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Telehealth models could be extended to conducting clinical trials- A Teletrial approach

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Access to specialist cancer care services is a significant issue faced by residents of rural, remote, Indigenous and some regional communities in countries with large rural populations (Hazin and Qaddoumi, 2010). Lack of access to specialist services may be due to lack of availability of specialist oncologists locally, limited scope of practice of other rural health professionals and/or overall rural workforce shortages. Poor access to such specialized health care services could be one of the contributors to the disparity in survival and disease related outcomes that exist between metropolitan and non-metropolitan patients (Australian Institute of Health and Welfare, 2008, Jong KE et al., 2004, Coory MD and PD, 2005, Sabesan and Piliouras, 2009), although it is acknowledged that this issue is complex and may also relate to other factors such as behavioural or cultural factors.

In relation to clinical trials, patients living outside of major metropolitan centres face many barriers in accessing clinical trials including those involving new, experimental therapies, though participation in clinical trials is recommended as the best option for many cancer patients by international guidelines such as the National Comprehensive Cancer Network (www.nccn.org) and an analysis of 21 SWOG studies supports the NCCN recommendation where trial participation was associated with better one year survival for all 10 poor prognosis studies (Unger JM et al., 2014). These barriers include the lack of availability of trial sites closer to home and as a result, the cost and inconvenience of travel to major centres undertaking clinical studies (Sabesan S et al., 2011, Comis RL et al., 2005).

Teleoncology models of care have been shown to satisfy many specialist health care needs of rural and regional patients in the field of medical oncology in countries with large rural populations (Hazin and Qaddoumi, 2010). Using teleoncology, internationally many cancer centres have been able to facilitate the

administration of complex chemotherapy in rural and regional areas (Sabesan S et al., 2012, Doolittle GC and Spaulding A, 2006, Palkhivala A, 2011). Around the world, such centres have implemented safe and successful teleoncology models that are acceptable to patients, families and health professionals, save money to the health system and enhance the capabilities of rural health systems in oncology services as part of core business (Doolittle GC and Spaulding A, 2006, Weinerman et al., 2005, Sabesan et al., 2012, Thaker D et al., 2013, Sabesan S et al., 2014b, Doolittle et al., 1997, Chan B et al., 2015). In addition, medical oncology services can be delivered to rural patients closer to home in a timely manner through this model (Sabesan S et al., 2014a). Yet, the current arrangements for conducting clinical trials do not allow for rural and regional sites with limited resources and low patient numbers to easily take part in clinical trials whether these relate to phase 3 comparative effectiveness trials or novel therapies.

We believe that the oncology community can take advantage of existing teleoncology models to enrol, consent, treat and follow up patients on clinical trials closer to home, not only providing these patients with access to best practice care, improving the quality of care locally, but also increasing the numbers of patients enrolled onto clinical studies.

Teletrial model

Teleoncology models offer the opportunity to provide access to clinical trials closer to home for patients living in rural or regional centres outside of major metropolitan hubs by providing availability of trials closer to home and reducing the need for travel to larger centres. The concept of the Australasian teletrial model was developed by the regional and rural group of the Clinical Oncology Society of Australia (COSA) and was endorsed by the COSA Council in August 2015. Using telehealth, patients from rural/regional sites (satellite sites) can be recruited and treated closer to home by established sites initiated as the primary trial sites (Figure 1). While broad principles for primary and satellite sites are the same across the board, site specific governance and processes need to be developed for effective implementation.

Figure 1: Australian Teletrial model

Broad principles of Teletrial governance can be summarised as below:

1. Satellite sites are created using teleoncology models without the need for separate site initiation and establishment costs and activated as part of trial clusters (Figure 2).

Figure 2: A teletrial cluster

Trial clusters may exist in the following settings:

- (1) Larger urban centres as primary sites with other larger centres as satellites even within the same city
- (2) Larger urban centres or regional centres as primary sites with regional or rural sites as satellites

2. Patients from satellite sites are consented, recruited and treated close to home (in collaboration with doctors and nurses at satellite sites) as if they are patients at the primary sites, using teleoncology models

3. During consultations, details of complications are recorded by the primary site. For treatment related data, unless the sites are connected by the same electronic medical records (EMR), scanning and sending the nursing notes to primary sites in a timely manner will be important. For more complex regimens, direct observation and monitoring at satellite sites can be performed using remote supervision models such as those based on the rural telehealth models

(<https://www.health.qld.gov.au/circs/Docs/QReCS%20Guide.pdf>).

Factors to consider in the development of implementation processes

Whilst many factors need to be considered and addressed before teletrial models can be adopted as a routine, none are insurmountable. Factors for consideration include workforce, clinical trial training, medico-legal issues, ethics and governance (including financial aspects), indemnity, pharmacy services (including trial drug documentation and handling where relevant) and the management of trial-specific toxicities.

Under current teleoncology models, specialists at a primary site provide their services using videoconferencing. The type of technology required depends on the complexity of the medical therapies provided at remote sites. While dedicated videoconferencing equipments may be ideal in complex situations, most centres around the world utilise web based systems to provide majority of their services. In this instance, only limitation might be the speed and connectivity of internet systems. Service delivery is supported and facilitated by doctors, nurses and allied health professionals at a satellite site. The nature of support required at satellite sites would be determined by the complexity of the clinical services to be provided locally as well as the training and experience of those based at satellite sites (Sabesan S, 2014, Doolittle and Allen, 1997). Using the teleoncology medical oncologists and trial coordinators from primary sites can help obtain consent, recruit, treat and monitor patients at satellite sites during routine or trial-specific consultations depending on the type of study as illustrated in figure 1. Clinical encounters can be documented at both the primary and satellite sites (if both sites share the same electronic medical records (EMR), data entry will be simultaneous). Therefore, most of the source data is available at the primary site. When EMR is not available, data can be collected and coordinated using standard methods by the primary site trial coordinators. This enables the trial coordinators based at the primary site to monitor and attend to issues without travelling to satellite sites.

One advantage of the collaboration between primary and satellite sites is in the area of ongoing education and training, notwithstanding that a key investigator at each site should have undertaken one of the many on-line Good Clinical Practice training courses. When training for all the sites in a cluster is required, videoconferencing is an effective method to cover a large geographical area.

As is the case in most teleoncology models, it is important to establish certain aspects of trial management at the outset. Defining roles and allocating specific responsibilities to staff within a cluster can ensure the safe and efficient conduct of clinical trials. This is particularly important for reporting and managing serious adverse events. When serious adverse events occur, mechanisms need to be in place for alerting

the primary sites, review and management of patients by primary and satellite site medical officers using videoconferencing and documentation.

The primary site should be the coordinating site for trial related matters including management of medications and funds within a cluster, so that trial organisations (pharmaceutical companies, co-operative trial groups or contract-research organizations) have a central point of contact. In terms of remuneration of sites, there are administrative efficiencies if invoices for trial related expenses at satellites sites are also dealt with by the primary site. Generally most of the expenses related to staff will be covered by existing work contracts and funding mechanisms that exist for routine operations. Not all the expenses may be covered but reimbursement of such expenses can be managed by simple site-site agreements, although comparative-effectiveness studies should not incur any substantial additional costs in any case. In our view, indemnity should not be an issue as more and more institutions are covered by State-wide indemnity agreements. Notwithstanding such processes, it is possible that some negotiations may have to occur at jurisdictional levels to elucidate any outstanding indemnity related matters, depending on the type of trial. Contractual, ethical and governance processes can be expedited when common standards and strong collaboration are established between primary and satellite sites within clusters.

Once the primary sites are chosen, allocation of trials for each site within a cluster would depend on the complexity of the trials and the medical, nursing and pharmacy capabilities of those satellites. For sites that have never participated in clinical trials before, it is likely that there would be a staged approach as suggested by existing remote chemotherapy supervision models (<https://www.health.qld.gov.au/circs/Docs/QReCS%20Guide.pdf>). Initial stages could include comparison of standard practices and studies involving less complex medications. When larger centres are involved in a cluster or when smaller satellite sites have become more capable, it will be easier for site to undertake trials involving intravenous and more complex medical therapies.

Expected benefits:

Based on the model outlined, many smaller satellite sites can be created as part of trial clusters without the need for separate site initiation and establishment costs. This model has the potential to make clinical trials accessible to patients from rural, regional and other low income and underprivileged settings closer to home. It may also allow recruitment of patients with rare tumours into trials open in only one centre in

a large city or indeed a country! In terms of trial recruitment, the number of patients participating in clinical trials when a teletrial is broadly implemented across multiple regional and rural centres is likely to increase thus making the recruitment timeframes shorter. In addition, more collaboration and networking between rural and metropolitan centres and improved regional and rural capabilities are likely to result in better cancer care across these areas that could potentially reduce the disparity in cancer outcomes in geographically dispersed populations.

What is next?

While some of the governance issues mentioned herein can only be resolved by inter-jurisdictional policies, implementation of teletrial models is feasible if investigators, pharmaceutical companies and cooperative trial groups consider these opportunities and incorporate these models into their protocols from the outset. Funding bodies can also play a role by favourably considering protocols that accommodate teletrial models or indeed other models that expand the access of geographically, culturally or economically disadvantaged patients to multicentre trials.

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