as a regulated approved product which will hopefully widen access to APS in the future.[12]

The Association of British Clinical Diabetologists in the UK are supporting work on DIY APS. They plan to deliver a national clinical audit; this large, observational study will provide much-needed objective data on the impact on glycaemic control, quality of life and risk. The outcomes will help guide health care professionals to more accurately describe the risks and benefits of such systems,

Whatever construct is used to move DIY APS algorithms forward, it is clear that the end users want interoperability: the ability to use their artificial pancreas system with any CGM and any insulin pump so they are not tied into one manufacturer's eco-system and costs, as reflected in the JDRF open protocol automated insulin delivery initiative in 2017.

Conclusion

DIY APS is here to stay. The risks are unknown but one thing is certain: users report positive feedback and the uptake will no doubt continue to grow. Health care professionals can support users by ensuring the person with diabetes has a good understanding of the component parts which they are using, how to safely manage their glucose monitor and pump, how to access support from the community if they have concerns, and what to do if things fail. Users of DIY APS do so at their own risk.

In agreement with JDRF, there is a need for clarity on the issue of indemnity so that health care professionals feel they can continue to care for patients who choose to use DIY systems without medicolegal repercussions.

Ultimately, health care professionals have a role to support people living with diabetes, regardless of their choice of therapy.

Key points

- The number of people living with type 1 diabetes who choose to build their own DIY closed-loop system is increasing
- DIY artificial pancreas systems are not regulated or approved. Outcomes and safety of these systems have not been investigated in randomised controlled trials and safety data are lacking
- The benefits and risks of DIY artificial pancreas systems are considered and the risks debated

Declaration of interests

Thomas SJ Crabtree has no conflicts of interest to declare.

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Emma G Wilmot has received personal fees from Abbott, Eli Lilly, Dexcom, Medtronic, Novo Nordisk and Sanofi.

References

1. Stone MP, *et al.* Retrospective analysis of 3-month real-world glucose data after the MiniMed 670G system commercial launch. *Diabetes Technol Ther* 2018;20(10):689–92.
2. Racklyeft N. The History of Loop and LoopKit. https://medium.com/@loudnate/the-history-of-loop-and-loopkit-59b3caf13805 [accessed 24 Nov 2018].
3. OpenAPS website. https://openaps.org/outcomes/ [accessed 24 Nov 2018].
4. Lewis DM. Real-world use of Open Source Artificial Pancreas Systems – Poster presented at American Diabetes Association Scientific Sessions. 2016. https://openaps.org/2016/06/11/real-world-use-of-open-source-artificial-pancreas-systems-poster-presented-at-american-diabetes-association-scientific-sessions/ [accessed 24 Nov 2018].
5. Lewis DM, *et al.* Improvements in A_{1c} and time-in-range in DIY closed-loop (OpenAPS) users. *Diabetes* 2018;67(Suppl 1). doi:10.2337/db18-352-OR.
6. Litchman M, *et al.* Twitter analysis of #OpenAPS DIY artificial pancreas technology use suggests improved A_{1c} and quality of life. *J Diabetes Sci Technol* 2019;13(2):164–70.
7. Choi SB, *et al.* Open artificial pancreas system reduced hypoglycemia and improved glycemic control in patients with type 1 diabetes. *Diabetes* 2018;67(Suppl 1). doi:10.2337/db18-964-P.
8. Provenzano V, *et al.* Closing the Loop with OpenAPS in people with type 1 diabetes – experience from Italy. *Diabetes* 2018;67(Suppl 1). doi:10.2337/db18-993-P.
9. Street T. #WeAreNotWaiting at the Type1AndTech Conference. http://circles-of-blue.winchcombe.org/index.php/2018/11/11/wearenotwaiting-at-the-type1andtech-conference/ [accessed 10 Nov 2018].
10. Juvenile Diabetes Research Foundation. JDRF's UK Position Statement on type 1 diabetes 'DIY' technologies. 19 Feb 2019.
11. Liebrand S. 2018. Gitter.im – Nightscout/Intend-to-bolus channel [accessed 25 Oct 2018].
12. https://tidepool.org/tidepool-delivering-loop/ [accessed 29 Nov 2018].