Cancerworld

Telemedicine on the path to personalised treatment

Adriana Albini / 19 October 2022

Telemedicine has been defined as the use of telecommunications technology to deliver health care to populations with limited access to care. However, its increased adoption in the past couple of years, triggered by the Covid-19 pandemic and the constant development of new technological solutions, are showing a vaster range of benefits for everyone, from financial to quality of life, from timesaving to better allocation of resources, ease of multidisciplinary consultations, monitoring, and so on.

Telemedicine has now been tested in multiple settings and has demonstrated to be at almost equivalent to in-person care in certain situatios. Furthermore, it has the potential to deliver a more personalised care, through AI, patient questionnaires and interprofessional consultations. Because of the complexity of cancer care, which requires multidisciplinary teams, teleoncology has proven particularly successful, so much so that is has been hailed as the fourth (albeit the youngest) pillar of oncology, next to surgical, radiation, and medical oncology (Puneet Pareek et al., JCO Global Oncol 6:1455-1460.) Due to a dearth of oncologists around the world and an ageing population, the possibility of performing remote or supervised surgery and chemotherapy treatment is being explored with good results. In the Queensland Remote Chemotherapy Supervision (QReCS) model, rural generalist nurses administer chemotherapy and other therapy agents under the supervision of specialised nurses from a tertiary centre via videoconferencing. Implementation of QReCS started as far back as 2014. In Spain in May 2022, a breast cancer surgery was performed for the first time, which was remotely supervised by a second surgeon using augmented reality and 5G.

In cancer treatment, beside remote intervention, telemedicine can help towards devising and implementing more personalised, patient-centred therapies, partly because of its overlap with digital health and Real-World Evidence. At the SPCC and ASCO online conference “Telemedicine in Cancer Care Continuum: implementation and integration”, **Massimo Di Maio**, medical oncologist at the

University of Turin, Italy, gave a presentation on the potential and the limits of telemedicine from Real World Data to Real World Evidence. **What is the role of Real-World Data and Real-World Evidence in oncology?** We usually consider large randomised control trials (RCTs) as the most solid source of evidence for clinical practice. However, they have a number of limitations, for instance they might ask questions of commercial rather than clinical interest, show statistically significant but clinically not so relevant results, or select patients who do not represent those seen in everyday practice (Ian Tannock et al., Relevance of randomised controlled trials in oncology, *Lancet Oncology* 2016; 16: e560-567). Such weaknesses are reasons to search for Real-World Data and Real-World Evidence to integrate the results coming from pivotal trials and from randomised control trials.

The FDA definition of Real-world data (RWD) is: "the data relating to patient health status and/or the delivery of health care routinely collected from a variety of sources" (such as electronic health records, product and disease registries, etc.) While "Real-world evidence (RWE) is the clinical evidence regarding the usage and potential benefits or risks of a medical product derived from analysis of RWD." Real-World Data and Real-World Evidence are not just valuable in terms of our scientific knowledge. The FDA and other agencies are increasingly recognising their role in regulatory decisions and regulatory approval of treatments.

In 2020, Di Maio and his colleagues Franco Perrone and Pierfranco Conte, published a review on *The Oncologist* to discuss the opportunities and limitations of Real-World Evidence, specifically in the oncology field (Di Maio M, Perrone F, Conte P. Real-World Evidence in Oncology: Opportunities and Limitations. *Oncologist*. 2020 May;25(5):e746-e752). Some of the strengths of RWE in the description of treatment efficacy compared to RCT are a lower selection bias, focus on efficacy in special patients' populations, and production of evidence in settings suffering from the absence of an RCT. While among the limitations there can be a lower quality of data sources. Other opportunities are, for instance, the use of treatments within specific geographic and/or economic context which allows to produce pharmacoeconomic data within specific countries and specific health systems different from those where the randomised control trial has been produced.

Another important field of Real-World Evidence in oncology is the **description of treatment toxicity** and tolerability. For instance, description of rare toxicities based on a potentially larger number of patients compared to those enrolled in randomised trials; description of tolerability in a population which is more heterogeneous compared to the randomised control trials; description of tolerability in a special patient population; description of long-term toxicities, as the follow-up in clinical practice can be longer compared to the limited follow-up which often characterises pivotal trials. And, most important, the incorporation of Patient-Reported Outcomes (PROs) into the description of toxicity, which could enhance the description of adverse events from the patients' perspective. Of course, the limitations of RWE are that it is potentially less accurate than RCTs.

What are the challenges for telemedicine in RWD & RWE? Advances in digital health, a proliferation of digital devices, new support tools for medical decision, can all generate big data and hence novel types of Real-World Evidence in cancer care. There are **four main stages** in this process. The first is the **patient and caregiver consent**. The changes in this stage brought by digital technology include new ways for patient consent, for instance in electronic form. There are also increasing opportunities for patient engagement and a more holistic disease and treatment approach. The challenges, of course, are the patient's comfort with data and information sharing; there can be patient concerns over data misuse and security; there may be a selection "bias", because less digitally literate patients could be under-represented. And last, but not least, we are still dealing with multiple interfaces and multiple technical solutions, that should be linked. The second stage is **data collection**. The changes here are new ways to collect data and new data types and sources; location of data collection can be decentralised and closer to the patient, and we have

the ability to collect data 24/7. The challenges are the implementation of the necessary technical infrastructure; maintaining patient engagement in digital activities; there must be patient willingness for all stakeholders to have access to all the collected information. The third stage is **data storage**, transmission, and aggregation. Changes we will observe in the near future are improved server capacity to store high volume, high velocity, and a wide variety of data. We will witness new ways to process data and will be able to link data from digital devices to the patient's electronic health record. This is crucial for a large-scale use of RWE in clinical practice. The challenges in this stage are the very high volume of data to be stored and transmitted; there is still lack of interoperability across multiple systems and technologies; transmission of data requires reliable internet connection; and all necessary requirements for data security, integrity, and harmonisation must be met. The final stage is the **use by stakeholders**. The changes are a wider variety of data sources; additional data will increase clinical decision support. And, to summarize, we will see a transition from population health management to patient-level support. The challenges are: uncertainty over stakeholder acceptability of digitally derived insights; stakeholder's ability to transfer, receive, store and process large volumes of data. Also, inadequate application of digital health could drive up healthcare costs.

The future: remote monitoring of symptoms during routine cancer care

Traditionally, we have measured Patient-Reported Outcomes with paper questionnaires but now the time has come to use remote monitoring, allowing the patient to use a mobile phone or other electronic devices. The flow of information coming from the patient can be implemented in real-time in the Electronic Health Record and generate alerts to nurses and oncologists to manage the symptoms reported by the patient. So, this is not only a way to produce and store data, but also a way to improve the management of cancer patients. The Covid pandemic made the oncology community more aware of the importance of remote monitoring, of the adoption of electronic PROs in cancer clinical practice.

In the meeting Dr Paul Cornes discussed the cost-effectiveness of telemedicine and the post-Covid: "many of the programmes that started during the "lockdown" phase of the COVID pandemic were in fact born as a stop-gap measure. But given the great impact they will probably remain long term".

The advantages of the adoption of ePROs are: systematic check of the clinical trend of important symptoms and side-effects; prevention of severe adverse events needing ER access and hospitalization; efficient screening of patients who need further phone assistance or direct medical intervention; prompt management of medical needs; positive psychological impact on patients and increased patient satisfaction with healthcare services. The challenges are lack of awareness among clinicians of the cost-effectiveness of this adoption, lack of awareness by hospital management of the importance of the incorporation of ePROs into medical health records, the need for education of patients and caregivers to fill in the questionnaires, and for clinicians on how to manage them. This year ESMO has produced the first guideline on the role of Patient-Reported Outcome measures in the continuum of cancer clinical care. This effort was coordinated by Dr. di Maio.

Florian Scotté is Medical Oncologist at the Institute Gustave Roussy, Villejuif, France, and has been a regular speaker at the SPCC webinars on telemedicine. On this occasion he spoke about the pros and cons of **Teleoncology for remote monitoring of treatments**. Remote medical monitoring is the interpretation of data collected at the patient's place of living by a professional and sent to other professionals in order to manage the patient. It can manage anticancer treatment, monitor and manage adverse events, monitor the patient's journey, but also it allows for patient-professional interactivity.

As pointed out by Ethan Basch in 2010 in his article for the *New England Journal of Medicine*,

entitled "The Missing Voice of Patients in Drug-Safety Reporting", there is a gap between patients living with symptoms and the clinician's perception. This gap can be decreased by the use of digital devices. There are discrepancies between the patient's and the professional's perspectives concerning, for instance, side effects and their intensity. The two visions need to be combined in order to provide the best approach. **PROCHE** (programme for the optimisation of chemotherapy administration) was developed at the Georges-Pompidou European Hospital with the objective of anticipating drug delivery and evaluating toxicity profile by a medical call centre dedicated to the oncology unit. A nurse phoned the patient two days before the appointment with a questionnaire. The information collected, together with biological data, was forwarded to the day hospital where the oncologist decided whether to go ahead with the treatment session, adapt protocols, postpone, or cancel. The use of this programme proved to decrease patient waiting time in day hospital, but also to alleviate certain symptoms, such as fatigue, pain, etc.

The next step was the **STAR** (Symptom Tracking and Reporting) study presented by Ethan Basch at the ASCO meeting in 2017. Cancer patients receiving out-patient chemotherapy were randomly assigned to self-report 12 common symptoms via tablet computers or to usual care. Outcomes showed a survival gain for patients under remote monitoring compared to usual care. There was also improved quality of life with remote monitoring, and a significant decrease in emergency visits. The study had a huge impact on the future development of digital health.

The same year Fabrice Denis published the article "Randomized Trial Comparing a Web-Mediated Follow-up with Routine Surveillance in Lung Cancer Patients". The results of that study demonstrated that it was possible to detect early relapse in patients with lung cancers by using symptoms monitoring.

The **CAPRI** (CAncérologie, Parcours, Région, Ile de France) study also compared one cohort on standard of care and another with nurse navigators using a digital device or telephone calls. The study demonstrated increased relative dose intensity, but also a decrease of grade 3-4 toxicities, a decrease in emergency visits and improvement in patient experience.

Remote monitoring of patients with PROs could play an important role towards more personalised cancer care, but information is still limited about the clinical utility and user perceptions of these systems. **PRO-TECT** is a trial evaluating the implementation of PROs in cancer care. To elicit feedback, surveys were administered to participating patients and clinicians. In 2020 Ethan Basch published the first results of the study. While the vast majority of patients were satisfied with the questionnaires and felt that the information they provided was used by the clinicians for care, nurses were still positive, but less keen, with 30% of them stating that they would not use the system in the future. Nurses and patients involved in such a process can have different perceptions, and some of them do not want to use this kind of programme. It is important to understand why in order to improve the system. Nurses, for instance, raised concerns about potential added workload from symptom alerts. As to physicians, most of them actively reviewed PROs and stated that the information was useful. Yet only 20% of them used the reports to make treatment decisions. In daily practice, physicians are still not ready to use digital reports to manage their patients. Again, this is probably due to a clash of perspectives, whereby the way questions are tailored in order for the patient to understand them, can make the answers too vague for the physician to gain enough information for decision making.

Widespread use of Real-World Data and Real-World Evidence needs to overcome many technical, logistical, financial, and educational challenges, and remote monitoring of symptoms with PROs needs to find a formula that allows for all the parties' perspectives to be clearly understood, but both forms of telemedicine will eventually lead to more personalised and safe treatment.