“The study population should be defined in advance, stating unambiguous inclusion (eligibility) criteria. The impact that these criteria will have on study design, ability to generalize, and participant recruitment must be considered.”

—Friedman, et al., pg. 30
Study Population

- Eligibility = inclusion + exclusion criteria
- Consider . . .
  - Feasibility
  - Generalizability
  - Risk/benefit
  - Subject characteristics
  - Disease characteristics
  - Enrichment
Overall Picture

- Population at large
  - Definition of condition
  - Entry criterion
  - Enrollment

- Population with condition

- Study population

- Study sample
Example: Women with Breast Cancer

Population at large

Definition of condition

Entries criterion

HER2+, distant metastases, no prior chemotherapy, no serious intercurrent illness

Enrollment

Study sample
How It Happens in Practice

Population at large

Population w/o condition

Definition of condition

Population with condition

With condition but ineligible

Entry criteria

Study population

Eligible but not enrolled

Enrollment

Study sample

And these we randomize
Eligibility Criteria

- Identify subjects:
  - Likely to benefit
  - In whom benefit can be discerned
  - In whom risks are acceptable
- Function of trial phase and objectives
- Basis for generalizability of results
- Improve precision of effect
- Quantitative or otherwise clearly interpretable criteria should be used
Eligibility Criteria

- **Inclusion**
  - Hospitalized patients 18 years-of-age or older
  - Oral temperature >38.5°C

- **Exclusion**
  - History of hypersensitivity to new treatment (and control)
  - Pregnant or breastfeeding
  - Hospitalized for CHD or for treatment of endocarditis
An Example in Obesity

- The epidemiology
  - 20% adults BMI > 30—increases with age
  - At least 20% of all patients would fall into a high-risk category
  - 50% of these high-risk patients will have a BMI > 27
Epidemiology

- Taking any 100 adults on GP list:
  - 20 patients will have a BMI > 30
  - 10 patients will have at least one risk factor and BMI > 27
- Allowing for overlap and ineligibles, it was estimated that 20 adults out of every 100 will qualify
12 Mailshots and advertising

<table>
<thead>
<tr>
<th>Mailshot known high-risk patients</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>320</strong> Responses for telephone screening</td>
</tr>
<tr>
<td>25% success rate</td>
</tr>
<tr>
<td><strong>80</strong> Patients pre-screened</td>
</tr>
<tr>
<td><strong>40% selected for screening</strong></td>
</tr>
<tr>
<td><strong>32</strong> Patients formally consented and screened</td>
</tr>
<tr>
<td>Enrolment success rate following formal screening</td>
</tr>
<tr>
<td><strong>20</strong> Patients randomised and treated with study medication</td>
</tr>
</tbody>
</table>
A Critical Question . . .

- To whom do the results apply?
  - All patients?
  - All patients who meet the disease criteria?
  - All patients who meet the disease criteria but are not subject to any of the exclusion criteria?
  - All patients who . . . [as above] . . . and who are willing to take part in a trial?
  - Your next patient?
In the Next Lecture We’ll Look at . . .

- Study designs issues
  - Randomization
  - Blinding (masking)
  - Stratification, blocking