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What do know improves recruitment to trials: and what might improve the situation?

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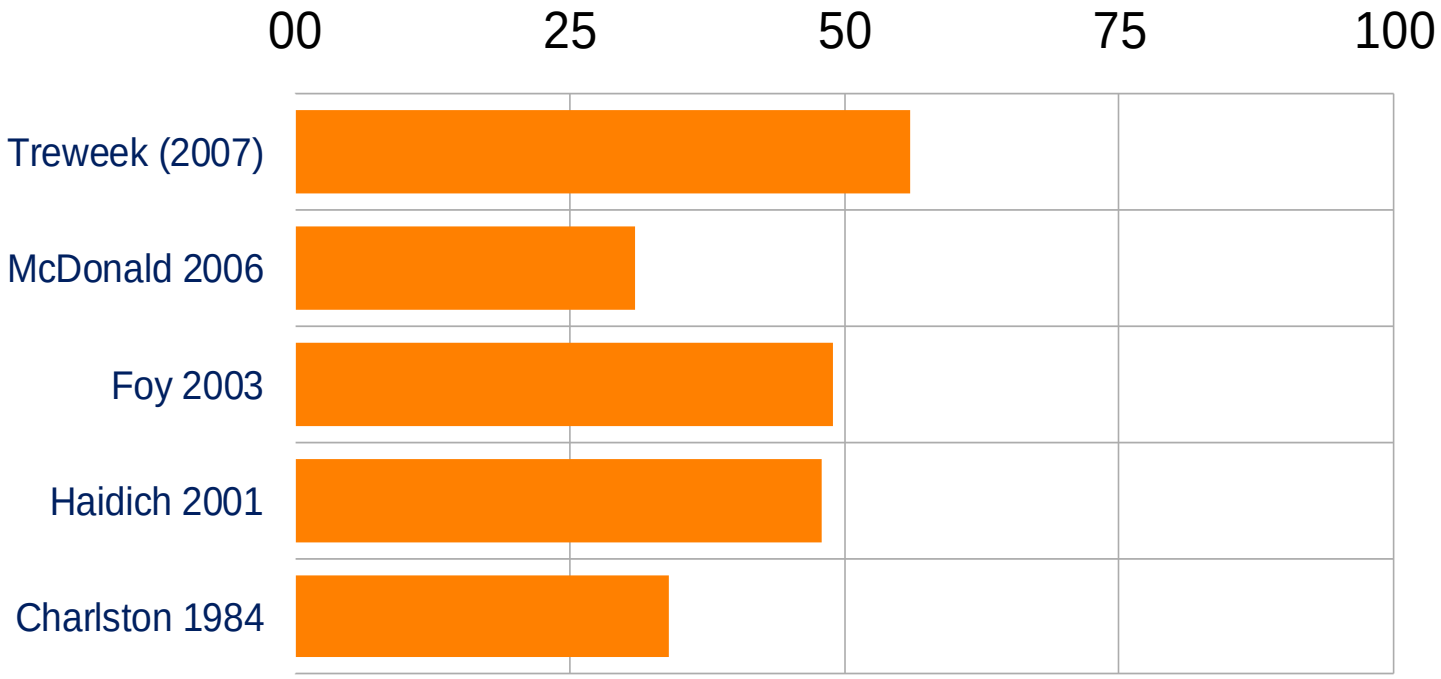
NORTH YORK GENERAL
Making a World of Difference

What do you think we know?

1. How often do clinical trials fail to recruit to target?
2. Which of the following strategies have been shown to increase recruitment rates?
   a) Open designs
   b) Opt out V Opt in
   c) Telephone reminders
   d) Audiovisual aids
   e) Trial Booklets
   f) Study Questionnaires
   g) Financial Incentives
3. What other strategies might be effective?
   a) Intervention modelling
   b) Via EMRs (Incident, Prevalent)
   c) PBRNs

1. How often do clinical trials fail to recruit to target?



Seget S, Optimizing patient recruitment and retention in late stage clinical trials, 2010 Business Insights Ltd

- 45% failed to reach 80% of the pre-specified sample size.
- Sampling frame 60 studies funded by the MRC & HTA

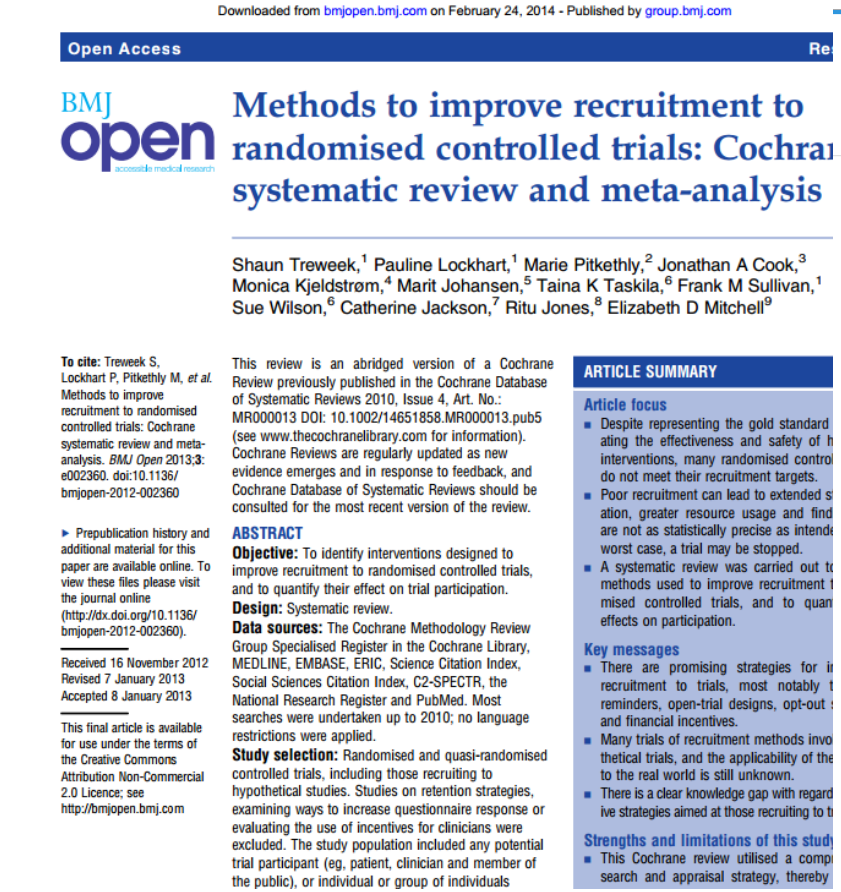
Health Technology Assessment 2007; Vol. 11: No. 48

Recruitment to randomised trials: strategies for trial enrolment and participation study. The STEPS study

MK Campbell, C Snowdon, D Francis, D Elbourne, AM McDonald, R Knight, V Entwistle, J Garcia, I Roberts and A Grant (the STEPS group)

2. What works?

a-g



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Methods to improve recruitment to randomised controlled trials: Cochrane systematic review and meta-analysis

Shaun Treweek,[1] Pauline Lockhart,[1] Marie Pitkethly,[2] Jonathan A Cook,[3] Monica Kjeldstrøm,[4] Marit Johansen,[5] Taina K Taskila,[6] Frank M Sullivan,[1] Sue Wilson,[6] Catherine Jackson,[7] Ritu Jones,[8] Elizabeth D Mitchell[9]

To cite: Treweek S, Lockhart P, Pitkethly M, *et al*. Methods to improve recruitment to randomised controlled trials: Cochrane systematic review and meta-analysis. *BMJ Open* 2013;**3**: e002360. doi:10.1136/bmjopen-2012-002360

► Prepublication history and additional material for this paper are available online. To view these files please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2012-002360).

Received 16 November 2012
Revised 7 January 2013
Accepted 8 January 2013

This review is an abridged version of a Cochrane Review previously published in the Cochrane Database of Systematic Reviews 2010, Issue 4, Art. No.: MR000013 DOI: 10.1002/14651858.MR000013.pub5 (see www.thecochranelibrary.com for information). Cochrane Reviews are regularly updated as new evidence emerges and in response to feedback, and Cochrane Database of Systematic Reviews should be consulted for the most recent version of the review.

ABSTRACT

Objective: To identify interventions designed to improve recruitment to randomised controlled trials, and to quantify their effect on trial participation.

Design: Systematic review.

Data sources: The Cochrane Methodology Review Group Specialised Register in the Cochrane Library, MEDLINE, EMBASE, ERIC, Science Citation Index, Social Sciences Citation Index, C2-SPECTR, the National Research Register and PubMed. Most searches were undertaken up to 2010; no language restrictions were applied.

Study selection: Randomised and quasi-randomised controlled trials, including those recruiting to hypothetical studies. Studies on retention strategies, examining ways to increase questionnaire response or evaluating the use of incentives for clinicians were excluded. The study population included any potential trial participant (eg, patient, clinician and member of the public), or individual or group of individuals

ARTICLE SUMMARY

Article focus

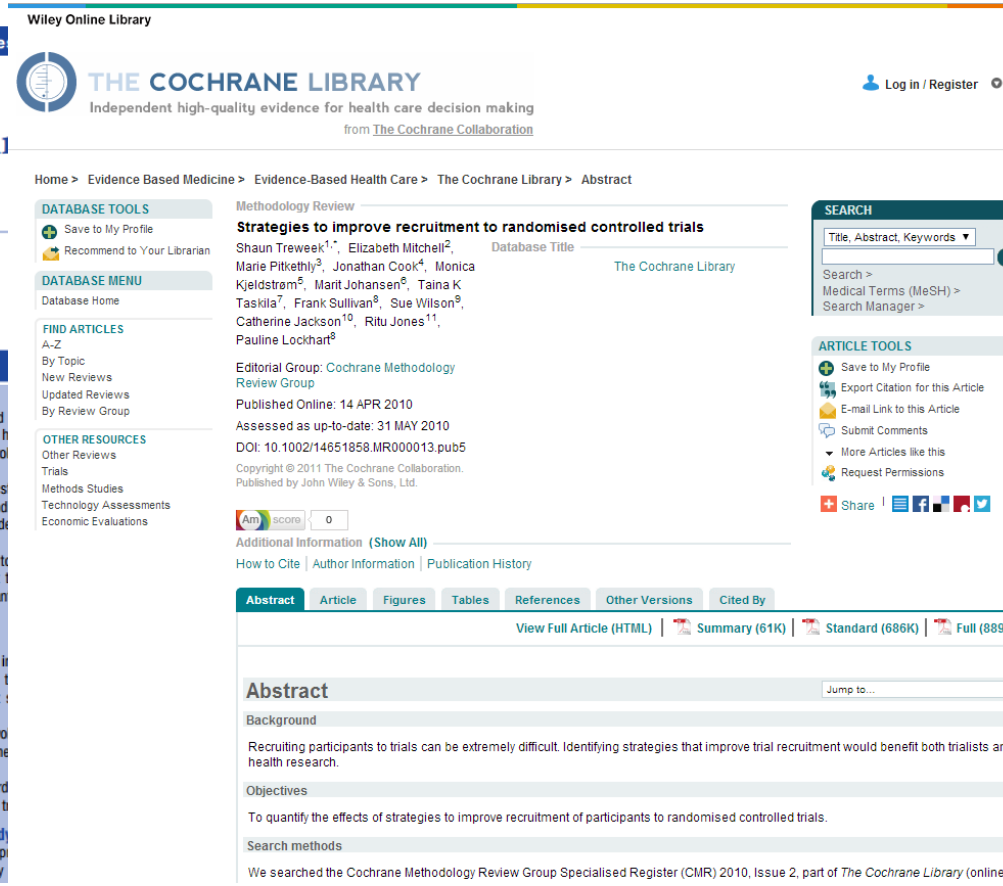
- Despite representing the gold standard ating the effectiveness and safety of h interventions, many randomised contro do not meet their recruitment targets.
- Poor recruitment can lead to extended s ation, greater resource usage and find are not as statistically precise as intende worst case, a trial may be stopped.
- A systematic review was carried out t methods used to improve recruitment mised controlled trials, and to quan effects on participation.

Key messages

- There are promising strategies for i recruitment to trials, most notably reminders, open-trial designs, opt-out and financial incentives.
- Many trials of recruitment methods invo thetical trials, and the applicability of the to the real world is still unknown.
- There is a clear knowledge gap with regard ive strategies aimed at those recruiting to t

Strengths and limitations of this study

- This Cochrane review utilised a compr search and appraisal strategy, thereby



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Methodology Review

Strategies to improve recruitment to randomised controlled trials

Shaun Treweek[1,*], Elizabeth Mitchell[2], Marie Pitkethly[3], Jonathan Cook[4], Monica Kjeldstrøm[5], Marit Johansen[6], Taina K Taskila[7], Frank Sullivan[8], Sue Wilson[9], Catherine Jackson[10], Ritu Jones[11], Pauline Lockhart[8]

Database Title: The Cochrane Library

Editorial Group: Cochrane Methodology Review Group

Published Online: 14 APR 2010

Assessed as up-to-date: 31 MAY 2010

DOI: 10.1002/14651858.MR000013.pub5

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Abstract

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Background

Recruiting participants to trials can be extremely difficult. Identifying strategies that improve trial recruitment would benefit both trialists ar health research.

Objectives

To quantify the effects of strategies to improve recruitment of participants to randomised controlled trials.

Search methods

We searched the Cochrane Methodology Review Group Specialised Register (CMR) 2010, Issue 2, part of *The Cochrane Library* (online

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6 comparisons

41 comparisons

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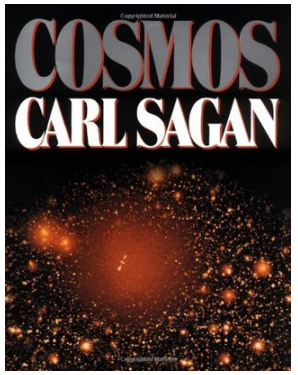
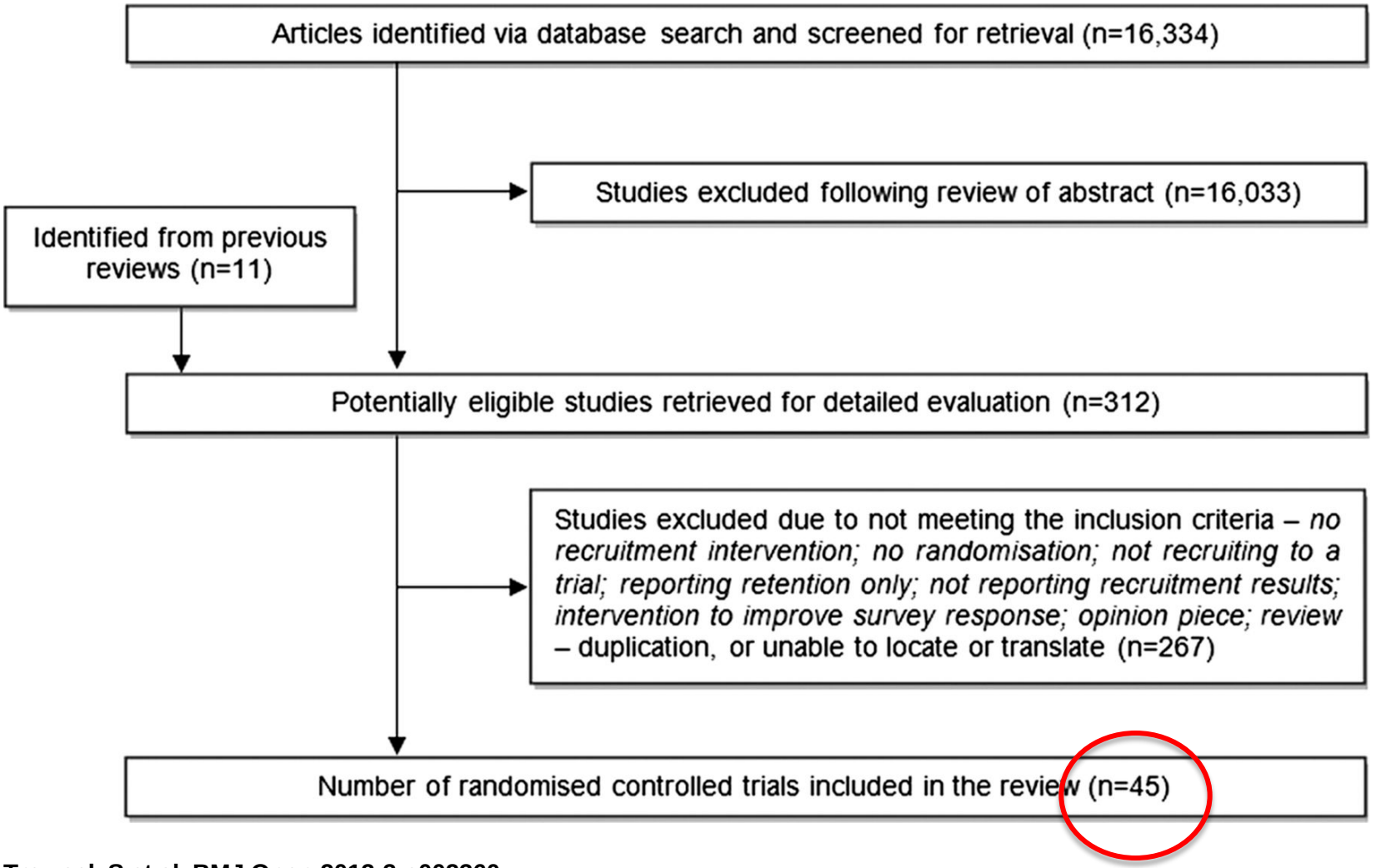
The absence of evidence is not the evidence of absence.



a) Open designs
b) Reducing the burden of consent
c) Telephone reminders
d) Audiovisual aids
e) Trial Booklets
f) Study Questionnaires
g) Financial incentives

Flow of studies into the review.



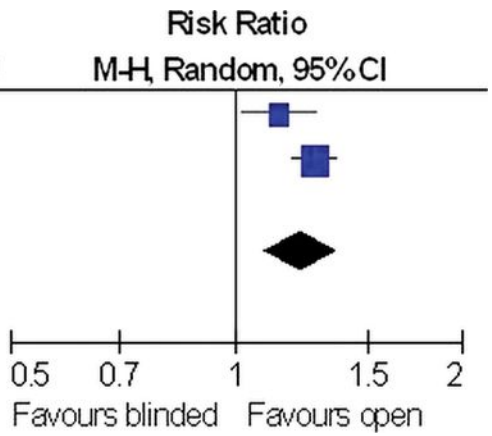
Treweek S et al. BMJ Open 2013;3:e002360

a Recruitment with open and blinded trial design.

Study or Subgroup	Open Events	Open Total	Blinded Events	Blinded Total	Weight	Risk Ratio M-H, Random, 95% CI
Hemminki 2004	134	180	233	358	41.8%	1.14 [1.02, 1.28]
Avenell 2004	1027	2159	796	2136	58.2%	1.28 [1.19, 1.37]
Total (95% CI)		**2339**		**2494**	**100.0%**	**1.22 [1.09, 1.36]**
Total events	1161		1029			

Heterogeneity: Tau² = 0.00; Chi² = 2.74, df = 1 (P = 0.10); I² = 64%

Test for overall effect: Z = 3.54 (P = 0.0004)



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b Opt out V Opt in

Analysis 4.1. Comparison 4 Opt-out consent vs opt-in consent, Outcome 1 Participant recruited.

Review: Strategies to improve recruitment to randomised controlled trials

Comparison: 4 Opt-out consent vs opt-in consent

Outcome: 1 Participant recruited

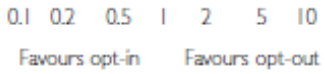
Study or subgroup	Opt-out n/N	Opt-in n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Trevena 2006	40/60	44/92		100.0 %	1.39 [1.06, 1.84]
Total (95% CI)	**60**	**92**		**100.0 %**	**1.39 [1.06, 1.84]**

Total events: 40 (Opt-out), 44 (Opt-in)

Heterogeneity: not applicable

Test for overall effect: Z = 2.34 (P = 0.019)

Test for subgroup differences: Not applicable



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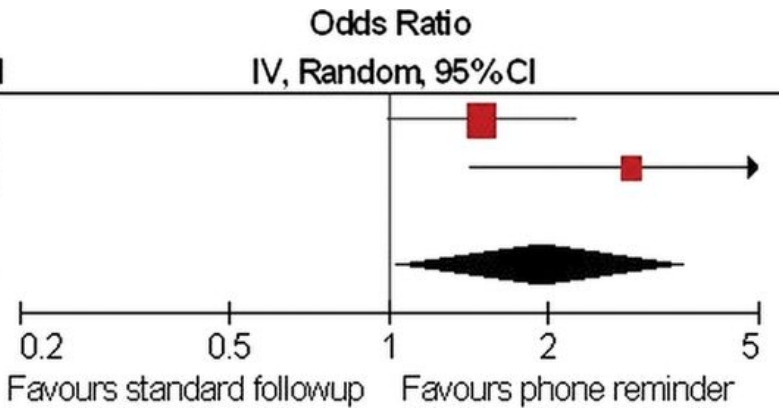
c Recruitment with telephone reminder V standard follow-up.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Harris 2008	0.405	0.212	60.1%	1.50 [0.99, 2.27]
Nystuen 2004	1.061	0.363	39.9%	2.89 [1.42, 5.89]
Total (95% CI)			**100.0%**	**1.95 [1.04, 3.66]**

Heterogeneity: Tau² = 0.13; Chi² = 2.44, df = 1 (P = 0.12); I² = 59%

Test for overall effect: Z = 2.08 (P = 0.04)



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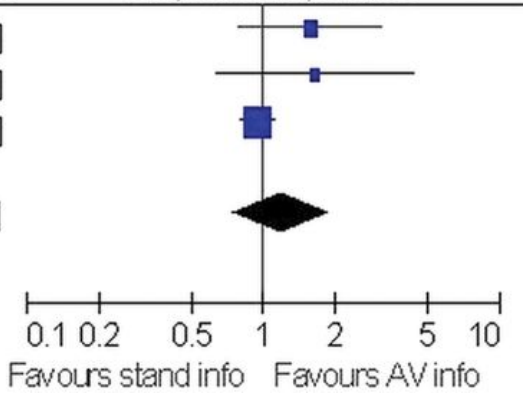
d Recruitment with audiovisual V standard trial information.

Study or Subgroup	AV information Events	Total	Standard information Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Du 2008	16	63	10	63	25.7%	1.60 [0.79, 3.25]
Du 2009	10	98	6	98	16.9%	1.67 [0.63, 4.41]
Hutchison 2007	62	86	66	87	57.3%	0.95 [0.80, 1.13]
Total (95% CI)		**247**		**248**	**100.0%**	**1.20 [0.75, 1.91]**
Total events	88		82			

Heterogeneity: Tau² = 0.09; Chi² = 4.00, df = 2 (P = 0.14); I² = 50%

Test for overall effect: Z = 0.75 (P = 0.46)



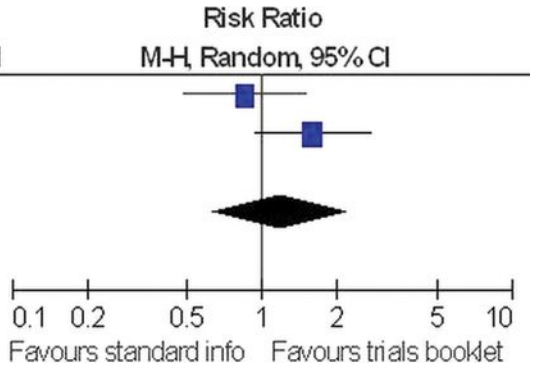
Treweek S et al. BMJ Open 2013;3:e002360

e Recruitment with clinical trials booklet V standard trial information.

Study or Subgroup	Trials booklet Events	Total	Standard information Events	Total	Weight	Risk Ratio M-H, Random, 95% CI
Ellis 2002	12	30	14	30	48.6%	0.86 [0.48, 1.53]
Ives 2001	15	23	11	27	51.4%	1.60 [0.93, 2.76]
Total (95% CI)		53		57	100.0%	1.18 [0.64, 2.18]
Total events	27		25			

Heterogeneity: $Tau^2 = 0.11$; $Chi^2 = 2.38$, df = 1 (P = 0.12); $I^2 = 58\%$

Test for overall effect: Z = 0.53 (P = 0.59)



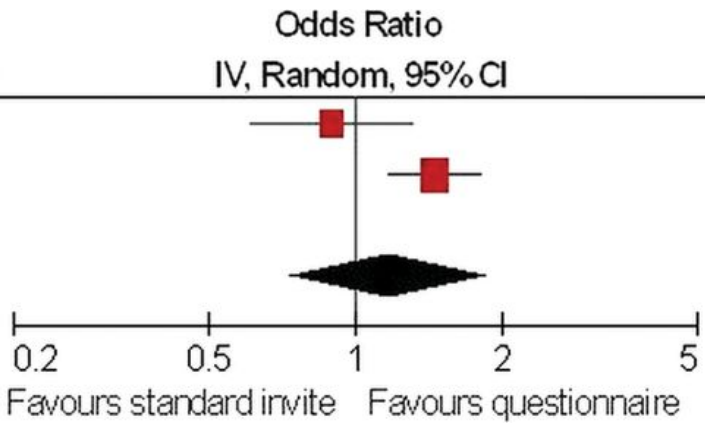
Treweek S et al. BMJ Open 2013;3:e002360

f Recruitment with invitation including study questionnaire V standard invitation.

Study or Subgroup	log[Odds Ratio]	SE	Weight	Odds Ratio IV, Random, 95% CI
Harris 2008	-0.105	0.197	44.3%	0.90 [0.61, 1.32]
* Kendrick 2001	0.372	0.113	55.7%	1.45 [1.16, 1.81]
Total (95% CI)			**100.0%**	**1.17 [0.74, 1.87]**

Heterogeneity: Tau² = 0.09; Chi² = 4.41, df = 1 (P = 0.04); I² = 77%

Test for overall effect: Z = 0.68 (P = 0.50)



Treweek S et al. BMJ Open 2013;3:e002360

g Financial Incentives

Analysis 40.1. Comparison 40 Financial incentive vs no incentive, Outcome 1 Participant recruited.

Review: Strategies to improve recruitment to randomised controlled trials

Comparison: 40 Financial incentive vs no incentive

Outcome: 1 Participant recruited

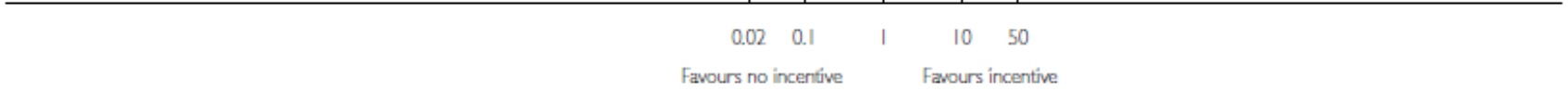
Study or subgroup	Financial incentive n/N	No incentive n/N	Risk Ratio M-H,Fixed,95% CI	Weight	Risk Ratio M-H,Fixed,95% CI
Free 2010	13/246	1/245		100.0 %	12.95 [1.71, 98.21]
Total (95% CI)	**246**	**245**		**100.0 %**	**12.95 [1.71, 98.21]**

Total events: 13 (Financial incentive), 1 (No incentive)

Heterogeneity: not applicable

Test for overall effect: Z = 2.48 (P = 0.013)

Test for subgroup differences: Not applicable



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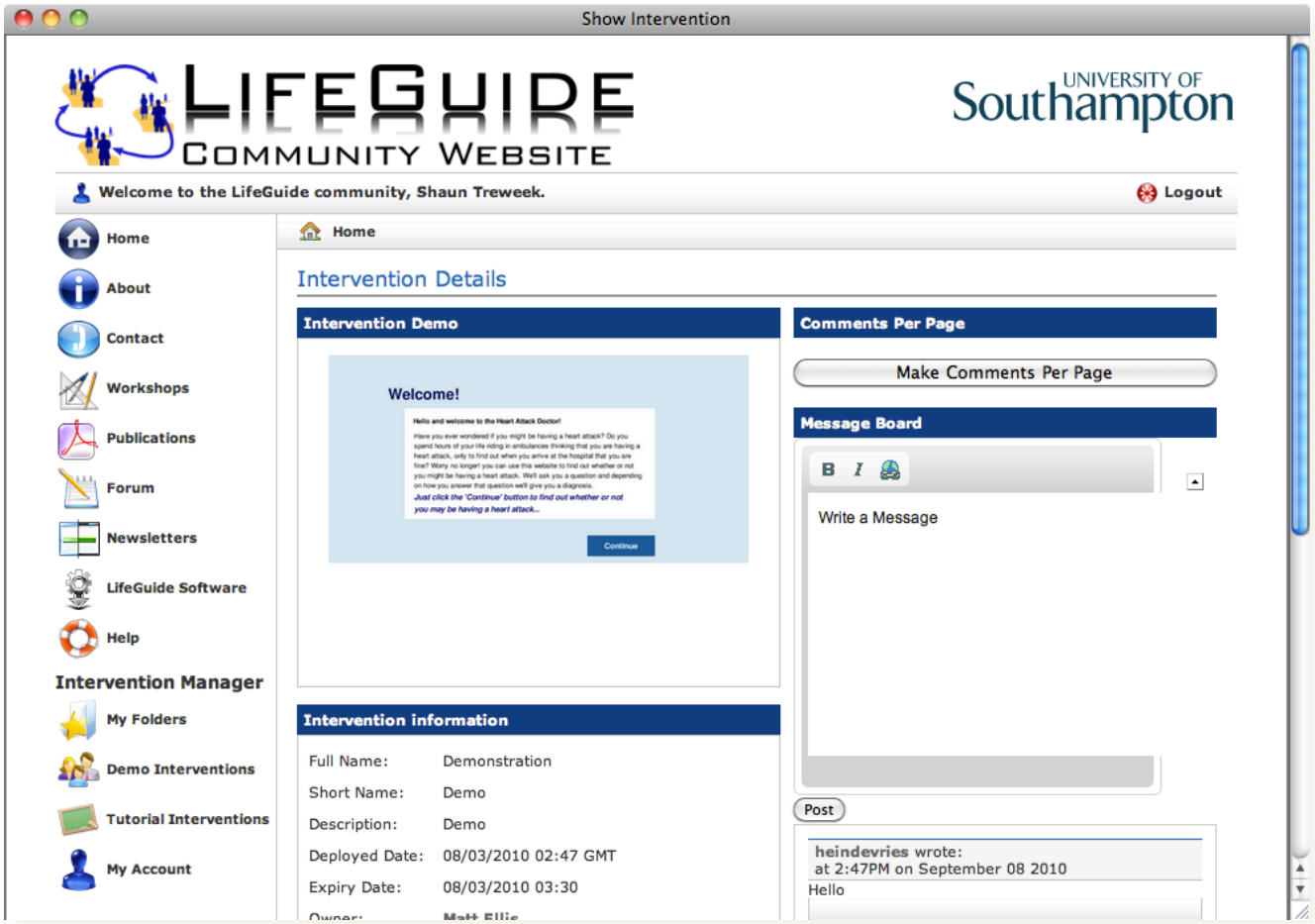
What other strategies might be effective?

a) Intervention modelling
b) Via EMRs (Prevalent, Incident)
    i. TrialTorrent
    ii. Searches
        Local
            Integrated with EMR
        Central
    iii. SHARE
c) Practice Based Research Networks

Web- Based Intervention Modelling (WIME) uses the LifeGuide system



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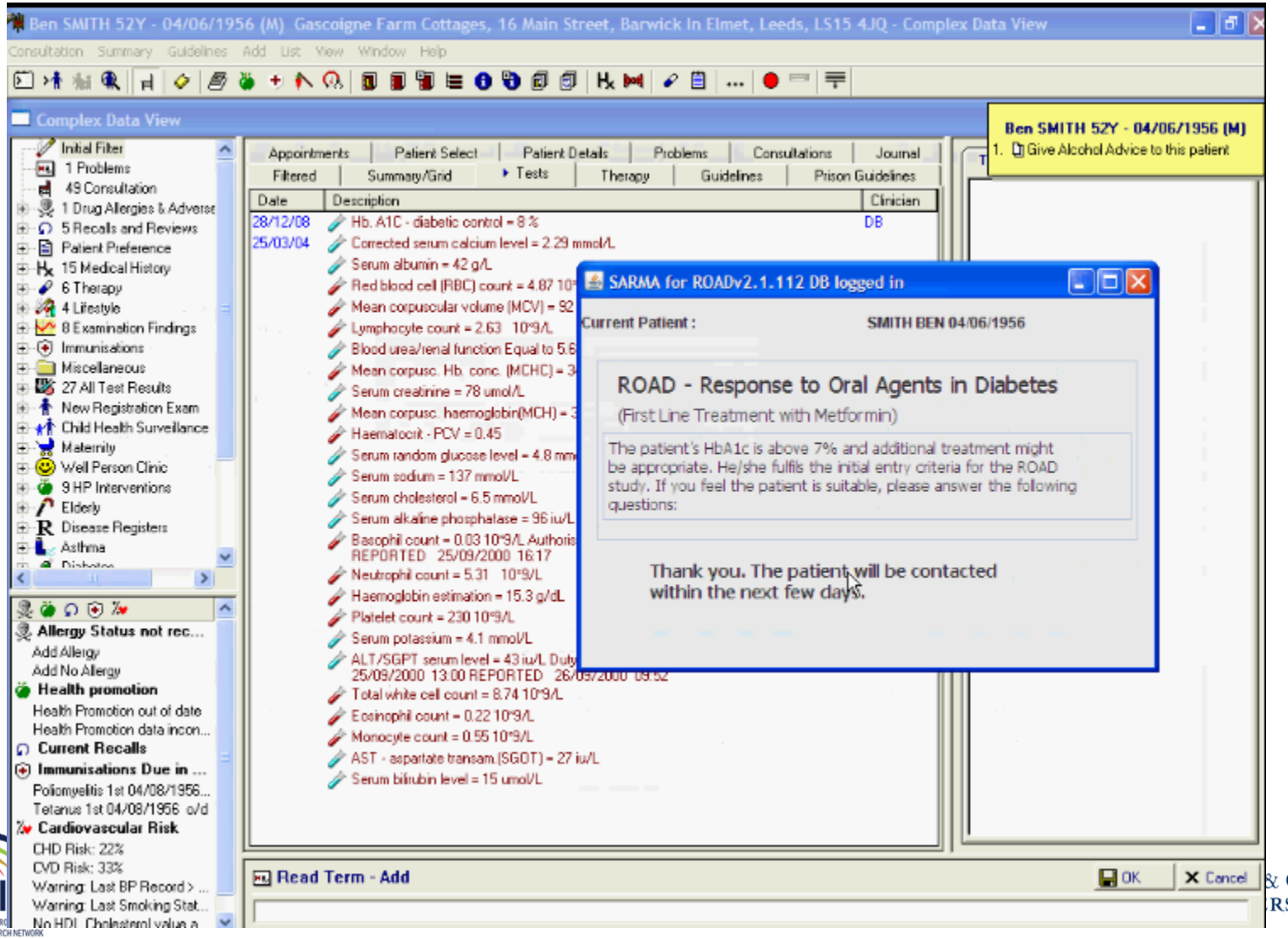
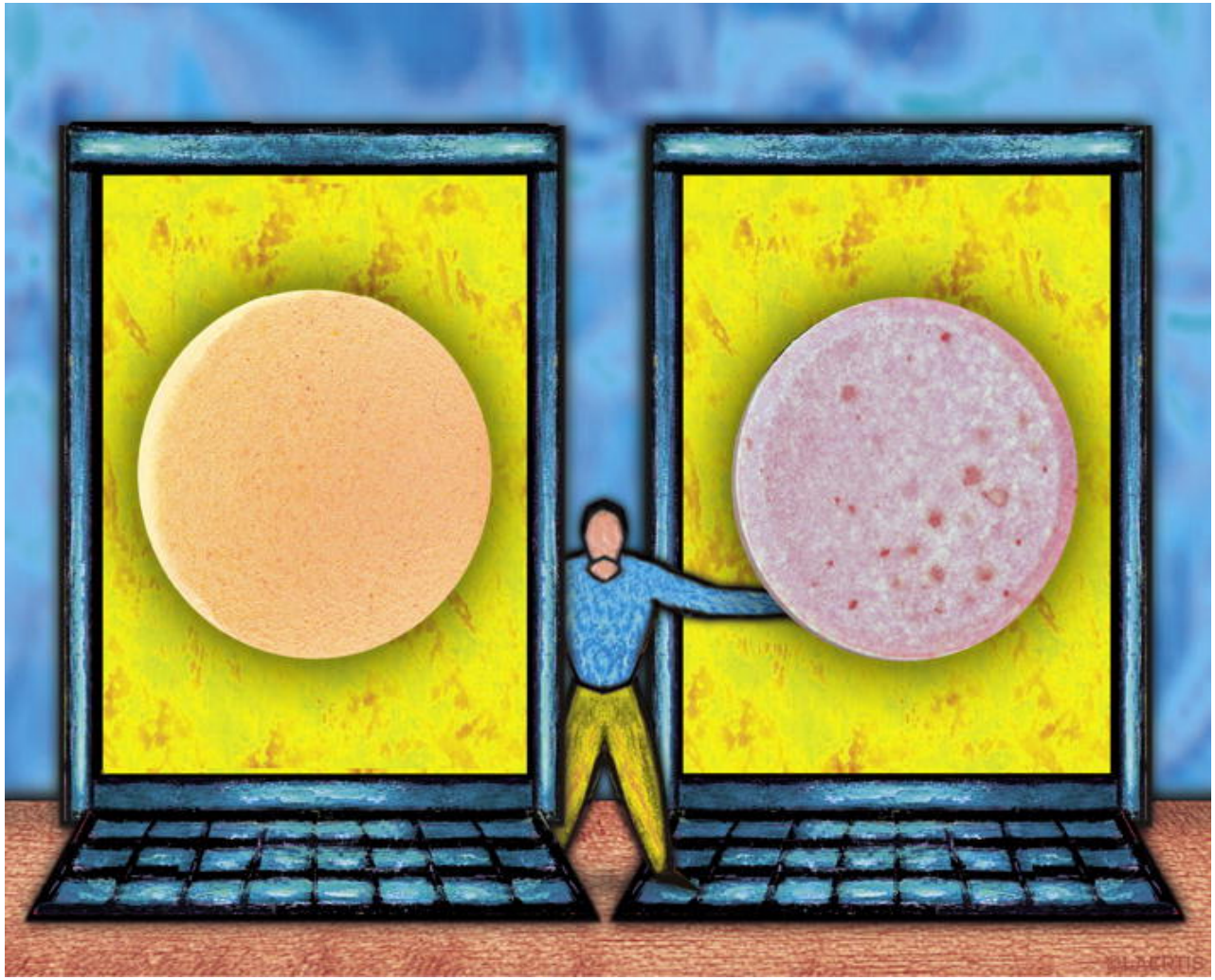
Acute Recruitment Tools



Pragmatic randomised trials using routine electronic health records
eLung (Antibiotics in COPD) RetroPro (Statins in 1y prevention)



Staa T v et al. BMJ 2012;344:bmj.e55

Embedding recruitment in software

- At appointment booking
- Before appointment
- In waiting room
- In consultation

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OceanWave lets patients register and change contact information online at home, or on a tablet in the waiting room. Your patient data stays accurate and up-to-date, you eliminate paper, and save time and hassle for front-desk staff.

BETTER PATIENT CARE

OceanWave generates accurate, focused patient histories with concise clinical notes in your EMR, allowing you to easily identify "red flags" before you even see the patient. You stay on schedule, spend less time typing, and more on patient

BETTER RESEARCH & QIPs

OceanWave makes it easy to recruit or follow up on patient surveys using specific inclusion criteria at check-in. Securely collect, aggregate and store anonymous patient data across multiple sites with PHIPA compliance.

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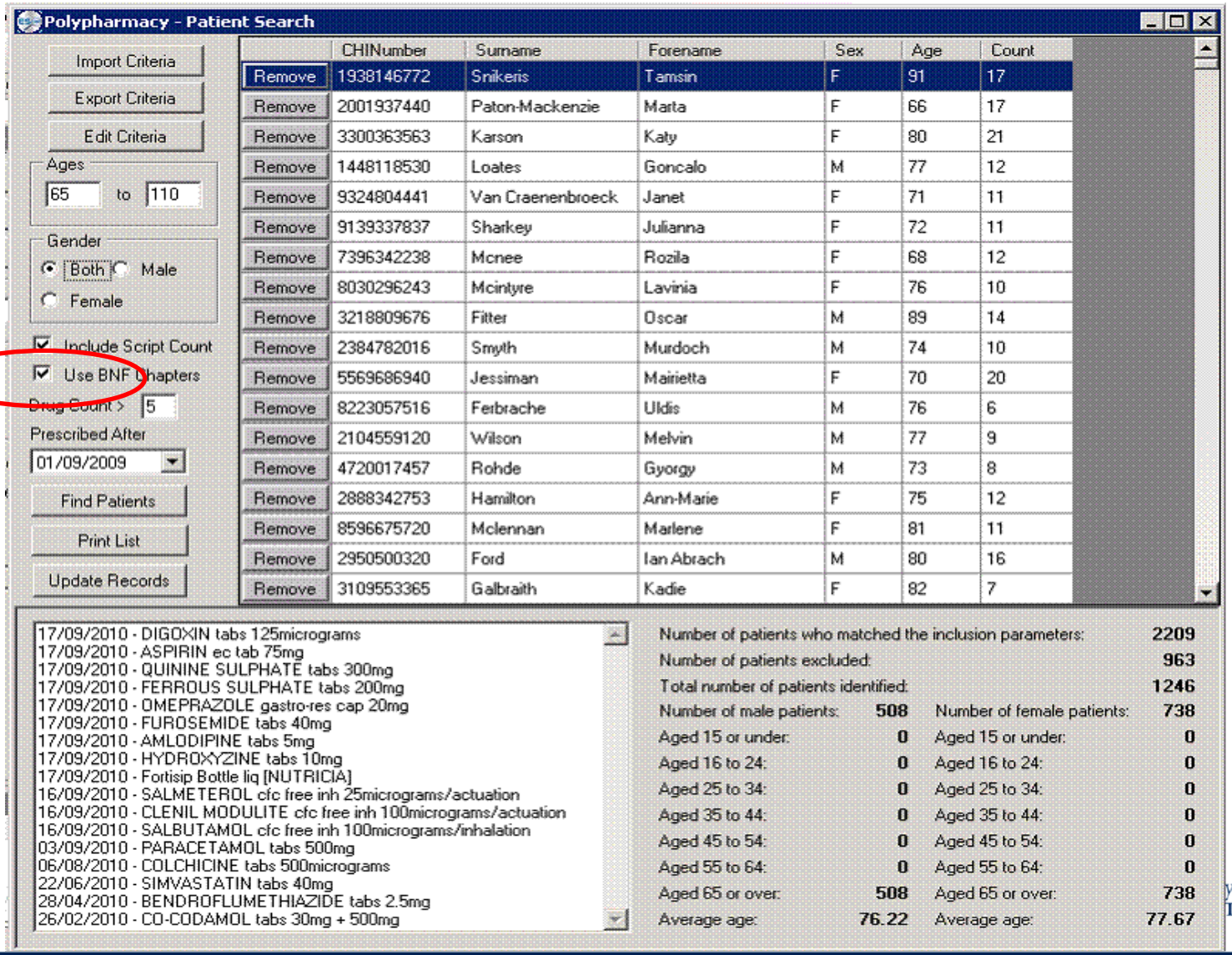
Remote Query on Central database of EMR data



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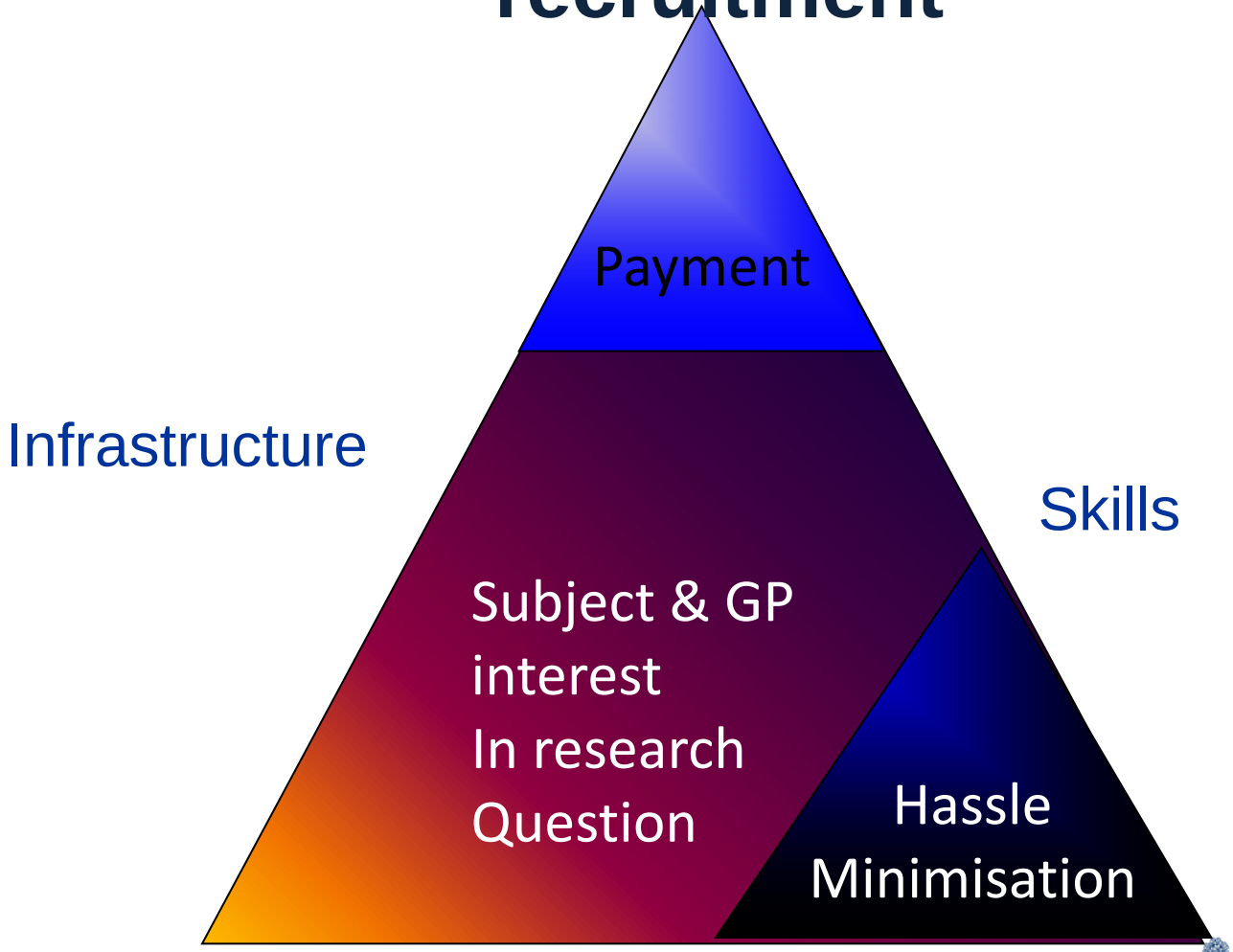
Key PBRN Concepts when engaging with practices and potential subjects for trial recruitment



What do you think we know now?

1. How often do clinical trials fail to recruit to target?
2. Which of the following strategies have been shown to increase recruitment rates?
   a) Open designs
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   c) Telephone reminders
   d) Audiovisual aids
   e) Trial Booklets
   f) Study Questionnaires
   g) Financial Incentives
3. What other strategies might be effective?
   a) Intervention modelling
   b) Via EMRs (Incident, Prevalent)
   c) PBRNs

Research Implications

1. Few effective strategies identified
2. Insufficient/Inadequate research
   - 45 papers included
3. Low contribution from primary care
   - 7
     - 4 UK, 1USA, 1Can,1 Aus
4. Novel ideas promising
5. PBRNs offer a valuable laboratory to test new approaches