RECRUITMENT IN PHASE 1 STUDIES

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HISTORY

Recruitment in Phase 1 Studies

Clinical Pharmacology

- As a discipline it was first recognised and named during 1930/40s.
- The flood of new drugs during the 1950/60s required a more systematic approach.
- Initial focus on drug safety following serious failures.
- Academia driving the expansion of the discipline and methods funded through research funding agencies.
- “Integrated” approach diverged into separate disciplines.

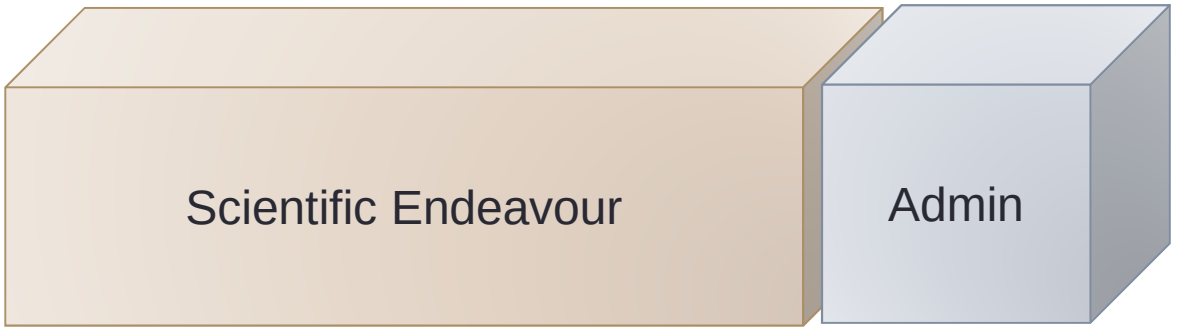
Pharmaceutical Research

- During the 1960/70s most companies systemised the role of Clinical Pharmacology.
- Many created their own trial facilities – based on fast turnaround using staff volunteers.
- Capacity was limited and most Companies started to use specialist commercial facilities.
- The increase in regulation and need for subject privacy caused the rapid decline in staff volunteers.

Current Challenges

- Most Clinical Pharmacology originates in Pharma – and is often remote from the Clinic.
- Academic contribution to the discipline is in decline.
- Commercial focus tends to restrict innovation.
- Demands of “narrow” Target Product Profiles pushes early research from exploratory to determinative.

Paradigm Shift



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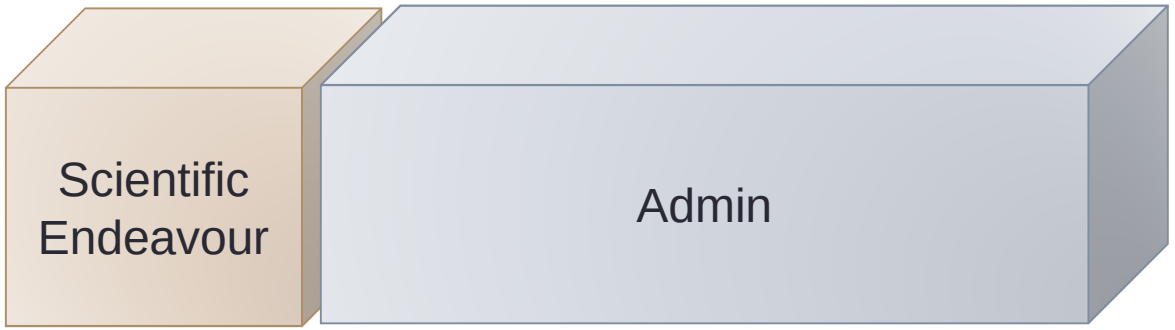


Now

PATIENTS VS HEALTHY VOLUNTEERS

Recruitment in Phase 1 Studies

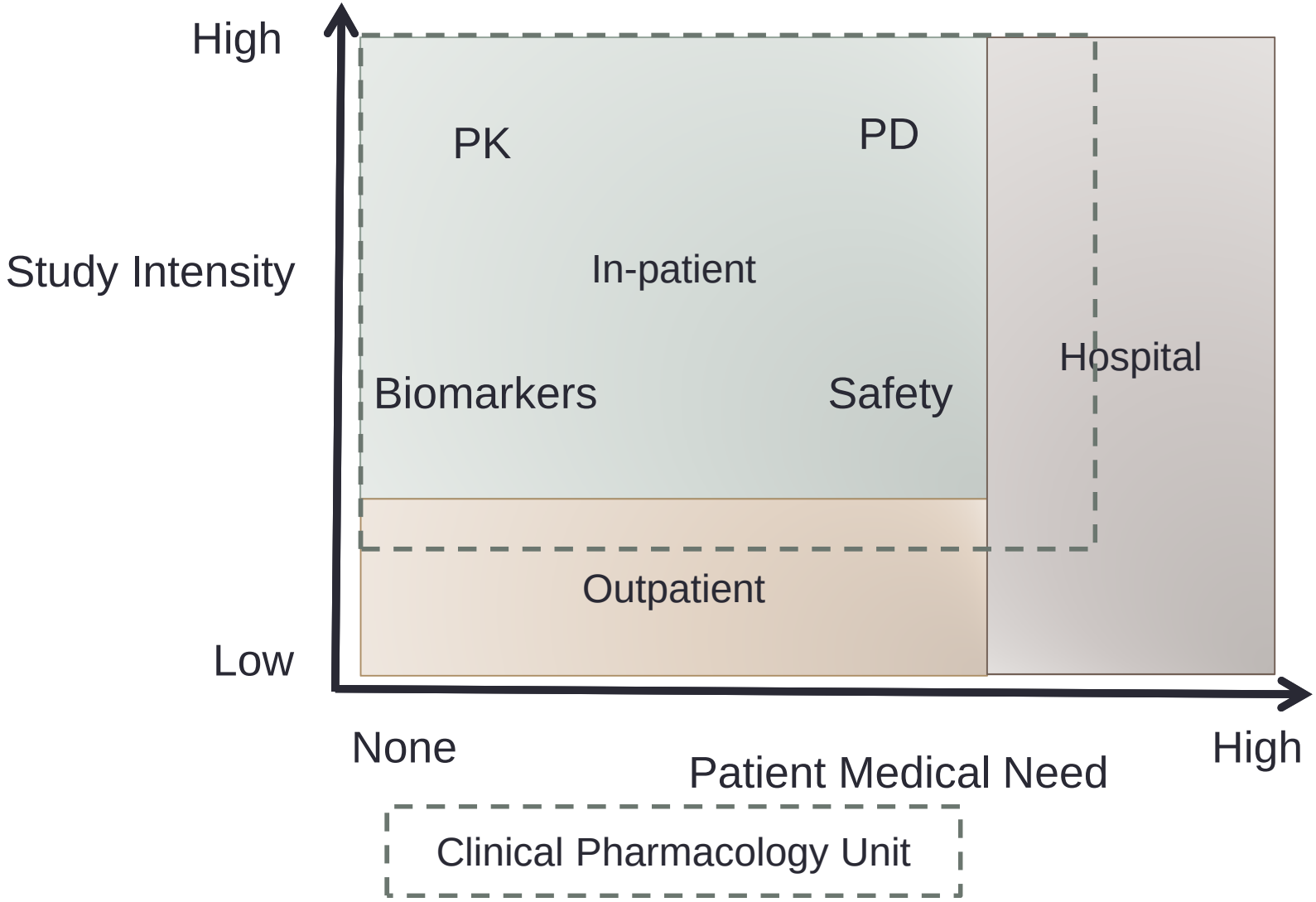
Phase 1 Trials

- Traditionally synonymous with young healthy volunteers.
- Regulation has redefined the area as “non-therapeutic trials”.
- Established Regulators and RECs do not have issues with a selected population.

When to use patients in Phase 1?

- When the subjects are otherwise well with a stable or chronic condition.
- Where a challenge agent is used to invoke a response.
- Cytotoxic drugs in cancer patients to assess PK.
- In special populations such as renal and hepatic impairment to assess clearance.

Where to study patients in Phase 1?



When not to use Patients in Phase 1?

- Where their use hasn’t been adequately justified.
- When appropriate feasibility work hasn’t been performed.
- Where time is a key component of the development strategy.
- Where the patient population is not representative of the general/target population.

METHODOLOGIES

Recruitment in Phase 1 Studies

Healthy Volunteers

- Focus on outcome and not methodology.
- Commercial CROs “survive” through effective recruitment.
- Tend to split into 2 modes:
  - Selected database of “repeat” subjects (pool).
  - Extensive database of willing individuals.
- Be aware of the likely population entering your study – demographics (UK≠EU≠US).
- “Recruitment” period is often very short – focus less on progress and more on outcomes.

Where have all the Aussies gone?

They stayed at home….

Patient Recruitment in Phase 1

- Avoid translating Phase 3 methodologies into Phase 1.
- Look for proactive mechanisms rather than passive recruitment mechanisms.
- Start with view that these people are “well”.
- Feasibility pre-work is usually essential.
- Adapt requirements where necessary (I/E criteria).
- Consider the medical environment as part of your feasibility.
- Select the fewest possible sites.
- Consider plurality in your outsourcing strategy.

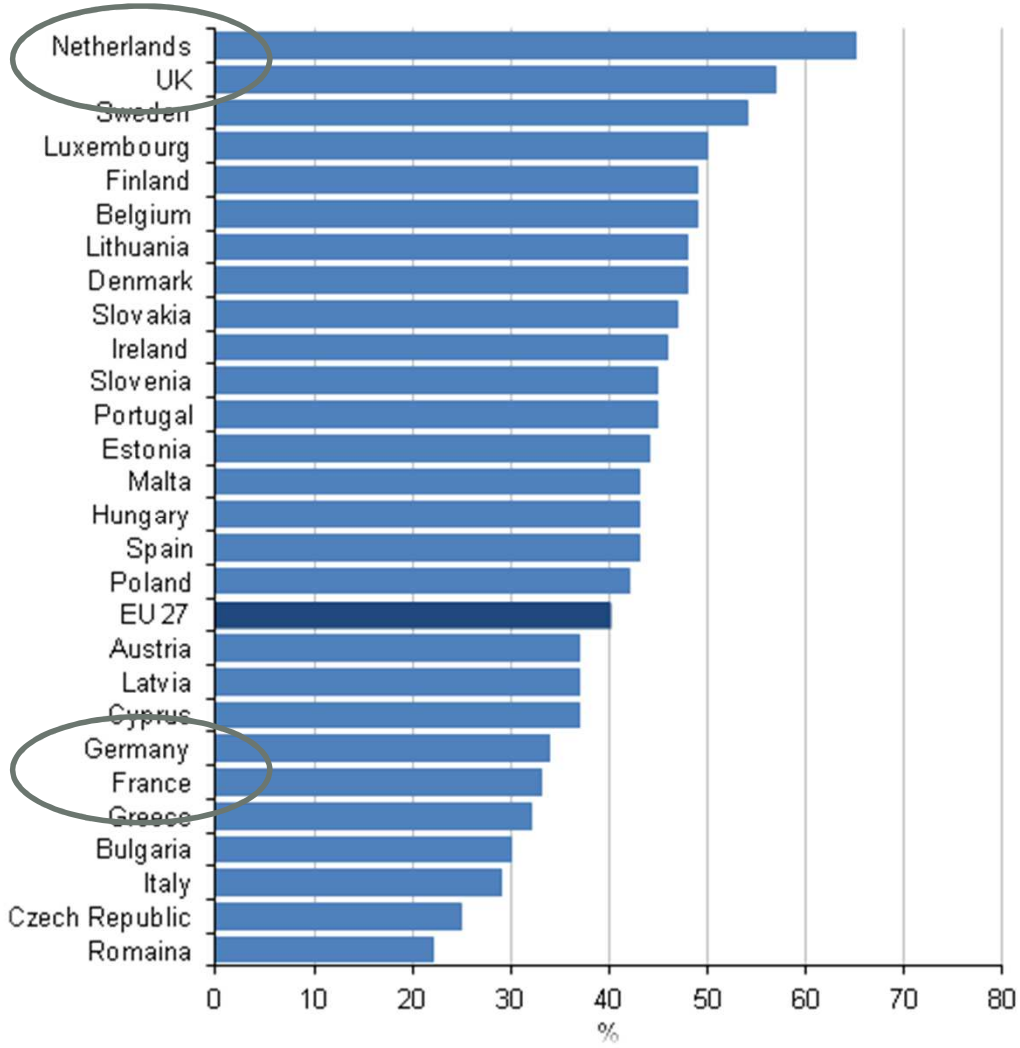
Message to Outsourcers

Share responsibility for the outcome of patient recruitment.

Role of Social Media in Recruitment

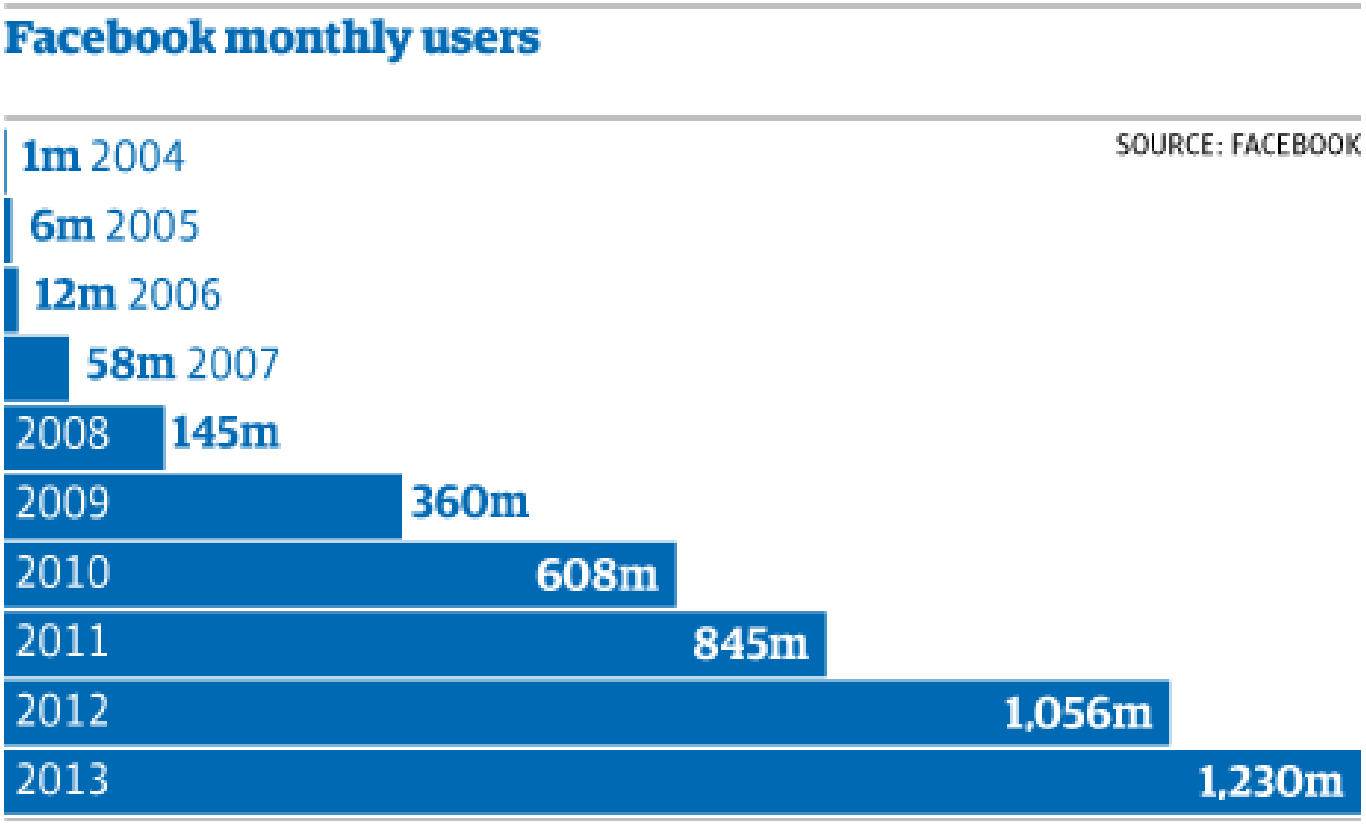
- Regulators and guidance lagging behind the “real world”.
- Same rules apply to social media as other advertising media (papers, radio, posters etc..)
- Social media is an engagement tool and is not used for direct recruitment.
- Leads routed through phone and e-mail.
- Reach and referral mechanisms transformative for both routine and specialist recruitment.

Social Media in EU



EUROSTAT 2012

Facebook is currently dominant



Role of Specialist Groups

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ETHICAL CONSIDERATIONS

Recruitment in Phase 1 Studies

Subject Payments in Phase 1

- Payment is the primary reason for participation.
- Payments are independent of the subject's underlying condition.
- UK REC procedures ensure sharing of information and experience across the industry.
- Less of an issue since EU CT Directive bought Phase 1 under direct regulation.
- Other EU Countries will have different approaches.

Procedures and Subject Demands

- HVs and patients in work have restricted availability.
- Seek advice before finalising protocol.
- Perform feasibility assessments where possible.
- Subjects are quite tolerant….push the envelope.
- RECs have the final say.

SPECIAL POPULATIONS

Recruitment in Phase 1 Studies

Japanese Recruitment

- Successful bridging strategies are an essential component of Global Drug development.
- Non-assimilation criteria (<5yr ex-Japan) hinders recruitment.
- UK/D/US are lead countries.
- Centres have restricted capacity (10-20/month)
- Consider “umbrella” protocols to incorporate ethnic considerations early.

Biologicals

- Recommendation 17 of the Duff Report.
  - “The decision whether to conduct a FIM trial in healthy volunteers or in volunteer patients should be carefully considered and fully justified,….”
  - “..the paramount factors should be the rights, safety and well-being of the volunteers, whether patients or healthy individuals,…”
- Work within an experienced regulatory and ethical environment.

CONCLUSIONS

Recruitment in Phase 1 Studies

Final Messages

- Recruitment is often critical to study success.
- Seek advice and invest before making decisions.
- Manage expectations about benefits of using patients in non-therapeutic trials.
- Share in success but accept responsibility for failures.
- Finally….

Questions