

Adaptation report

## Adaptation of the Dutch Quality Standard for anorectal malformations

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****Abstract****

**INTRODUCTION**

Anorectal Malformations (ARM) are rare conditions. Awareness and knowledge are essential among thehealthcare providers involved in the diagnosis and treatment of ARM. The complexity of ARM requires multidisciplinary and tailor-made care with expertise in this low prevalence condition.

**OBJECTIVES**

To adapt the Dutch Quality Standard recommendations for patients with ARM in order to enhance and protect the quality of care, specifically within the European context.

**METHODS**

This Adaptated Quality Standard was developed in adherence to the ADAPTE method. A Systematic literature review was conducted using Medline, Embase, and Cochrane databases to identify studies published after 2017. Systematic reviews or original studies focused on the diagnosis and treatment of ARM patients were considered for inclusion if they provided evidence that could potentially change the course of care outlined in the Dutch Quality Standard.

**RESULTS**

After completing the adaptation process the Adoption and Adaptation working group decided that 35 recommendations could be adapted, 11 adopted and 15 were developed de novo (new) for the diagnosis and treatment of patients with ARM. In order to enhance the rigor of development, newly created recommendations were accompanied with a Grade of Recommendation according to the Level of Evidence of the respective linked study. Justifications were reported, describing the areas of consensus, the development process of the recommendations and the discrepancies with the original Quality Standard.

**CONCLUSION**

Based on current evidence, an existing Dutch Quality Standard and according to the European context, a set of recommendations was developed for the diagnosis and treatment of ARM. However, further research is required to increase the certainty of evidence in areas of ambiguity and to develop more evidence-based recommendations for the diagnosis and treatment of ARM.

# Keywords

Anorectal Malformation, ARM, Quality Standard, Adaptation.

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Acronyms and abbreviations

|  |  |
| --- | --- |
| ARM | Anorectal Malformations |
| ERN | European Reference Network |
| AAWG | Adoption and Adaptation Working Group (expert panel) |
| TC | Tethered cord |
| TCS | Tethered Cord Syndrome |
| (V)UD | (Video)-urodynamic study |
| SD | Spinal Dysraphia |
| ATS | Anal Target Sign |
| HMA | Heineke-Mikulicz anoplasty |
| AGREE II | Appraisal of Guidelines for Research and Evaluation II |

1. Introduction
   1. General

Anorectal malformations (ARM) are rare conditions. The incidence of ARM varies between 1:3500 to 1:5000 live births.1 There is a great need for more awareness and knowledge among all healthcare providers involved in the care of patients with an ARM in order to reduce the sometimes occurring diagnostic delay, improve diagnostics and treatment, and prevent complications and comorbidities in the short and long term as much as possible and improve the quality of life for patients. The care for patients with ARM is complex, where multidisciplinary, tailor-made care by healthcare providers with expertise is essential. An extensive introduction of ARM and associated malformations can be found in the Dutch Quality Standard.2

* 1. Scope and Objectives

The scope of this adaptation report follows the scope of the original Dutch Quality Standard. This includes the care pathway from the prenatal detection until lifelong follow-up care and transition care for patients with all types of ARM. A full overview of all types of ARM and associations is to be found in the original Dutch Quality Standard.2 The primary objectives of this adaptation are:

1. To assess currency and validity of the Quality Standard recommendations to improve and safeguard the quality of care for patients with ARM.
2. To assess applicability and acceptability of the Quality Standard recommendations for ARM to fit the European context.
3. Methods
   1. Target Population

The target population for this Quality Standard Adaptation is patients with ARM. Additionally, the primary target audience of the Quality Standard Adaptation consists of all members of the professional groups involved in the care of patients with an ARM, such as paediatric surgeons, paediatricians, nurse practitioners, nurses, (paediatric) gastroenterologists, paediatric anaesthesiologists, physiotherapists, dieticians, psychologists, clinical geneticists, nephrologists, general practitioners, (paediatric) urologists, (paediatric) neurosurgeons, (paediatric) gynaecologists, sexologists and (paediatric) orthopaedic surgeons.

* 1. ADAPTE

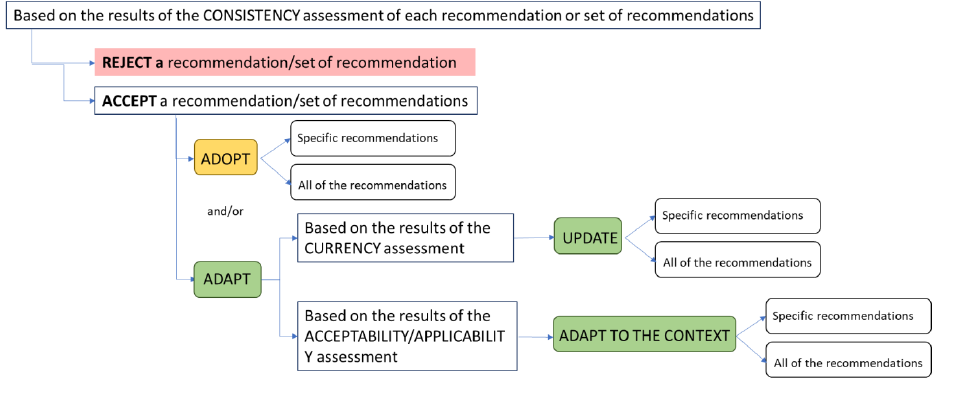
For the Adaptation of the Quality Standard the ADAPTE method was used.3 First, the existing Quality Standard was appraised for its methodological quality with the AGREE II tool. To assess if the recommendations were current, or if new literature could update the advises in the Quality Standard, a literature review was performed. Applicability and acceptability were assessed during meetings between the ERN eUROGEN Adoption and Adaptation Working Group (AAWG) and team members from Qualicura.

Once the assessment has been completed, the AAWG considered the results of the assessment to obtain a conclusion for each recommendation. The existing recommendations from the original Quality Standard were adopted as a whole or modified in order to be adapted. New recommendations emerged based on the new evidence found. In this document, the recommendations have been referred as either adopted, adapted or new. The definitions of adapted, adopted and new recommendations are displayed in [Table 1](#table1). The decision for each recommendation was reached by consensus based on the methods of a consensus development conference.4

|  |  |
| --- | --- |
| Adopted | Recommendation was not changed from the original Quality Standard |
| **Adapted** | Recommendation was modified and adapted to the needs of the ERN |
| **New** | Recommendation was createdfrom the new evidence found |

**Table 1.** *Definition of adopted, adapted and new recommendations.*

A decision-making algorithm is displayed below to show the process towards a conclusion about the recommendations to create an adopted or adapted guideline (see [Figure A](#decision_making_algorithm)).



**Figure A.** *Decision making algorithm for the acceptance of a recommendation or set of recommendations.*

* 1. Search Strategy

The literature searches were conducted by a professional information specialist in the following databases, (Ovid/Medline (PubMed), Cochrane CENTRAL, Embase) to identify any new relevant studies published between 2017 and March 2023. Databases were searched using relevant medical subject headings and free-text terms. The search strategy was conducted in the electronic databases in March 2023 and the searches were restricted to retrieve articles in English language. To ensure that the report contains current and relevant evidence, studies published prior to 2017 were excluded. The literature searches yielded a total number of 2248 studies (after removal of duplicates) and were subsequently screened for title and abstract (see [Appendix Table 1](#systematic_literature_search)). The screening was conducted by two methodologists (WI) and (KM). Both screened results based on title and abstract utilising the Systematic review app Rayyan,5 and identified useful publications according to the inclusion/exclusion criteria displayed in [Table 2.](#table2)

Literature Selection Criteria

|  |
| --- |
| **Inclusion** |
| * Research covering Anorectal Malformations, Congenital AND (diagnosis), (treatment) within the scope of clinical questions in the original quality statements |
| * Evidence that possibly changes the course of care as described in the Quality Standard |
| * Systematic review or study reporting original data. |
| * English language |
| **Exclusion** |
| * Studies with < 10 patients |
| * Acquired malformations/fistulas (i.e., Crohn’s related) |
| * Published before 2017 |

**Table 2**. *Inclusion and exclusion criteria of publications on Diagnosis and Treatment of children with ARM*

After completing the screening of all tiles and abstracts decision discrepancies were discussed. After the first screening round, two methodologists (WI, KM) and three pediatric surgeons (JG, ML, IB) screened the included publications and categorized them in two topics: Diagnosis, Treatment. Any results that did not match with one of these preselected topics were excluded in the second screening round. Seven new studies for the diagnosis module and seven new studies for the treatment module were identified, adding value in the adaptation of the Quality Standard. Prisma flow diagram with the literature selection is available in [Appendix Figure A](#prisma_diagram).

1. Results
   1. Guideline Methodologic Review
      1. Appraisal of the Dutch Quality Standard for Anorectal malformations

In order to make a decision about the adoption or adaptation of the Dutch “Quality Standard for Anorectal Malformations”, assessment of its quality and reporting was sought.

The Appraisal of Guidelines for Research and Evaluation (AGREE II) instrument was used to independently appraise the Dutch Quality Standard on anorectal malformations.6 Four reviewers carried out the appraisal (two reviewers from the Aragon Institute of Health Sciences (IACS) and two from the ERN eUROGEN expert panel).

Domain scores were calculated by summing up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain. The overall standard domain score given by the reviewers was 38%. For additional information about the appraisal of the Dutch Quality Standard and the domain scores see Appendix: [Dutch Quality Standard Appraisal](#dutch_quality_standard_appraisal).

The AAWG and methodologists decided that the recommendations from the original Quality Standard could be adapted, however some improvements were desirable based on the consistency assessment.

* + 1. Levels of evidence and Grades of recommendation

To improve the rigor of development the AAWG and methodologists suggested to accompany all new recommendations with a Grade of recommendation if applicable. Therefore, the working group chose to use an appraisal method that can be applied on study level. The possible levels of evidence were I, II, III and IV (OCEBM, 2011) orexpert opinion and this was paired with a Grade of recommendation (Adapted from OCEBM, 20097) (see [Table 3](#table3)).

|  |  |
| --- | --- |
| A | Based on consistent level 1 studies |
| **B** | Based on consistent level 2 or 3 studies or extrapolations from level 1 studies |
| **C** | Based on level 4 studies or extrapolations from level 2 or 3 studies |
| **D** | Based on expert opinion **or** inconclusive/inconsistent studies of any level. |

**Table 3.** *Correspondence between grades of recommendations and study level of evidence.*

To improve the reporting of of the adapted recommendations with more clarity, transparency and explicitness, the AAWG and methodologists will provide the adaptation report following the RIGHT-Ad@pt preferred reporting items.8

* 1. Currency, Acceptability, Applicability and Clarity
     1. Diagnostics in a child with ARM

**Key question 1**

In patients with ARM, which diagnostic examinations are important for making the diagnosis, for evaluating the postoperative phase and for evaluation during follow-up, and at what time should which examination be performed?

The key question consists of the following sub-questions:

1. Which diagnostics do you need to make a diagnosis of ARM and to determine which type of ARM is involved, and which diagnostics do you need to determine additional comorbidity?
2. Which diagnostic examinations are performed during and after the various surgeries and which diagnostics are important during follow-up?
3. Which urological examination should be performed and when?
4. Which diagnostic exams of the reproductive system should be performed and when?
5. What are the indications for additional neurological examination?

Recommendations for sub-question 1a

For this sub-question, seven new studies were included and considered by the panel.9-15 Six (6) recommendations were adapted, two (2) were adopted and seven (7) were developed de novo (new). All recommendations are reported in [Table 4](#table4). A summary of all newly included studies for this sub-question is available in [Appendix Table 2](#Summary_prenatal_postnatal).

|  |  |  |
| --- | --- | --- |
| PRENATAL | | Grade of Recommendation |
| 1 | It is recommended to increase the awareness of ultrasound technicians / sonographers about the possible diagnosis of ARM before birth with prenatal ultrasound examination. **[adapted]** | B9 |
| 2 | A dilated bowel with absence of the anal target sign (ATS) might be indicative of high ARM type. **[new]** | D |
| 3 | In case of an increased risk of abnormalities, it is recommended to perform an advanced ultrasound examination between 18 and 22 weeks of pregnancy. **[adapted]** | - |
| 4 | Sonographers must be aware of dilation of the last part of the colon/rectum. ARM may be suspected if the distal bowel is dilated on the first trimester ultrasound or if intraluminal echogenic foci are seen on the second trimester ultrasound. **[adopted]** | - |
| 5 | The visualization of the anal target sign is feasible by prenatal ultrasound and may aid in the detection of less severe ARM sub-types. **[new]** | B10 |
| 6 | Identification of a peri-anal muscular complex during prenatal US evaluation is useful for prenatal diagnosis but its sensitivity and specificity for ARM is low and a positive finding doesn't exclude low type ARM. **[new]** | C11 |
| 7 | The possibility of a present cloaca should be suspected antenatally in case of a cystic mass in the pelvis, that matches a hydrocolpos, and, in some cases, also by the presence of an expanded intestinal loop in the pelvis. Later in the pregnancy (more than 24 weeks) it is possible to visualize and assess the anal target sign. **[adapted]** | - |
| 8 | It is recommended to follow up early (1st trimester) a cystic abdominal mass while maintaining a high index of suspicion for ARM even if the cystic mass disappears on follow up scans, especially in isolated cases with normal genetics. **[new]** | D12 |
| 9 | Foetal MRI may be considered in case of ultrasound identified hydrocolpos and suspected cloacal malformation. **[new]** | C13 |
| **NEONATAL** | | |
| 1 | In the acute phase, the first 24-48 hours after birth, ARM must be diagnosed by history and physical examination. **[adopted]** | - |
| 2 | In the diagnostic phase, the type of ARM (according to Krickenbeck classification) and any additional anomalies should be carefully mapped out prior to any attempts to repair the ARM. Different diagnostic methods are available to map the phenotype but there is no evidence of superiority of one over the other. **[adapted]** | - |
| 3 | To qualify the condition, the digestive tract, the urogenital tract, the neuromuscular tract, the circulatory tract, and the respiratory tract must be or should be examined. In particular, disorders of the VACTERL association are also looked for:  V = Vertebrae, anomalies of the vertebrae  A = Anus, an anorectal malformation  C = Cardiac, anomalies of the heart  TE = Tracheoesophageal abnormality, occlusion or narrowing of the esophagus with possibly a connection to the trachea  R = Renal, abnormality of the kidney, urinary tracts, or bladder  L = Limb, limb abnormalities  **[adapted]** | - |
| 4 | Spinal and renal ultrasound in the first weeks of life are recommended to screen for spinal cord and urological anomalies. **[new]** | B14 |
| 5 | In case of ARM with at least one other anomaly, consultation with a clinical geneticist is strongly recommended. **[new]** | B15 |
| 6 | At the end of the diagnostic phase, the patient-specific abnormality must be clearly documented and saved throughout the life of the patient. Any digital data, (diagnostic data) should also be saved. **[adapted]** | - |

**Table 4.** *Recommendations for sub-question 1a.*

Justification for sub-question 1a

**Prenatal**

Recommendations have been made in favour of evaluating different signs and symptoms of ARM prenatally through ultrasound. The AAWG addressed that the probability of advanced ultrasound examination to diagnose ARM is enhanced when it is performed by highly skilled ultrasound specialists and at an academic center.2 Evidence from cohort studies and case series suggest that ARM may be suspected if the distal bowel is dilated or if intraluminal echogenic foci are seen on prenatal sonography.9-12 Ultrasound technicians/sonographers should be aware of these sonographic signs of possible diagnosis of ARM. However, because the condition is rare, the diagnosis will not often be made prenatally. Awareness of sonographers could be improved by when checking the sex, also assessing the target sign.9, 10 However, AAWG referred to a study by Bischoff 10 concluding that the anal target sign has the highest detection rate between 28-33 weeks, which should be taken into account since gender screening is predominantly done at an earlier term. The combination of a dilated bowel and the absence of the anal target sign (ATS) might be indicative of a high ARM type, but due to scarce evidence the specificity is not yet determined. In one of the new included studies,11 the authors reported that detection of the fetal anal canal and anal muscular complex may aid in the detection of anal atresia. The AAWG recognizes this but wants to emphasize that the diagnostic accuracy seems to be low and presence of a normal anal muscular complex on ultrasound cannot exclude ARM. The AAWG members agreed that a cystic abdominal mass finding should raise suspicion as it may be a cloaca or other ARM types in the differential diagnosis.12 Sonographers should search for cysts in the foetal pelvis during the first and early second trimester. After considering a study on prenatal MRI,13 the panel agreed that in case of ultrasound findings suspecting ARM, a complementary MRI may be useful without being necessarily superior to ultrasound. Although the qualification of the screening technician may play a role in the quality of the examination, the AAWG supports that there is insufficient evidence to prove ultrasound inferior to MRI. MRI may add value in the diagnosis of ARM, but the consequences must be weighted in each case. Additionally, gynaecologists must be aware how important the diagnosis of ARM is during prenatal consultation.

The AAWG considered the favourable benefit-risk balance, the acceptability and applicability in order to adopt, adapt or to form new recommendations. Antenatal diagnosis of ARM seems to be accurate and does not lead to over diagnosing and unnecessary concerns. In return, it could lead to improved counselling of parents and better planning of postnatal care. Prenatal counselling of parents and timely transfer (before birth to expert centers) could lead to parental and physician stress reduction and more adequate care for the newborn.

**Neonatal**

In the Dutch Quality Standard this section is referred as postnatal diagnosis.2 However, the AAWG acknowledged that the included recommendations covered only the neonatal period and thus the section was renamed accordingly. Recommendations have been made on the best methods of diagnosing ARM neonatally. The panel considered most recommendations on neonatal diagnosis acceptable and applicable and only slightly changed the wording of the adapted recommendations to improve their clarity. More information regarding the diagnostic modalities for ARM can be found in the Dutch Quality Standard.2

Evidence from 1 newly included study (diagnostic test accuracy) confirms that spinal ultrasound is an accurate method to help in the diagnosis of spinal cord anomalies14 and the panel agreed that this is beneficial because it is a low invasive test that can provide important information. Clinicians pointed out that the provision of care in areas without specialization would increase the risk of misdiagnosis, but the expertise exists within the ERN.

The ARM type (according to Krickenbeck classification) and any additional anomalies must be explicitly specified and documented. The AAWG considered mapping the phenotype an important part of neonatal diagnostics and recognizes that there are multiple modalities to do so, including modern 3D measures, but that there is no evidence to recommend one modality over the other. It is preferable to offer screening by a clinical geneticist in case of ARM and coexisting anomalies.15 The AAWG discussed the value of measuring the pouch-perineum distance in neonates with and without a fistula and if this can prevent an incorrect surgical procedure based on misdiagnosis of the type of ARM.16 The AAWG pointed out that measuring the distance can be controversial as there is no clear evidence that contributes to mapping the phenotype or planning the surgery. The group concluded that the pouch-perineum distance is not the most important marker and therefore no recommendations on this measure are made.

* + 1. Diagnostic examinations performed during and after surgeries and during follow-up

**Sub question 1b and 1c**

b) Which diagnostic examinations are performed during and after the various surgeries and which diagnostics are important during follow-up?

c) Which urological examination should be performed and when?

Recommendations for sub-questions 1b and 1c

For these sub-questions, no new studies were included. Two (2) recommendations were adapted, none were adopted or developed de novo (new). All recommendations are reported in [Table 5](#table5). A summary of all newly included studies for these sub-questions is available in [Appendix Table 3](#Summary_during_after_surgeries_followup).

|  |  |  |
| --- | --- | --- |
| DURING and AFTER SURGERIES and DURING FOLLOW-UP | | Grade of Recommendation |
| 1 | After reconstructive surgery the patient should be monitored closely (within 3 week period). A diagnostic examination must be conducted on the function and integrity of the perineal reconstruction of the digestive tract and the urogenital tract. In case of a stoma creation a proper stoma care is recommended. **[adapted]** | - |
| 2 | A possible follow-up (V)UD study will take place no earlier than 6 months after the reconstructive surgery, and only on indication (including persistent large residues or absence of spontaneous micturition postoperatively, dilation of the urinary tract postoperatively, follow-up of bladder dysfunction or vesicoureteral reflux established in previous (V)UD study, or tethered cord syndrome (TCS) follow-up). The indication for this must be determined during urological follow-up. **[adapted]** | - |

**Table 5.** *Recommendations for sub-questions 1b and 1c.*

Justification for sub-questions 1b and 1c

Recommendations have been made on diagnostic examinations that should be performed both before and after surgery. The AAWG considered the favorable benefit-risk balance, the acceptability and applicability in order to adopt, adapt or to form new recommendations.

In the Dutch Quality Standard,2 a diagnostic examination of the digestive tract and the urogenital tract on to assess the function and integrity was considered optional after a reconstruction surgery or stoma creation. The AAWG proposed that this diagnostic examination and assessment should be mandatory within a 3 week period after the reconstructive surgery and within 6 week period after a stoma creation.

Additionally, it is recommended that a possible follow-up (V)UD study should take place no earlier than 6 months after the reconstructive surgery, and only on indication. The AAWG suggested that the indications must be determined by any means during urological follow-up.

* + 1. Diagnostic exams of the reproductive systems

**Sub question 1d**

d) Which diagnostic exams of the reproductive systems should be performed and when?

Recommendations for sub-question 1d

For this sub-question, no new studies were included by the panel. Three (3) recommendations were adapted, four (4) were adopted and none were developed de novo (new). All recommendations are reported in [Table 6](#table6).

|  |  |  |
| --- | --- | --- |
| REPRODUCTIVE SYSTEMS | | Grade of Recommendation |
| 1 | Proper evaluation and documentation of the external and, if possible, internal genitalia of patients with ARM is required prior to, or at the time of reconstructive surgery. **[adopted]** | - |
| 2 | To optimize the results for the patient during a possible surgical intervention, in the case of abnormalities in the genitourinary area of patients with ARM, it is recommended to always consult a multidisciplinary team and document well their findings. Prior to the onset of puberty, a (paediatric) gynaecologist (preferably with expertise in the field of malformations) should assess and document the anatomical situation to optimize follow-up treatment in menarche / adolescence. **[adopted]** | - |
| 3 | A hydrocolpos (occlusion of the vagina / uterus with mucus build-up) may appear as a cystic swelling in the lower abdomen, especially in females with a cloaca, but can also be seen with an imperforate hymen. The filled vagina can compress the urethra and ureters and thus obstruct the flow of urine and cause hydronephrosis. In case of no or poor urination, careful examination must be done. A diagnosed hydrocolpos must be surgically relieved. Any hydronephrosis should be monitored closely in the context of a hydrocolpos in at least the first months of life. **[adopted]** | - |
| 4 | Attention is also recommended for the prevention of gynaecological anomalies in females with ARM as this can prevent (distal) vaginal stenosis, which can hinder tampon use and sexual contact. **[adopted]** | - |
| 5 | At the beginning of adolescence, females and males with ARM must be provided with information about the possibilities of problems in sexuality, fertility and reproduction. **[adapted]** | - |
| 6 | Females with ARM must be supervised and examined by a gynaecologist (preferably with experience in ARM and have access to a paediatric surgeon experienced in the field of ARM) during pregnancy. **[adapted]** | - |
| 7 | In females with a history of ARM and an abnormal perineum, it is recommended that the perineum be properly examined both pre-conceptually and during the entire pregnancy. An individual recommendation must be made on how the patient can give birth. When in doubt, the choice of Caesarean section should be strongly considered. **[adapted]** | - |

**Table 6.** *Recommendations for sub-question 1d.*

Justification for sub-question 1d

The AAWG considered the favourable benefit-risk balance, the acceptability and applicability in order to adopt, adapt or to form new recommendations.

In the original Quality Standard, recommendations have been made on the gynaecological examinations that should be performed for patients with ARM.2 As suggested by the AAWG, the sub-question was reshaped and the section has been renamed to 'Diagnostic exams of the reproductive systems. By broadening the scope to encompass both male and female reproductive health, the group aimed in a more holistic approach to care, ensuring that patients receive thorough examinations and appropriate interventions tailored to their unique anatomical variations.

Additionally, the AAWG highlighted that it is of high importance to raise ARM patients’ awareness of potential problems in sexuality, fertility and reproduction at the beginning of their adolescence and not on a later stage.

* + 1. Indications for performing additional neurological examinations

**Sub question 1e**

1. What are the indications for additional neurological examination?

Recommendations for sub-question 1e

For this sub-question, no new studies were included and considered by the panel. One (1) recommendation was adapted, two (2) were adopted and none were developed de novo (new). All recommendations are reported in [Table 7.](#table7)

|  |  |  |
| --- | --- | --- |
| NEUROLOGICAL EXAMINATION | | Grade of Recommendation |
| 1 | Spinal dysraphia (SD) can be an additional condition in patients with ARM and it is recommended that all patients with ARM must be screened. **[adopted]** | - |
| 2 | In addition to the radiological evaluation of the vertebra and sacrum, it is recommended to perform an ultrasound of the spinal canal. The spinal canal ultrasound is performed shortly after birth, but at least in the first month, because otherwise the vertebral arches may close, and an ultrasound scan of the spinal canal is less reliable to rule out anomalies. If there are abnormalities on the ultrasound of the spinal cord, follow up is needed for symptoms preferably with the help of a paediatric neurologist. **[adopted]** | - |
| 3 | If indicated, in case of neurological symptoms or abnormal findings on spinal ultrasound, a MRI can be conducted before the age of 12 months.  Work-up:  • All children receive an ultrasound scan of the spinal cord within 1 month of birth.  • A deteriorating neurological image (sensorimotor and / or continence) during follow-up can be an indication to consult a paediatric neurologist to evaluate the presence or not of a tethered cord or any other spinal anomaly. **[adapted]** | - |

**Table 7.** *Recommendations for sub-question 1e.*

Justification for sub-question 1e

Recommendations have been made on the indications for performing additional neurological examinations in patients with ARM. The AAWG considered the favourable benefit-risk balance, the acceptability and applicability in order to adopt, adapt or to form new recommendations.

Patients with ARM may have associated congenital conditions, including tethered cord spinal dysraphia. Tethered spinal cord or other spinal anomalies occur in 10-60% of ARM patients.15

The AAWG suggested that an MRI can be conducted in case of neurological symptoms and if indicated at the age of 12 months and not in an earlier age as recommended in the Dutch Quality Standard.2 It is also advised that an ultrasound scan of the spinal cord must be conducted within the 1st month of birth and not later. The panel did not recommend the use of an MRI as first line diagnostics in case of a deteriorating neurological image during follow-up as it is suggested in the original Quality Standard. Instead, a paediatric neurologist should be consulted to evaluate if a tethered cord or any other spinal anomaly is present or not.

* + 1. Treatment of a child with ARM

Key question 2

What (evidence-based and expert-based) treatment options are there for patients with ARM and when do they apply?

The key question consists of the following sub-questions:

1. Which treatments are suitable for patients with ARM? Which reconstructive operations are performed, and which treatments are still needed afterwards?
2. What instructions are given to parents for actions after the reconstructive operations? Which healthcare provider gives the instruction and when is this instruction given?
3. What is the work-up for the treatment of urinary and faecal continence problems and any associated complications?
4. What individually adaptable protocol can be followed for toilet training and at what age is this offered?
5. What is good prevention and treatment for diaper dermatitis?
6. Which aids are available (incontinence materials, rinse aids)? Which care provider can advise on this?
7. How is / are the parents of the patient with ARM supported in self-management?

Sub-question 2a

Which treatments are suitable for patients with ARM? Which recovery operations are performed, and which treatments are still needed afterwards?

Recommendations for sub-question 2a

For this sub-question, six studies were included and considered by the panel.17-22 Six (6) recommendations were adapted, none were adopted and six (6) were developed de novo (new). All recommendations are reported in [Table 8](#table8). A summary of all newly included studies for this sub-question identified is available in [Appendix Table 4](#Summary_treatment_modalities).

|  |  |  |
| --- | --- | --- |
| TREATMENT MODALITES | | Grade of Recommendation |
| 1 | Refer patients with an ARM diagnosis to a paediatric surgery department when available. The following measures are recommended:   * Patient examination in the first 24 hours on whether there is meconium discharge and which type of ARM is involved. * Exclusion of other potentially lethal pathology, especially congenital heart disorder. * Intravenous fluid management in case of bowel obstruction or enteral nutrition if defecation is possible. * Parental counselling on the condition.   **[adapted]** | - |
| 2 | Patients with cloaca and cloacal exstrophy should be referred to a reference centre with experience in the multidisciplinary treatment of these patients and long-term follow-up. **[new]** | D17 |
| 3 | In patients with insufficient or absent meconium discharge, establish a venous access and insert a nasogastric tube. Provide IV antibiotics. Inform the parents not to feed the baby or child. **[adapted]** | - |
| 4 | For forms of ARM in which there is no meconium discharge after birth, surgery is performed. Often, three surgeries are required:   * Creating a colostomy * The reconstruction surgery * Reversal/Closure of the stoma   **[adapted]** | - |
| 5 | If there is a phenotype of ARM in which (sufficient) meconium is discharged (e.g. ARM with perineal or vestibular fistula or anal/rectal stenosis), the anus should be calibrated and/or painlessly dilated until the daily evacuation of meconium is possible. If there is no sufficient meconium evacuation, a stoma should be considered. **[adapted]** | D18 |
| 6 | Choose the timing of reconstructive surgery (either in the neonatal period or during infancy) based on the height of the rectum and the presence of a connection to the urinary tract. **[adapted]** | - |
| 7 | Primary reconstruction and restoring bowel continuity should be done within the first year of life, unless there are contra indications for surgery such as life-threatening comorbidities (e.g., cardiac). **[new]** | C19 |
| 8 | In certain cases of perineal fistula non-operative treatment might be considered. **[new]** | B20 |
| 9 | Type of colostomy: no evidence for superiority between either loop vs split.  Place: descending sigmoid stoma is preferred but, in some cases, (cloacal malformations or associated gastrointestinal anomalies) a transverse stoma might be an option. **[new]** | D |
| 10 | The chosen surgical technique depends on the abnormalities found and the surgeons’ expertise. The most common surgical techniques are the application of an anoplasty, ASARP, PSARP, LAARP (ASARP: anterior sagittal anorectoplasty; PSARP: posterior sagittal anorectoplasty; LAARP: laparoscopically assisted anorectoplasty), or a combination of the different techniques. **[adapted]** | C21 |
| 11 | In case of anal stenosis at the skin level during follow-up after anorectoplasty, anal dilatation under general anesthesia should be considered, otherwise a Heineke-Mikulicz anoplasty (HMA). **[new]** | B22 |
| 12 | Postoperative routine calibrations at home may be considered but are not mandatory. Painful calibrations must by all means be avoided. If a calibration programme is started, it should not be longer than 3-4 months, and an intensive follow-up is needed. **[new]** | D |

**Table 8.** *Recommendations for sub-question 2a.*

Justification for sub-question 2a

Recommendations have been made regarding the various treatment modalities for patients with ARM. The AAWG considered the favourable benefit-risk balance, the acceptability and applicability in order to adopt, adapt or to form new recommendations.

The AAWG suggested, from evidence found in a study by Kubota et al.,17 that patients with cloaca and cloacal exstrophy should be referred to a specialised treatment center with expertise in multidisciplinary care and long-term follow-up.

The AAWG agreed that the treatment of ARM depends on the type of the malformation, sex, weight, possible comorbidities and time or age at diagnosis. To make particular recommendations regarding initial treatment options, the AAWG considered it necessary to assess the presence and degree of meconium discharge. When absent or insufficient, the group noted that calibration should be started until daily evacuation is possible.18

Depending on the local surgical expertise and the condition of the neonate, primary reconstruction and restoring the bowel continuity is feasible within the first year of life and should be done within this period, unless there are contra indications for surgery such as life threatening comorbidities.19

According to a study by Amerstorfer et al.,20 evidence supports that in some cases of perineal fistula (the anal orifice surrounded by 80% of the anal sphincter and no stenosis) a non-operative treatment might be considered, thus the group formed a recommendation in favour of this treatment method.

Regarding the surgical techniques, the AAWG did not recommend single-stage over multi-stage surgery approaches, as evidence was mainly limited to females with recto-vestibular fistulae and was considered insufficient to make a general statement.23 The group addressed that this is a complex issue in which there is also an ongoing debate. The AAWG considered it essential to take into consideration the surgeons’ expertise when choosing the specific method, in addition to the patient’s abnormalities and/or comorbidities, with which they join the concluding statement of Lauriti et al.21 Among the updated evidence, the group observed a lack of long-term data on functional outcomes and insufficient data on cosmetic appearance or patient satisfaction. Given this, the group could not make any particular recommendations on specific surgical techniques for ARM patients with enough confidence.

In addition, the necessity of anal calibration for prevention of anal stenosis was discussed together with the results of an RCT on routine postoperative dilatation.22 Results of the RCT indicated that routine postoperative dilatation did not lead to less skill level strictures but these results were imprecise. The AAWG considered this a very sensitive topic, in which there is an ongoing debate on whether to dilatate for which higher level evidence is warranted. The panel unanimously agreed that the dilatations should be by any means painless and the benefits and harms of doing this should be carefully discussed with parents. In case of painful anal calibrations the group pointed out that they should be performed exclusively under general anaesthesia as an alternative treatment.22 The Heineke-Mikulicz anoplasty (HMA) was presented by Ahmad et al. as an alternative to routine dilatations and was found to be a viable treatment option in case of stricture on skin-level, 22 thus it was included in the recommendations.

The AAWG emphasised that not all surgical methods for treating ARM are viable in every healthcare center. In these cases a nonoperative management considered and patients can remain with a colostomy without a reconstruction and referred to a center specializing in ARM treatment.

Finally, the AAWG suggested that, when surgeons select a surgical technique, they should consider that perineal wound infection is usually limited and does not affect the functional long-term outcome. However, in case of extended and destructive wound infection, a colostomy may be required and the final functional outcome, in this case, may be affected.

* + 1. Postoperative instructions to parents: which, from whom and when

Sub-question 2b

What instructions are given to parents for actions after the reconstructive operations? Which healthcare provider gives the instruction and when is this instruction given?

Recommendations for sub-question 2b

For this sub-question, no new studies were included and considered by the panel. Two (2) recommendations were adapted, one (1) was adopted and none were developed de novo (new). All recommendations are reported in [Table 9](#table9).

|  |  |  |
| --- | --- | --- |
| INSTRUCTIONS TO PARENTS | | Grade of Recommendation |
| 1 | Paediatric surgeons and nurses must inform parents on available ARM resources such leaflets, brochures, website, webinars on the neonatal aspects of ARM in an understandable way (i.e., lay language) etc. as well as patient associations. **[adapted]** | - |
| 2 | The paediatric surgeon should provide relevant information to parents whose children undergo ARM surgery about conditions, treatment, and care after surgery and possible complications. **[adopted]** | - |
| 3 | A specialized nurse in ARM should always be involved after the operations of a child receiving a stoma. **[adapted]** | - |

**Table 9.** *Recommendations for sub-question 2b.*

Justification for sub-question 2b

Recommendations have been made regarding what instructions, from which healthcare provider and when they should be given to the parents after the reconstructive operations. The AAWG considered the favourable benefit-risk balance, the acceptability and applicability in order to adopt, adapt or to form new recommendations.

The AAWG considered the provision of correct information among the most important things for parents with a child with ARM and therefore adapted the recommendations on this. The AAWG suggested that if there is not a specific patient’s association for ARM in their own country, parents should link to other existing international patient organisation for support. Compared to the original Quality Standard, the recommendations were adapted to be more generally applicable throughout European countries.

* + 1. Toilet training and treatment of urinary and faecal continence problems

Sub-question 2c

What is the work-up for the treatment of urinary and faecal continence problems and any associated complications?

Sub-question 2d

What individually adaptable protocol can be followed for toilet training and at what age is this offered?

Recommendations for sub-question 2c and 2d

For these sub-questions, one new study was included and considered by the panel. Nine (9) recommendations were adapted, one (1) was adopted and none were developed de novo (new). All recommendations are reported in [Table 10](#table10).

|  |  |  |
| --- | --- | --- |
| TOILET TRAINING | | Grade of Recommendation |
| 1 | It is crucial to strive for urinary and faecal continence. If continence cannot be achieved, the highest possible quality of life should be aimed. (e.g. by facilitating pseudo-continence with bowel management). **[adapted]** | - |
| 2 | It is important to keep in mind at all times of the patient's course, the association between ARM and urological malformations and to act accordingly, involving the relevant healthcare professionals. **[adapted]** | - |
| 3 | An individually tailored protocol according to the children’s ARM sub-type and form is recommended for toilet training.  This is, on the one hand, to be done in connection with the different degrees and forms of ARM and comorbidity and on the other hand in connection with the differences per child in maturity and development phase. **[adapted]** | - |
| 4 | In case of problems with toilet training (unsuccessful management, whether or not related to complex problems) it is recommended that the toilet training problem should be discussed and treated within a multidisciplinary team. **[adopted]** | - |
| 5 | The approach to toilet training in children with ARM, depending on complexity, comorbidity and social context, can be initiated at the age of 1-5 years (as with all children). **[adapted]** | - |
| 6 | It is recommended during faecal toilet training to pay attention to   * care of the perineal skin * toilet posture, toilet seat reducer, relaxation of the child during toilet use, using fixed times on the toilet * paediatric pelvic floor physiotherapy * optional supervision by a psychologist / remedial educationalist   **[adapted]** | - |
| 7 | Patient-parents should be educated to recognise constipation and subsequent overflow incontinence. **[adapted]** | - |
| 8 | Bowel incontinence may require an enema or rectal irrigation, which could be temporary. **[adapted]** | - |
| 9 | If rectal irrigation is not working or not possible -e.g., rectal trauma, physical inability- antegrade irrigation should be considered. **[adapted]** | - |
| 10 | In case of persistent and specific problems of incontinence, re-do surgery may be considered, in coordination with an experienced surgeon or centre. If redo-surgery is not recommended, definite stoma may be considered as a last resort. **[adapted]** | C24 |

**Table 10.** *Recommendations for sub-question 2c and 2d.*

Justification for sub-question 2c and 2d

Recommendations have been made for toilet training. The AAWG considered the favourable benefit-risk balance and adapted all recommendations. Changes from the original Quality Standard were made to improve clarity of the statements and adjust them to European context.

The panel recommended to implement a personalised protocol for toilet training which takes into account the specific sub-type of ARM in children. Furthermore, this protocol should also consider any associated comorbidities, as well as individual differences in maturity and developmental stages. The toilet training strategies should be flexible and adaptable, taking into consideration several aspects of ARM and the individual variations in each child's growth and development. The AAWG considered also that the social context of a child with ARM is an additional factor that should be accounted for in the optimal approach for toilet training. If incontinence or relevant challenges persist (e.g. a failed reconstructive surgery), the group indicated that a re-do surgery should be considered, in coordination with an expert centre.24

* + 1. Prevention and treatment of diaper dermatitis

Sub-question 2e

What constitutes good prevention and treatment for diaper dermatitis?

Recommendations for sub-question 2e

For this sub-question, no new studies were included and considered by the panel. One (1) recommendation was adapted, none were adopted and none were developed de novo (new). All recommendations are reported in [Table 11](#table11).

|  |  |  |
| --- | --- | --- |
| DIAPER DERMATITIS | | Grade of Recommendation |
| 1 | Wound, stoma and perianal care should be monitored by skin and /or stoma nurse in or out of the hospital on regular basis. **[adapted]** | - |

**Table 11.** *Recommendations for sub-question 2e.*

Justification for sub-question 2e

One recommendation has been made regarding the prevention and treatment of diaper dermatitis in patients with ARM. The AAWG considered the necessity of a professional medical supervision to ensure proper care and management to prevent diaper dermatitis. As a result, the panel recommended involving a skin and/or stoma nurse on a regular basis for wound, stoma, and perianal care, whether in a hospital setting or not.

* + 1. Information about available products to aid incontinence

Sub-question 2f

Which aids are available (incontinence materials, rinse aids)? Which care provider can advise on this?

Recommendations for sub-question 2f

For this sub-question, no new studies were included and considered by the panel. Two (2) recommendations were adapted, none were adopted and one (1) was developed de novo (new). All recommendations are reported in [Table 12](#table12).

|  |  |  |
| --- | --- | --- |
| AVAILABLE AIDS | | Grade of Recommendation |
| 1 | Patients should be provided with good information about incontinence materials and rectal irrigation products, ideally in collaboration between a specialised ARM nurse and a physician or surgeon. **[adapted]** | - |
| 2 | Patients and parents should be informed of additional aids for incontinence, together with their limitations. **[adapted]** | - |
| 3 | It is recommended that parents and/or patients contact their ARM patient associations for further support. **[new]** | - |

**Table 12.** Recommendations for sub-question 2f.

Justification for sub-question 2f

Recommendations have been made regarding the available aids, materials and products that can be used in the care of ARM patients. The AAWG considered the favourable benefit-risk balance, the acceptability and applicability in order to adopt, adapt or to form new recommendations.

There are all kinds of incontinence materials. Which aids a patient with ARM needs depends, among other things, on the type of incontinence and the extent of the urine and / or stool loss. Based on an intake questionnaire, the specialised nurse will inform and help parents choose the right aids.

The panel considered that the availability of aids such as incontinence materials, rinse aids, and reimbursement options may substantially differ between the European countries. Therefore, the recommendations were either modified or were rejected and the respective sub-question was adjusted accordingly.

* + 1. The support of parents with ARM patients in self-management

Sub-question 2g

How is / are the parents of the patient with ARM supported in self-management?

Recommendations for sub-question 2g

For this sub-question, no new studies were included and considered by the panel. Three (3) recommendations were adapted, one (1) was adopted and one (1) was developed de novo (new). All recommendations are reported in [Table 13.](#table13)

|  |  |  |
| --- | --- | --- |
| AVAILABLE AIDS | | Grade of Recommendation |
| 1 | Refer patients with ARM to patient associations for support and education about self-management of the disease, or to other patients for peer learning. **[adapted]** | - |
| 2 | Include in the patient information material an up-to-date point of contact or a named person to whom patients can reach out to when needed, for information and/or support in 24/7. **[adapted]** | - |
| 3 | It is recommended to work jointly with (the parents of) a patient with ARM a care plan to reach personal treatment goals. **[adapted]** | - |
| 4 | Healthcare professionals should document information about agreed treatment goals in the medical records and/or individual care plans. **[adopted]** | - |
| 5 | It is recommended to review the treatment goals and care plan periodically. **[new]** | - |

**Table 13.** *Recommendations for sub-question 2g.*

Justification for sub-question 2g

Recommendations have been made regarding the support that the parents receive in self-management of their children with ARM. The AAWG considered the favourable benefit-risk balance, the acceptability and applicability in order to adopt, adapt or to form new recommendations.

The AAWG agreed with most recommendations and mainly made adjustments in the wording to come to a set of recommendations that are applicable in all European countries. The AAWG discussed that the periodical review of the treatment goals, is as important as creating the goals; therefore the group formed a new recommendation. Care providers are responsible for thorough documentation of the treatment plan and the panel members agreed that the point of contact does not need to be a specific person, as long as it is clear to everyone who takes on this role. ARM patient associations can provide additional (psychological/social) support to parents and assist them in the management of their child’s condition.

* 1. Implementation, Validity and Evaluation
     1. Implementation

In the different phases of adapting the Quality Standard, the implementation of the Quality Standard and the practical feasibility of the recommendations have been taken into account. In doing so, explicit attention was paid to factors that could promote or hinder the implementation of the Quality Standard in practice.

The panel highlighted that varying resources and priorities in different European countries, limited investments in specialized facilities, equipment, or trained personnel, and the absence of established mechanisms for interdisciplinary collaboration may hinder the implementation of the ARM Quality Standard. Furthermore, variations in regulatory frameworks, legal systems, and knowledge gaps among healthcare professionals, policymakers, and the general public also pose barriers the implementation of a Quality Standard across Europe.

In addition to the challenges mentioned, the panel suggested several manners to promote a widespread adoption of the European Quality Standard for ARM. As eUROGEN is a network consisting of healthcare providers across Europe, panel members can actively contribute by sharing the Quality Standard in their respective countries and advocating for its implementation. Local webinars or workshops can be organized ensuring that the knowledge spreads effectively to healthcare providers who may have limited access to educational resources about the Quality Standard. Furthermore, the AAWG aims to publish topic-specific articles in relevant journals to disseminate information about the Quality Standard. Moreover, eUROGEN organises European webinars on a regular basis, part of which are dedicated to proact the awareness of ARM among healthcare providers. Additionally, translating the Quality Standard into different languages could facilitate its implementation from healthcare professionals who may not be fluent in English.

* + 1. Validity

This Quality Standard is valid from the moment of publication, until the publication of its update. In general, a guideline will undergo evaluation every 5 years. Consequently, the board of the eUROGEN will install a new workgroup in 2028 to evaluate which modules are in need of an update and if there is a need to develop new modules based on the latest insights.

1. Discussion

The purpose of this paper was to adapt the Dutch Quality Standard for patients with Anorectal Malformation to fit the European context. By tailoring the Dutch quality standard, the AAWG aimed to establish a framework that would effectively guide healthcare providers in delivering standardized, high-quality care for patients with ARM throughout Europe, and thus improving overall diagnostics and treatment outcomes by ensuring equitable access to care. The AAWG considered the favorable benefit-risk balance, the acceptability and applicability in order to adopt, adapt or to form new recommendations.

During the process, areas of consensus were identified and areas of ambiguity that require further research were revealed. Upon review of existing literature, the panel verified that the majority of studies lack sufficient evidence, being restricted to retrospective reviews and case series. Important areas of consensus and ambiguity and their research implications are addressed below.

Diagnostic examinations for ARM

The panel did reach consensus on the benefits of improving the prenatal ultrasound diagnostics. Additionally, the panel emphasised that a complementary MRI may add value in the prenatal diagnosis of ARM,13 but the consequences have to be assessed in each case and further research is required to address the benefit-risk balance of the prenatal MRI. The AAWG underlined that the awareness of sonographers should be improved by assessing the anal target sign among others, especially during 28-33 weeks of the prenatal phase.9, 10 The panel was able to form a recommendation, suggesting that a combination of a dilated bowel and the absence of the target sign might be indicative of a high ARM type. However, it was claimed that further research should be conducted to enhance the quality of evidence. Furthermore, sonographers are encouraged to search for cysts in the foetal pelvis during the first and early second trimester, since a cystic abdominal mass finding could raise suspicion for a cloaca or other ARM types.12

The panel strongly agreed on that neonatal ultrasound screening examinations for the urinary tract, spinal cord and heart within the first living month should be mandatory and comprise the gold standard. Screening of malformations within VACTERL association but also genital and gastrointestinal malformations should be performed and documented both in medical chart and in individual patient information. In case of at least one other concomitant malformation in ARM a referral to a clinical genetician or a genetic screening should be conducted.

The panel also reached consensus in broadening the section consisting of the gynecological diagnostic examinations by renaming it to ‘Diagnostic exams of the reproductive systems’. By doing so, the group aimed in broadening the scope ensuring that patients receive thorough examinations based on their unique anatomical variations and also including males. Future research should focus on providing insights for the diagnostic examinations of both genders and their reproductive systems, respectively.

Treatment of ARM

The panel did not reach consensus on a preferable surgical technique for patients with ARM. There are multiple surgical modalities used for treating ARM depending on the abnormalities and comorbidities found in each individual patient or the surgeons’ expertise. Further investigation is necessary through clinical trials in ARM expertise centers to assess the effectiveness of various treatment modalities and make specific recommendations for (subgroups of) patients.

The best timing of primary reconstruction and restoring the bowel continuity reached consensus. Unless there are contra indications such as life-threatening comorbidities, the panel agreed that the surgical procedure should be conducted within the first year of life.19 Importantly, a careful preoperative diagnostic work-up in rare and complicated ARM sub-types should be prioritized.

Furthermore, the AAWG unanimously agreed that certain questions from the original Quality Standard, related to the treatment module, had to be modified or to be rejected. These questions were assessed to not be suitable for inclusion in a European Quality Standard due to heterogeneity in healthcare practices and policies across Europe. For these reasons, no appropriate recommendations could be formed for the management of frequent urinary tract infections. If recommendations are updated in the future, evaluation of best practices could be more thorough if specific PICO-questions and GRADE-methodology is applied.

1. Conclusion

ERN eUROGEN aims to form a Quality Standard for ARM that can be applicable in every European country. A set of recommendations was developed for the diagnosis and treatment of ARM according to the European context and based on current evidence. Close attention should be paid to the dissemination and the implementation of this adapted Quality Standard across the target groups. Further research is required to enhance the certainty of evidence in areas of ambiguity and to develop more evidence-based recommendations for the diagnosis and treatment of ARM.

About this document

# Disclosures

We would like to disclose that two of the authors of this adaptation report, (IDB, CEJS) were also authors of the Dutch Quality Standard. However, it is important to note that neither IDB, nor CEJS have any conflict of interest to declare and they did not advocate for any particular viewpoints or positions in relation to the content of the Dutch Quality Standard. No conflicting interests were declared from the authors.

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# Collaboration

This work was performed in collaboration with experts involved in ERN ERNICA, EUPSA and Qualicura.





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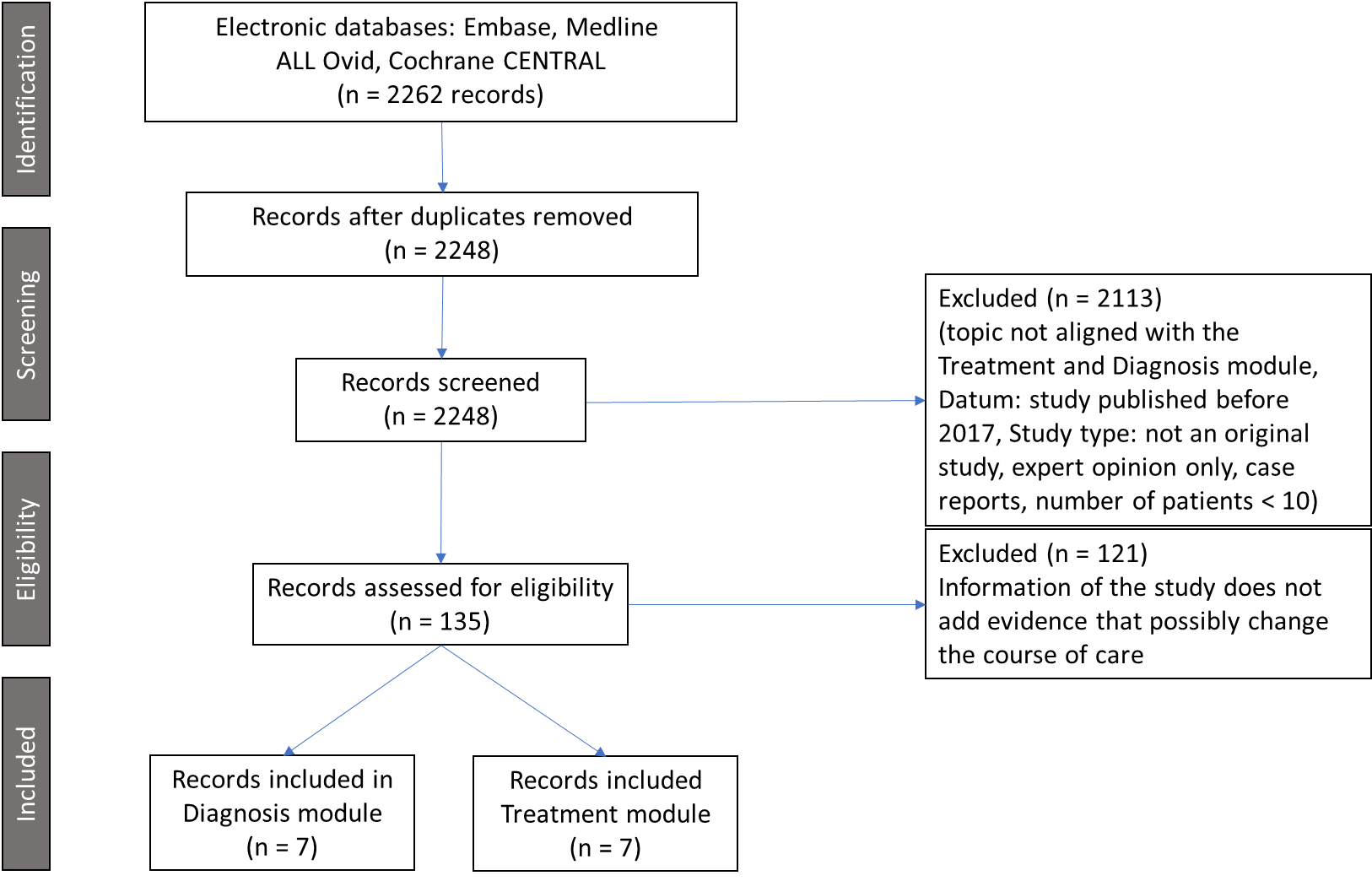
Appendix

**SYSTEMATIC LITERATURE SEARCH**

|  |  |  |  |  |
| --- | --- | --- | --- | --- |
|  | EMBASE | OVID/MEDLINE | Cochrane CENTRAL | Deduplicated |
| SRs | 223 | 135 |  | 249 |
| RCTs | 411 | 155 |  | 475 |
| Observational studies | 1356 | 884 |  | 1526 |
| Other |  |  | 58 | 12 |
| **Total** |  |  |  | 2262 |

**Appendix Table 1.** Systematic literature search

**LITERATURE REVIEW**



**Appendix Figure A.** Prisma flow diagram of literature selection

**Summary of the evidence for sub-question 1a**

Sub-question 1a

Five (5) new studies, published between 2018 and 2022, were found for prenatal diagnosis and one (1) new study published in 2020 was found for neonatal diagnosis.

|  |  |
| --- | --- |
| PRENATAL | Author |
| Study type: Retrospective chart review (case series)  Aim: review of diagnostic approaches for diagnosing foetal imperforate anus.  Population: neonates with ARM  Results: Ultrasonography was performed in 19 cases of foetal imperforate anus from 2016 to 2019 at the prenatal diagnostic centre. Foetuses at 21–24 weeks and 30–34 weeks were examined for anal deformity. The ability to recognize the most typical ultrasound findings in imperforate anus can improve the detection rate.  Conclusion: The absence of the ‘target sign’ and then the presence of the ‘line sign’ can assist in the diagnosis of imperforate anus. The ‘line sign’ can be used as a secondary assessment to determine the type of the malformation following non-visualization of the ‘target sign’ | Yin et al., 20229 |
| Type of study: Prospective Case series  Population: 900 ultrasounds in 372 different pregnant women.  Interventions: Prenatal ultrasound to visualize anal dimple  Results: In the fetuses with more than one ultrasound, the anal dimple (AD) was visualized at least once in 164 (81%) cases, and not visualized in any ultrasound in 39 (19%). The optimal gestational age range for AD visualization was 28–33 weeks + 6 days, with 78.1% visualization rate (*p* < 0.001). Only one baby was found to have ARM.  Conclusion: The study concludes that visualization of the anal dimple by prenatal ultrasound is feasible and may aid in the detection of less severe ARM  Level of evidence: Level III study (OCEBM, 2011) | Bischoff et al. 202110 |
| Type of study: Prospective cohort  Population: Between January 2008 and January 2016, 63,101 foetuses (gestational age, 20–38 weeks) were prospectively evaluated using 2-dimensional US scans.  Results: Among the investigated foetuses, 28 showed evidence of anorectal atresia on US scans, and 22 of those with anorectal atresia had additional anomalies. Six cases of isolated anorectal atresia were successfully detected during the preclusive prenatal US scans.  Conclusion: Identifying the abnormal appearance or absence of the foetal anal canal and rectum on preclusive US anomaly scans is useful for prenatal diagnosis or exclusion of anorectal atresia, which may help improve the detection of isolated anorectal atresia. However the diagnosic accuracy is low and detection of a muscular complex does not exclued low ARM types.  Level of evidence: Level III study | Su et al., 201911 |
| Type of study: Systematic review of case reports  Population: Patients where ARM was diagnosed prenatally  Results: In 12 of the 14 cases reported in the literature of ARM diagnosed in the first trimester, the first sonographic sign was a hypoechoic cystic mass in the abdomen. In four cases, the hypoechoic content converted into a hyperechoic mass during the second trimester. In four other cases, the cystic mass disappeared and the bowel had a normal appearance at mid gestation. In five cases, the cystic mass remained unchanged until mid-gestation.  Conclusion: The study emphasizes the importance of maintaining a high index of suspicion for ARM when a cystic mass appears in the lower abdomen in the first trimester  Level of evidence: Level IV (OCEBM, 2011) | Liberty et al., 201812 |
| Type of study: Retrospective comparison  Population: A retrospective study included 13 US and 8 MRI exams, with 7 children having both exams.  Results: All cases (n=14) had associated congenital anomalies. The detection rate of US was 31% [95% CI 0.25–0.37] (4/13; 3 anorectal malformations and 1 cloaca), and for MRI was 50% [95% CI 0.41–0.59] (4/8; 1 anorectal malformation and 3 cloacae). The study conclude that the foetal perineum should be carefully examined in prenatal US screening exams, especially in foetuses with urinary and spinal anomalies.  Conclusion: Complementary MRI should be performed in foetuses with cloaca or multiple congenital anomalies at US screening  Level of evidence: Level III | Rohrer et al., 202013 |
| **NEONATAL** | **Author** |
| Type of study: Diagnostic test accuracy Aim: The study aimed to correlate spinal ultrasound and magnetic resonance imaging findings in patients with ARM.  Population: 193 patients with ARM. Results: Spinal ultrasound had an overall sensitivity of 91% and specificity of 75% compared to MRI for detecting spinal cord anomalies in children with ARM.  Conclusion: spinal ultrasound performed in a tertiary paediatric imaging department was a good screening test for spinal cord anomalies in children with ARM. The finding of a low, borderline low or tethered cord on US mandates an MRI to confirm the findings and correlates with the need for operative correction of spinal cord tethering | Jehangir et al., 202014 |

**Appendix Table 2.** Summary of evidence for prenatal and neonatal diagnostics

**Summary of the evidence for sub-questions 1b and 1c**

One (1) new study published in 2018 was found.

|  |  |
| --- | --- |
| BEFORE SURGERY | Author |
| Study type: Case series on diagnostic features  Aim: To evaluate the difference in pouch-perineum distance (PPD) between neonates with a low-type ARM with and without an opened fistula. Populations: Retrospective analysis of 24 neonates with low-type ARM who underwent sonography before surgery.  Results: The mean PPD in neonates with an opened fistula was 10.6 mm ± 3.4 mm (range, 5.6–14.0 mm), compared to 7.1 ± 1.7 mm (range 3.3–10.0 mm) without an opened fistula (*p*<.02).  Conclusion: The study found that the pouch-perineum distance is substantially longer in neonates with an ARM with an opened fistula than in those without an opened fistula. Therefore, caution should be exercised by the sonographic examiner in evaluating pouch-perineum distance in neonates with an opened fistula to prevent an incorrect surgical procedure based on misdiagnosis of the type of ARM  Level of evidence: Level III study (OCEBM, 2011) | Hosokawa et al., 201816 |

**Appendix Table 3.** Summary of evidence for diagnostic examinations performed during and after surgeries and during follow-up

**Summary of the evidence for treatment of ARM**

Seven (7) new studies published between 2017 and 2022 were found form the systematic literature search.

|  |  |
| --- | --- |
| SINGLE-STAGE AND MULTI-STAGE ANORECTOPLASTY | Author |
| Type of study: systematic review with meta-analysis (5 retrospective studies and 1 randomized controlled trial (RCT); n = 199 female patients)  Interventions: one-stage sagittal anorectoplasty (SARP) without prior colostomy vs conventional two or three-step sagittal anorectoplasty (SARP).  Population: females with recto-vestibular fistula (RVF).  Results: one-stage approach increases the risk of postoperative complications, such as wound infection, dehiscence and anorectal stenosis. Nevertheless, the one-stage approach was not associated with reduced faecal continence and constipation compared to the multi-stage repair.  Level of evidence: Level III study (OCEBM)  Authors’ conclusions: choose the surgical approach based on the surgeon’s experience and the patient’s general conditions. | Lauriti et al, 201921 |
| Type of study: RCT  Interventions: single-stage procedures vs two or three-step procedures.  Population: Females with low-type ARM (85% VF), mean age  Results: Wound dehiscence (superficial and deep) occurred in 13 of 33 (39.4%) children in Group I and in 6 of 31 (18.2%) children in Group II. This difference was significant (P = 0.038). On logistic regression analysis, the odds ratio of wound dehiscence associated with a staged procedure was 0.55 (95% confidence interval = 0.31-0.98; P = 0.042).  Level of evidence: Level III study (OCEBM) (rated down for high risk of bias)  Authors’ conclusions: Females with low-type ARM treated with primary definitive procedure have a significantly higher incidence of wound dehiscence, immediate and early postoperative complications. Intraoperative faecal contamination of the surgical site significantly increased the incidence of wound dehiscence. | Gupta et al., 201723 |
| **ANAL DILATIONS /CALIBRATIONS** |  |
| Type of study: randomised controlled trial.  Population: 50 patients (40% females) with ARM who underwent a posterior sagittal anorectoplasty (PSARP).  Interventions: postoperative dilation with Hegar protocol vs no postoperative dilations (except if a stricture was detected during follow-up).  Results: no statistically significant differences in stricture formation between both groups.  13% of patients in the dilation group vs 16% of patients in the control group needed surgery to manage skin-level strictures;  A redo PSARP was needed in 8% of patients of both groups to manage deep strictures.  Level of evidence: Level II study (OCEBM, 2011)  Authors’ conclusions: parents should be given a choice whether or not to perform routine dilations at home. Close follow-up is recommended if they choose not to perform. Contemplate non-dilation as a viable alternative, with Heineke-Mikulicz anoplasty as a backup plan when a stricture develops. | Ahmad et al., 202122 |
| **OTHER SURGICAL APPROACHES** |  |
| Type of study: treatment guidelines (TGs)  Population: patients with persistent cloaca (PC), cloacal exstrophy (CE), or Mayer–Rokitansky–Küster–Häuser syndrome (MRKH).  Results: Clinical questions (CQs) concerning treatment outcomes of the genitourinary system, pregnancy and delivery, and quality of life in adulthood were prepared as six themes for PC and CE and five themes for MRKH. We were able to publish statements on chronic renal dysfunction, hydrometrocolpos, and pregnancy, based on four CQs about PC, four about CE, and two about MRKH, respectively  Level of evidence: Level IV study (OCEBM, 2011)  Authors’ conclusions: due to the paucity of proper manuscripts, we were unable to make conclusions about the correct timing and method of vaginoplasty for patients with PC, CE, and MRKH or the usefulness of early bladder closure for patients with CE. These TGs may help clarify the current treatments for PC, CE, and MRKH in childhood, which have been carried out on an institutional basis. To improve clinical outcomes, systematic clinical trials revealing comprehensive clinical data of the urinary and reproductive systems, especially the length of the common channel in PC, are essential. | Kubota et al., 201917 |
| Type of study: retrospective cohort study.  Interventions: surgical complications and postoperative defecation function between neonates and infants undergoing anterior sagittal anorectoplasty (ASARP).  Population: 35 females with AVF (17 undergoing surgery as neonates and 18 as infants).  Results: Surgery duration was shorter for neonates, as well as time to restart oral intake. Postoperative complications more frequent in infants (mostly wound dehiscence). No significant differences in long-term defecation function scores, though less patients in neonatal group required every day enemas or defecation assistance during a follow-up of 4 years.  Level of evidence: Level IV study (OCEBM, 2011)  Authors’ conclusions: single-stage ASARP for anovestibular fistula can be performed even in the neonatal period. | Shirota et al., 201819 |
| Type of study: systematic review and consensus statements  Population: patients with normal Anus, Anterior anus (AA) and milder types of ARM such as congenital anal stenosis (CAS) and perineal fistula (PF).  Results: a consensus on definitions, clinical characteristics, diagnostic management, and treatment modalities was established, and a diagnostic algorithm was proposed. The algorithm enables pediatricians, midwives, gynecologists, and surgeons to make a timely correct diagnosis of any abnormally looking anus and initiate further management if needed.  Level of evidence: Level II study (OCEBM, 2011)  Authors’ conclusions: the routine physical inspection of a newborn should include the inspection of the anus and define its position, relation to the external sphincter, and caliber. A correct diagnosis and use of the presented terminology will avoid misclassifications and allow the initiation of correct management. This will provide a reliable comparison of different therapeutic management and outcomes of these patient cohorts in the future. | Amerstorfer et al, 202020 |
| Type of study: case series.  Population: 153 patients (29% females) with previous ARM repair.  Aims: assess the benefit of a redo posterior sagittal anorectoplasty (PSARP) in patients still suffering from faecal incontinence.  Results: significant improvement in validated faecal incontinence and quality of life scores (Baylor and PedsQL scores) after a redo PSARP. All patients included for a redo procedure were also placed on an aggressive bowel management program with either a laxative or an enema-based regimen.  Level of evidence*:* Level IV study (OCEBM, 2011)  Authors’ conclusions: a redo procedure in patients with a previously repaired ARM along with intensive bowel management can significantly improve both faecal continence, cleanliness for stool and quality of life in a majority of patients. | Wood et al., 202024 |

**Appendix Table 4.** Summary of evidence for treatment modalities

**DUTCH QUALITY STANDARD APPRAISAL**

|  |  |
| --- | --- |
| Domain | Signaling question |
| **Domain 1. Scope and purpose** | Item 1. The overall objective(s) of the guideline is (are) specifically described. |
|  | Item 2. The health question(s) covered by the guideline is (are) specifically described. |
|  | Item 3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described. |
| **Domain 2. Stakeholder Involvement** | Item 4. The guideline development group includes individuals from all relevant professional groups. |
|  | Item 5. The views and preferences of the target population (patients, public, etc.) have been sought. |
|  | Item 6. The target users of the guideline are clearly defined. |
| **Domain 3. Rigour of Development** | Item 7. Systematic methods were used to search for evidence. |
|  | Item 8. The criteria for selecting the evidence are clearly described. |
|  | Item 9. The strengths and limitations of the body of evidence are clearly described. |
|  | Item 10. The methods for formulating the recommendations are clearly described. |
|  | Item 11. The health benefits, side effects, and risks have been considered in formulating the recommendations. |
|  | Item 12. There is an explicit link between the recommendations and the supporting evidence. |
|  | Item 13. The guideline has been externally reviewed by experts prior to its publication. |
|  | Item 14. A procedure for updating the guideline is provided. |
| **Domain 4. Clarity of Presentation** | Item 15. The recommendations are specific and unambiguous. |
|  | Item 16. The different options for management of the condition or health issue are clearly presented. |
|  | Item 17. Key recommendations are easily identifiable. |
| **Domain 5. Applicability** | Item 18. The guideline describes facilitators and barriers to its application. |
|  | Item 19. The guideline provides advice and/or tools on how the recommendations can be put into practice. |
|  | Item 20. The potential resource implications of applying the recommendations have been considered. |
|  | Item 21. The guideline presents monitoring and/or auditing criteria. |
| **Domain 6. Editorial Independence** | Item 22. The views of the funding body have not influenced the content of the guideline. |
|  | Item 23. Competing interests of guideline development group members have been recorded and addressed. |

**Appendix Table 5.** AGREE II domains and items.

Results

Domain scores were calculated by summing up all the scores of the individual items in a domain and by scaling the total as a percentage of the maximum possible score for that domain.

* Domain 1 (scope and purpose) had a standard domain score of 88%. The objectives and population were clearly described in the guideline; however, the health questions covered by the guideline were only vaguely described.
* Domain 2 (stakeholder involvement) was the highest scoring domain with full marks being awarded by each reviewer for each signaling question resulting in a standard score domain of 1.
* Domain 3 (rigour of development) had a standard domain score of 78%. There was a variety of responses and disagreement in this domain between reviewers. It was clearly described in the guideline that systematic methods were used and that there is a procedure in place for updating the guideline. However, the other questions in this domain were more ambiguous throughout the methods of the guideline development.
* Domain 4 (clarity of presentation) had a standard domain score of 75%. The recommendations were evaluated as being unspecific and ambiguous and the key recommendations were not easily identifiable.
* Domain 5 (applicability) was the lowest scoring domain with a standard domain score of 46%. However, there was a high level of disagreement between reviewers in this domain for all of the signaling questions.
* Domain 6 (editorial independence) had a standard domain score of 75%. The competing interests wasn´t clear to some of the reviewers.

The overall standard domain score given by the reviewers was 38%. The guideline was recommended for use with some modifications by two reviewers and recommended for use without modifications by the other two reviewers.

AGREE II quality scores

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Quality Standard for Anorectal Malformation | | ES | PG | ML | JG | Total | Min | Max | Standard Domain  Score |
| **Domain 1. Scope and purpose** | Item 1. The overall objective(s) of the guideline is (are) specifically described. | 7 | 6 | 7 | 7 | 27 | **12** | **84** | **88%** |
| Item 2. The health question(s) covered by the guideline is (are) specifically described. | 7 | 3 | 7 | 7 | 24 |
| Item 3. The population (patients, public, etc.) to whom the guideline is meant to apply is specifically described. | 4 | 6 | 7 | 7 | 24 |
|  | **Total** | 18 | 15 | 21 | 21 | **75** |
|  |  |  |  |  |  |  |  |  |  |
| **Domain 2. Stakeholder Involvement** | Item 4. The guideline development group includes individuals from all relevant professional groups. | 7 | 7 | 7 | 7 | 28 | **12** | **84** | **100%** |
| Item 5. The views and preferences of the target population (patients, public, etc.) have been sought. | 7 | 7 | 7 | 7 | 28 |
| Item 6. The target users of the guideline are clearly defined. | 7 | 7 | 7 | 7 | 28 |
|  | **Total** | 21 | 21 | 21 | 21 | **84** |
|  |  |  |  |  |  |  |  |  |  |
| **Domain 3. Rigour of Development** | Item 7. Systematic methods were used to search for evidence. | 7 | 7 | 7 | 7 | 28 | **32** | **224** | **78%** |
| Item 8. The criteria for selecting the evidence are clearly described. | 5 | 4 | 7 | 7 | 23 |
| Item 9. The strengths and limitations of the body of evidence are clearly described. | 3 | 1 | 7 | 7 | 18 |
| Item 10. The methods for formulating the recommendations are clearly described. | 5 | 3 | 7 | 7 | 22 |
| Item 11. The health benefits, side effects, and risks have been considered in formulating the recommendations. | 5 | 4 | 7 | 7 | 23 |
| Item 12. There is an explicit link between the recommendations and the supporting evidence. | 1 | 3 | 7 | 7 | 18 |
| Item 13. The guideline has been externally reviewed by experts prior to its publication. | 7 | 4 | 7 | 7 | 25 |
| Item 14. A procedure for updating the guideline is provided. | 7 | 3 | 7 | 7 | 24 |
|  | **Total** | 40 | 29 | 56 | 56 | **181** |
|  |  |  |  |  |  |  |  |  |  |
| **Domain 4. Clarity of Presentation** | Item 15. The recommendations are specific and unambiguous. | 3 | 4 | 7 | 7 | 21 | **12** | **84** | **75%** |
| Item 16. The different options for management of the condition or health issue are clearly presented. | 7 | 6 | 7 | 7 | 27 |
| Item 17. Key recommendations are easily identifiable. | 3 | 1 | 7 | 7 | 18 |
|  | **Total** | 13 | 11 | 21 | 21 | **66** |
|  |  |  |  |  |  |  |  |  |  |
| **Domain 5. Applicability** | Item 18. The guideline describes facilitators and barriers to its application. | 1 | 2 | 7 | 7 | 17 | **16** | **112** | **46%** |
| Item 19. The guideline provides advice and/or tools on how the recommendations can be put into practice. | 4 | 1 | 5 | 5 | 15 |
| Item 20. The potential resource implications of applying the recommendations have been considered. | 1 | 1 | 7 | 7 | 16 |
| Item 21. The guideline presents monitoring and/or auditing criteria. | 1 | 1 | 5 | 5 | 12 |
|  | **Total** | 7 | 5 | 24 | 24 | **60** |
|  |  |  |  |  |  |  |  |  |  |
| **Domain 6. Editorial Independence** | Item 22. The views of the funding body have not influenced the content of the guideline. | 7 | 7 | 7 | 7 | 28 | **8** | **56** | **75%** |
| Item 23. Competing interests of guideline development group members have been recorded and addressed. | 7 | 7 | 1 | 1 | 16 |
|  | **Total** | 14 | 14 | 8 | 8 | **44** |
|  |  |  |  |  |  |  |  |  |  |
| **Overall assessment** Please, rate the overall quality of this guideline | | 5 | 4 | 7 | 7 | 23 | **7** | **49** | **38%** |
|  | **Total** | 5 | 4 | 7 | 7 | **23** |
|  |  |  |  |  |  |  |  |  |  |
| **Would you recommend this guideline for use?** | | **Yes, with modifications** | **Yes, with modifications** | **Yes** | **Yes** |  |  | |  | | --- | |  | |  |

**Appendix Table 6.** AGREE II quality scores

Standardised scores per AGREE II domain

|  |  |
| --- | --- |
| **AGREE II Instrument** | Quality Standard for Anorectal Malformation |
| Domain 1. Scope and Purpose | 88% |
| Domain 2. Stakeholder Involvement | 100% |
| Domain 3. Rigour of Development | 78% |
| Domain 4. Clarity of Presentation | 75% |
| Domain 5. Applicability | 46% |
| Domain 6. Editorial Independence | 75% |

**Appendix Figure 2.** Standard domain scores of each domain

**SYSTEMATIC LITERATURE SEARCH STRATEGY**

**Embase**

|  |  |  |
| --- | --- | --- |
| No. | Query | Results |
| #11 | #9 NOT #8 NOT #7 OBS | 1356 |
| #10 | #8 NOT #7 Clinical trials, RCT | 411 |
| #9 | #2 AND (#5 OR #6) | 1564 |
| #8 | #2 AND #4 | 346 |
| #7 | #2 AND #3SR | 223 |
| #6 | 'case control study'/de OR 'comparative study'/exp OR 'control group'/de OR 'controlled study'/de OR 'controlled clinical trial'/de OR 'crossover procedure'/de OR 'double blind procedure'/de OR 'phase 2 clinical trial'/de OR 'phase 3 clinical trial'/de OR 'phase 4 clinical trial'/de OR 'pretest posttest design'/de OR 'pretest posttest control group design'/de OR 'quasi experimental study'/de OR 'single blind procedure'/de OR 'triple blind procedure'/de OR (((control OR controlled) NEAR/6 trial):ti,ab,kw) OR (((control OR controlled) NEAR/6 (study OR studies)):ti,ab,kw) OR (((control OR controlled) NEAR/1 active):ti,ab,kw) OR 'open label\*':ti,ab,kw OR (((double OR two OR three OR multi OR trial) NEAR/1 (arm OR arms)):ti,ab,kw) OR ((allocat\* NEAR/10 (arm OR arms)):ti,ab,kw) OR placebo\*:ti,ab,kw OR 'sham-control\*':ti,ab,kw OR (((single OR double OR triple OR assessor) NEAR/1 (blind\* OR masked)):ti,ab,kw) OR nonrandom\*:ti,ab,kw OR 'non-random\*':ti,ab,kw OR 'quasi-experiment\*':ti,ab,kw OR crossover:ti,ab,kw OR 'cross over':ti,ab,kw OR 'parallel group\*':ti,ab,kw OR 'factorial trial':ti,ab,kw OR ((phase NEAR/5 (study OR trial)):ti,ab,kw) OR ((case\* NEAR/6 (matched OR control\*)):ti,ab,kw) OR ((match\* NEAR/6 (pair OR pairs OR cohort\* OR control\* OR group\* OR healthy OR age OR sex OR gender OR patient\* OR subject\* OR participant\*)):ti,ab,kw) OR ((propensity NEAR/6 (scor\* OR match\*)):ti,ab,kw) OR versus:ti OR vs:ti OR compar\*:ti OR ((compar\* NEAR/1 study):ti,ab,kw) OR (('major clinical study'/de OR 'clinical study'/de OR 'cohort analysis'/de OR 'observational study'/de OR 'cross-sectional study'/de OR 'multicenter study'/de OR 'correlational study'/de OR 'follow up'/de OR cohort\*:ti,ab,kw OR 'follow up':ti,ab,kw OR followup:ti,ab,kw OR longitudinal\*:ti,ab,kw OR prospective\*:ti,ab,kw OR retrospective\*:ti,ab,kw OR observational\*:ti,ab,kw OR 'cross sectional\*':ti,ab,kw OR cross?ectional\*:ti,ab,kw OR multicent\*:ti,ab,kw OR 'multi-cent\*':ti,ab,kw OR consecutive\*:ti,ab,kw) AND (group:ti,ab,kw OR groups:ti,ab,kw OR subgroup\*:ti,ab,kw OR versus:ti,ab,kw OR vs:ti,ab,kw OR compar\*:ti,ab,kw OR 'odds ratio\*':ab OR 'relative odds':ab OR 'risk ratio\*':ab OR 'relative risk\*':ab OR 'rate ratio':ab OR aor:ab OR arr:ab OR rrr:ab OR ((('or' OR 'rr') NEAR/6 ci):ab))) | 13923341 |
| #5 | 'major clinical study'/de OR 'clinical study'/de OR 'case control study'/de OR 'family study'/de OR 'longitudinal study'/de OR 'retrospective study'/de OR 'prospective study'/de OR 'comparative study'/de OR 'cohort analysis'/de OR ((cohort NEAR/1 (study OR studies)):ab,ti) OR (('case control' NEAR/1 (study OR studies)):ab,ti) OR (('follow up' NEAR/1 (study OR studies)):ab,ti) OR (observational NEAR/1 (study OR studies)) OR ((epidemiologic NEAR/1 (study OR studies)):ab,ti) OR (('cross sectional' NEAR/1 (study OR studies)):ab,ti) | 6767914 |
| #4 | 'clinical trial'/exp OR 'randomization'/exp OR 'single blind procedure'/exp OR 'double blind procedure'/exp OR 'crossover procedure'/exp OR 'placebo'/exp OR 'prospective study'/exp OR rct:ab,ti OR random\*:ab,ti OR 'single blind':ab,ti OR 'randomised controlled trial':ab,ti OR 'randomized controlled trial'/exp OR placebo\*:ab,ti | 3302394 |
| #3 | 'meta analysis'/exp OR 'meta analysis (topic)'/exp OR metaanaly\*:ti,ab OR 'meta analy\*':ti,ab OR metanaly\*:ti,ab OR 'systematic review'/de OR 'cochrane database of systematic reviews'/jt OR prisma:ti,ab OR prospero:ti,ab OR (((systemati\* OR scoping OR umbrella OR 'structured literature') NEAR/3 (review\* OR overview\*)):ti,ab) OR ((systemic\* NEAR/1 review\*):ti,ab) OR (((systemati\* OR literature OR database\* OR 'data base\*') NEAR/10 search\*):ti,ab) OR (((structured OR comprehensive\* OR systemic\*) NEAR/3 search\*):ti,ab) OR (((literature NEAR/3 review\*):ti,ab) AND (search\*ti,ab OR database\*:ti,ab OR 'data base\*':ti,ab)) OR (('data extraction':ti,ab OR 'data source\*':ti,ab) AND 'study selection':ti,ab) OR ('search strategy':ti,ab AND 'selection criteria':ti,ab) OR ('data source\*':ti,ab AND 'data synthesis':ti,ab) OR medline:ab OR pubmed:ab OR embase:ab OR cochrane:ab OR (((critical OR rapid) NEAR/2 (review\* OR overview\* OR synthes\*)):ti) OR ((((critical\* OR rapid\*) NEAR/3 (review\* OR overview\* OR synthes\*)):ab) AND (search\*:ab OR database\*:ab OR 'data base\*':ab)) OR metasynthes\*:ti,ab OR 'meta synthes\*':ti,ab | 733409 |
| #2 | #1 AND [1-1-2017]/sd NOT ('conference abstract'/it OR 'editorial'/it OR 'letter'/it OR 'note'/it) NOT (('animal'/exp OR 'animal experiment'/exp OR 'animal model'/exp OR 'nonhuman'/exp) NOT 'human'/exp) | 3517 |
| #1 | 'anorectal malformation'/exp OR 'cloacal malformation'/exp OR 'cloacal anomaly'/exp OR (((rectal OR anorectal OR anal OR anus OR cloaca\*) NEAR/3 (atres\* OR anomal\* OR malformat\* OR atret\* OR imperforat\* OR agenes\*)):ti,ab,kw) OR ((currarin\* NEAR/3 (syndrome\* OR triad)):ti,ab,kw) OR (((lumbar OR townes OR pallister) NEAR/3 syndrome\*):ti,ab,kw) OR 'hypothalam\* hamartoblastom\*':ti,ab,kw OR 'hydrocolpos'/exp OR 'urethra fistula'/exp OR hydrocolpos:ti,ab,kw OR (((urethra OR perineal OR rectovestibular OR rectobulbar OR 'recto bulbar' OR 'recto vestibular' OR rectourinary OR 'recto urinary' OR 'recto bladder' OR 'peri anal' OR perianal) NEAR/3 fistula):ti,ab,kw) OR 'perineal fistula'/exp OR 'rectovestibular fistula'/exp OR 'rectobulbar fistula'/exp OR 'rectal stenosis'/exp OR 'rectal stenos\*':ti,ab,kw | 16668 |

**Ovid/Medline**

|  |  |  |
| --- | --- | --- |
| **#** | **Searches** | **Results** |
| 12 | 10 not 9 not 8 OBS | 884 |
| 11 | 9 not 8 Clinical trials, RCTs | 155 |
| 10 | 3 and (6 or 7) | 1078 |
| 9 | 3 and 5 | 190 |
| 8 | 3 and 4 SR | 135 |
| 7 | Case-control Studies/ or clinical trial, phase ii/ or clinical trial, phase iii/ or clinical trial, phase iv/ or comparative study/ or control groups/ or controlled before-after studies/ or controlled clinical trial/ or double-blind method/ or historically controlled study/ or matched-pair analysis/ or single-blind method/ or (((control or controlled) adj6 (study or studies or trial)) or (compar\* adj (study or studies)) or ((control or controlled) adj1 active) or "open label\*" or ((double or two or three or multi or trial) adj (arm or arms)) or (allocat\* adj10 (arm or arms)) or placebo\* or "sham-control\*" or ((single or double or triple or assessor) adj1 (blind\* or masked)) or nonrandom\* or "non-random\*" or "quasi-experiment\*" or "parallel group\*" or "factorial trial" or "pretest posttest" or (phase adj5 (study or trial)) or (case\* adj6 (matched or control\*)) or (match\* adj6 (pair or pairs or cohort\* or control\* or group\* or healthy or age or sex or gender or patient\* or subject\* or participant\*)) or (propensity adj6 (scor\* or match\*))).ti,ab,kf. or (confounding adj6 adjust\*).ti,ab. or (versus or vs or compar\*).ti. or ((exp cohort studies/ or epidemiologic studies/ or multicenter study/ or observational study/ or seroepidemiologic studies/ or (cohort\* or 'follow up' or followup or longitudinal\* or prospective\* or retrospective\* or observational\* or multicent\* or 'multi-cent\*' or consecutive\*).ti,ab,kf.) and ((group or groups or subgroup\* or versus or vs or compar\*).ti,ab,kf. or ('odds ratio\*' or 'relative odds' or 'risk ratio\*' or 'relative risk\*' or aor or arr or rrr).ab. or (("OR" or "RR") adj6 CI).ab.)) | 5381225 |
| 6 | Epidemiologic studies/ or case control studies/ or exp cohort studies/ or Controlled Before-After Studies/ or Case control.tw. or cohort.tw. or Cohort analy$.tw. or (Follow up adj (study or studies)).tw. or (observational adj (study or studies)).tw. or Longitudinal.tw. or Retrospective\*.tw. or prospective\*.tw. or consecutive\*.tw. or Cross sectional.tw. or Cross-sectional studies/ or historically controlled study/ or interrupted time series analysis/ [Onder exp cohort studies vallen ook longitudinale, prospectieve en retrospectieve studies] | 4391876 |
| 5 | exp clinical trial/ or randomized controlled trial/ or exp clinical trials as topic/ or randomized controlled trials as topic/ or Random Allocation/ or Double-Blind Method/ or Single-Blind Method/ or (clinical trial, phase i or clinical trial, phase ii or clinical trial, phase iii or clinical trial, phase iv or controlled clinical trial or randomized controlled trial or multicenter study or clinical trial).pt. or random\*.ti,ab. or (clinic\* adj trial\*).tw. or ((singl\* or doubl\* or treb\* or tripl\*) adj (blind$3 or mask$3)).tw. or Placebos/ or placebo\*.tw. | 2566361 |
| 4 | meta-analysis/ or meta-analysis as topic/ or (metaanaly\* or meta-analy\* or metanaly\*).ti,ab,kf. or systematic review/ or cochrane.jw. or (prisma or prospero).ti,ab,kf. or ((systemati\* or scoping or umbrella or "structured literature") adj3 (review\* or overview\*)).ti,ab,kf. or (systemic\* adj1 review\*).ti,ab,kf. or ((systemati\* or literature or database\* or data-base\*) adj10 search\*).ti,ab,kf. or ((structured or comprehensive\* or systemic\*) adj3 search\*).ti,ab,kf. or ((literature adj3 review\*) and (search\* or database\* or data-base\*)).ti,ab,kf. or (("data extraction" or "data source\*") and "study selection").ti,ab,kf. or ("search strategy" and "selection criteria").ti,ab,kf. or ("data source\*" and "data synthesis").ti,ab,kf. or (medline or pubmed or embase or cochrane).ab. or ((critical or rapid) adj2 (review\* or overview\* or synthes\*)).ti. or (((critical\* or rapid\*) adj3 (review\* or overview\* or synthes\*)) and (search\* or database\* or data-base\*)).ab. or (metasynthes\* or meta-synthes\*).ti,ab,kf. | 655973 |
| 3 | 2 not ((exp animals/ or exp models, animal/) not humans/) not (letter/ or comment/ or editorial/) | 2394 |
| 2 | limit 1 to yr="2017 -Current" | 2548 |
| 1 | Anorectal Malformations/ or Anus, Imperforate/ or Hydrocolpos/ or Rectovaginal Fistula/ or ((rectal or rectum or anorectal or anal or anus or cloaca\*) adj3 (atres\* or anomal\* or malformat\* or atret\* or imperforat\* or agenes\*)).ti,ab,kf. or (currarin\* adj3 (syndrome\* or triad)).ti,ab,kf. or ((lumbar or townes or pallister) adj3 syndrome\*).ti,ab,kf. or hypothalam\* hamartoblastom\*.ti,ab,kf. or hydrocolpos.ti,ab,kf. or ((urethra or perineal or rectovestibular or rectobulbar or recto bulbar or recto vestibular or rectourinary or recto urinary or vesicorectal or vesico rectal or rectobladder or recto bladder or perianal or peri anal) adj3 fistula).ti,ab,kf. or rectal stenos\*.ti,ab,kf. | 11279 |

**Cochrane CENTRAL**

#1  (“anorectal malformation” OR “perineal fistula” OR “rectovestibular fistula” OR “recto-bulbar urethral fistula” OR “recto-bladder neck fistula” OR “anus atresia” OR “rectal atresia” OR “rectal stenosis” OR “hydrocolpos” OR “bulbar fistula” OR “recto-urethral fístula” OR “urethra fistula” OR “anus malformation” OR “rectum malformation” OR “urogenital tract malformation” OR “anal atresia” OR “imperforate anus”):ti,ab,kw (Word variations have been searched)

#2  MeSH descriptor: [Anorectal Malformations] explode all trees  113

#3 2017 -

Chart, bubble chart

Description automatically generated

<https://ec.europa.eu/health/ern_en>



<https://eurogen-ern.eu/>

Blue text on a black background

Description automatically generated