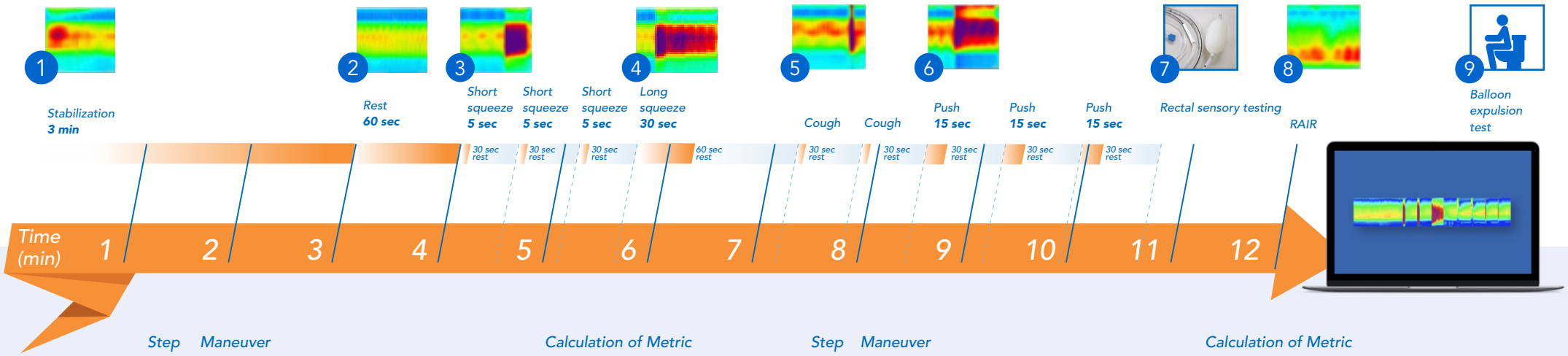
SUMMARY OF LONDON PROTOCOL AND CLASSIFICATION FOR HRAM[1]



Step	Maneuver	Calculation of Metric
0	**Preparation** Explain procedure to the patient. Fix balloon, Presoak, Zero, Insert.	
1	**Stabilization period | 3 minutes** "No talking with patient, no intervention"	
2	**Rest | 60 seconds** "No talking with patient, no intervention"	- Anal resting pressure - Ultraslow wave
3	**3x Short squeeze | 5 seconds (each)** "Please squeeze in tight with muscles around your bottom and hold until I say stop". 30-s between-maneuvres recovery interval.	- Squeeze pressure
4	**1x Long squeeze | 30 seconds** 60-s between-maneuvres recovery interval.	- Endurance squeeze time

Step	Maneuver	Calculation of Metric
5	**2x Strong single cough** 30-s between-maneuvres recovery interval.	
6	**3x Push | 15 seconds (each)** 30-s between-maneuvres recovery interval.	- Rectal pressure increase - Anal pressure decrease
7	**RST (Rectal Sensation Test)** Inflate the balloon and mark the sensations of the patient.	Rectal sensation thresholds (ml) - First constant sensation volume - Desire to defecate volume - Maximum tolerated volume
8	**R1x RAIR** Fast balloon inflation, min 30 ml in ± 2 sec. Remove air after 5 sec. Repeat with larger volume if no reflex is observed.	- RAIR observed
9	**BET (Balloon Expulsion Test)** Balloon pre-filled with 50ml body temperature water. Patient in sitting position in private room.	- Balloon expulsion time

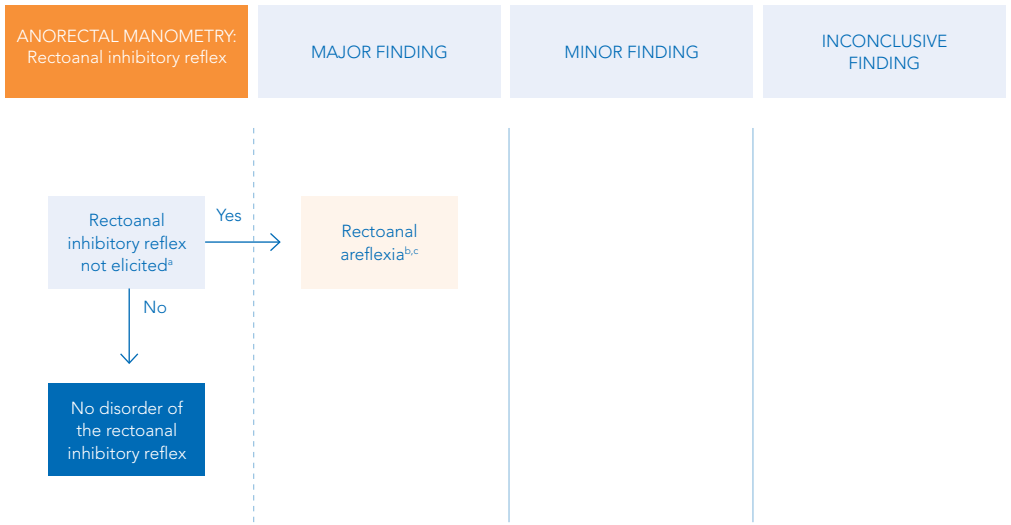
References: 1) E. Carrington, et.al. The IAPGW recommendations; standardized testing protocol and London classification, NGM. doi.org/10.1111/nmo.13679, 2019;

0073-MAI-012-EN-V1.02 London protocol leaflet PRC- 026549.

LABORIE

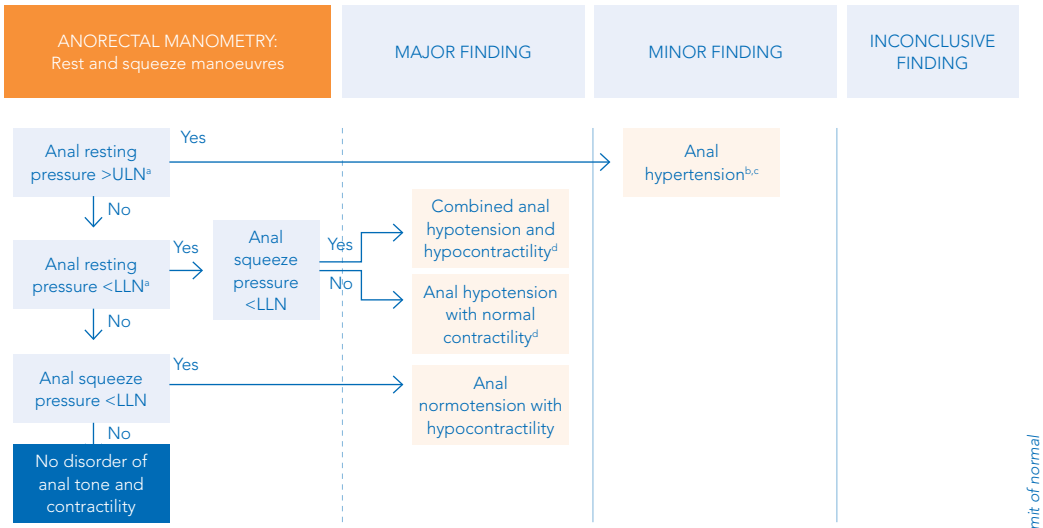
The diagrams are color-coded for clarity: (i) light blue boxes represent manometric findings or decision points; (ii) light orange boxes represent the resultant diagnosis; and (iii) blue boxes represent a 'negative/normal' study.

LONDON CLASSIFICATION PART I:
DISORDER OF THE RECTOANAL INHIBITORY REFLEX



[a]*Minimum volume required to elicit reflex not established in the literature: failure to elicit a RAIR may be seen with low distending volumes in a large capacity rectum.* [b]*RAIR not elicited is a pattern not seen in health but may be found in asymptomatic patients following rectal resection / ileal pouch anal anastamosis, anal hypotonia, faecal loading or megarectum.* [c]*May indicate the need for further investigation to exclude aganglionosis expecially in paediatric populations and adult patients with coexistent megarectum/megacolon. All results to be interpreted in the context of adjunctive testing.*

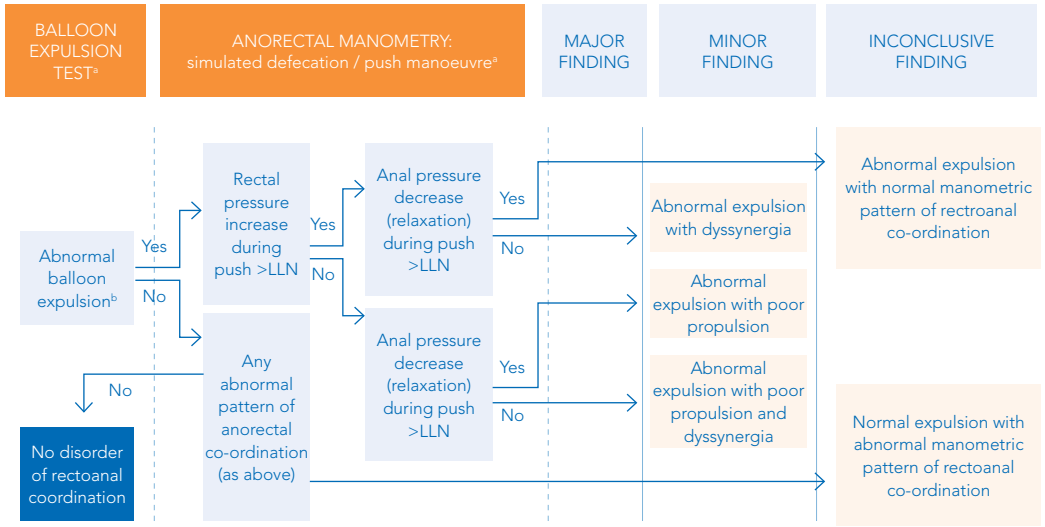
LONDON CLASSIFICATION PART II:
DISORDERS OF ANAL TONE AND CONTRACTILITY



[a]*The functional anal canal length may be measured, as a short anal canal can be associated with anal hypotonia, but its use as a diagnostic criterion in isolation is unproven.* [b]*may be associated with slow and/or ultraslow waves, however the clinical significance of these has not been established.* [c]*this finding may have greater clinical significance in certain patient groups (e.g. chronic anal fissure, levator ani syndrome or proctalgia fugax).* [d]*addition of an abnormal cough response may indicate a more severe phenotype (whereas preservation may suggest a target for biofeedback) but its use as a diagnostic criterion is unproven. All results to be interpreted in context of adjunctive testing.*

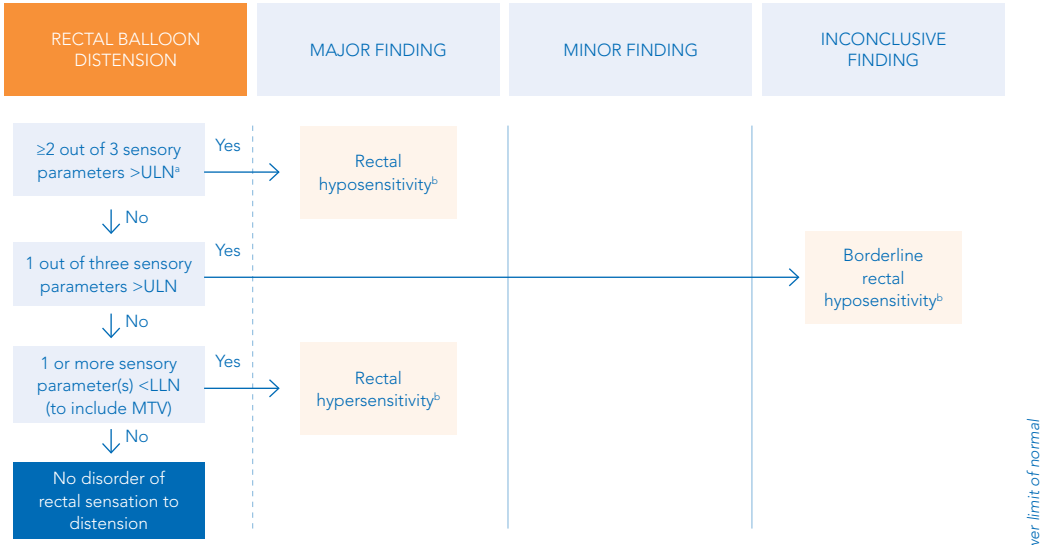
LLN : Lower limit of normal
ULN: Upper limit of normal

LONDON CLASSIFICATION PART III:
DISORDERS OF RECTOANAL COORDINATION



[a]*requires the use of both balloon expulsion test and anorectal manometry.* [b]*or impaired evacuation of contrast medium (prolonged evacuation end time and/or reduced percentage of contrast emptied) on alternative testing e.g. barium or MR defaecography. All results to be interpreted in context of adjunctive testing.*

LONDON CLASSIFICATION PART IV:
DISORDERS OF RECTAL SENSATION



[a]*sensory parameters are: first constant sensation volume (FCSV), desire to defecate volume (DDV) and maximum tolerated volume (MTV).* [b]*abnormal results may be further described using additional methods (e.g. barostat to assess compliance). All results to be interpreted in context of adjunctive testing.*

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ULN: Upper limit of normal