

New treatment approaches for people with psychosis

Shôn Lewis

There is no money



Schizophrenia

- Onset in early adult life
- Psychotic illness with positive and negative symptoms, plus cognitive impairments
- 1 in 200 people
- Direct costs of health and social care in UK : £3 billion.
- Life expectancy reduced by 17 years

Outcome in schizophrenia

- 80% will recover from first episode, usually within 3 months
 - BUT
- Relapse in 30% by one year; 80% by 5 years
- Negative symptoms often persist
- Suicide in 5%

Three sorts of intervention

- Drug treatments
- Psychological treatments
- Service-level interventions

How to tell what works

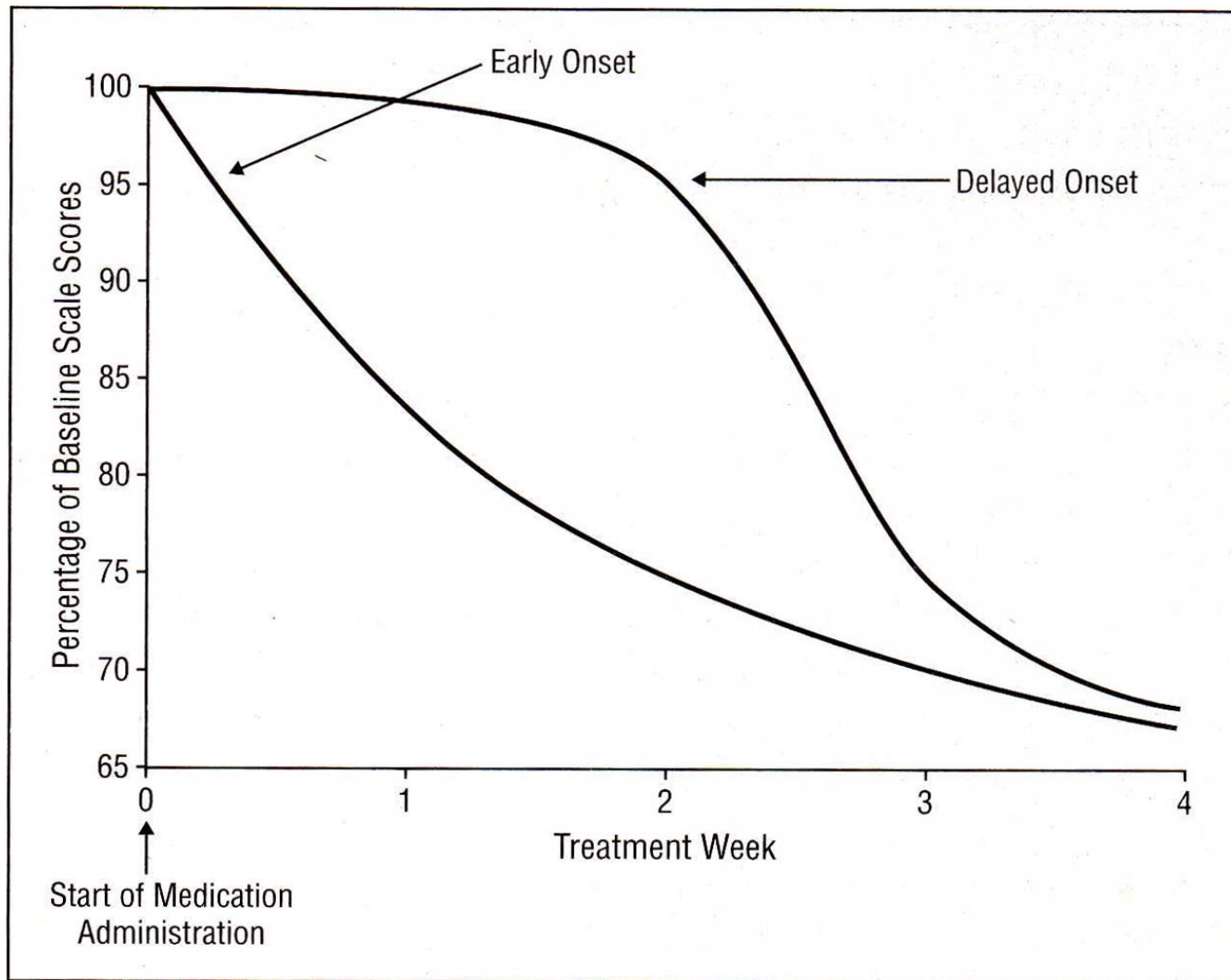
- **Randomised controlled trials**
 - Difficult and expensive to do well

Drug treatments

Antipsychotic drugs

- Chlorpromazine 1954
- Two indications:
 - *Acute treatment*: getting people better: effective for positive symptoms in 70%; less effective for negative symptoms
 - *Maintenance treatment*: keeping people well: reduce relapse by five fold over 1 year
- Cause a range of side effects

Early versus delayed acute drug action

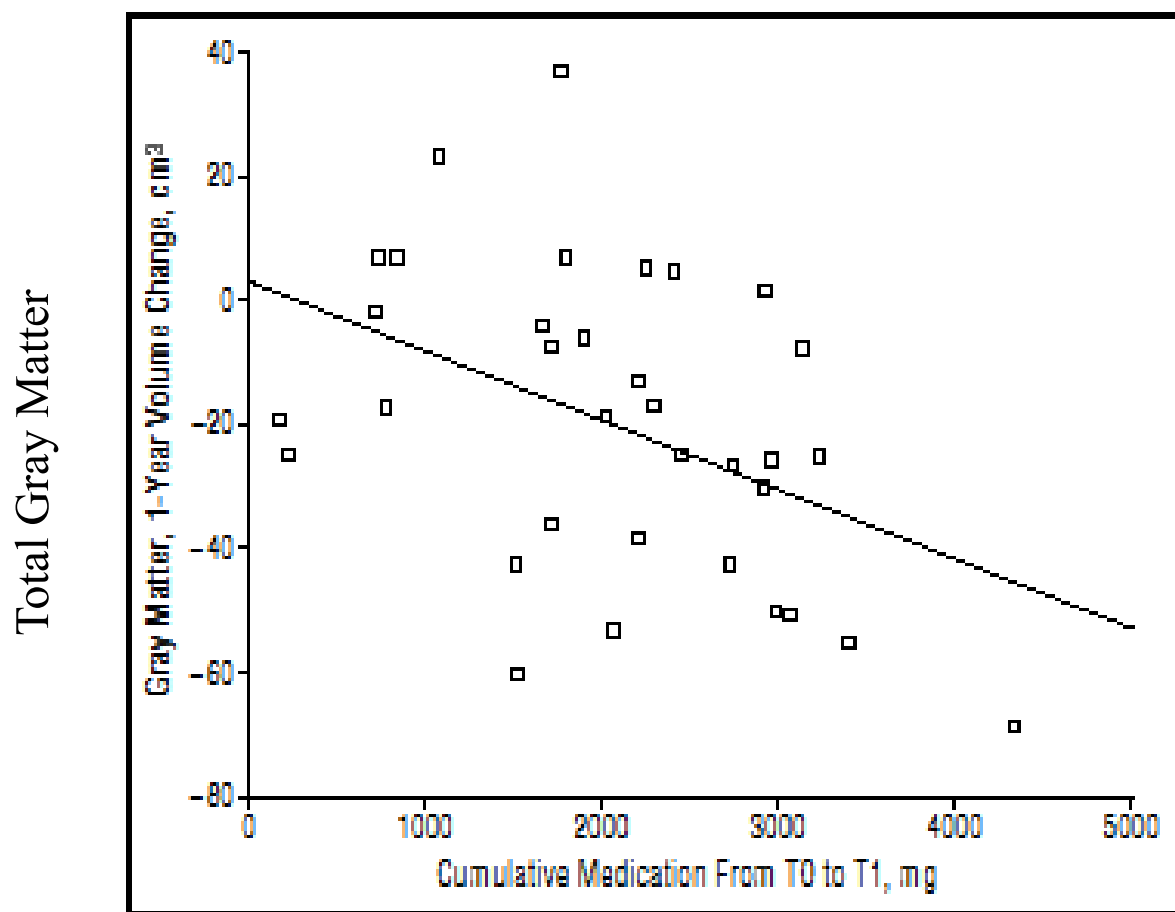


Agid, Kapur et al 2003

Early antipsychotic response

- Ziprasadone IM double blind vs placebo: PANSS positive subscale score at 4 hours $p < 0.05$ (Agid et al, 2008)
- 30% reduction in PANSS total at 2 weeks best predicts 6 week outcome (PPV 70%; NPV 80%)
- Patients with no or minimal improvement of symptoms during the first week of treatment are unlikely to respond to a 4 week trial

Total grey matter volume change over one year after first episode psychosis and antipsychotic drug load



This correlation was evident even when controlling for poor clinical outcomes.

Cahn et al 2002

Figure 3. Change in gray matter volume and cumulative dosage of antipsychotic medication from baseline (T0) to 1 year after study inclusion (T1) in patients with schizophrenia.

Do antipsychotic drugs damage your brain?

Dorph-Petersen et al (2005)

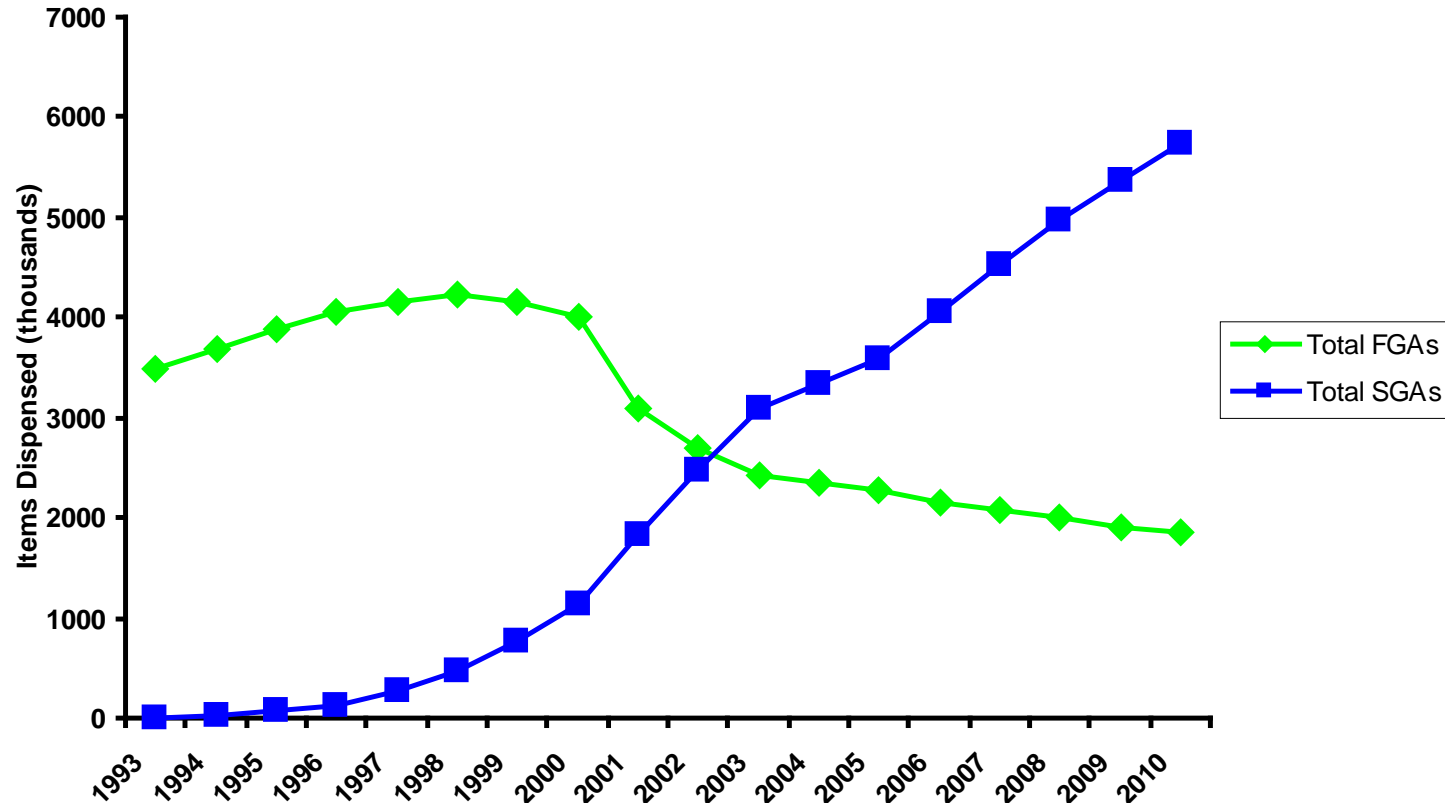
18 macaque monkeys assigned to 2 year course of **placebo**, **haloperidol** or **olanzapine** at doses equivalent to therapeutic human doses

Brain volume change at 2 years:

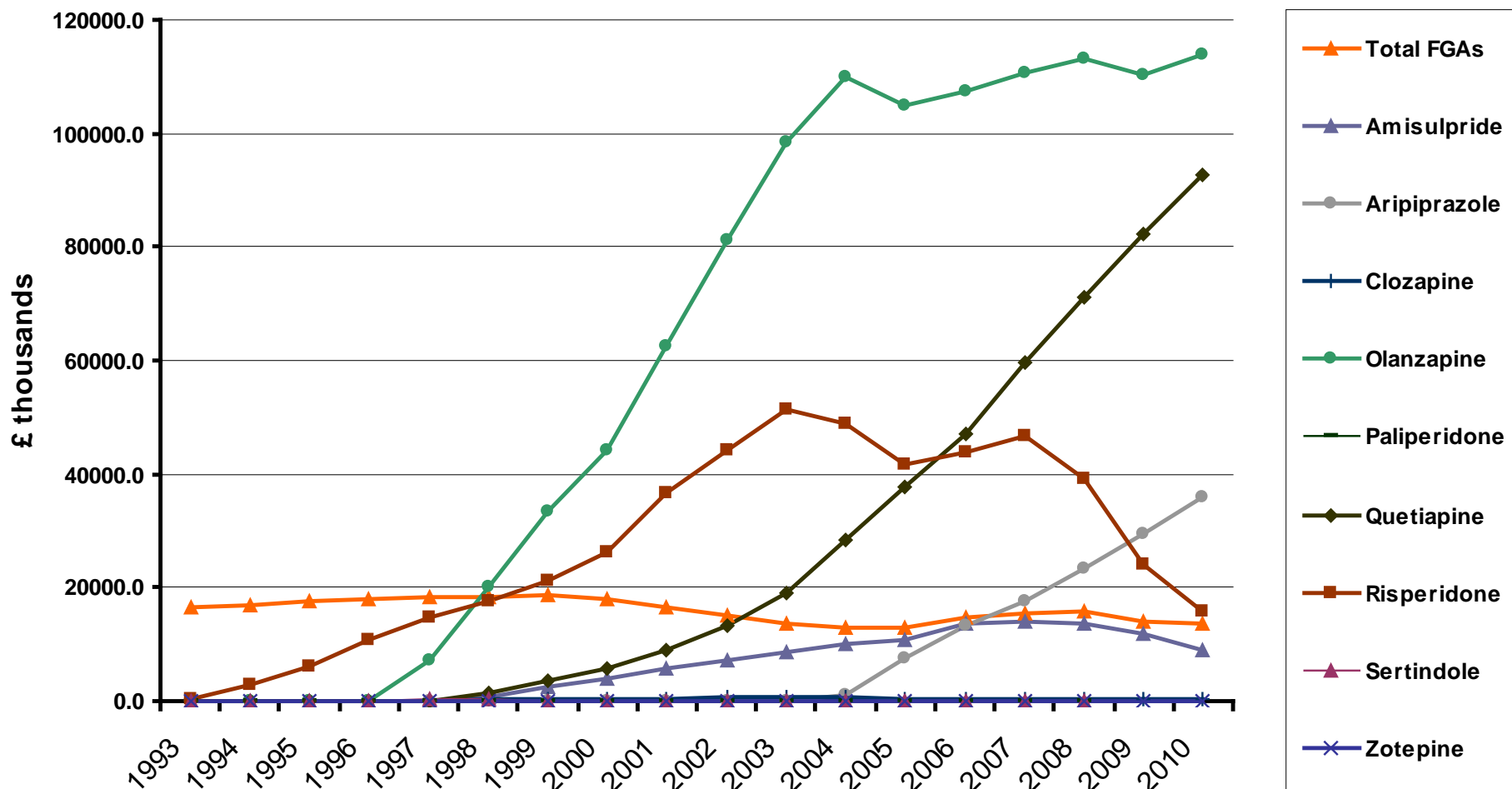
- | | |
|--------------|--------|
| ▪Placebo | 0% |
| ▪Haloperidol | -8.8% |
| ▪Olanzapine | -10.5% |

$p < 0.05$ for both drugs

FGA vs SGA prescriptions primary care England 1993-2010

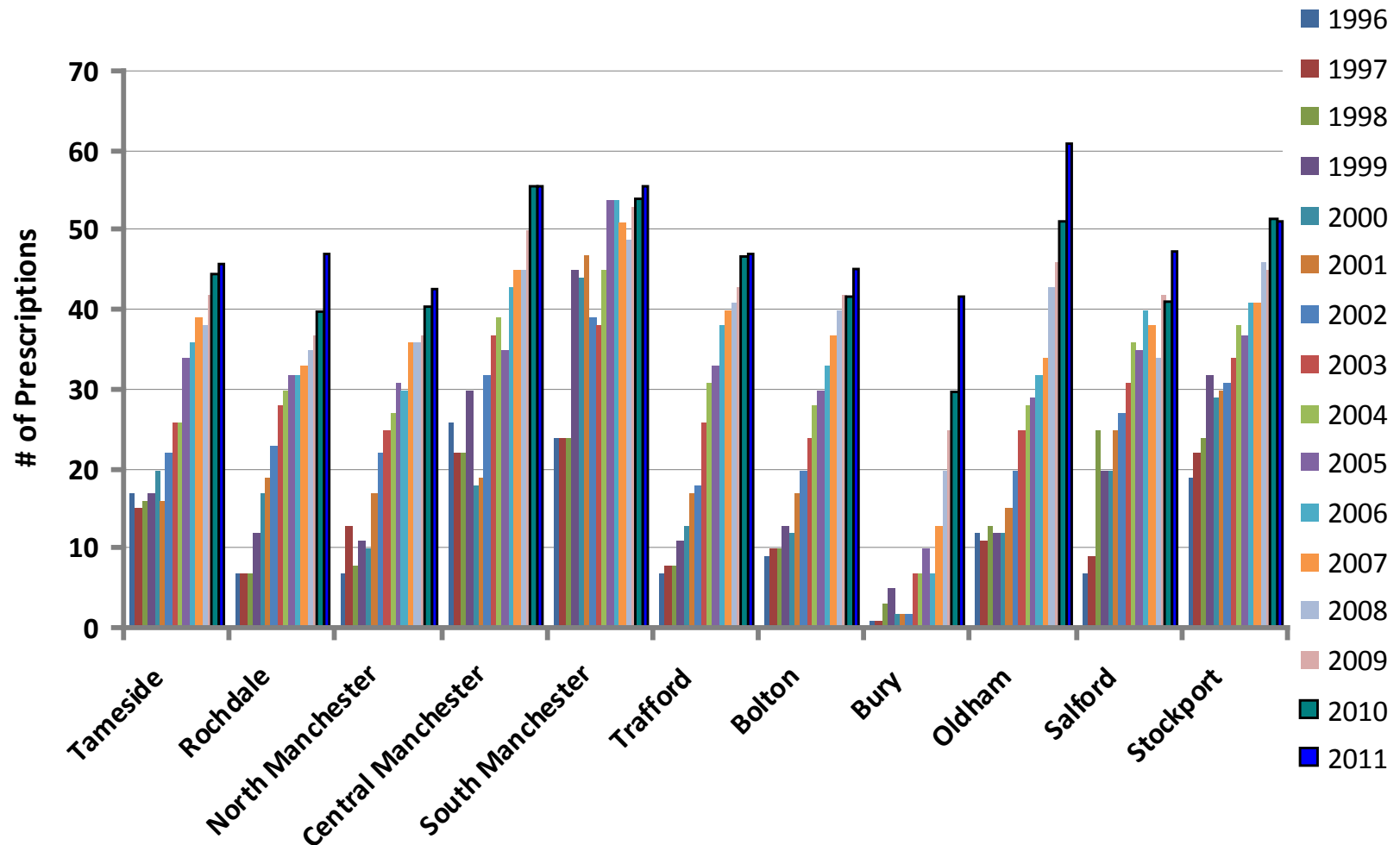


Expenditure primary care England

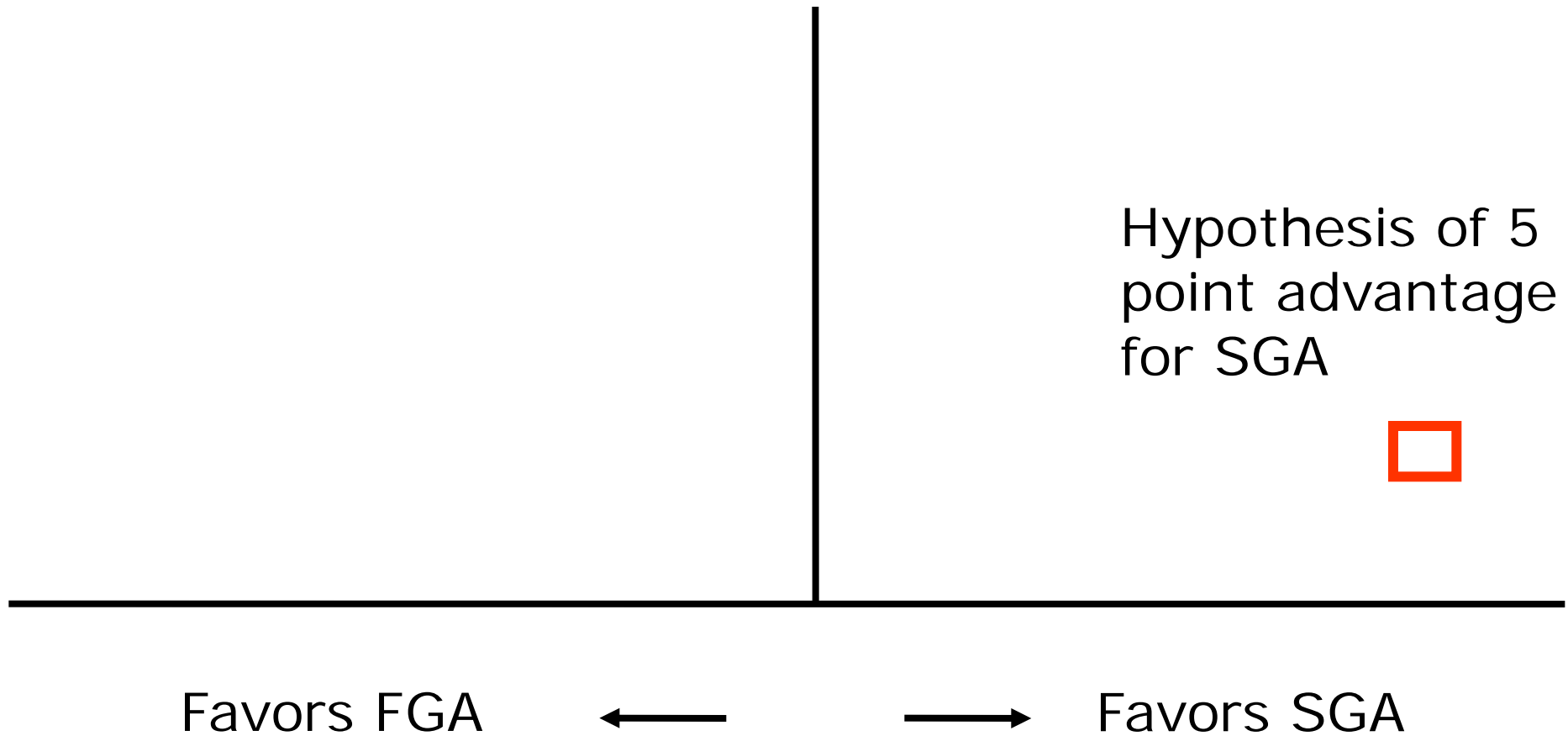


Postcode prescribing: clozapine Greater Manchester 1996-2011

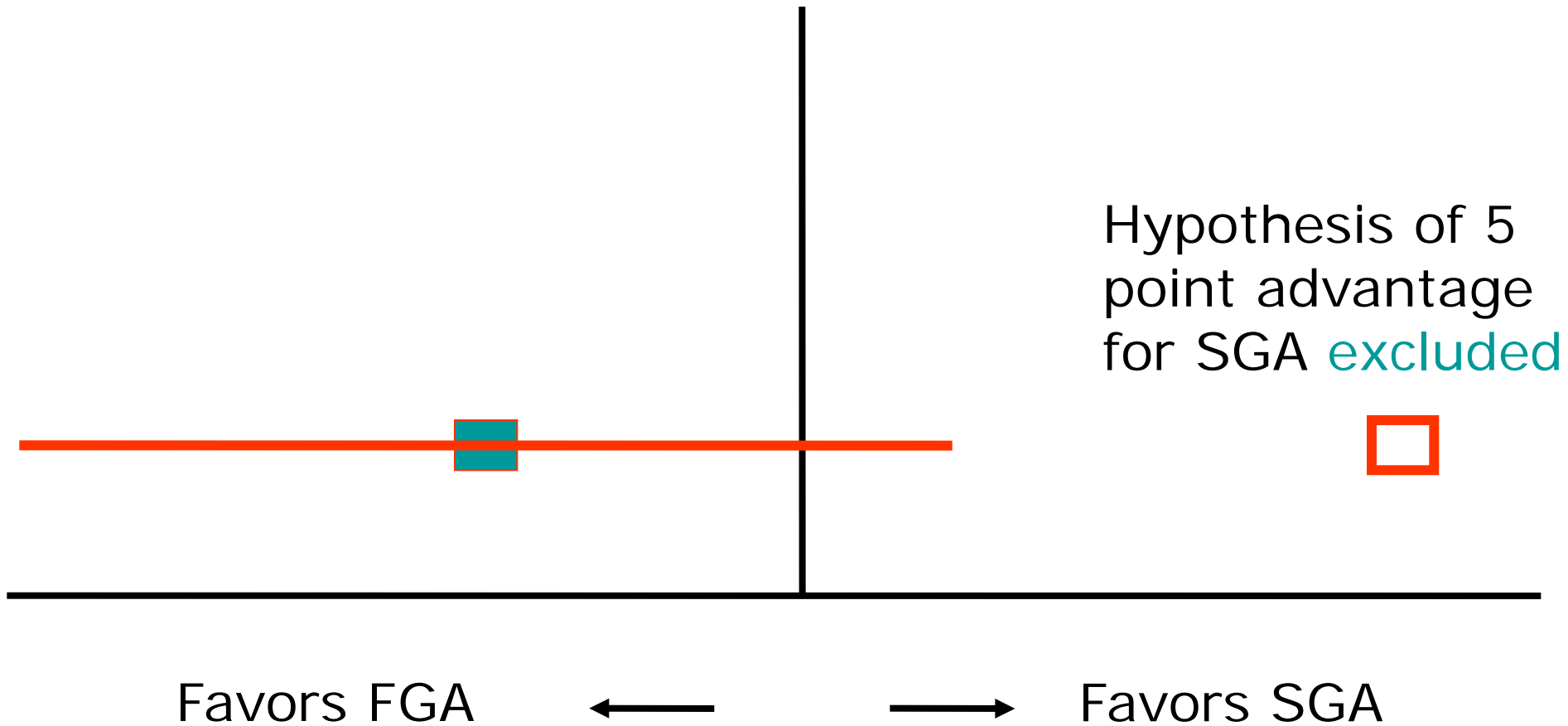
Population & Need Adjusted Data



CUtLASS 1 Quality of Life



CUtLASS 1 Quality of Life



In Antipsychotics, Newer Isn't Better Drug Find Shocks Researchers

By [Shankar Vedantam](#)

Washington Post Staff Writer

Tuesday, October 3, 2006; Page A01

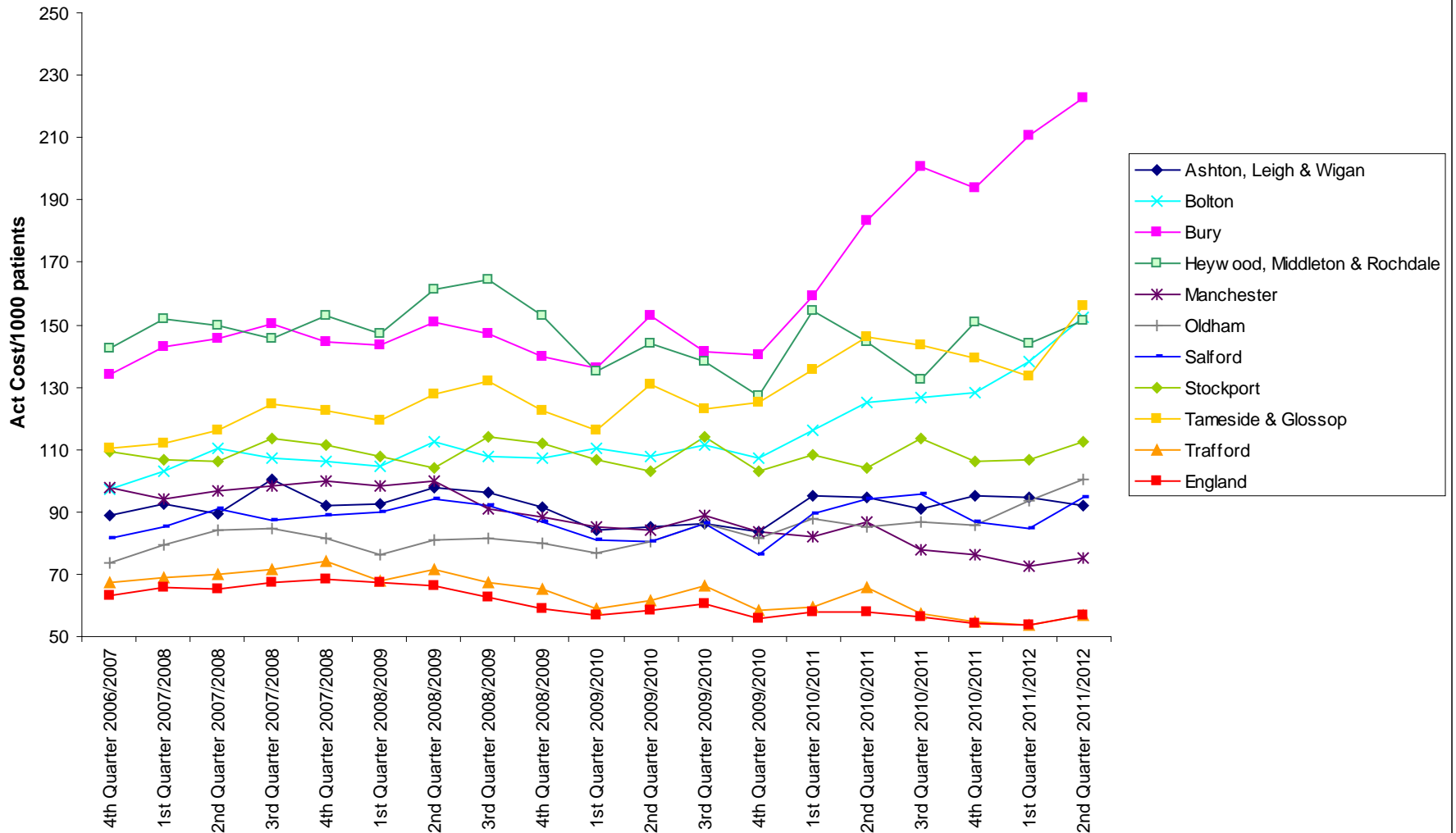
Schizophrenia patients do as well, or perhaps even better, on older psychiatric drugs compared with newer and far costlier medications, according to a study published yesterday that overturns conventional wisdom about antipsychotic drugs, which cost the United States \$10 billion a year. The results are causing consternation. The researchers who conducted the trial were so certain they would find exactly the opposite that they went back to make sure the research data had not been recorded backward.

The study, funded by the British government, is the first to compare treatment results from a broad range of older antipsychotic drugs against results from newer ones. The study was requested by Britain's National Health Service to determine whether the newer drugs -- which can cost 10 times as much as the older ones -- are worth the difference in price.

Highlights of Phase I

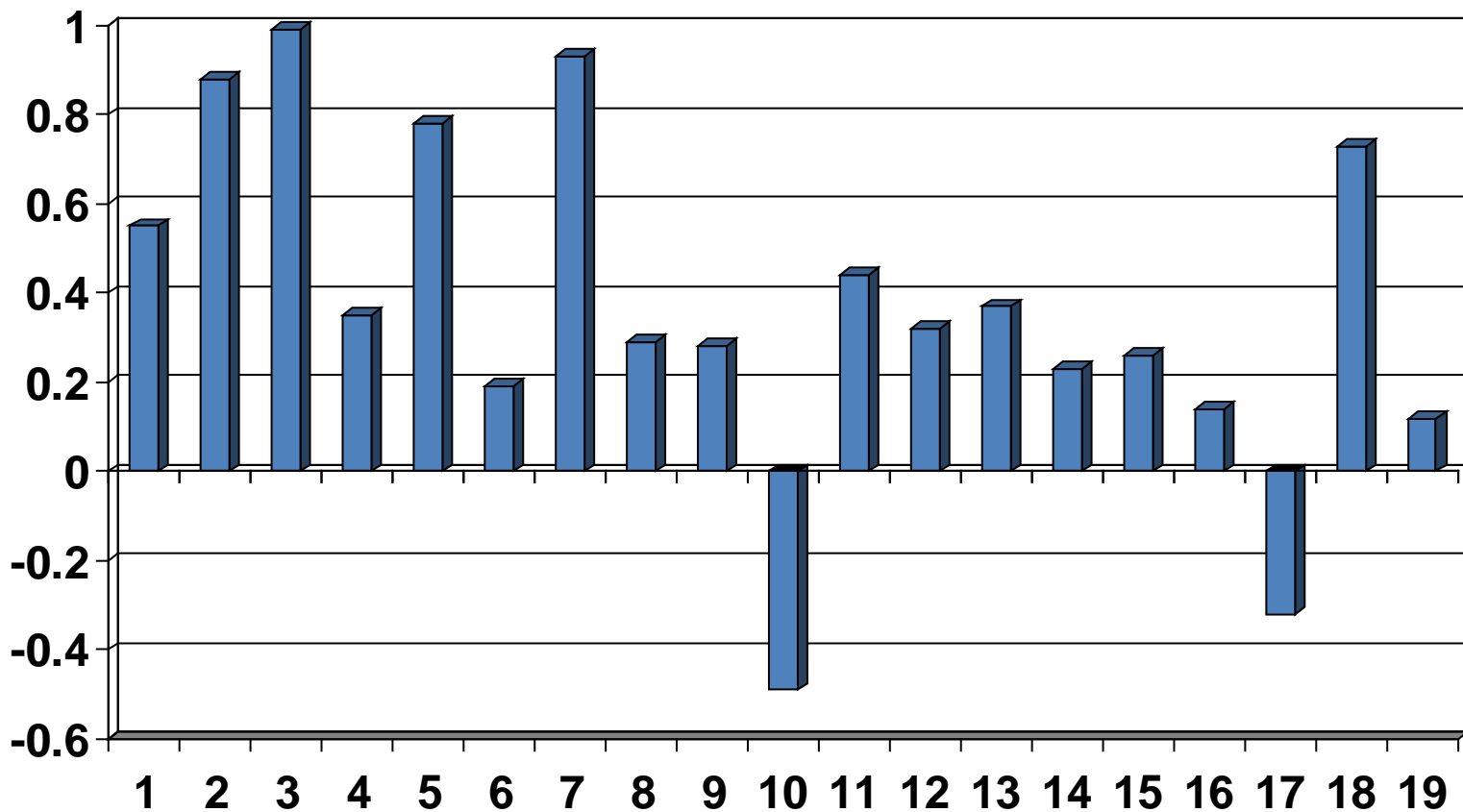
- High rate of discontinuation (switching)
 - Hypothesized 60%
 - Consistent with practice and clinical trials
- OLZ most effective
 - Best efficacy, worst side effects
- PER comparably effective to SGAs
 - Slightly higher EPS
- No differential effects of SGAs on Sxs including negative Sxs
 - Cognition, substance abuse, violence
- Differences in types and severity of side effects
- Consistent results across multiple measures within domains
- Full dose range not explored before switching

Greater Manchester PCTs - Weighted prescribing cost of 'typical antipsychotics' since January 2007: (All)

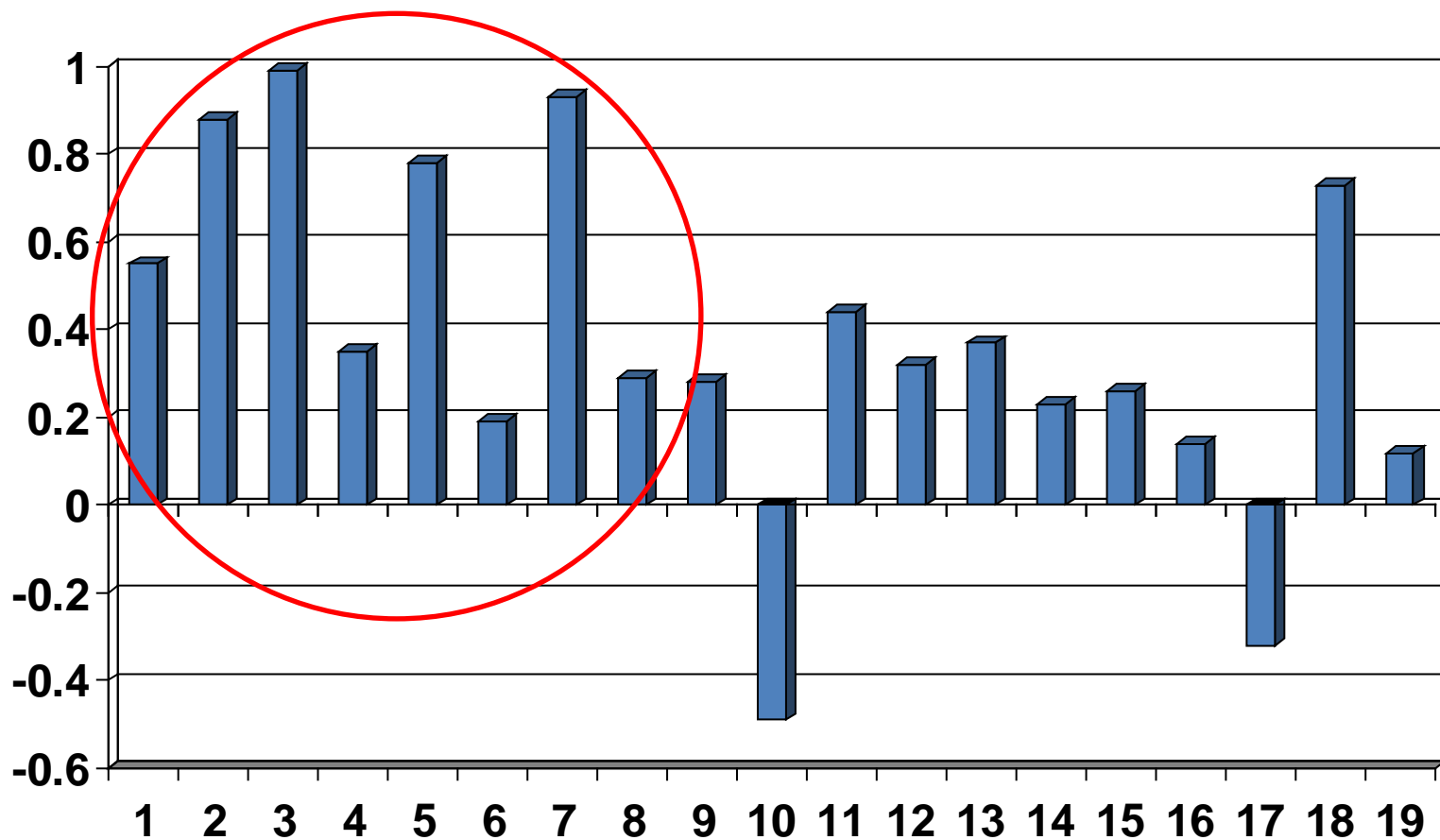


Psychological treatments

CBT Effect Size by trial quality



CBT Effect Size by trial quality



SoCRaTES trial

- Independently rated as highest quality CBT/psychosis trial. MRC-funded trial of brief 6-week CBT vs supportive counselling vs usual care in n=308 acute 1st/2nd episode clients.
- Results
 - CBT accelerates improvement in acute symptoms
 - leads to improved outcomes at 18 months
 - effects small, but measurable and durable
 - BUT SO DID SUPPORTIVE COUNSELLING

Lewis et al (2003),
Tarrier et al (2004)

All psychological treatments work

- So-called Dodo bird hypothesis
 - “everyone’s won and all must have prizes!”
- Supportive counselling as good as CBT
- BUT what drives this effect might be the therapeutic alliance: *“the quality of the relationship between therapist and client, characterised by trust and a sense of common purpose”*.
- How to prove this?

SoCRaTES trial

- Therapeutic alliance rated by therapist (Frank and Gunderson scale) and client (CALPAS scale).
- CALPAS showed
 - With a **good TA**, attending more sessions causes a significantly better outcome on PANSS total score (effect size -2.91, 95% confidence interval -0.90 to -4.91)
 - With a **poor TA**, attending more sessions is detrimental (effect size +7.74, 95% confidence interval +1.03 to +14.45).
- No-one has shown this before.

Service redesign
- through connected health

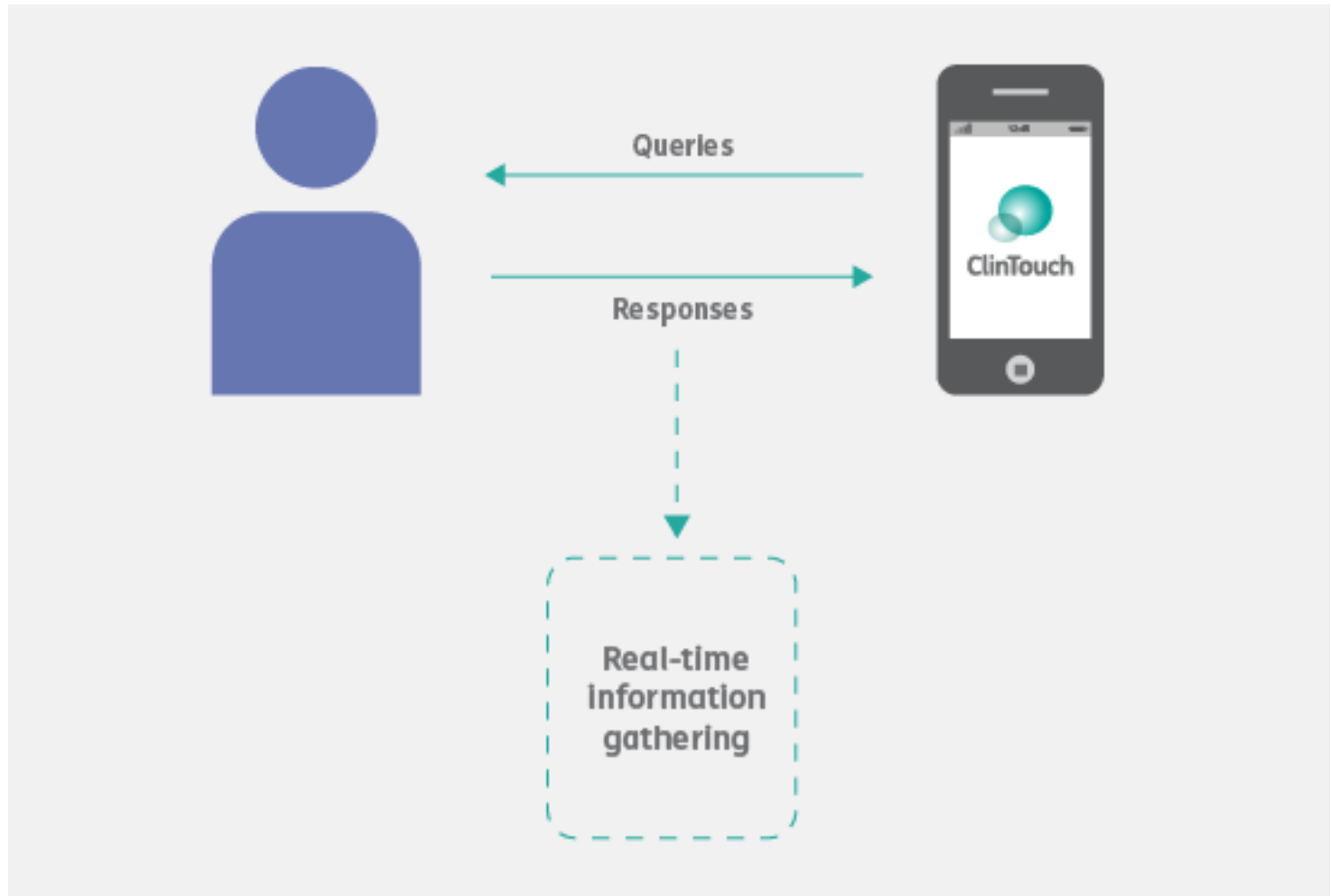


ClinTouch

m-Health for people with psychosis

www.clintouch.com

How it works



ClinTouch/Careloop

- **Careloop**

- **Aim: an end-to-end solution linking client and professional in the co-production of care.**
- **Customisable, secure interface for clinical teams**
- **Real-time data summaries streamed to team base, ECRs**
- **Personalised relapse signature/EWS triggers alert at team base.**

Four impacts

Improved user
experience of
care

User health
self-
management

Early
intervention
and prevention

Research
capability

People with SMI: opinions of health professionals 2010

They said

- Few users own and use a mobile
- Users won't be interested
- They'll lose or sell the handset
- It will make users paranoid
- It will be too complicated
- It will take too long to complete
- They will stop using it
- Responses might be made up
- Responses won't resemble interview data

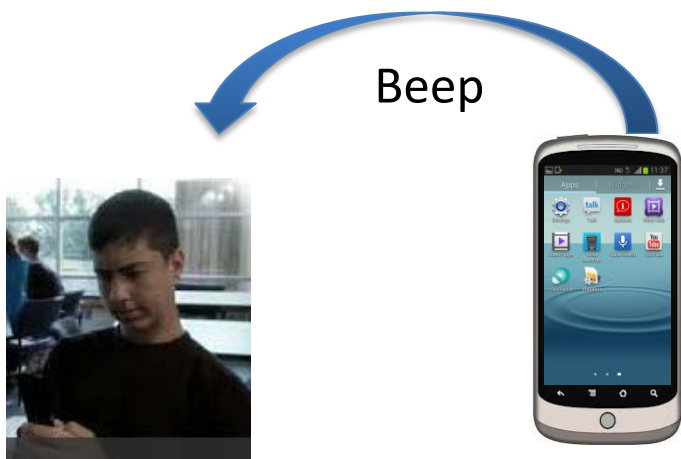
We found

- 85% do.
- 80% of those approached agreed
- 1/44 lost handset
- 2/44 discontinued for this reason
- 36/44 completed >33% of 36
- Average 70 seconds
- 81% completed a week
- Not the case.
- Very high correlations on key items

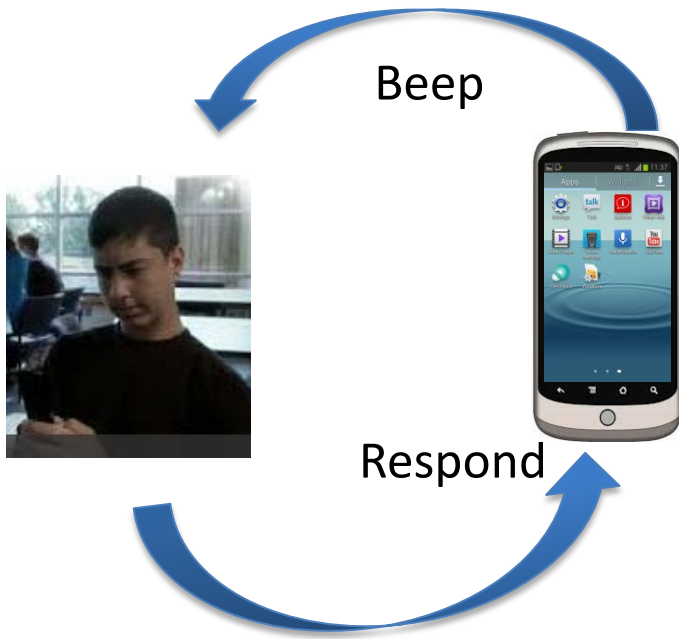
How it works



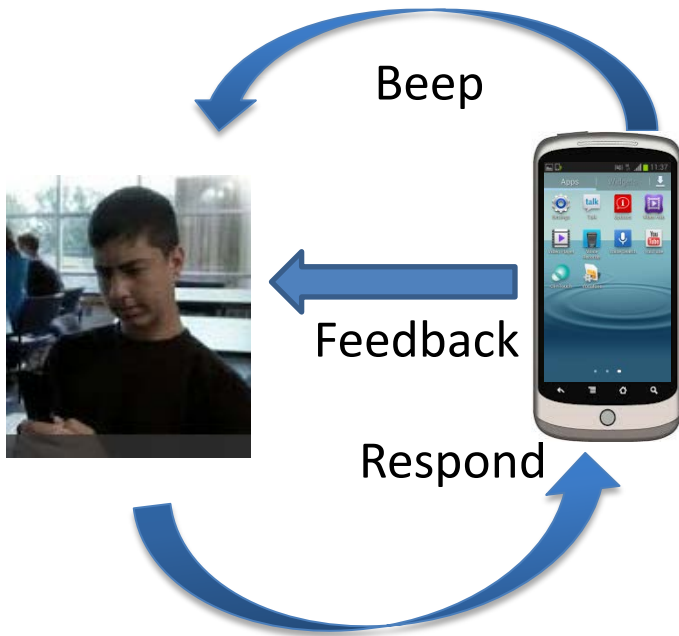
How it works



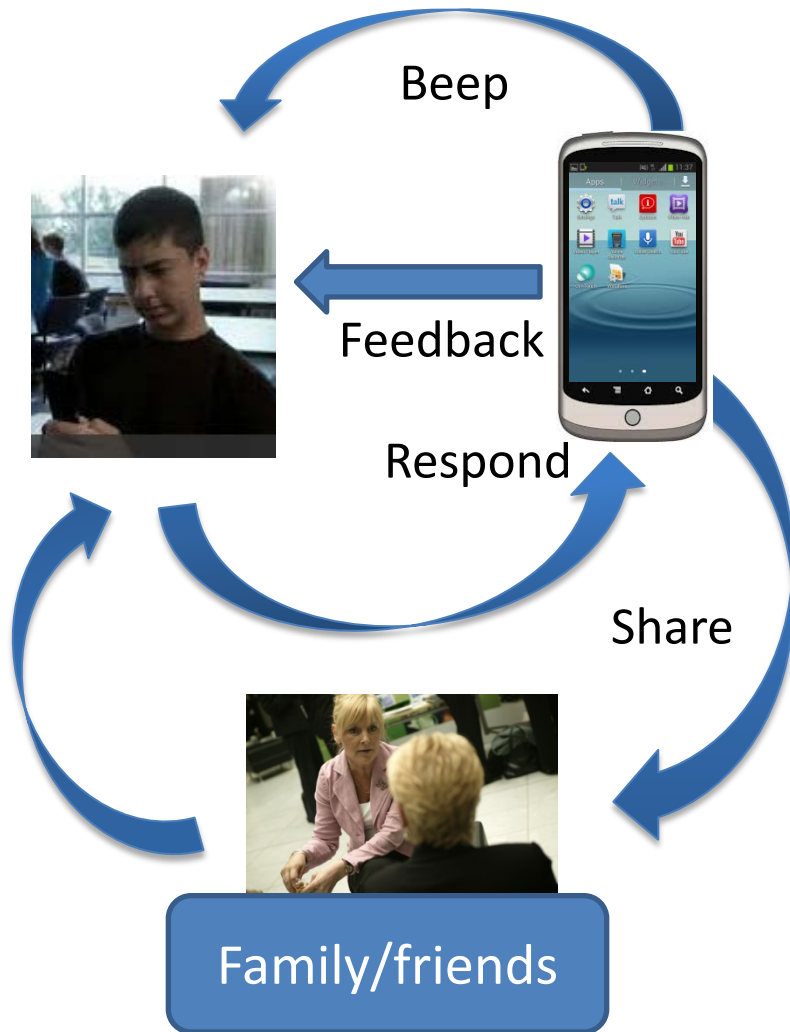
How it works



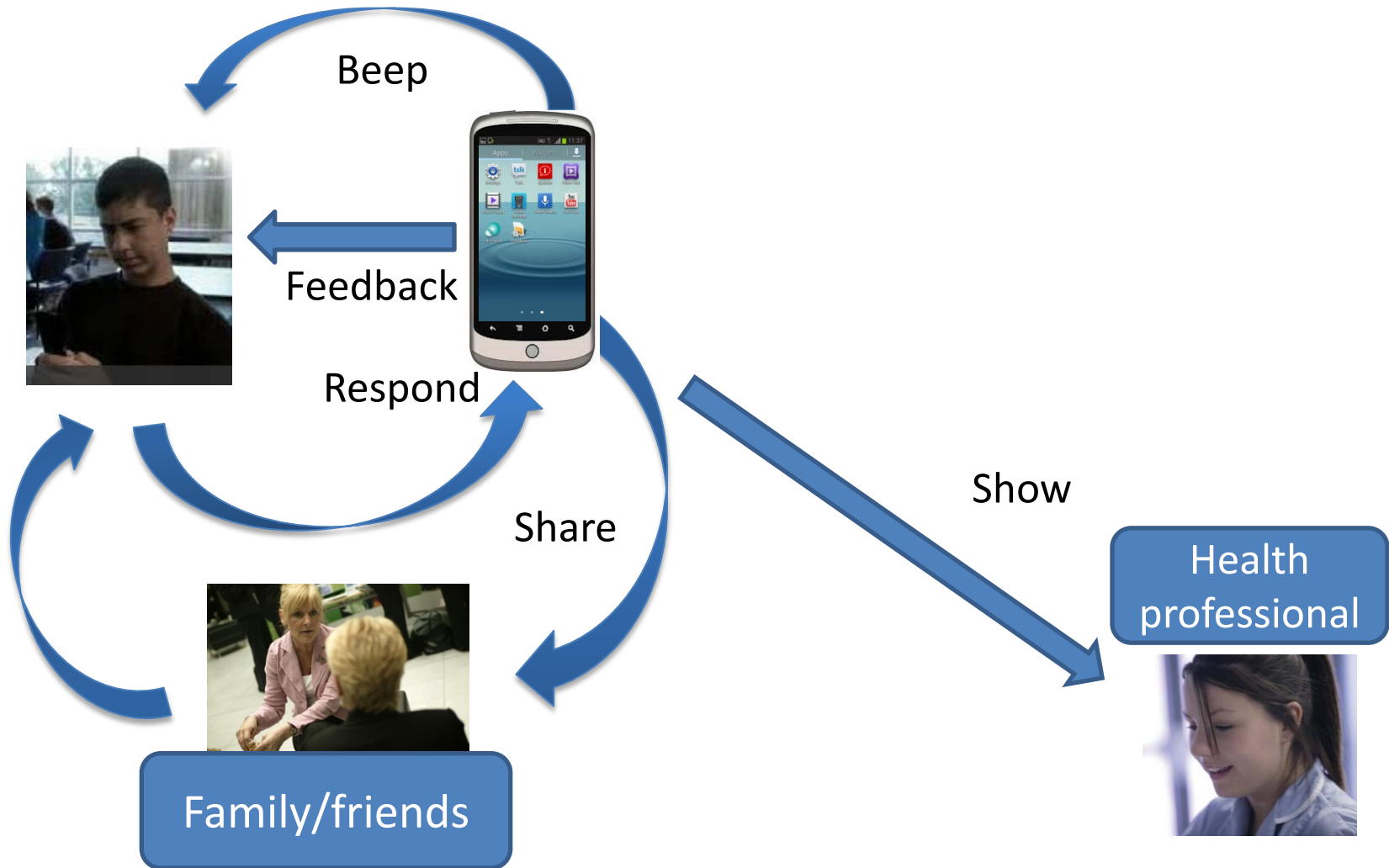
How it works



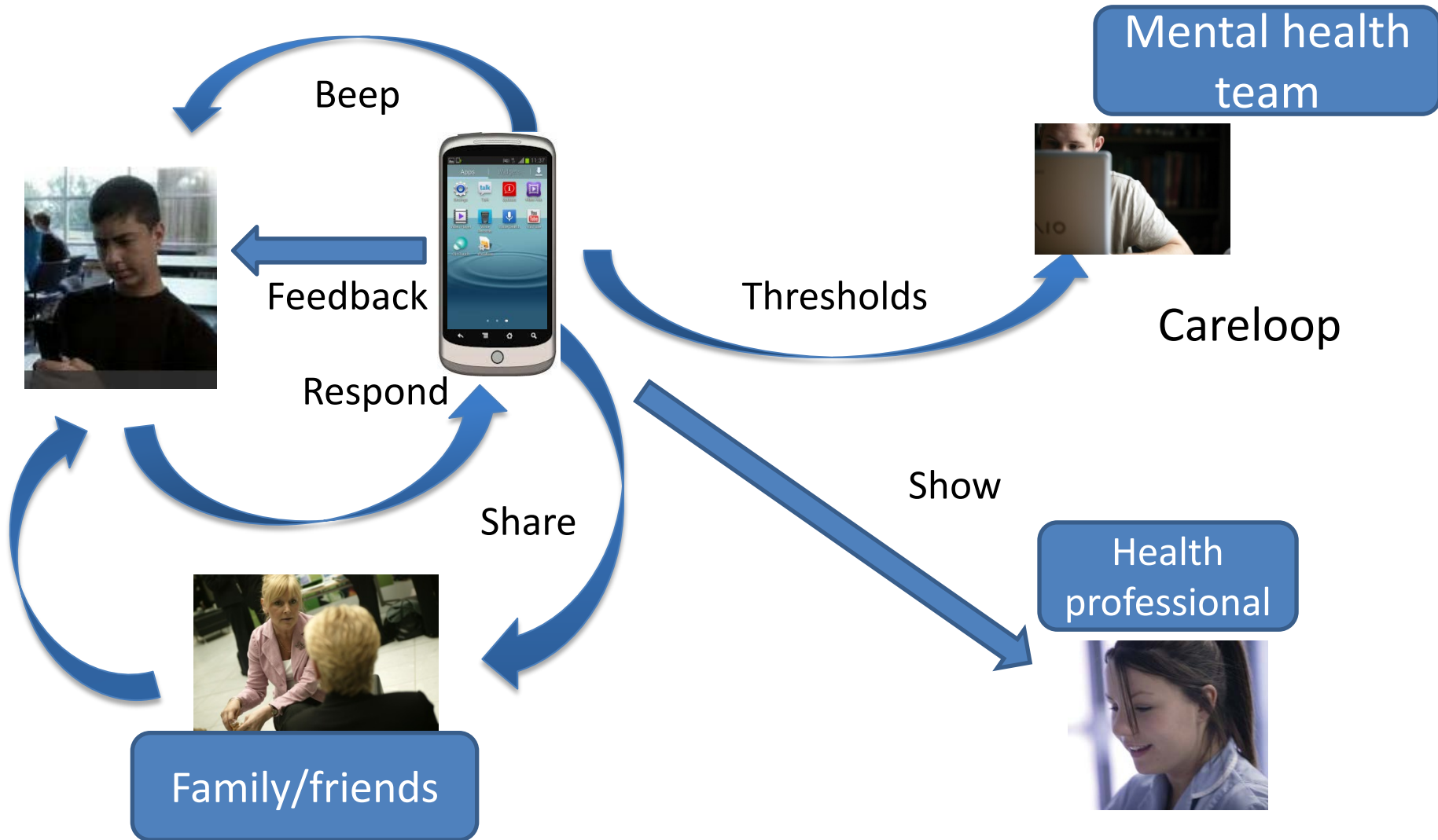
How it works



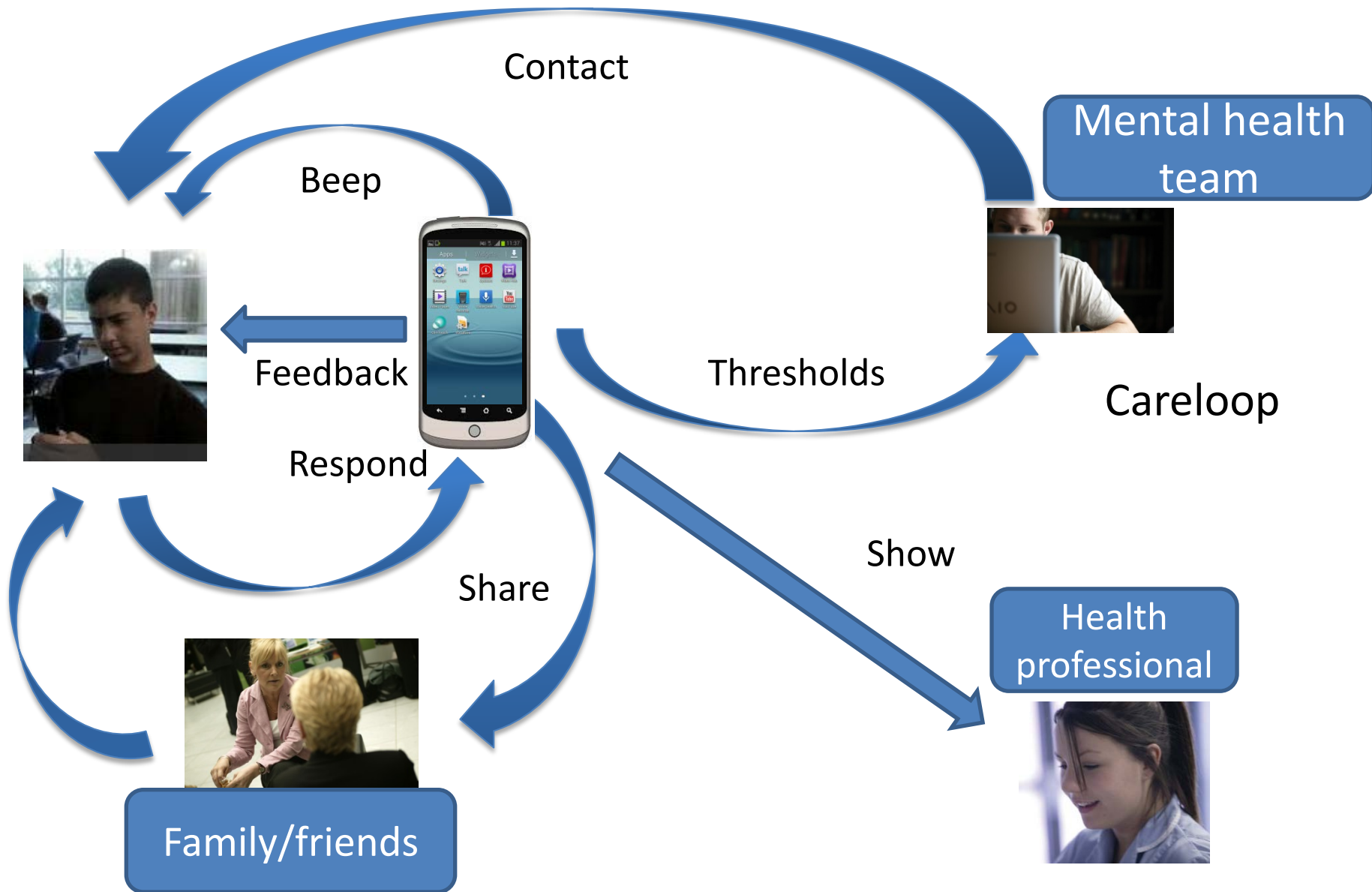
How it works



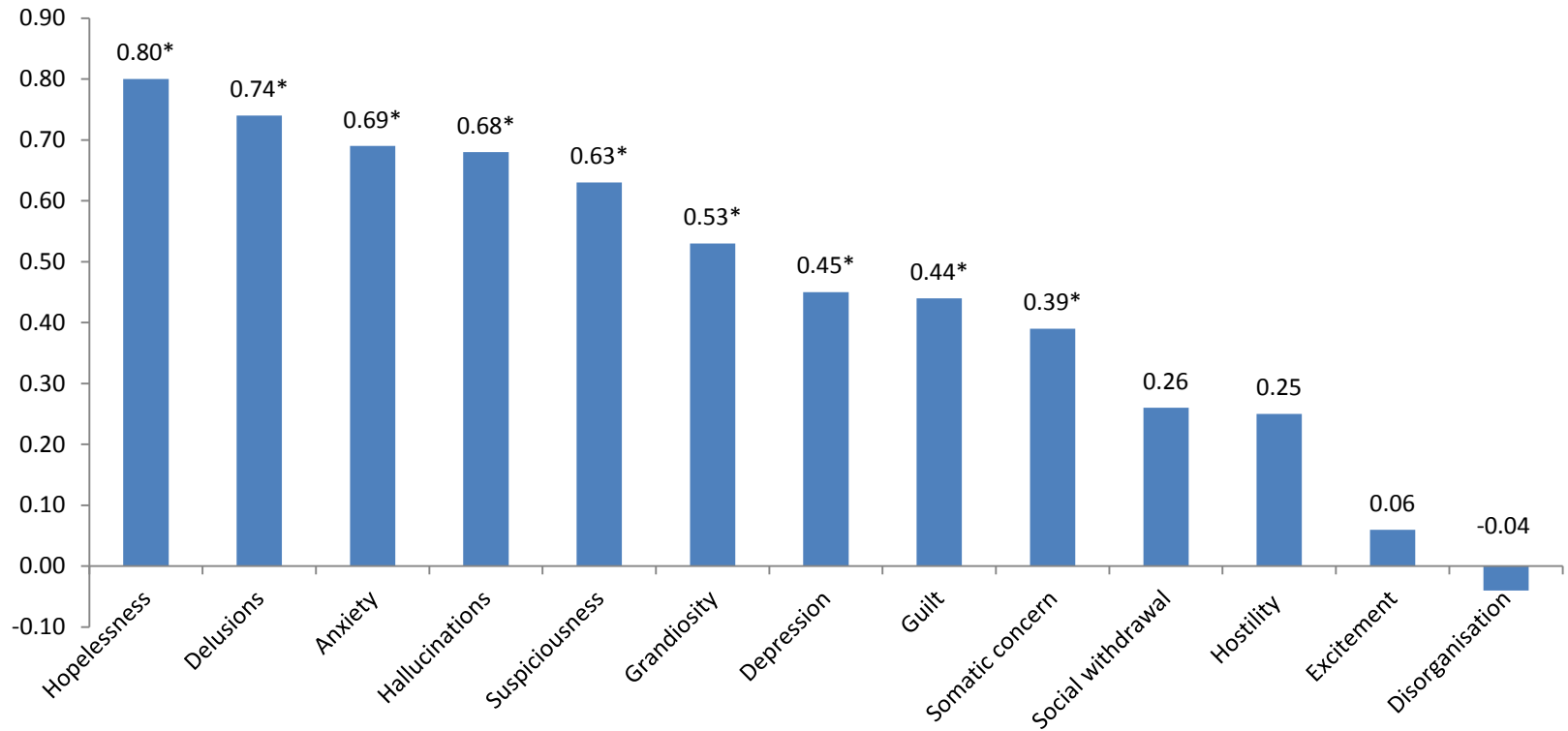
How it works



How it works

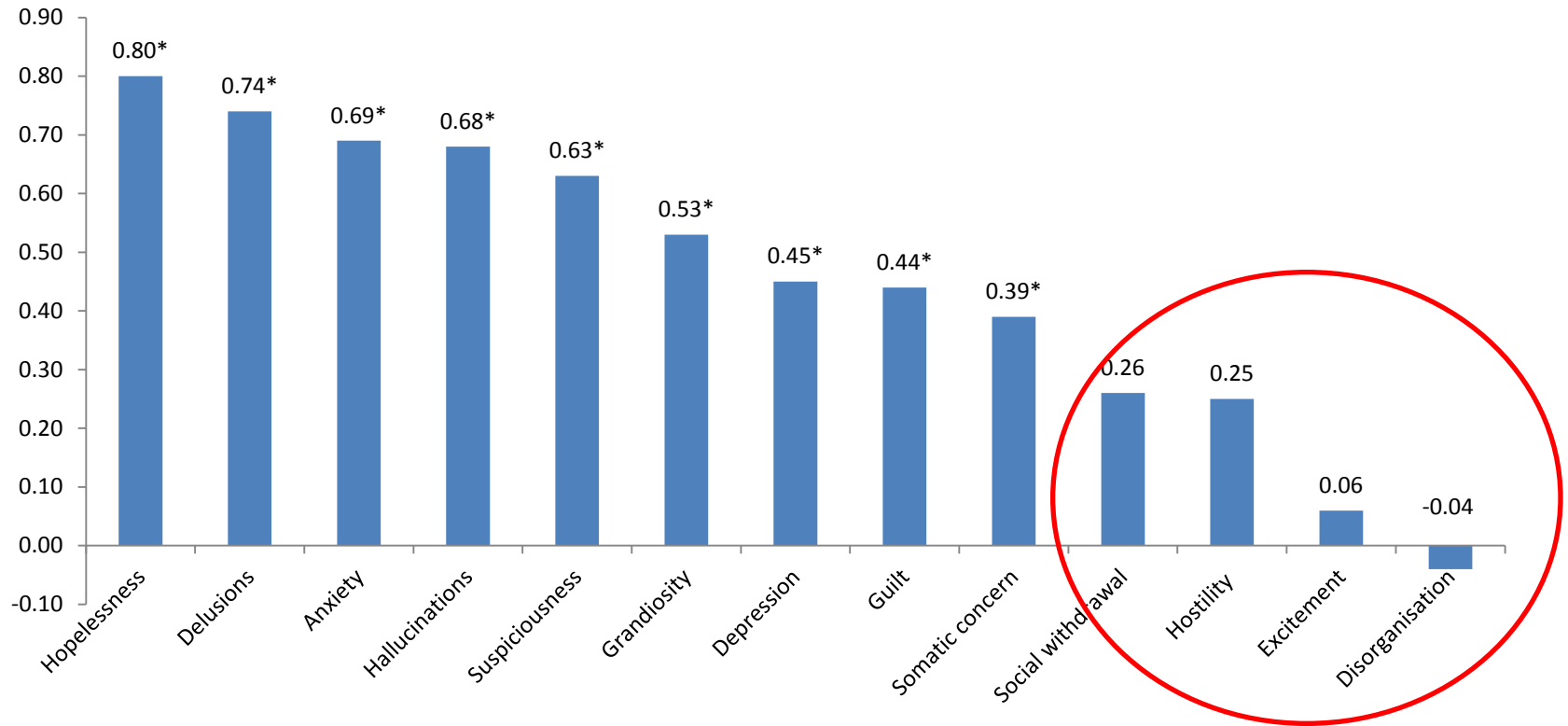


Correlations with gold standard interviews



* $p < .05$

Correlations with gold standard interviews



* $p < .05$

Experience-based design

Service user advisory group:

Dawn Perry, Jamaal Hatton, Neal Sinclair, George, Kate Lurie, Deborah Peer

<https://www.facebook.com/MakingMentalHealthPositive>

- Advice on study information, design of methods, focus group topics and questions, feedback/ suggestions for app design changes. Barriers to adoption.
- Focus groups: 23 SMI users, 5 carers, 30 staff

EBD is a user-focused design process with the goal of making user experience accessible to the designers.

(Bate & Robert, 2006)

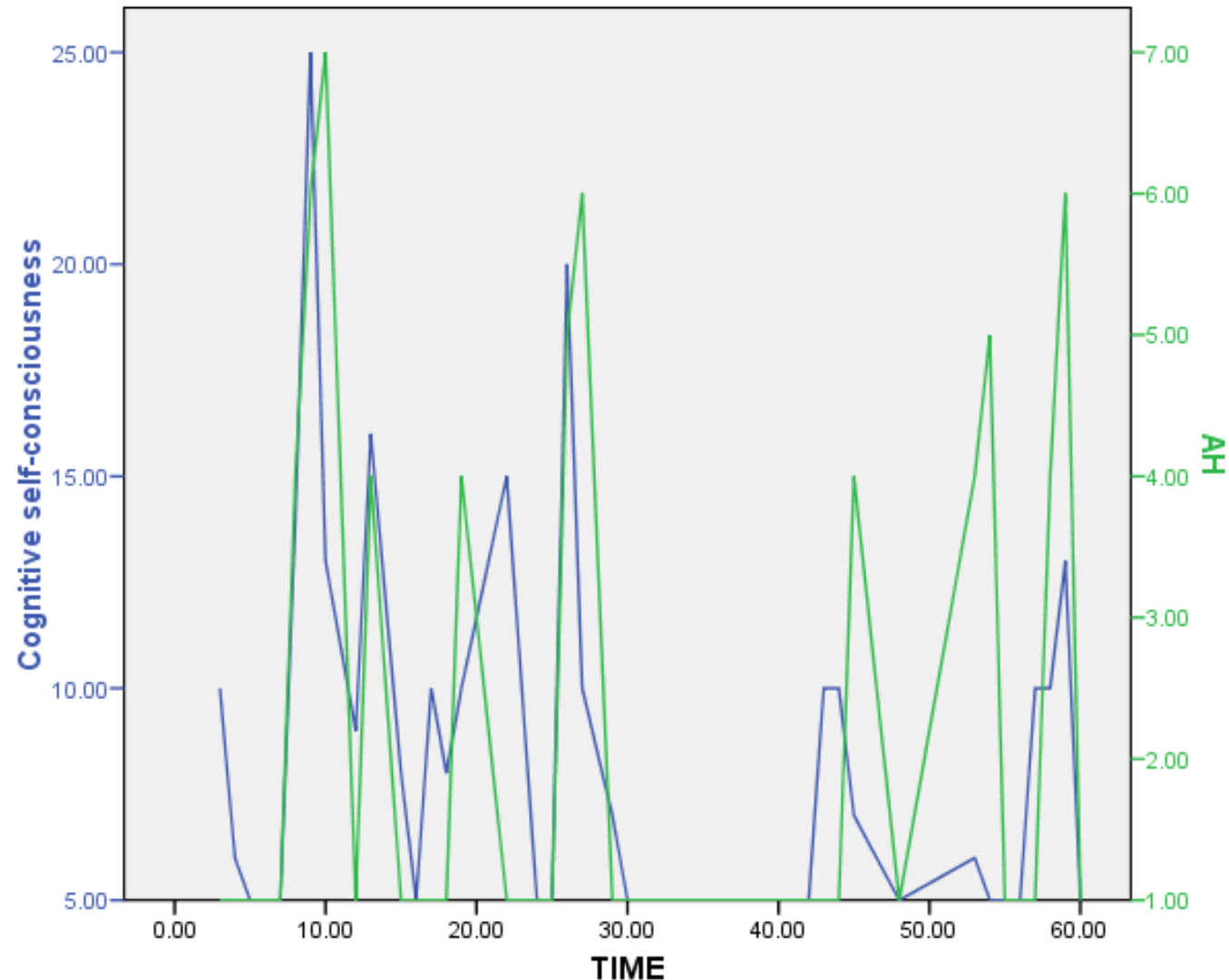
Staff: operational issues

What are users' expectations?... if it's a red signal for me, are they expecting -that I'm going to ring them within eight hours?

I mean with recovery in mind... we're moving towards more of stepping up and stepping down, it's maybe reassuring for service users to have that device when they step down...

Moving towards self autonomy and recovery, when we see them in a couple of days, we say...how did you manage?... The system recognises the reality of the world.

An example: temporal association between metacognition and auditory hallucinations



Processes in proof of concept

- Standards and governance: a medical device.
- Feasibility
- Acceptability (service users; professionals)
- Safety
- Privacy, security
- Data analytics
- Validity; reliability
- Operational integration
- Efficacy; effectiveness; cost.



ClinTouch



@clin_touch

ClinTouch/Careloop Team

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That's all, folks!



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Do antipsychotic drugs damage your brain?

Dorph-Petersen et al (2005)

18 macaque monkeys assigned to 2 year course of **placebo, haloperidol or olanzapine** at doses equivalent to therapeutic human doses

Brain volume change at 2 years:

■ Placebo	0%
■ Haloperidol	-8.8%
■ Olanzapine	-10.5%
	$p < 0.05$ for both drugs

Clintouch/Careloop

- **Clintouch**

- Development funded by 3 MRC grants
- Commodity mobile phone technology, using existing device, so minimal lifestyle intrusion. Familiar operability and interface.
- Safety assessed first
- Generalisable: 80% of SMI clients own and use mobile phones
- Acceptable: (short term at least): 81% compliant
- Personalisable; modular, with machine learning of responses
- Clinical data shown to be valid
- Platform technology for monitoring and interventions across long term conditions

- **Careloop**

- provides an end to end solution linking client and professional in the co-production of care

Recent and next steps

- Attachable modules
 - Medication management support,;side effects monitoring: Optimise trial
 - Contextual assessment
 - Social networking: “virtual drop in”
 - CBT support
 - Biosensors: sleep and exercise sensors; mood recognition
 - Neurocognition
 - Ecologically-valid functional assessment

What do you think?

LAIs in first episode

Open rct of risperidone LAI versus oral risperidone in 57 people with first episode schizophrenia over 1 year

- Relapse 5% vs 32%
- Hospitalisation 5% vs 18%
- All cause discontinuation 12% vs 33%
- Perfect adherence 73% vs 7%
- Improved working memory, visual learning (MCCB)
- Better work outcomes

Three sorts of intervention

- Drug treatments
- Psychological treatments
- Service-level interventions



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Depot (long acting) medication

- About 35% of people with schizophrenia will receive LAI medication
- SGA LAIs (risperdal consta, paliperidone) now widely used but expensive, and no strong evidence that they are better than FGA LAIs
- May have a role in first episode

CUtLASS 3?

- Risperidone LAI
 - Since 2002
 - 50mg 2 weekly £4000 pa
 - High wastage
 - Manchester MHSCTrust spend Consta £560k 08/09
 - Depixol 40mg monthly £90
 - No evidence for better effectiveness/ tolerability
 - Paliperidone, olanzapine LAIs due 2011