Registry based trials: the ultimate platform for representative enrolment

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ESC Cardiovascular Round Table: The future of clinical trials: Towards Diversity and Inclusion
Steps to inclusion

Facilitate research

Public understanding of research
Support for research among healthcare professionals

Be eligible → Be invited → Be interested → Be willing → Be committed

<table>
<thead>
<tr>
<th>Protocol</th>
<th>Invitation method</th>
<th>Participant materials</th>
<th>Participant materials</th>
<th>Staff interactions</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Site location</td>
<td></td>
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<td></td>
<td>Staff burden</td>
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</table>

Society

Trial team

Facilitate research

Public understanding of research
Support for research among healthcare professionals
Definitions

**Registry**: An organised system that collects uniform data (clinical and other) to identify specified outcomes for a population defined by a particular disease, condition or exposure

**Registry-based trial**: Participants are recruited and followed up within an existing registry
Example: VALIDATE-SWEDEHEART
Bivalirudin versus Heparin Monotherapy in Myocardial Infarction

Eligibility: Admitted with STEMI or NSTEMI and urgent PCI planned

Intervention: Open-label

1:1 randomisation
Intravenous bivalirudin vs intra-arterial unfractionated heparin

Outcome: Death, myocardial infarction, or major bleeding at 180 days
VALIDATE-SWEDEHEART: How were participants recruited?

- Be eligible: Simple, broad eligibility criteria
- Be invited: 22 sites across Denmark. All relevant patients assessed
- Be interested: Low burden for participants
- Be willing: Verbal consent for STEMI participants
- Be committed: Telephone follow-up at 7 and 180 days
VALIDATE-SWEDEHEART: Participant enrolment

Assessed for eligibility (n=12561)

- Excluded (n=6555)
  - Not meeting inclusion criteria (n=3584): (not able to give informed consent, not to be treated with potent P2Y12-inhibitors, to high dose heparin was given)
  - Declined to participate (n=392)
  - Other reasons (n=2579): (Was not asked to participate, could not be asked)

Randomized (n=6006)

Allocation

- Allocated to Heparin (n=3002)
  - Received allocated intervention (n=2982)
  - Did not receive allocated intervention (n=20)
    - Received Bivalirudin (n=13)
    - Other deviation (n=7)
- Allocated to Bivalirudin (n=3004)
  - Received allocated intervention (n=2971)
  - Did not receive allocated intervention (n=33)
    - Received >5000U Heparin (n=19)
    - Other deviation (n=14)
VALIDATE-SWEDEHEART: Selected baseline characteristics

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>All Patients Enrolled in the Trial (N=6006)</th>
<th>Screened Patients Not Enrolled in the Trial (N=6555)</th>
</tr>
</thead>
<tbody>
<tr>
<td>STEMI — no. (%)</td>
<td>3005 (50.0)</td>
<td>2318 (35.4)</td>
</tr>
<tr>
<td>Male sex — no. (%)</td>
<td>4406 (73.4)</td>
<td>4555 (69.5)</td>
</tr>
<tr>
<td>Median age— yr</td>
<td>68.0</td>
<td>71.0</td>
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<tr>
<td>Current smoker — no. (%)</td>
<td>1426 (23.7)</td>
<td>1361 (20.8)</td>
</tr>
<tr>
<td>Diabetes — no. (%)</td>
<td>999  (16.6)</td>
<td>1631 (24.9)</td>
</tr>
<tr>
<td>Hypertension — no. (%)</td>
<td>3105 (51.7)</td>
<td>4080 (62.2)</td>
</tr>
<tr>
<td>Previous MI — no. (%)</td>
<td>974  (16.2)</td>
<td>1831 (27.9)</td>
</tr>
</tbody>
</table>

STEMI = ST Elevation Myocardial Infarction
LENS: fenofibrate for diabetic retinopathy

- **Trial design**: Randomised double-blind placebo-controlled trial
- **Run-in**: active, 2-3 months
- **Treatment**: 145mg fenofibrate tablet or placebo
- **Eligibility**: adults, T1DM and T2DM, observable eye disease
- **Sample size**: >1000 patients
- **Primary outcome**: progression to referable eye disease or treatment
- **NHS data linkage**: recruitment and most outcomes
- **Contact**: two visits in person, then by telephone + post

LENS trial (www.ctsu.ox.ac.uk/lens)
Registry trials - key elements for inclusivity

- Broad, simple eligibility (where-ever possible)
- Low burden of data collection for sites and participant
- Recruitment embedded in clinical care (acute/one-off interventions)
- Opportunities for direct-to-participant national mail-based recruitment (long-term treatments)