NHMRC additional evidence and grades for recommendations for developers of guidelines

The following tables based on the NHMRC evidence guidelines demonstrate how treatment of osteoarthritis with ACBI is Graded C (Satisfactory) i.e. The body of evidence provides some support for use with osteoarthritis but care should be taken in its application.

Table 1: Body of evidence matrix

Component	A	B	C	D
	Excellent	**Good**	**Satisfactory**	**Poor**
Evidence base[1]	one or more level I studies with a low risk of bias or several level II studies with a low risk of bias	one or two level II studies with a low risk of bias or a SR/several level III studies with a low risk of bias	one or two level III studies with a low risk of bias, or level I or II studies with a moderate risk of bias	level IV studies, or level I to III studies/SRs with a high risk of bias
Consistency[2]	all studies consistent	most studies consistent and inconsistency may be explained	some inconsistency reflecting genuine uncertainty around clinical question	evidence is inconsistent
Clinical impact	very large	substantial	moderate	slight or restricted
Generalisability	population/s studied in body of evidence are the same as the target population for the guideline	population/s studied in the body of evidence are similar to the target population for the guideline	population/s studied in body of evidence differ to target population for guideline but it is clinically sensible to apply this evidence to target population[3]	population/s studied in body of evidence differ to target population and hard to judge whether it is sensible to generalise to target population
Applicability	directly applicable to Australian healthcare context	applicable to Australian healthcare context with few caveats	probably applicable to Australian healthcare context with some caveats	not applicable to Australian healthcare context

SR = systematic review; several = more than two studies

[1] Level of evidence determined from the NHMRC evidence hierarchy – Table 3, Part B

[2] If there is only one study, rank this component as 'not applicable'.

[3] For example, results in adults that are clinically sensible to apply to children OR psychosocial outcomes for one cancer that may be applicable to patients with another cancer

NHMRC Evidence Statement **ATTACHMENT 1**

(If rating is not completely clear, use the space next to each criteria to note how the group came to a judgment. Part B of this document will assist with the critical appraisal of individual studies included in the body of evidence)

Key question(s):			**Evidence table ref:**
1. Evidence base *(number of studies, level of evidence and risk of bias in the included studies)*			
Seven level IV studies on hip and knee osteoarthritis with SVF demonstrated symptom improvement. Of the seven publications six reported tissue improvements by MRI One level IV meniscus study demonstrated repair by MRI One conference proceedings of 1,128 patients with symptom improvement	A	**One or more level I studies with a low risk of bias or several level II studies with a low risk of bias**	
	B	**One or two Level II studies with a low risk of bias or SR/several Level III studies with a low risk of bias**	
	C	**One or two Level III studies with a low risk of bias or Level I or II studies with a moderate risk of bias**	
	D	**Level IV studies or Level I to III studies/SRs with a high risk of bias**	
2. Consistency *(if only one study was available, rank this component as 'not applicable')*			
All studies (eight, N=1299) are consistent with symptom improvement of osteoarthritis in the majority of patients. All studies (six, N= 48) that conducted MRI studies are consistent with evidence of tissue regeneration. One meniscus study (N=1) reported MRI repair	A	**All studies consistent**	
	B	**Most studies consistent and inconsistency can be explained**	
	C	**Some inconsistency, reflecting genuine uncertainty around question**	
	D	**Evidence is inconsistent**	
	NA	**Not applicable (one study only)**	
3. Clinical impact *(Indicate in the space below if the study results varied according to some <u>unknown</u> factor (not simply study quality or sample size) and thus the clinical impact of the intervention could not be determined)*			
The clinical impact is substantial as OA can only be treated by pain management prior to partial or total knee replacement. Osteoarthritis affects the ability to work, quality of life, has associated co-morbidities, and in comparison to joint replacement surgery it appears to have less serious adverse events	A	**Very large**	
	B	**Substantial**	
	C	**Moderate**	
	D	**Slight/Restricted**	
4. Generalisability *(How well does the body of evidence match the population and clinical settings being targeted by the Guideline?)*			
There is one caveat with generalizing this finding to the target population. Symptom relief and tissue repair is not the only desirable feature in the healthcare setting. The others are user acceptability in both patient and clinician, and cost.	A	**Evidence directly generalisable to target population**	
	B	**Evidence directly generalisable to target population with some caveats**	
	C	**Evidence not directly generalisable to the target population but could be sensibly applied**	
	D	**Evidence not directly generalisable to target population and hard to judge whether it is sensible to apply**	
5. Applicability *(Is the body of evidence relevant to the Australian healthcare context in terms of health services/delivery of care and cultural factors?)*			
There are some caveats in the Australian healthcare context. The main one is vested interests, revenue from standard practice in the joint replacement industry is high and the cultural divide between scientists and clinicians	A	**Evidence directly applicable to Australian healthcare context**	
	B	**Evidence applicable to Australian healthcare context with few caveats**	
	C	**Evidence probably applicable to Australian healthcare context with some caveats**	
	D	**Evidence not applicable to Australian healthcare context**	

Other factors *(Indicate here any other factors that you took into account when assessing the evidence base (for example, issues that might cause the group to downgrade or upgrade the recommendation)*

Strikingly positive results have been reported in some patients but there have been few prospective controlled studies. Also, the reasons for the beneficial effects are frequently unclear, as a result there has been a heated debate. One of the strongest arguments for regenerative medicine is that human cell-based therapies have the potential, which most molecular medicines for chronic conditions do not, of returning the patient to health with respect to that condition without further intervention. The major cost implications of side effects with present medicines are potentially in favour of regenerative medicine.

EVIDENCE STATEMENT MATRIX

Component	Rating	Description
1. Evidence base	D	
2. Consistency	A	
3. Clinical impact	B	Large clinical impact
4. Generalisability	B	Generalisable to adult osteoarthritis population
5. Applicability	B	Applicable to most osteoarthritis patients

Evidence statement

There is consistent level IV evidence of tissue repair and symptom relief in osteoarthritis patients.

RECOMMENDATION *What recommendation(s) does the guideline development group draw from this evidence? Use action statements where possible.*	**GRADE OF RECOMMENDATION**	**C**

The body of evidence provides some support for use with osteoarthritis but care should be taken in its application. The ACTS Code of Practice should be followed.