How Integrated Technology Benefits Patients and Investigators in Diabetes Clinical Trials

Doctors are warning of the 'absolute pandemic' of diabetes. In the US alone, 100 million are diagnosed with diabetes, with many millions more undiagnosed or unaware of their condition. In July 2017, the Centers for Disease Control and Prevention (CDC) reported that more than 100 million Americans have diabetes or prediabetes[1]. By 2035 it is predicted that diabetes will be the seventh leading cause of death, affecting more than 592 million people worldwide[2]. Given these statistics, it is not surprising that pharmaceutical companies are heavily investing in this area. Researchers are, therefore, adopting technology to elevate their clinical trials for better data, reduced burden on patients, and increased patient safety. This article explores how connected technology and electronic solutions can be integrated specifically into diabetes clinical trials to meet the needs of clinicians and patients.

Connected Devices

Clinical research is changing due to the Internet of Things (IoT) and the Internet of Medical Things (IoMT). New data from Juniper Research predicts the number of connected IoT devices will reach over 46 billion in 2021[3]. IoT connected devices currently include standard smartphones, tablets and bluetooth speakers. While 5G is not expected until 2020, this low-bandwidth technology has the potential to be included in devices with IP addresses and battery lives of up to ten years, designed to passively collect and transmit data as required. 5G's speed and capacity will therefore enable an even more connected future.

IoMT connected medical devices can be defined as wireless, wearable or implantable digital technologies used in healthcare and clinical research to passively collect biometric data about a patient's health. These devices may be regulated or not. For example, Class I, II, and III regulated medical devices include glucometers, spirometers, weights, scales, and implantables, while unregulated devices include activity trackers, smartwatches, cardiac monitors and body temperature devices. As noted, these devices are collectively part of the IoMT network, and can be applied to clinical trials in several beneficial ways, including the capture of better quality data.

Integrating Technology into Diabetes Clinical Trials

Diabetes is a complex condition for patients to manage, with significant impact on patients' daily lives. Managing the condition can involve a variety of demanding tasks including taking regular measurements of blood glucose, monitoring the nutritional value of meals and tracking insulin usage. Diabetes clinical trials typically seek to capture this data, as well as expecting participants to complete a variety of additional patient-reported outcomes, often while having to alter their normal established routine to align with the study protocol. It is difficult for patients to remember to report everything at the right time and this increased complexity can lead to higher patient burden and risks, resulting in additional worry and lower compliance within the study. The key to optimising data collection is to understand the patient perspective and how each activity affects their everyday life. Managing diabetes clinical trials can similarly be a challenge to the investigators if patients are not reporting data accurately, as they use this data to closely monitor patients' wellbeing. A 1984 publication concluded that, "Two thirds of the subjects had reported values (on paper) in such a manner as to obscure hyper- and hypoglycemia, leading to misleading clinical impressions about the fluctuation in metabolic control[4]." This leads to the conclusion that paper collection impacts data quality and therefore also impacts monitoring patient safety.

Robust and intuitive systems for use in diabetes clinical trials are needed to capture clinically relevant data, decrease patient burden and increase patient safety.

Developing an Effective Electronic Solution

A leading provider of patient-centred eSource and electronic solutions for the life sciences industry, CRF Health, identified a need for a diabetes solution that not only caters to the clinical team and sponsors' needs for accurate data collection, but is also relevant to a patient's symptoms and typical daily routine, thereby limiting any additional burden to the patient. The company implemented a project to identify what constitutes a good electronic solution. The process took the following stages:

1. Collect feedback from sponsors and patients
    a. Client interviews to gather requirements and challenges
    b. Online survey of diabetic patients
2. eDiary design for collecting ePRO data in trials
3. Test and refine the eDiary design
    a. Diabetes focus group testing
        1. Revisions based on focus group
    b. Independent usability testing
        1. Revisions based on usability testing
    c. Second round of independent usability testing
        1. Revisions based on second round of usability testing
4. Final eDiary solution

Let's take a deeper dive into the process:

Collecting Feedback from Sponsors and Patients

While designing this solution, feedback from sponsors on previous studies was used to identify the specific challenges associated with capturing patient data in diabetes populations. Input was also gathered from the intended users of the solution: the patients. An online survey was used to assess aspects of diabetes patients' daily routines. The survey was completed by patients from a diabetes support group, with a wide mix of ages, sexes and type I and type II diabetes.

eDiary Design, Testing, and Refinement

The feedback from sponsors and patients was used to implement the design and layout of the initial diary (CRF Health's TrialMax Touch® software for handheld devices). This alpha version of the solution was then tested in focus groups formed of members of a diabetes support group, providing hands-on user testing data. This feedback was used to update the content, design and layout of the diary.

Once the diary had been refined, it was sent to an independent third party for usability testing with diabetes patients. The purpose

was to determine how suitable the tailored eDiary was and to ensure it fit in with the daily routines of diabetic patients. The feedback was used to further refine the diary and a final round of testing was done to gather evidence that proved the intended population deemed the product intuitive and easy to use. The patients from this study expressed a preference for the integrated electronic diary over traditional paper and electronic reporting methods, as they found it to be less burdensome, and given the option, they would choose to use it in a clinical trial setting.

Final eDiary Solution

The solution developed to minimise burden incorporates a handheld device, a bluetooth-enabled wireless glucose meter (MyGlucoHealth) which allows data transfer to the diary, and a site management software tool (see Figures 1 and 2).

- The home-based eDiaries are integrated with a glucometer, allowing for the automatic capture of glucose readings (Figure 1)
- The diary indicates what tasks have been accomplished for the day and what still needs to be done
- Reports for investigators are available in near real time because of automated data sending

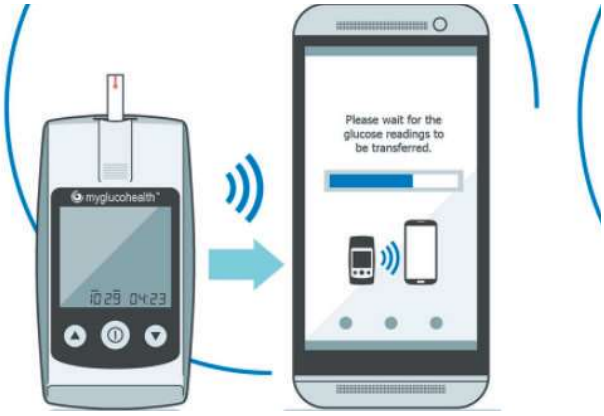

Figure 1: Data transfer from MyGlucoHealth meter to the diabetes diary

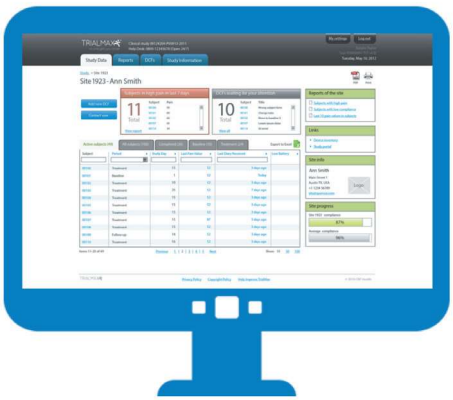

Figure 2: Reporting available to investigators via TrialManager® with automatic data sending

The benefits of this solution include higher data quality because the removal of paper leads to a reduction in errors. In addition, engagement and compliance are enhanced because of the patient-centric design. Finally, because patients can submit data from home via the eDiary, the investigators are able to effectively monitor the data. This provided a real-time picture of the patient and the ability to react (for instance, adjusting the insulin dose).

Key Considerations When Using eCOA in Diabetes Trials

The wireless integration of eDiaries with medical devices results in more accurate data by removing the need for manual transcription of the data values. Date and time stamps of the reading and the device serial number are also transferred, providing evidence of the timeliness of the data and an attributable source. Once the eDiary receives the values from the glucometer, the values can automatically be sent to the ePRO database for review by the site personnel or study team. This allows very close to real-time monitoring of the patient's status and permits timely intervention for safety or compliance concerns.

Patient experience is key. The patient should be able to report meals, blood glucose, insulin and hypoglycemic symptoms and events. The devices should have well-designed user interfaces for a pleasant user experience, with reminders, prompts and notifications to encourage reporting to boost compliance and complete data. A good system should also deploy common diabetes instruments, such as pre-approved questionnaires that can be deployed electronically.

From a site perspective, a system should allow near real-time view on the patient's wellbeing including glycemic control and hypoglycemic events, as well as insulin use, to allow follow-up on patient compliance.

The Electronic Revolution

By utilising sophisticated wireless biometric sensors and devices, real-time patient readings can be collected and seamlessly uploaded to cloud-based platforms, for data aggregation, reporting and analysis. This in turn leads to improved data quality and study efficiency, meeting the needs of the trial sponsor. From a clinical trial perspective, electronic solutions and connected devices result in cleaner, faster data and better management of the patient.

REFERENCES

1. www.cdc.gov/media/releases/2017/p0718-diabetes-report.html, visited on 29 November 2017.
2. http://www.einstein.yu.edu/centers/global-health/global-diabetes-institute/about-us/global-diabetes/, visited on 13 December 2017.
3. www.juniperresearch.com/home, visited on 29 November 2017.
4. Mazze, R. S., Shamoon, H., Pasmantier, R. et al. Reliability of Blood Glucose Monitoring by Patients with Diabetes Mellitus, The American Journal of Medicine. 77: 211-217 Published August 1984

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