Design, Implementation and Management of an International Medical Device Registry

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Abstract

Background

Registries are powerful clinical investigational tools. More challenging, however, is an international registry conducted by industry. That requires considerable planning, clear objectives and endpoints, resources and appropriate measurement tools.

Methods

This paper aims to summarize our learning from ten years of running a medical device registry monitoring patient-reported benefits from hearing implants.

Results

We enlisted 113 participating clinics globally, resulting in a total enrolment of more than 1500 hearing-implant users. We identify the stages in developing a registry specific to a sensory handicap such as hearing loss, its challenges and successes in design and implementation, and recommendations for future registries.

Conclusions

Data collection infrastructure needs to be maintained up to date throughout the defined registry lifetime and provide adequate oversight of data quality and completeness. Compliance at registry sites is important for data quality and needs to be weighed against the cost of site monitoring. To motivate sites to provide accurate and timely data entry we facilitated easy access to their own data which helped to support their clinical routine.

Trial registration:

ClinicalTrials.gov NCT02004353

Introduction

There are many types of medical registries, the vast majority of which are concerned with drug safety and efficacy, disease-specific registries, including rare diseases, and medical devices focused on safety and effectiveness. Most are supported as part of a regional or national mandate. Thorough overviews to developing a safety registry can be found in several publications [IMDRF 2015, Gliklich 2020, Zaletel 2015] and for a medical device registry [Mandavia 2018, Banerjee 2019, Medtech Europe 2017, Melvin
2019]. It is rare for a patient-related outcomes registry to be corporate funded and international. In 2015, there were 1028 registries listed in the EU, of these only 13 were multinational, 83 were for medical devices and only 5 (3%) were sponsored by a company [Zaletel 2015].

Cochlear Ltd (Australia) manufactures hearing implants such as bone conduction hearing solutions (‘Baha’), cochlear implants (CI), auditory brainstem implants (ABI) and over the duration of the registry several middle-ear implants. These devices serve to overcome various dysfunctions in the auditory system from the outer ear to the inner ear and further up the auditory pathway. As such, although sensitivity to sound may be restored in all cases, functional hearing such as speech understanding is the main aim of such devices [James 2021]. Probing speech understanding capacity has been incorporated into generic health utility measures such as the Health Utility Index (HUI) [Feeny 2002] so that the benefit of a hearing implant may be calibrated against interventions for other health attributes. Disease-specific questionnaires for hearing loss, such as the Speech Spatial Qualities (SSQ) developed by Gatehouse and Noble [Gatehouse 2004] have also been developed to allow more fine-tuned measures; for example, to allow comparison between devices. We note that cochlear implantation is generally accepted to be the standard of care for profound neurosensory hearing loss [Buchman 2020] where conventional acoustic hearing aids are not sufficient to restore functional speech understanding. Similarly, other technologies such as Baha and middle-ear implants are used where conventional sound-amplifying acoustic hearing aids are not able to overcome physical barriers between the outer and inner ear.

It was a pioneering endeavour for the company’s subsidiary Cochlear AG (Switzerland) to consider establishing an international registry in 2009. At that time, in the hearing device domain there existed only the voluntary Swiss CI registry, started in the 1990s. The Swiss CI registry collected performance and safety data from clinics but did not involve patient-reported outcome measures [Brand 2014, Senn 2020]. At its inception, the primary aim of Cochlear’s registry was to produce a real-world view of the impact of CI on hearing ability and QoL in daily life, a topic that continues to be of interest to researchers [Andries 2020], by reporting on self-assessed benefits following hearing-implant treatment.

The formal name given to the Cochlear registry was the Implant Recipient Observational Study (IROS) [ClinicalTrials.gov NCT02004353]. The concept for the registry arose from the realization that the available clinical evidence supporting the benefit of CI did not lend itself to meta-analysis. Furthermore, due to limited inclusion criteria for smaller cohorts in research with relatively short observation times, outcomes were not generalizable. Typically, hearing treatment outcome data, such as speech recognition measures or non-standardized patient-reported outcome measures used routinely across clinics and cultures, is diverse and thus difficult to collate and analyse collectively. Prior to this registry, any group data with diversified input could only be reported as results of strictly controlled clinical trials where applying outcome data to broader populations was not possible. In contrast to clinical trial participation, a registry involving cross culturally adapted patient-reported outcome measures (PROMs) would offer the opportunity for broader participation by clinics, and their treatment groups, representative of less biased target populations [Zaletel 2015, Suvarna 2018]. This would be best supported as an international registry (International Organization for Standardization (ISO), 2020) using
widely accepted questionnaires. The HUI instrument was already available in many languages and the SSQ was available in a few language versions. One of the first tasks was to ensure further validated translations and cultural adaptations of the SSQ questionnaire in collaboration with the author developer (Gatehouse 2004) and for the HUI Mark III version in collaboration with HUI inc. (Canada). These two questionnaires served as the primary endpoints for IROS. Both PROMs enable capture of real-world experience and treatment benefits for implant users. To characterize the nature of hearing loss and further help the definition of user profiles versus the primary endpoints, collection of clinically relevant data points such as etiology, duration of hearing loss, progression of hearing loss, type and degree of hearing loss were also collected. Unlike mandated registries with a primary focus on safety aspects, collection of safety data was part of established vigilance systems. Ongoing vigilance information complemented the annual report of serious events and select non-serious events (such as tinnitus or dizziness) for registry participants.

This paper provides insight into crucial decisions that may be encountered in the pursuit of efficient data collection, ultimately leading to useful data analysis and reporting. The details are particularly relevant when conceptualizing the potentials offered in creating better registries using modern data collection methods that reduce, or even eliminate, the workload on participating sites that was identified as one of the major challenges faced during the operation of IROS. Our paper, thus, reflects the experience with the first large hearing-implant device registry using electronic data capture. We present details that relate to decision-making in the design, implementation, management, follow-up and decision to continue or close a registry. Note that the IROS registry was closed mid-2020, see Figure 1 for a timeline.

**Design**

**Purpose and primary aims:** The type of evidence defines the purpose of the registry, whether it be to collect real-world evidence (RWE) or yield safety data for regulatory certifying bodies, federal and local funding authorities and other healthcare agencies, or to provide support for clinical or market access activities; each will have its own set of advantages and limitations [Suvarna 2018]. Regardless of the type, there will always be shifting sub-goals as stakeholders may request broader application of the registry, such as mining of available data for specific clinical or development purposes. It is, therefore, important to maintain a clear focus as to the fundamental aim of the registry. In our case, there was also interest for Cochlear to use the registry to monitor hearing outcomes for recipients of other implantable hearing devices as made available. Furthermore, it was realized that data could equally be collected for adolescents (>10 y.o.) who were able to complete the PROM questionnaires. Collecting similar data for children <10 years of age is more complex and involves surveying parental perspectives and observations. Under a parallel project and scope, Cochlear therefore started in 2015 a paediatric registry (P-IROS), a description of which is available in [Sanderson 2014].

**Selection of Measures:** Consistent with the aim of the registry, it is necessary to consider language and culture, that is, the measures must have the potential to be adapted cross-culturally. The IROS registry utilized two PROM questionnaires that would represent real-world experiences and included general
demographics and other patient characteristics. The selection of measures impacted IROS in two ways: one concerned the need for pre- and postoperative assessment due to the nature of the questionnaires that concerned current perceived status of hearing and, the other, the absolute need for long-term repeated-measure outcome data, particularly for CI recipients, because optimal benefit from the hearing implant might only be obtained after several months. The ultimate impact was that the postoperative measures needed to be suitable for repeat assessment at several annual time points up to 3-years following implant.

**Type:** All registries are in essence observational, collecting data from routine clinical practice and therapy, but they can be implemented as voluntary or mandated. Inherent in a corporate-sponsored registry like IROS is that it must be voluntary [Gomes 2017]. It can be a so-called patient registry, which systematically collects data concerning a defined treatment population, or a study registry that is designed to answer specific research questions or provide supporting evidence. IROS was designed and implemented as a patient registry focusing on real-world patient-related benefits.

**Stakeholders:** Stakeholders share common interests but also have specific expectations [Gliklich 2020]. Consideration should be given to the scientific community, healthcare professionals, health economists, healthcare payers and reimbursers, healthcare authorities, regulatory agencies, medical device manufacturers and, often not sufficiently considered, respective patients and their associations. It is important that the registry design and implementation not be overloaded to enable delivering on its primary objectives, which may require compromises between stakeholder interests. Once defined, success of the registry will be guided by clear communication that enables coordinated efforts and well-defined ongoing measures of success. Our stakeholder group grew as the utility of the registry became more apparent.

**Governance:** The overall governance of a registry lies best with a small steering committee, including the project manager. The steering committee interacts with stakeholders and gives particular attention to documenting ethical approvals, data entry and retrieval and monitoring procedures [Mandavia 2018]. This is especially significant in a diverse and wide-reaching international corporation. In-house governance versus contracting an external contract research organisation (CRO) may facilitate rapid changes but in our experience may not always be practical from a cost or resource point of view.

**Degree of Flexibility:** Part of good planning is deciding how long the registry will run, or defining when it will end in terms of the required number of data points meeting set objectives, or the criteria for termination (such as poor recruitment or follow-up rates). Amendments are necessary for technical updates (browser version, etc.), data transfers and expanding the registry to meet stakeholder requests and also to incorporate changed regulatory demands, which are to be expected. For instance, IROS was adapted to provide mandated Post Market Clinical Follow-up (PMCF) data for medical devices, initially under EU Active Implantable Medical Devices Directive (AIMDD) [90/385/EEC] in 2014 and more recently under EU Medical Device Regulation [EU MDR 2017/745]. Prior to 1st enrolment in 2011, the IROS registry was designed to meet the requirements for data protection of patient personal information and
registration with the Commission for Data Privacy in Belgium on behalf of all European countries (CPVP). Subsequently further refinements were made to ensure compliance to the EU General Data Protection Regulation (EU GDPR 2016/679) requirements in 2018. It is key to keep the registry current with the regulatory environment; however, there are no harmonized regulatory requirements for registries across countries [Artyomenko 2018]. Deciding on the operating term of the registry and keeping to a minimum duration required will help avoid accumulation of regulatory imposed changes, which may lead to further cost and resource drain. We might add that addressing evolving commercial needs such as release of new products and their iterative inclusion in an established registry platform may equally impose resource intensive changes to documentation, training and support. Before doing so it may be worth considering whether the evidence landscape has evolved that warrants a new registry design and concept.

**Transparency**: Essentially, this involves letting stakeholders know how and why data are being collected and providing a means for reasonable access to their own data. Data ownership is an inherent part of transparency, privacy and security. It has become more relevant in study designs in the last decade [Artyomenko 2018]. For IROS, it was communicated and well understood that clinics had full access to their own data for analysis and reporting as desired and that collaborative permission from other participating clinics was required to access and use any other group’s data. Furthermore, Cochlear owned all data for analysis and reporting to stakeholders as required. Transparency also carries the responsibility of assuring data anonymity when data-reporting to any parties.

**Legal and Ethics Aspects**: It is important to determine whether patient consent needs to be obtained from each patient, or whether anonymization can be considered a substitute for patient consent [Bisdas 2019, Zaletel 2015]. When designing a patient consent form, it is important to include clear reference of utilizing analysed data for publication and reports as well as any secondary uses of data (e.g. data mining or exploratory research). Important to emphasize that any published data will maintain patient privacy through anonymized group reporting. It is beneficial to define the potential data uses broadly enough, already foreseeing potential data analysis requests outside the primary registry objectives. A clear definition of purpose of end-use for data collected is also a requirement by EU GDPR. If registries are designed in a way not collecting patient identifiable information and the data collected is fully aligned with clinical routine, it might be possible to obtain a waiver from ethics committees, allowing data collection directly from the patients without Informed Consent (IC) process. This tremendously reduces the burden of ongoing compliance on a project. Another possibility for streamlining registries is to use PROMs that can be responded to directly by patients via marketing type surveys, without the involvement of a clinician in the data collection. We recognize that certain detailed clinical data that requires the health care professional’s input will not be accessible via this route.

**Financial Commitment**: As a long-term project, it is important to properly assure financial resources. Design, implementation, and maintenance costs, including upgrades as needed, are concerned with different facets of the registry (Figure 2). Even before actually starting the data collection, adequate investment plans are needed for all levels of documentation that may include translation of test tools,
providing various information for Ethics Committees in local languages, information materials to clinics and patient participants and various other communications. Other activities such as development of the database, webinars, travel costs, as well as in-house registry support personnel must also be considered. The database, also called Electronic Data Capture (EDC) system, may need to undergo technological iterations over the years which is an aspect to consider and financially plan for.

Implementation

**Recruitment:** Participating clinics may be recruited directly by the company, its local distributors, or via interest groups. Patients are typically recruited by the clinical professionals involved in their care and treatment; thus, their selection criteria can carefully be delineated. For the data to be representative, aim to enrol enough patients from different clinics in different countries. However, this should be balanced against the cost of translations and implementations in different regulatory regions.

**Data entry:** Clinics should be vetted for appropriate infrastructure to provide data input and resources to provide long-term follow-up. Data entry, in addition to everyday clinical tasks, is burdensome. These might be standard expectations for a clinical trial but not so for a voluntary registry. During the selection process of clinics, clearly define and confirm reciprocal responsibilities and expectations. We chose, at the time, to notify clinics that they could review the proposal to participate online, register and receive access to the registry platform. Registries are suitable investigational projects where investigators with variable experience levels can be involved. This opens opportunities for less experienced investigators to participate in research projects. Such sites may, however, lack proficiency in regulatory aspects and may need more assistance to maintain compliance.

**Incentives:** To motivate ongoing participation, all contributing stakeholders will need general incentives. The registry can be offered as a service that provides a means for the clinics to collect data systematically and access their own collated data for publication or patient counselling, as well as be part of the collective research on a larger scale.

**Clear documentation** means developing concise and easy-to-understand materials that assist in fulfilling all aspects of a registry. It involves creation of the master protocol, registry agreements, master versions of all instructions and report forms, data-entry portal frameworks, etc., all of which may require translations for international registries. There needs to be checks and validation of the accuracy of translations and any appropriate cultural adaptations. This can be time consuming and costly. In some regulatory domains the registry may be considered a retrospective study, in others as non-invasive, but still a clinical study. This can have implications for additional documentation requirements (for example, applying the ISO 14155 standard to a registry “study” under EU MDR 2017/745).

**Data Collection Procedures:** Make every effort to reduce the barriers to data entry. The process through which data is collected needs to be seamless, easy and require as little time as possible and, to be sustained, the amount of data requested needs to be concise. Including a paper-and-pen mode of collecting data is potentially more time consuming; requiring report forms to be printed, given to
participants, and then re-entered, often by the clinic personal, into the registry’s web portal. Re-entry of data may not only generate entry errors but is time consuming and may lead to reduced compliance over time, especially as more subjects are enrolled in the registry [Zaletel 2015].

**Ongoing Management**

**Data Management:** If it is deemed necessary to have external builders/contractors for the database, it is essential to keep an overview of data completeness and quality through diligent monitoring and reports. Dashboard views available to the steering committee aid in spotting problems as early as possible so that timely rectifications can be implemented. It may be possible to build in recruitment targets and use risk-based triggers for initiating monitoring actions to improve recruitment or increase data completeness. The registry platform should enable a fully automated electronic audit trail to allow traceability of all changes to data-entry made over time, including by whom.

**Data Completion Reporting:** We learned that the best option were automated and more frequent reports of data completion for registered patients. Also keep informing clinics that all data intervals were acceptable; that is, skipping a test period does not eliminate that subject from later analysis as long as baseline data had been collected. Strict oversight of missing data and attrition rates is paramount for the registry to enable identification of issues readily, implement mitigation and ensure delivery on its objectives.

**Monitoring:** A monitoring plan needs to be in place before data collection begins. It includes monitoring on a site-by-site basis at either all or select participating sites. Monitoring involves oversight of all administrative and regulatory aspects in participation in the registry. Keep in mind that applying compliance requirements normally associated with clinical investigations may overload a voluntary registry and cause failure to deliver. Monitoring, which can be done on site, remotely or a combination of both, should occur at regular intervals throughout the life of the registry [Gliklich 2020]. The budget impact of monitoring activities should not be underestimated.

**Training:** Upfront planning of an appropriate mode of training that can readily reach all contributors is key. Often this may require the availability of online training platforms and specific guidelines in different languages, as contributors will be widely distributed nationally and internationally. Local visits by sponsor representatives, as well as question-and-answer regional webinars will help to confirm the efficiency of data entry and follow up. Introduce the relevance of the registry along with the registry protocol and its procedures. Describe the outcomes and potential opportunities for their report and publication and why complete datasets are more powerful and remain essential to the goal of the registry [Zaletel 2015]. Regular newsletters, summaries of reports and publications, yearly investigator meetings and refresher training sessions can add to a sense of shared responsibility in the study group, and help increasing compliance to data provision and procedures. Training records should be collected to maintain oversight.
**Personnel on and off-boarding:** Registries running over a long timeframe will see staff changes at participating sites as well as with the sponsor. Clear processes for contributor on- and off-boarding are required, including creation and closure of accounts, onboarding training and respective documentation. A part of the off-boarding process must be a critical check of all necessary documentation (i.e. CVs, training logs) being filed as retrospective requests may not be possible.

**Financial commitment:** Registries may suffer from insufficient funding, especially if they run over a long period of time. Sponsoring a registry requires the far-reaching vision to see the project through delivery on its objectives and acknowledge the high costs involved [Berettini 2011]. It is, therefore, important to have regular progress reviews with the sponsors, ensuring the registry is delivering on their expectations [Gliklich 2020].

**External and Internal Audits:** Audits are concerned with checking the overall study conduct at the sponsor level, ensuring adequate study oversight and documentation according to the sponsor’s Standard Operating Procedures (SOP) which in turn should now be compliant with ISO14155:2020. They are therefore more associated with quality assurance [Ravi 2018, Maddock 2007]. These audits ultimately required much more oversight than anticipated for IROS. Internal audits are voluntary; initiated by the sponsor and eventually conducted by a qualified consultant. Audits are valuable in informing the sponsor of potential compliance weaknesses at any given time, allow addressing them in a timely manner. This can prevent more drastic actions as a result of an unannounced (external) audit, for example, by a Notified Body.

**Data Analysis**

**Statistics:** Statistical analysis should be planned and described in the planning phase. Keep in mind that a long-term registry acquires large amounts of data. This potentially allows stratification by patient profile. Registries offer an opportunity to mine the data for analysis of different subgroups, given adequate statistical numbers are accrued. It is, however, essential to first address primary goals of the registry, while being open to learn from interesting and valuable new information that may be revealed. Non-inferential data ‘analytics’ can be useful, but high-quality statistical analyses should be the main aim. We note that this can be time-consuming and expensive.

**Measure of Success:** These are concerned with being able to make projections as to how the data will unfold and further guide the planning of monitoring activities. As progress is checked against specifications of the protocol (goals), it is important to interact with each centre to address deficiencies and data problems and to then make adjustments promptly. For Cochlear, the measure of success was primarily the capture and report of sufficient patient-related longitudinal outcome data from a broad population of implant recipients to represent benefits in the real world. This enabled further analysis and interpretation of treatment benefits for the various patient subgroups involved.

**Missing data:** It is not possible to mandate data entry for a commercial patient-registry; therefore, it is wise to anticipate and account for a greater attrition rate than in rigorous clinical trials [Gomes 2017].
This can be factored in when considering the end points of the registry. Rigorous statistical treatment of data sets including enrolled individuals that are followed-up versus those that are lost to follow-up should be performed (Lenarz 2017, James 2021). It also is prudent to consider accounting for aspects that may influence or skew interpretation of the data in a voluntary registry such as how a registrant was recruited; the guidance provided to subjects on the completion methods of forms and questionnaires; and by whom and timing of evaluations.

**Data Access:** In addition to the statistical analysis strategy driven by the registry sponsors, contributors need to have access to their own data in a comprehensive form and format [Gliklich 2020]. This may include raw data access in a compatible form that can be used with common statistical packages. However, our experience revealed that when requested, provision of data reports that investigators could utilize in their own locally generated reports and presentations was greatly appreciated.

**Closing the registry**

**Closure timing:** A registry should have a defined lifespan, with trigger-points for reappraisal of the needs and conditions for continuation. In the case of IROS, we chose to close the registry for a number of reasons, including changes in regulations including related documentation requirements; a decline in patient recruitment and follow-up; and changing requirements for PMCF.

**Database closure:** Clinics need to be informed of the pending closure of the database in good time. This is somewhat opposite to the general rule for planned closure of clinical studies where all subjects would be required to complete evaluations according to the clinical protocol. Initially, the database should be frozen to allow for data queries to be answered before the database is closed.

**End-of-study report:** It is good practice to produce a final report which describes and analyses all the data collected according to the original registry plan. In some regulatory environments the registry may have been granted approval as a clinical study and, thus, the required Clinical Investigation Report (CIR) will need to be filed within a prescribed frame (e.g. one year) after closure. Notifications and reports to approving Ethical Committees will be required at study closure.

**Publication:** Some aspects of the registry data may be of more interest than others for publication; however, like clinical studies, publishing the primary and secondary outcomes from the registry for all or select patient groups as far as possible is advisable, both for transparency and to share the learnings and knowledge gained. In addition, summary reports describing the registry findings may need to be completed where the registries have been listed on public clinical trial portals.

**Outcomes**

Alongside considerable learning about the conduct of a company sponsored registry, the IROS registry was considered a success, achieving its goal in providing a view to real world benefits from hearing implant treatment.
The IROS registry succeeded in enrolling a large cohort of users of an implantable hearing solution, in particular CIs, who provided longitudinal real-world data. These data were utilized at various intervals to generate a wide range of local and international conference posters or presentations as well as articles and publications in peer-reviewed journals. Scientific findings for CIs from the IROS registry have been published in several papers [Czerniejewska-Wolska 2015, Lenarz 2017, Wyss 2019, Müller 2021, James 2021]. Pooled data could identify outcome trends as well as provide input for the design for more robust comparative studies.

Furthermore, it serves as an example of a large prospective observational study design yielding meta-analysis possibilities. The available data from adult CI-users was used to investigate the potential to reduce the number of SSQ49 questions administered while maintaining the required sensitivity to changes in self-reported hearing benefits over time. Statistical comparison was performed to compare the outcomes from the administered long version SSQ49, to the extracted subset of 12 questions for the SSQ12 [Noble 2013]. The analysis confirmed clinical equivalence between the long and short version questionnaires and thus a potential to save response time [Wyss 2019]. Consequently, the SSQ12 is now used standardly by Cochlear for studies and evaluation in the field of implantable hearing solutions.

**Recommendations For The Future**

There is an abundance of recommendations for developing a registry [Gliklich 2020] available but given our 10-year experience, we can succinctly focus on four points for distinct recommendations:

**Reduce site workload as much as possible**

Moving forward, two options are either to establish a clinic-based registry where source data derives from information collected by investigators or utilise directly generated patient-sourced data. The first faces the greatest challenge we experienced, which was insufficient resources in some sites. Since IROS deployed a combination of clinician-reported and patient-reported data collection, our recommendation is to focus on employing PROMs that can be filled-in directly by patients [Mandavia 2018] and without the need for a clinician to be involved with data entry.

**Develop an interactive registry**

Utilise web-based data entry with a simple interface, the operative word being simple. The more automatization in data collection and management the better; nonetheless, this will come at increased design and implementation costs. An online chat advisor to participants and clinics to support data entry may be useful, as well as something such as a hotline for those having special enquiries. Choosing a Software as a Service (SAAS) registry platform provider might be of advantage, as a state-of-the-art provider will ensure their platform stays current with new developments, including evolving regulations for data privacy. A truly interactive registry however, is better supported by newer technologies only available within the last decade [Christian 2018].
Utilise modern-day digital communication modes

As early as 2016, social media platforms have been called out as a potential medium for data collection opportunities [Thwaites 2016]. Social media is widely utilized by individuals of all ages, via mobile devices that include smart phones and tablets [Melvin 2019, Callahan 2019]. As such, these devices present an opportunity for further consideration and leverage as data entry tools for health-related data within today's communications environment. In a study conducted on this topic, it was concluded that it is an efficient means for patients to enter their own data, particularly QoL data, and that participants are keen to contribute to data entry via apps [Mandavia 2018].

Cochlear has already successfully instituted several proprietary applications for use as patient surveys. Issues in addressing patients directly must be considered and overcome by various methods. For example, making information obtained from patients directly available simultaneously to their health care professional, and as appropriate, to the sponsoring company. At the simplest level, there only needs to be appropriate access control and automated announcements and reminders for survey completion. Developing an app for remote responses may lead to the creation of new and better registries using modern data retrieval methods. The future of international registries lies in direct digital interaction with patients and reduction or elimination of clinic overload. The idea is to provide ease of data entry at any time and place; to be able to partially enter data and complete at the patient's convenience. This may lighten the load of data entry for the patient in offering more flexibility and choice in how and when data is provided, ultimately leading to more patient empowerment. Note that the ability to use an app could be, in itself, a built-in bias: participants must have the financial means to own a smart phone and be able to use the technology.

Find the most efficacious means to motivate all participants with varying levels of feedback

Consider and monitor motivation to clinics and what their rewards might be for committing to the patient recruitment and data collection process such as publication and access to data after a reasonable dataset is acquired to enable valid reporting. Confirm progress towards agreed milestones that may include patient enrolment, complete data sets, commitment to publish papers or present data over a given period of time and offer assistance in their creation. These may also serve as incentives to investigators to continue to collaborate. Patients may see benefit by self-monitoring their progress over time on self-reported measures, having appropriate access to their own data in an understandable summary format. More frequent and relatable feedback may also help incentivise patient responses over time which may be possible via applications for smart phones and or home-based computers.

Regardless of whether a traditional registry or one run via a specially designed application for mobile devices, it is worthwhile to conduct a feasibility test for the registry application; in particular, first run a pilot test of implementation.

Closing remarks
It is no small endeavour to collect a large dataset over an extended observation time frame that is representative of a treatment in a large population pool, especially one that is voluntary. IROS developed, maintained and effectively captured and harvested data through an international registry. It was the first international registry in the hearing field, pioneered by Cochlear to provide evidence from longitudinal self-reported, patient-related outcomes. Design and initial small-scale implementation proved to be relatively easy compared to longer-term conduct on a much larger scale. In particular, maintenance of required updates, cultural adaptations, sustaining data entry efforts for both new and existing registrants, performing data analysis, and providing reports demanded significant resources. We propose that it is necessary to focus resources to best support the primary end goals. Selecting and adapting meaningful self-reported patient-related outcome measures, coupled with data capture from large and small clinical facilities across countries and languages has enabled meta-analysis of the collective longitudinal data. The information provided has led to a better understanding of real-world benefits including hearing in daily life and generic quality-of-life benefits after treatment with hearing implant solutions, primarily CI for a broad treatment population.

**Declarations**

**Ethics approval and consent to participate**

This study involving human participants was reviewed and approved by Health Research Ethics Committee 1, Stellenbosch University, South Africa (reference N15/02/015). The patients/participants provided their written informed consent to participate in this study.

**Consent for publication**

Not applicable

**Availability of data and materials**

Not applicable

**Competing interests**

All authors (HM, JK, CI, JW) are employees of Cochlear Ltd or its regional subsidies

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**Author Contributions**

As a corporate project, all authors are employees of Cochlear. JW conceived of the registry and had conducted and analysed the running of the registry contributing insights. HM, JK and CI have contributed critical observations as to the long-term management and organization of IROS. JK initiated and led the
close out of IROS. HM and JW performed literature review and initial writing, all authors extended and revised the manuscript.

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**Figures**

**IROS REGISTRY TIMELINE**

Flow diagram depicting IROS from conception to closure
Figure 2

Main external cost items.

- LICENSES AND APPROVALS
  - Evaluation tools
  - Electronic Data Capture system (EDC) setup and maintenance (registry database)
  - EDC license per user/centre
  - Ethics Committee (EC) approvals (if required)

- INFORMATION DISSEMINATION AND MATERIALS
  - Statisticians
  - Medical writers
  - Publication fees
  - Translations

- MONITORING
  - Fees by external Contract Research Organization (CRO)
  - Clinical Research Associate (CRA) travel expenses

- TRAINING / COMMUNICATIONS
  - Communication platforms
  - Venues for meetings
  - Travel for Staff
  - Training forums