across specialties, particularly in the field of tissue and organ bioengineering, although they are currently limited to laboratory trials.

In contrast, five surgical specialities had category B evidence as the highest evidence category - these included General Surgery, Neurosurgery, Orthopaedic Surgery, Urology and Vascular Surgery. Based on the characteristic of category B the evidence is considered equivocal and the use of stem cell treatments unproven.

For the three remaining specialties (Otolaryngology Head and Neck Surgery, Paediatric Surgery and Plastic and Reconstructive Surgery), the evidence base was limited to category C. This indicates that there is little or no comparative evidence, and the use of stem cells is considered experimental.

The published evidence-base, demonstrates a large variability across a number of domains. Cell-based therapies vary depending on the origin of the stem cells, their manipulation and their intended use. In terms of the sources of stem cells, this report identified that (autologous) ASC and BMSC are commonly used for treatments. ASC is most commonly collected by liposuction from abdomen adipose tissue. Bone marrow is harvested from the posterior iliac crest. However, the stem cells density and dose for each treatment varied so the ideal dose for each treatment is unknown.

The lack of standardisation between published stem cell trials and other research studies in terms of isolation, manipulation and expansion protocols makes comparison between studies difficult.

What does it mean for surgeons and their patients?

Unfortunately, stem cells are not an established or recognised intervention for surgical practice. There remain a concerning amount of unknowns. None of the stem cell treatments provided in the private clinics in Australia and New Zealand had proven evidence for safety and effectiveness. As such, surgeons should not feel pressured to undertake these novel procedures simply because they are aware of others who are providing them. Unproven stem cell treatments risk harming patients and also bring risk to the clinicians themselves. Such treatments should be discouraged. A number of professional organisations including the Australian Rheumatology Association[5], Australian College of Sports and Exercise Physicians[6] and Motor Neurone Disease Australia[7] raise concerns about patient safety, absence of unequivocal evidence regarding safety or efficacy of these treatments, and lack of knowledge in terms of many aspects of stem cells and their function.

Although the technology is moving quickly and there is huge potential in the use of stem cells, many questions remain regarding their use.

Uncertain components include the matching of cell source and type to specific diseases /conditions, the need to expand stem cells following harvesting and the impact of laboratory processing on stem cell function as well as the cell density required to affect tissue repair. Important questions include:

- What is the best source of stem cells?
- How should stem cells be manipulated and expanded?
- For each indication, what is the appropriate density or dose of stem cells?
- For each indication, what is the mechanism of action in vivo and how do stem cells impact local tissue and biological processes?
- Are there negative consequences in the long-term?

However, the good news is that high-quality research is underway both locally and around the world. At the time of the review 34 ongoing clinical trials registered with the Australian and New Zealand Clinical Trials Registry (ANZCTR) were identified. Continuing research was uncovered in the ANZCTR for five of the surgical specialities; these being Cardiothoracic Surgery, General Surgery, Neurosurgery, Orthopaedic Surgery and Urology. Close to 70 per cent of the ongoing clinical trials in the ANZCTR are assessing stem cell treatments for orthopaedic Collectively this indicates greater research interest in stem cell treatments by surgeons in this craft group. In contrast, it appears the specialty of Otolaryngology Head and Neck Surgery is less impacted by stem cell treatments and researched for its potential.

> *"Treatments are expensive, costing from A$9,000 to $60,000 per treatment. As these services are not reimbursed by Australian or New Zealand governments ... this cost is paid by the patient"*

The upcoming review is highly anticipated and should provide much needed clarity around the use of stem cells in Australia. In the meantime the evidence vacuum suggests that we should all take care, whether from the perspective of a patient or a surgeon, and wait and see what the future will bring.

1. National Health and Medical Research Council. Stem cell treaments - frequently asked questions. National Health and Medical Research Council; 2013 [cited 2016 21/09]; Available from: https://www.nhmrc.gov.au/_files_nhmrc/publications/attachments/rm001a_stem_cell_treatments_faq_131220.pdf.

2. Coroners Courts New South Wales. Inquest into the death of Sheila Drysdale. NSW State Coroner's Court; 2016 [cited 2016 21/09]; Available from: http://www.coroners.justice.nsw.gov.au/Documents/Findings%20Drysdale.pdf.

3. National Stem Cell Foundation of Australia, Stem Cells Australia. The Australian Stem Cell Handbook. National Stem Cell Foundation of Australia; 2015 [cited 2016 22/08]; Available from: http://www.stemcellfoundation.net.au/about-stem-cells/stem-cell-treatment-information/handbook.

4. Therapeutic Goods Administration. Stem cell treatments and regulation - a quick guide for consumers. Australian Government; 2016 [updated 2016 06/04; cited 2016 /08]; Available from: https://www.tga.gov.au/community-qa/stem-cell-treatments-and-regulation-quick-guide-consumers.

5. Australian Rheumatology Association. A.R.A Position Statement on Stem Cell Therapies. Australian Rheumatology Association; 2014 [cited 2016 29/08]; Available from: https://rheumatology.org.au/downloads/ARA%20Position%20Statement%20042014.pdf.

6. Osborne H, Anderson L, Burt P, Young M, et al. Australasian College of Sports Physicians-position statement: the place of mesenchymal stem/stromal cell therapies in sport and exercise medicine. British Journal of Sports Medicine. 2015.

7. Motor Neurone Disease Australia. Position Statement: Alternative and Unproven therapies and people diagnosed with MND Motor Neurone Disease Australia; 2014 [cited 2016 29/08]; Available from: http://www.mndaust.asn.au/Documents/Policies-and-position-statements/Unproven-therapies-for-MND-and-the-internet.aspx.

8. Imaizumi K, Nishishita N, Muramatsu M, Yamamoto T, Takenaka C, Kawamata S, Kobayashi K, Nishikawa S, Akuta T. 2014. PLoS One. 9(2):e88696. doi: 10.1371/journal.pone.0088696.