

# USE OF PROBIOTICS FOR THE PREVENTION AND TREATMENT OF DIARRHEA: A HTA FOR EVIDENCE-BASED HOSPITAL DECISION MAKING

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## OBJECTIVE AND METHODS

Probiotic utilization is increasing among healthcare settings but clinical use is quite heterogeneous and controversial.

### Objective

A health technology assessment (HTA) was conducted to assist decision making for the use of probiotics in the Centre hospitalier universitaire de Qu bec (CHUQ). The HTA was aimed to evaluate probiotics in the prevention of antibiotic-associated diarrhea (AAD) or *C. difficile*-associated diarrhea (CDAD), and in the treatment of acute infectious diarrhea in children and adults.

### Methods

- An interdisciplinary group was established and involved in the definition of the evaluation questions, interpretation of the study results, and contextualization.
- Scientific evidence review: Assessment and critical appraisal of the available literature on the effectiveness and safety of probiotics were carried on for any specified strain or dose (table 1). Article selection, quality assessment, and data extraction were performed by two independent reviewers using standardized forms (UETMIS, 2007). Disagreements were resolved by including a third reviewer to reach a consensus.

Table 1. Number of SRs and RCTs included in the scientific evidence review

	AAD prevention		CDAD prevention		CDAD treatment		Acute infectious diarrhea treatment	
	SRs	RCTs	SRs	RCTs	SRs	RCTs	SRs	RCTs
Children	4	12 (2)*	4	6	-	-	4	32 (4)*
Adults	2	15 (1)*	2	5 (1)*	2	4	1	4

AAD: Antibiotic-associated diarrhea; CDAD: *C. difficile*-associated diarrhea  
\* N RCTs added to the most recent SR

**Organisational and cost evaluation:** Results from a survey on the current management and clinical practices for probiotic uses conducted in other Canadian hospitals were compared to the situation in the CHUQ. Organisational and patient impacts related to the implementation of the recommendations were also estimated.

## FINDINGS

### Effectiveness

Probiotics have not been proven to be effective to prevent or treat AAD and CDAD. Results suggested a beneficial effect of *Lactobacillus* GG (LGG) for the treatment of acute infectious diarrhea in children. However, heterogeneity (dosing regimen, population, case definition of diarrhea) and methodological flaws were observed.

### Safety

Few adverse events were reported among RCTs. However, cases of proven sepsis associated with the use of probiotics have been reported with underlying conditions like immunodeficiency, presence of a central venous catheter, or premature birth (table 2).

Table 2. Description of case reports of proven<sup>a</sup> sepsis associated with probiotics

	Total cases	CVC	Prior antibiotics	Immunodeficiency
<b>Children</b>				
LGG	4	4	2 (2*)	2 <sup>b</sup>
<i>S. boulardii</i>	4	4	4	1
<b>Adults</b>				
LGG	2	0	*	0
<i>S. boulardii</i>	22	15 (1*)	13 (9*)	6 (1*)

LGG: *Lactobacillus rhamnosus* or *casei*; *S.*: *Saccharomyces*; CVC: central venous catheter

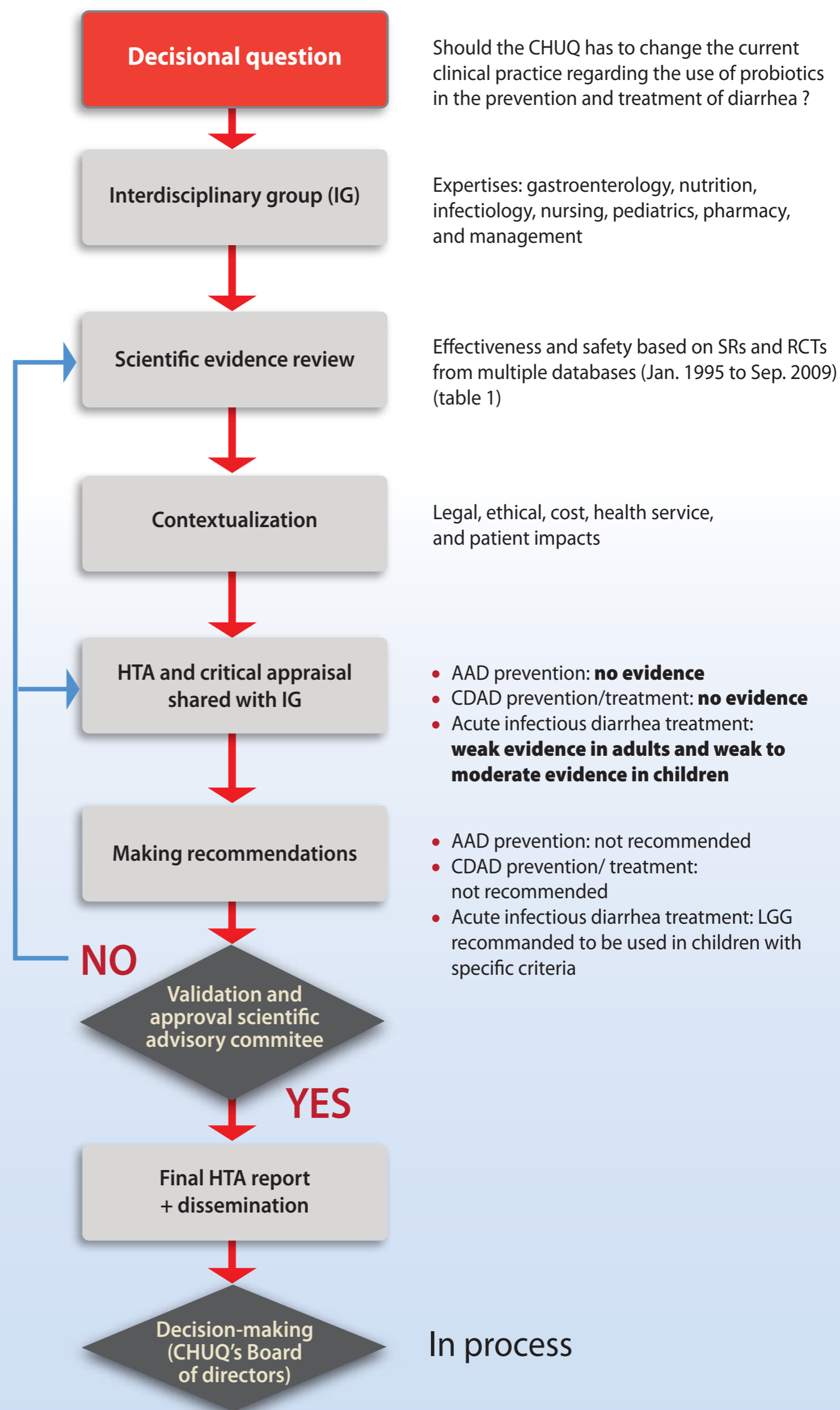
\*not reported

<sup>a</sup> Molecular test confirmed that sepsis was caused by the same microorganisms than those contained in the probiotic therapy

<sup>b</sup> Two infants were premature

- Discrepancies were noticed regarding prescription and distribution of probiotics in the CHUQ. These factors raise concerns about patient safety. In comparison with the CHUQ, probiotic use observed in the hospitals surveyed were mainly managed by their Pharmacy departments.
- There were 582 children treated for acute infectious diarrhea during the previous year in the CHUQ. The costs to treat these children with probiotics could approximate \$15,000 CDN. However, other costs have to be taken into account, for example, human resources.

Figure 1. HTA approach for the evidence-based decision making



## CONCLUSION

According to the HTA, the main recommendation was to limit the use of probiotics (LGG) for the treatment of acute infectious diarrhea in children. Probiotics should be administered to children without a CVC, not immunocompromised or premature. As part of the knowledge transfer and input for the decision making regarding probiotic use, the HTA results were disseminated to the clinical staff and stakeholders in the CHUQ. A review process to establish an efficient and safe clinical use of probiotics, from the prescription to the distribution, should be undertaken. These recommendations should be re-evaluated as more evidence becomes available.

### Reference

UETMIS, 2007. Guide m thodologique. <http://www.chuq.qc.ca/fr/evaluation/uetmis/demarche/>

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