PIPADOR REVISION

# MRCOG Part 1 Revision Notes

## *Genomic Medicine in the NHS*

MOLECULAR BIOLOGY • LECTURE 101

VISUAL EXAMINATION REVISION NOTES

*2026 Edition*

MRCOG Part 1 Revision Notes

# Lecture 101: Genomic Medicine in the NHS

*Molecular biology • Visual revision edition — final lecture of the section*

COLOUR CODE USED THROUGHOUT THESE NOTES

| NHS / GMS | LAB HUBS / ANALYSIS | PANELS / POLICY | CONSENT / FERTILITY | ONCOLOGY / RESULTS |
|---|---|---|---|---|

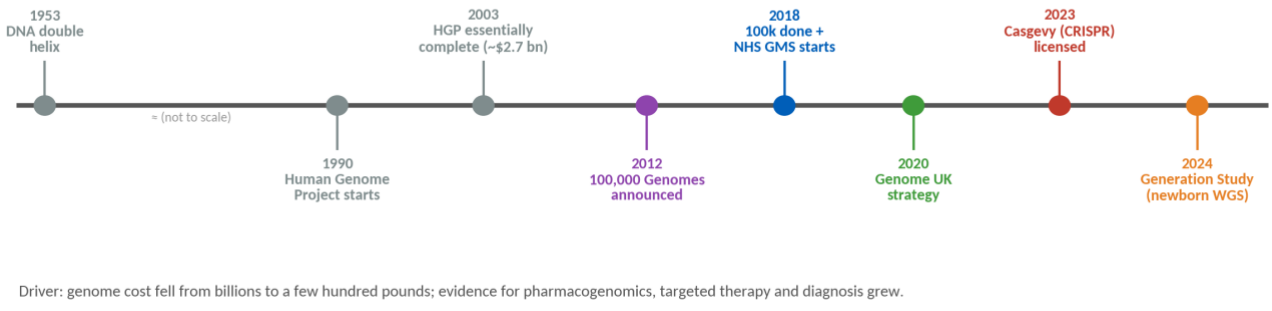
**LEARNING OBJECTIVES — tick off as you go**

- ☐ Outline the history and structure of the NHS Genomic Medicine Service.
- ☐ Explain the Test Directory, PanelApp, WGS and trio testing.
- ☐ Apply genomics to pregnancy, gynae-oncology, fertility/loss and pharmacogenomics.
- ☐ Describe mainstreaming, workforce and the Generation Study.
- ☐ Discuss consent, secondary findings, insurance, data and equity.

## 1 History and Structure

**IN ONE LINE:** *The 100,000 Genomes Project (2012–2018) built the evidence; the NHS Genomic Medicine Service (2018) made genomic testing routine — 7 lab hubs, one national test list, expert panels.*

**From double helix to NHS genomic medicine**




Driver: genome cost fell from billions to a few hundred pounds; evidence for pharmacogenomics, targeted therapy and diagnosis grew.

*Figure 1. Milestones.*

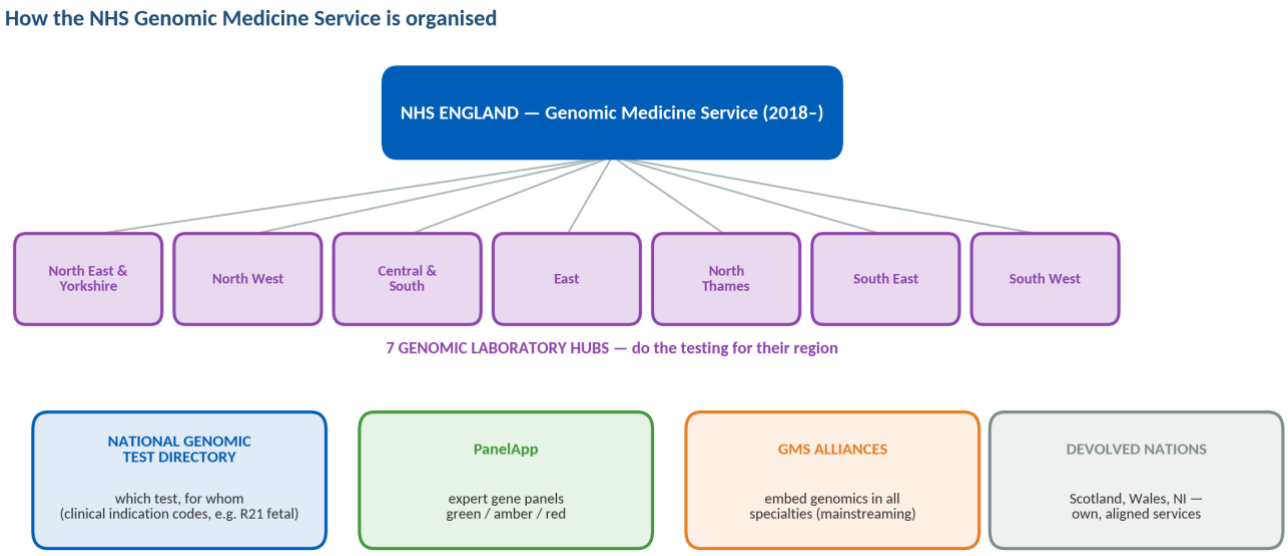



*Figure 2. NHS GMS structure.*

## 2 Testing Pathway

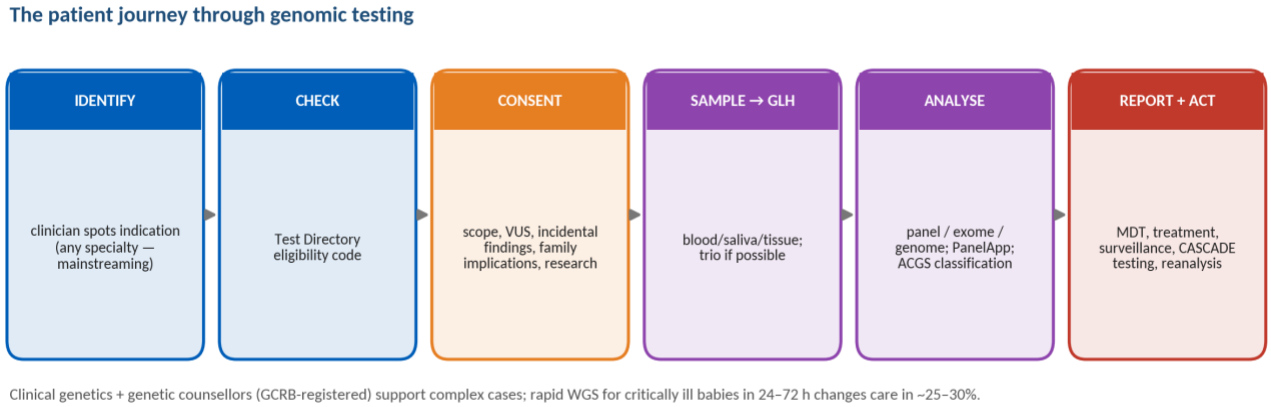



*Figure 3. Patient journey.*

| Test | Key points |
|---|---|
| **Gene panel** | Targeted to the indication (PanelApp) — fewer incidental findings and VUS |
| **Exome / genome** | Unexplained rare disease; solid tumour + germline WGS; TRIO (parents + child/fetus) finds de novo and recessive causes |
| **Rapid WGS / exome** | Critically ill babies and children (24–72 h); prenatal rapid exome (R21) |
| **Generation Study (2024–)** | Research: genome sequencing of up to 100,000 newborns for ~200+ treatable childhood conditions — ALONGSIDE (not replacing) the 9-condition heel prick |

**MNEMONIC / MEMORY HOOK**

**'Directory decides, PanelApp picks, Hub tests, MDT acts'** — the NHS genomic pathway.

# 3 Genomics in O&G

### Where genomics touches O&G

**PREGNANCY**

- NIPT (≥ 1 in 150): T21/T18/T13; fetal RhD and fetal sex are SEPARATE cfDNA tests
- CVS/amnio → QF-PCR → microarray
- Rapid prenatal EXOME (trio, R21): unexplained anomalies; yield ~8–10% (PAGE)
- Carrier couples: targeted tests; PGT-M via HFEA

**GYNAE-ONCOLOGY**

- ALL non-mucinous epithelial ovarian cancers: germline BRCA + tumour BRCA/HRD → PARP
- ALL endometrial (and colorectal) cancers: MMR IHC/MSI → MLH1 methylation → germline
- Cascade testing of relatives
- Solid-tumour WGS in selected cancers

**FERTILITY + LOSS**

- POI: karyotype + FMR1 premutation
- Recurrent miscarriage: array on pregnancy tissue; parental karyotype ONLY if unbalanced rearrangement found; antiphospholipid antibodies — NOT routine inherited thrombophilia panels (RCOG 2023)
- Male factor: karyotype, Y microdeletion, CFTR (CBAVD)

**PHARMACOGENOMICS**

- CYP2D6: avoid CODEINE in breastfeeding
- DPYD before 5-FU/capecitabine
- TPMT/NUDT15 before azathioprine
- CYP2C9/VKORC1 — warfarin (avoid in pregnancy)

*Figure 4. O&G touchpoints.*

# 4 Ethics, Law and Equity

### Ethical, legal and social issues

| | |
|---|---|
| LAYERED CONSENT | main indication • secondary findings • research use (e.g. Genomics England) • recontact + reanalysis policy |
| SECONDARY FINDINGS | UK: not routinely sought (unlike US ACMG list ~80 genes); actionable unexpected findings handled per lab policy + consent |
| INSURANCE CODE | Code on Genetic Testing and Insurance (2018): insurers may only ask for a PREDICTIVE result for Huntington's + life cover > £500,000; diagnostic results can be used |
| DATA | genetic data = special category (UK GDPR); held in Trusted Research Environments (NHS England, Genomics England) |
| EQUITY | databases skewed to European ancestry → more VUS for others; Diverse Data initiative, Our Future Health |
| HFEA | licenses PGT-M conditions (list keeps growing), PGT-SR; germline editing illegal |

*Figure 5. Ethical, legal and social issues.*

## 5 Mainstreaming and the Future

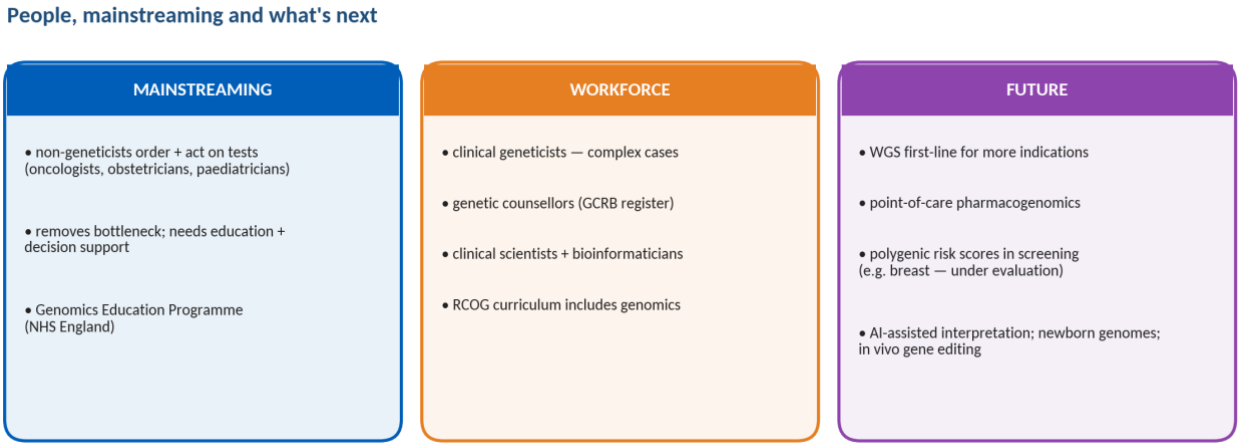



*Figure 6. People and the future.*

- **Genome UK** (2020; implementation plans from 2021–22): embed genomics in routine care, research leadership, equity, workforce. NHS Digital and Health Education England are now part of NHS England.

**★ PEARL**

**7 GLHs + National Genomic Test Directory + PanelApp = the NHS GMS (2018). Test ALL ovarian (BRCA) and endometrial (MMR) cancers.**

**Insurance: only a predictive Huntington's result, for life cover > £500,000. Recurrent miscarriage: no routine inherited thrombophilia panels.**

## 6 MRCOG Exam Pearls — Last-Minute Page

**Numbers to know**

| | | | |
|---|---|---|---|
| **7**<br>Genomic Laboratory Hubs | **2018**<br>GMS launch / 100k complete | **2012**<br>100k Genomes announced | **1 in 150**<br>NHS NIPT threshold |
| **~8–10%**<br>Prenatal exome yield | **24–72 h**<br>Rapid neonatal WGS | **£500,000**<br>Insurance code limit | **100,000**<br>Generation Study aim |

**HIGH-YIELD CHECKLIST**

- ☐ 100k Genomes (2012–18) → NHS GMS (2018).
- ☐ 7 GLHs; National Genomic Test Directory; GMS Alliances; devolved nations.
- ☐ PanelApp: green/amber/red genes.
- ☐ Panel vs exome vs genome; trio; rapid WGS for sick babies.
- ☐ NIPT for T21/18/13; RhD/sex separate; prenatal exome R21.
- ☐ Universal BRCA (ovary) and MMR (endometrium) testing; cascade.
- ☐ POI: FMR1 + karyotype; RM: array on tissue, no routine thrombophilia.
- ☐ PGx: CYP2D6 codeine, DPYD, TPMT, warfarin.
- ☐ Mainstreaming; genetic counsellors; Genome UK.
- ☐ Consent layers; secondary findings; insurance code; special category data; equity.

**Self-assessment** — cover the right-hand column

| Question | Answer |
|---|---|
| **How many Genomic Laboratory Hubs in England?** | Seven |
| **What does the Test Directory specify?** | Which tests are funded and for which indications |
| **What is PanelApp?** | Genomics England's expert-curated gene panel platform |
| **Why test a trio?** | Find de novo and recessive causes; improve yield |
| **Does the Generation Study replace the heel prick?** | No — it is research alongside it |
| **Which gynae cancers get universal genomic testing?** | Epithelial ovarian (BRCA/HRD) and endometrial (MMR) |
| **Routine thrombophilia panel for recurrent miscarriage?** | No (RCOG 2023) — antiphospholipid antibodies only |
| **What is 'mainstreaming'?** | Non-genetics clinicians ordering and acting on genomic tests |
| **When can UK insurers ask for a predictive test result?** | Huntington's disease, life cover > £500,000 |
| **Legal status of genetic data?** | Special category data (UK GDPR) |

## 7 References


- NHS England. National Genomic Test Directory; Genomic Medicine Service.
- HM Government. Genome UK: the future of healthcare (2020) and implementation plans.
- RCOG Green-top Guideline No. 17. Recurrent miscarriage. 2023; HM Government/ABI Code on Genetic Testing and Insurance. 2018.