Multi-Arm Randomised Controlled Trials: A Trial Manager's Perspective

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NHS
National Institute for Health Research

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Multi-arm RCTs

- Evaluates several new treatments simultaneously
- More cost-effective than conducting separate trials
- Potential to improve recruitment as all treatment options are offered

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PROSPECT

- **Two randomised controlled trials within a comprehensive cohort study**

- **Surgical options for pelvic organ prolapse**
  - **Three surgical options for primary repairs (RCT1)**
  - **Three surgical options for secondary repairs (RCT2)**
  - **Women not willing/eligible for randomisation entered Cohort study**

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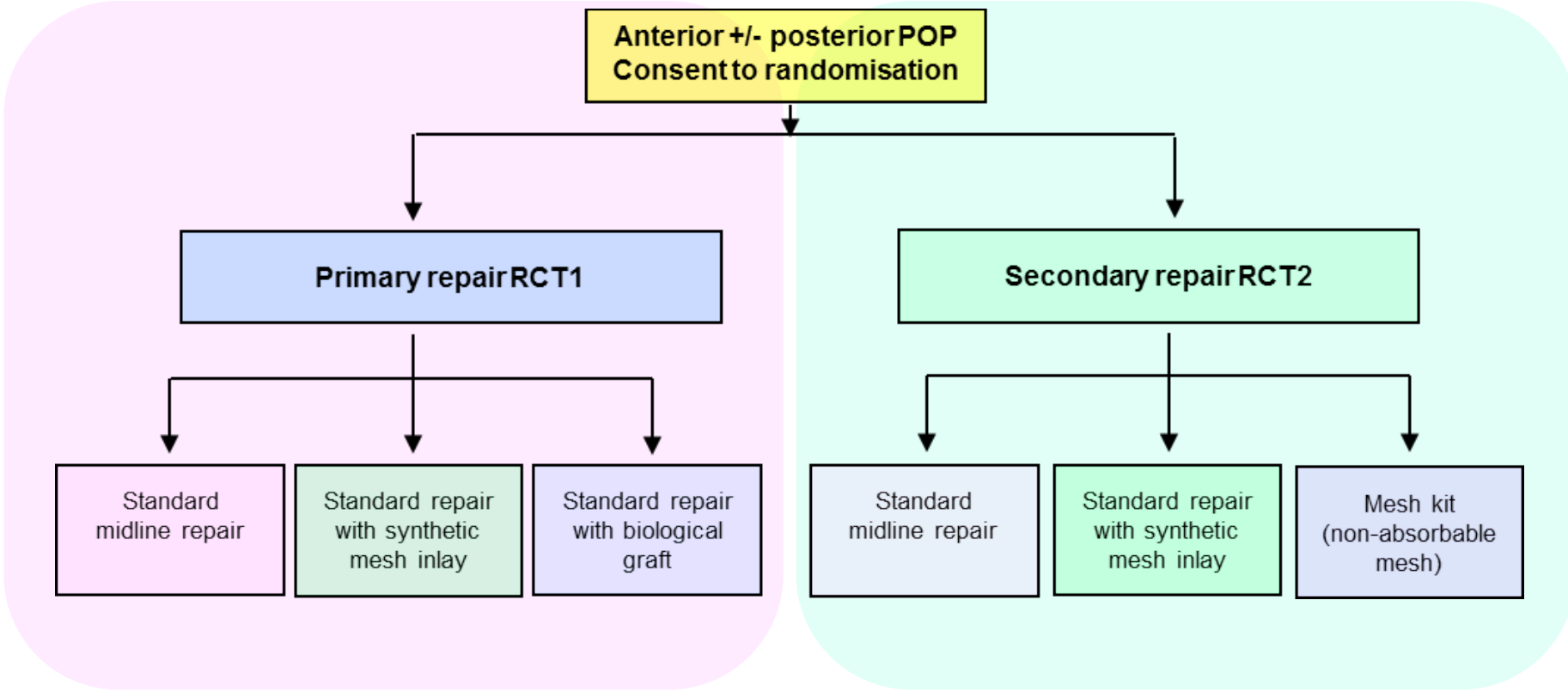
Flow Diagram



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Recruitment

- Recruitment slower than anticipated

- Due to a number of reasons:
  - cost of sourcing mesh
  - lack of availability of mesh
  - clinicians preference
  - Lack of training in a particular technique

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Solution

- **Decision**
  - **allow surgeons to randomise between no mesh and only one of the mesh types**

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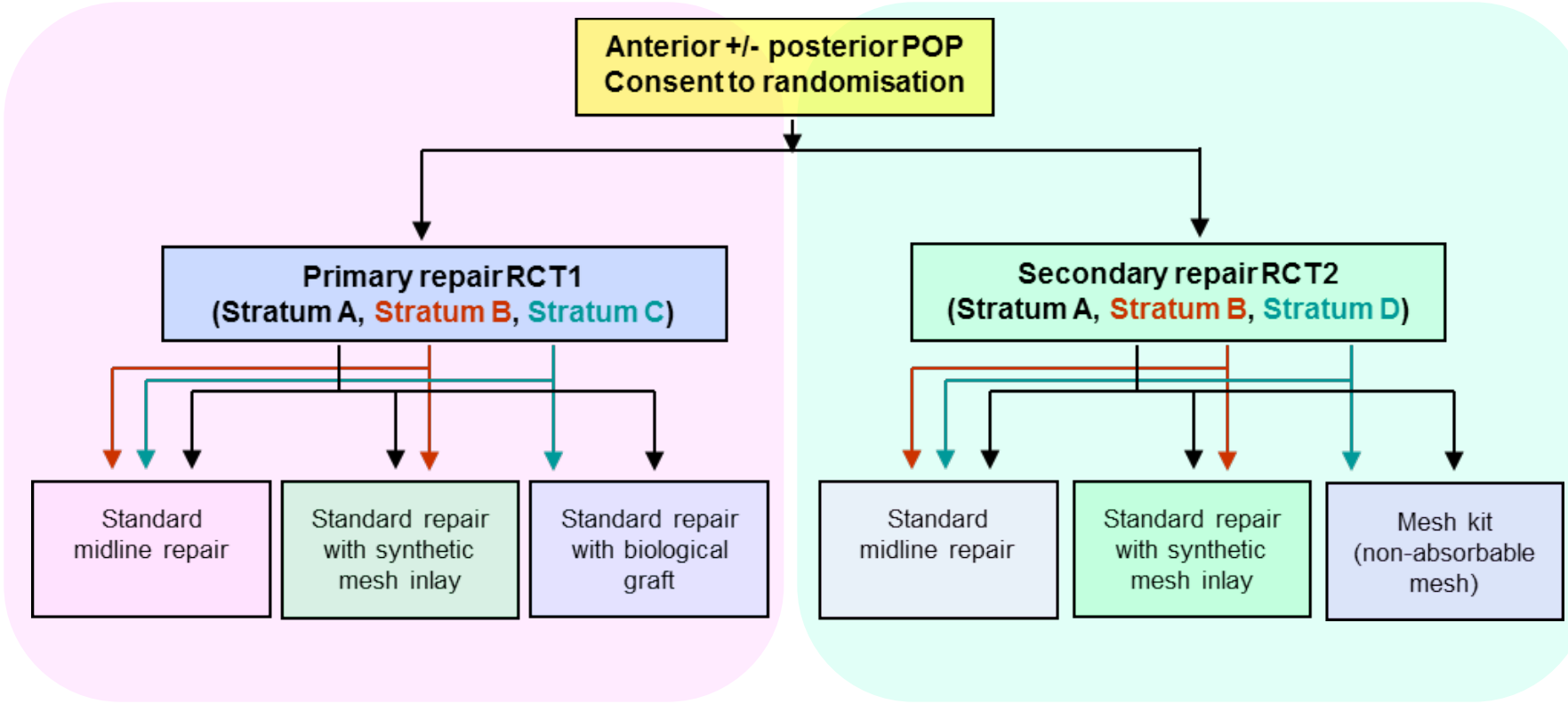
Flow Diagram



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Advantages

- Allowed more surgeons and centres to participate
- Access to larger number of potential recruits
- Increased recruitment
- Shortened the trial
  - Answer research question quicker
  - Reduces costs
  - Limits trial fatigue

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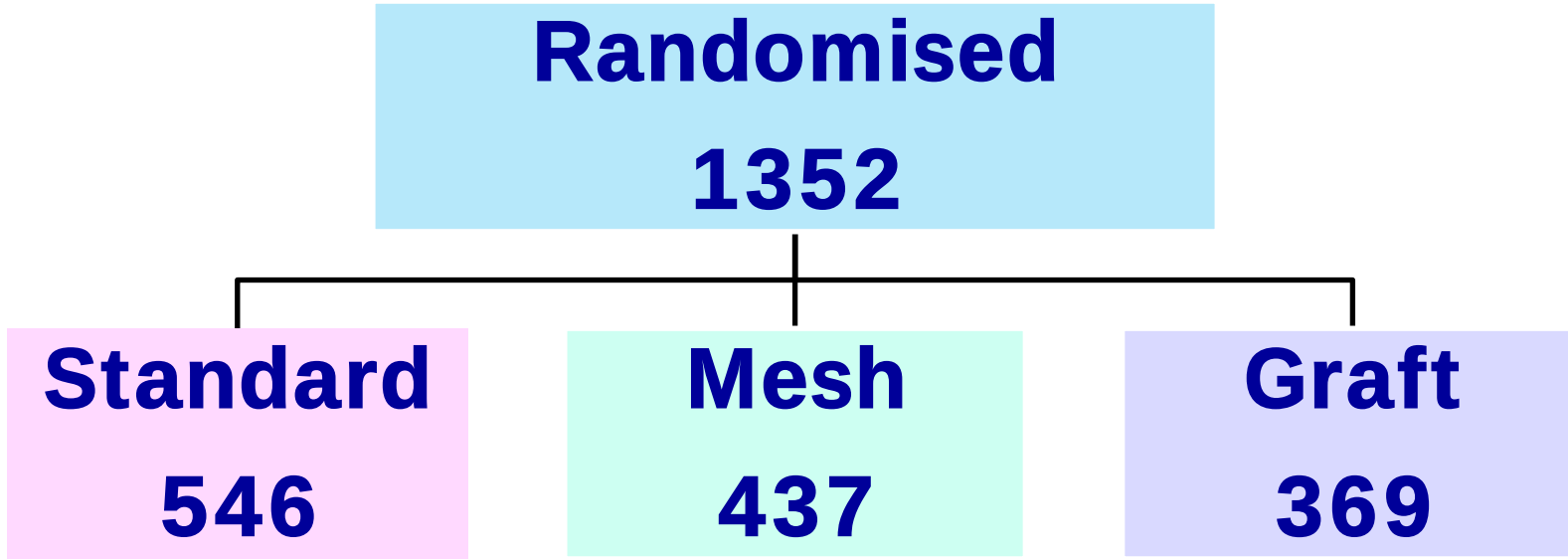
Limitations



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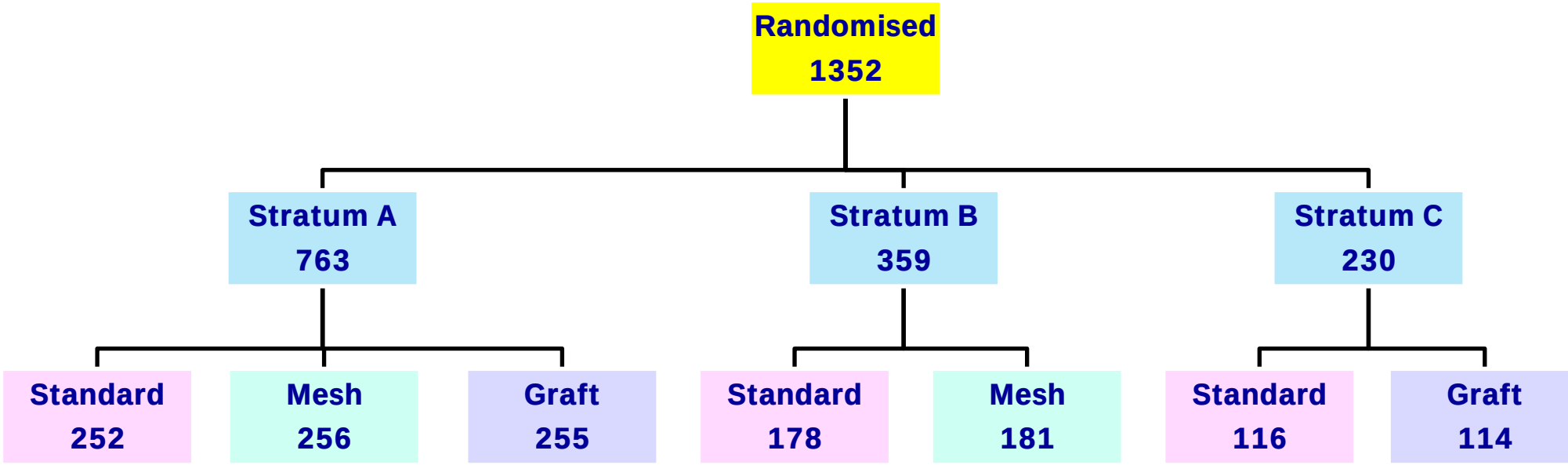
Strata



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Limitations

- To calculate unbiased estimates of treatment effects, only two out of three strata could be used in any analysis

- Primary trial
  - strata A+B for comparisons with synthetic mesh
  - strata A+C for comparisons with biological graft

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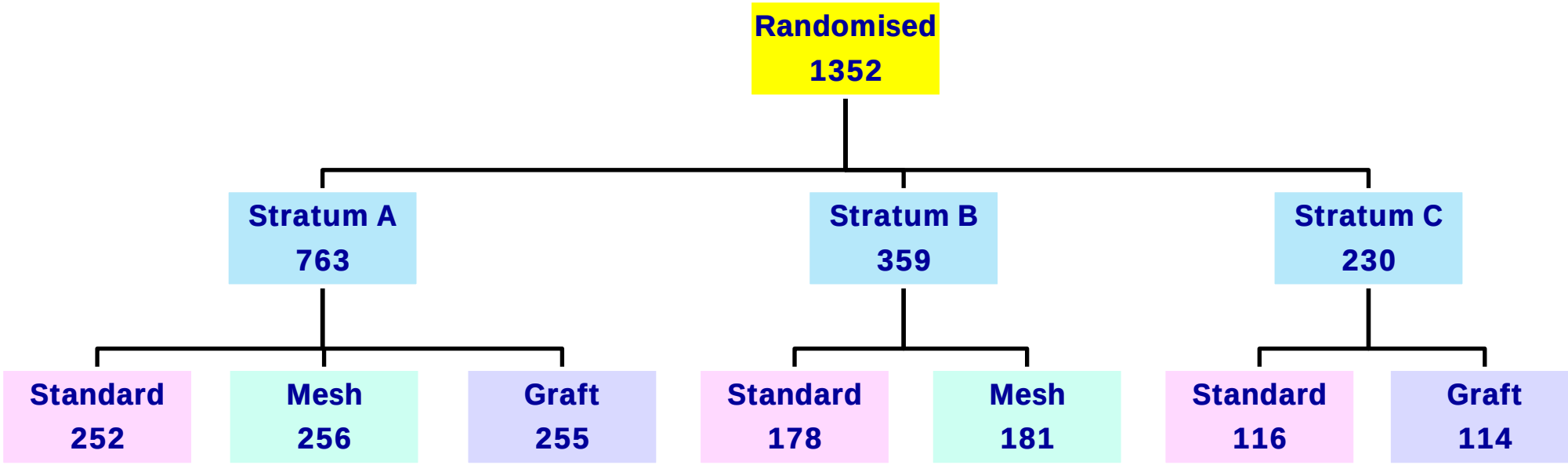
Strata



- **Mesh trial**
  - **Standard: 252 + 178 = 430**
  - **Mesh: 256 + 181 = 437**
- **Graft trial**
  - **Standard: 252 + 116 = 368**
  - **Graft: 255 + 114 = 369**

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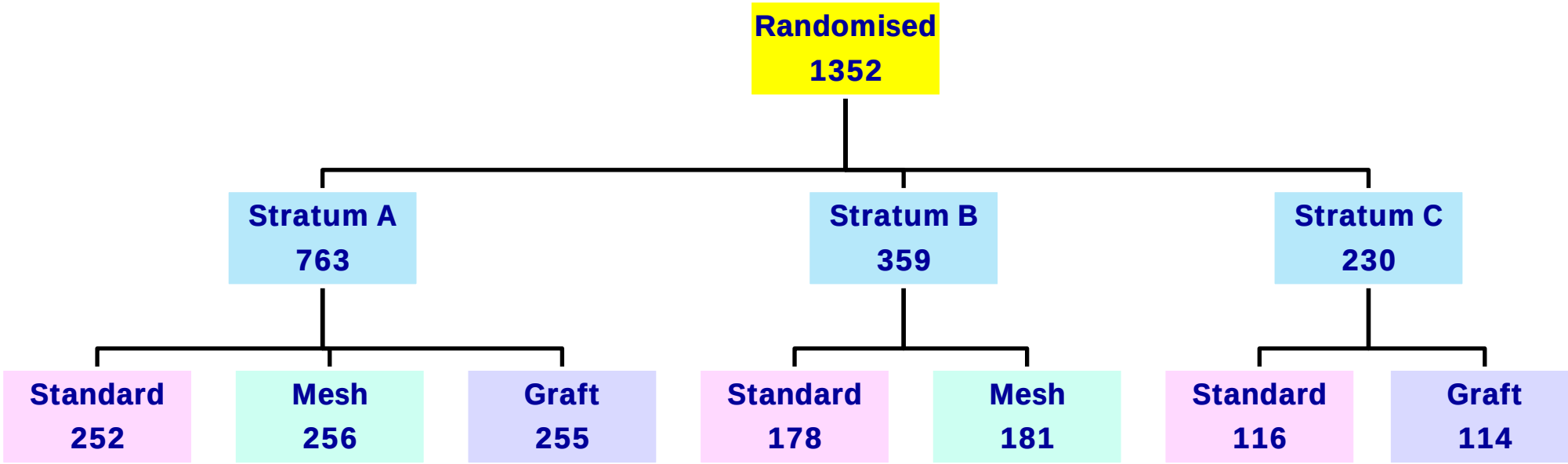
Strata



- **Mesh trial**
  - **Standard: 252 + 178 = 430**
  - **Mesh: 256 + 181 = 437**
- **Graft trial**
  - **Standard: 252 + 116 = 368**
  - **Graft: 255 + 114 = 369**

Total = 430 + 437 + 368 + 369 = 1604

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Limitations

- Reduction in power by a modest amount because the Stratum A was the largest stratum and was used in every analysis
- Challenges in reporting methodology / results due to the complex nature of the trial design / analysis
- Full CONSORT Diagram is HUGE!

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Summary

- Recruitment rates had to be improved
- Relaxation of trial design increased recruitment of centres and participants
- Shortened the length of the trial
- Resulted in three strata in each Trial
- More complex analysis
- Challenges when reporting

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Thank for your attention.

If you have any further questions please contact:

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