Policy Brief 2, June 2021

Clinical practice guidelines for recurrent miscarriage in high-income countries: a systematic review

We identified 32 clinical practice guidelines for the management, investigation and/or follow-up of recurrent first-trimester miscarriage within high-income countries. There were varying levels of consensus and quality across the included guidelines, with some conflicting recommendations

There is a need to build the evidence base for recurrent miscarriage, and to develop consensus on the definition of recurrent miscarriage and the terminology used to describe the condition. There is also a need to improve both the quality of evidence underpinning guidelines and the rigour of their development. This will influence guideline implementation and ultimately the care of women and men who experience recurrent miscarriage. More significant efforts should also be made to incorporate multi-disciplinary perspectives, including the involvement of those who experience recurrent miscarriage, in guideline development

What do we already know?

Recurrent miscarriage (RM) affects 1-2% of women of reproductive age, depending on the definition used. In 2017, the European Society of Human Reproduction and Embryology stated that a diagnosis of RM could be considered after the loss of two or more pregnancies. Before this, and indeed still in some countries, RM was defined as three or more consecutive pregnancy losses

Evidence-based, up-to-date guidelines are required to inform care decisions. At present, there is no national guideline for RM care in Ireland. An examination of published clinical practice guidelines (herein referred to as 'guidelines') for RM in high-income countries would help identify the degree of consensus in guideline recommendations and aid efforts to optimise and standardise care

Our study identifies, appraises and describes guidelines, published since 2000, for the investigation, management, and/or follow-up of RM within high-income countries

What did we do?

We conducted a **systematic review** following a pre-published protocol. We searched **six bibliographic databases, eight guideline repositories, and eleven professional organisations' websites**. Two reviewers independently screened abstracts and full texts against the eligibility criteria. One reviewer extracted the **characteristics and recommendations** of included guidelines, which were then double-checked by another reviewer

Quality of eligible guidelines was assessed by three appraisers independently, using the **Appraisal of Guidelines for Research and Evaluation (AGREEII)** tool. A **narrative synthesis** was conducted to appraise and compare guidelines and their recommendations

What did we find?

We identified **32 guidelines** for the the investigation, management, and/or follow-up of RM. These were published between 2011-2015 (n=12, 37%) and 2016-2020 (n=20, 53%)

Two thirds were described as guideline(s), clinical practice guideline(s)/clinical guideline(s), or practice guideline(s) (n=21, 66%)

The **focus of guidelines varied**: RM/recurrent pregnancy loss (RPL): 7 (22%); Early pregnancy loss, pregnancy loss/perinatal death: 4 (12%); Broader focus: 21 (66%)

Guidelines used various terms to describe the condition: 'Recurrent Pregnancy Loss' (n=15, 47%), 'Recurrent Miscarriage' (n=8, 25%), RPL/RM/Other (n=7, 22%); 2 guidelines (6%) did not specify a term

Definitions of RM/RPL also varied (n=17 guidelines): ≥3 losses (n=9, 53%), ≥2 losses (n=7, 41%), 2 consecutive spontaneous losses, or ≥3 spontaneous losses (n=1, 6%). 15 guidelines (47%) did not provide a definition, but 2 referred to 3 losses within their texts

The **majority of guidelines were country-specific**: US (n= 11, 34%), UK (n=5, 16%), Canada (n=2, 6%), Ireland (n=2, 6%), Australia (n=1, 3%), France, (n=1, 3%), Korea (n=1, 3%), Northern Ireland (n=1, 3%), Saudi Arabia (n=1, 3%); Germany/Austria/Switzerland (n=1, 3%); with 6 being Global (n=3, 9%) or European (n=3, 9%)

From the 32 guidelines, **373 recommendations** concerning first trimester RM were identified, across four sub-categories:

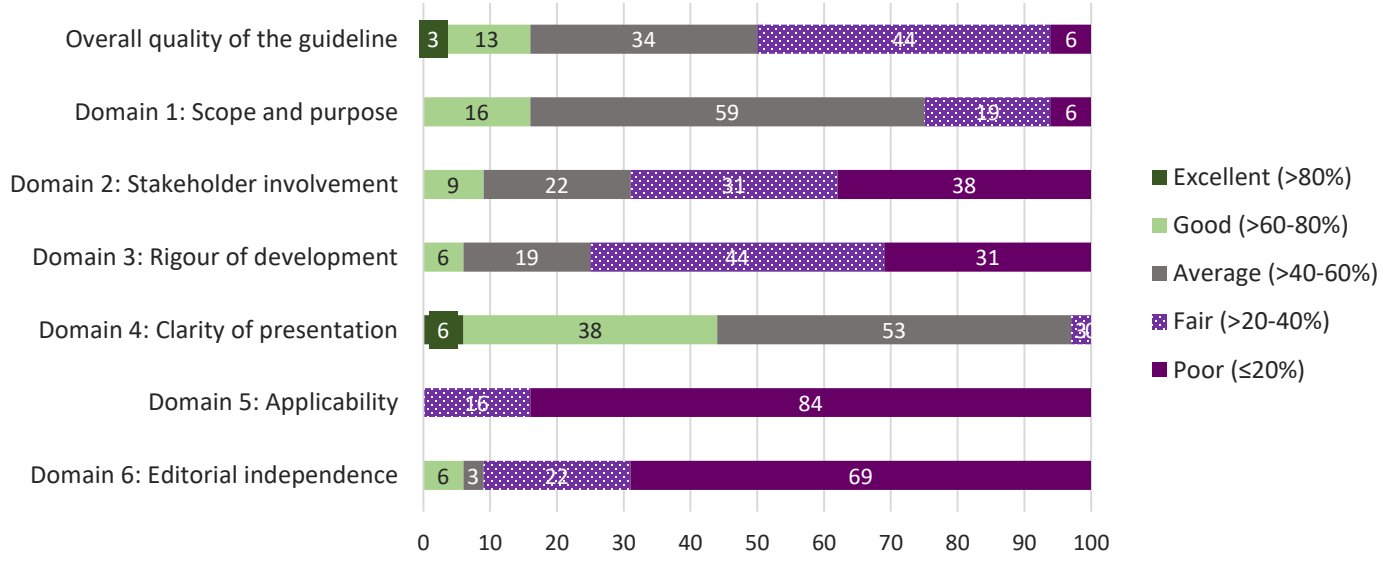
- **Structure of care** (42 recommendations, 9 guidelines)
- **Investigations** (134 recommendations, 23 guidelines)
- **Treatment** (153 recommendations, 24 guidelines)
- **Counselling/supportive care** (46 recommendations, 9 guidelines)

Variety of systems of rating evidence mentioned in 17 of 32 guidelines (53%); GRADE most commonly used (n=5 of 17, 29%). A further four guidelines (13%) described a system but did not specifically mention a name

There were **varying levels of consensus** across the included guidelines, with **some conflicting recommendations**

Quality of included guidelines varied. Only two were recommended for use; 29 were recommended for use with modification; one was not recommended. Most scored 'poor' on applicability (n=27, 84%) and editorial independence (n=22, 69%) using the AGREEII tool (see Figure 1)

Figure 1 AGREE II Domain scores for the 32 guidelines, percentage (%)



Further information

Hennessy M, Dennehy R, Meaney S, Linehan L, Devane D, Rice R, O'Donoghue K. Clinical practice guidelines for recurrent miscarriage in high-income countries: A systematic review. *Reprod Biomed Online.* 2021; 42(6):1146-1171. https://doi.org/10.1016/j.rbmo.2021.02.014. This study was funded by the Health Research Board (ILP-HSR-2019-011)

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