Professor Rob Horne  
University of London

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<th>Speaker Name</th>
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<tr>
<td>Prof Rob Horne</td>
<td>Received lecture and consultancy fees from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, Glaxo-Smith Kline, Janssen and Merck, Sharp &amp; Dome. He is a shareholder in Spoonful of Sugar.</td>
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| Date               | November 2013                                                                                                                                  |
Brian Gazzard Lectureship in HIV Medicine

Understanding patient beliefs and improving adherence

Rob Horne
Professor of Behavioural Medicine
UCL School of Pharmacy, University College, London
### SUPA Research Team
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- Kathryn King
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- Rosemary Mullett

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<th>Heather Leake-Date</th>
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<td>Mark Nelson</td>
<td>Paul McCrone</td>
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<td>Jane Anderson</td>
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<td>Caroline Sabin</td>
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<td>Nicky Perry</td>
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### SUPA Steering Group
| Alison Wearden     | Nick Freemantle    |
| Steve Morris       | John Walsh         |
| Rosy Weston        | Zoe Sheppard       |
| Paul Clift         | Ian Williams       |
| Brian Angus        | Annemiek de Ruiter |
| Memory Sachkonye   |                    |
Behaviour is a rate-limiting step between effective treatments and health gain.

Effective ART

1. Early testing
2. Prompt uptake
3. Optimal adherence

Optimum outcomes
Is delayed ART uptake and nonadherence still an issue?

HIV diagnosed

- CD4 > 350 cells/m$^3$
  - Accept treatment (87%)
  - Viral Suppression (87%)

- CD4 < 350 cells/m$^3$
  - Decline treatment (13%)
  - Not suppressed (13%)

- LTFU (14-19%)

UK-CHIC - later calendar year of follow-up is independently associated with more rapid ART uptake (adjusted relative hazard 1.20) (2)


Meta-analysis assessing effectiveness of interventions on adherence to ART (Simoni J et al, 2006)

- 1891 citations identified, 19 met eligibility criteria for meta-analyses (1999-2005)

- Four intervention categories: Education, “Interactive discussions”, Behavioural strategies, External reminders

- Two standardised outcome measures used, percentage achieving:
  - ≥95% adherence (18 studies)
  - undetectable viral load (14 studies)
Findings (Simoni et al., 2006)

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<tr>
<th>Measure</th>
<th>Intervention</th>
<th>Control</th>
<th>Effect size</th>
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<tr>
<td>Adherence</td>
<td>62%</td>
<td>50%</td>
<td>OR = 1.50, 95% CI: 1.16 to 1.94; N=1633 (significant)</td>
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<td>Undetectable viral load</td>
<td>62%</td>
<td>55%</td>
<td>OR = 1.25, 95% CI: 0.99 to 1.59; N=1247 (marginally significant)</td>
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- Only 37% of the interventions select for people with low adherence.
- Larger effect in studies using education on ART and interactive discussions
- Larger effect in studies with immediate post intervention follow up
A systematic review of adherence-enhancing interventions for ART (Mathes et al., 2013)

- 21 RCTs measuring BOTH adherence and clinical outcomes (viral load and/or CD4 count)
- Meta-analysis was not conducted due to the diversity of existing interventions
- Out of 21, 19 trials were not significant or were conflicting for adherence and/or clinical outcomes
- Two trials showed significant effects
  - Motivational interviewing vs information
  - Family support system

- Limitations
  - Categorisation of studies (Educational, Behavioural, Psychosocial, and Mixed) was too broad and the review does not evaluate the components of effective interventions
  - Only included studies with both adherence and clinical outcomes which restricts the sample size
  - Does not consider differences in the interventions in terms of tailoring to the individual or the use of theory to guide the intervention design

Perceptions and Practicalities Approach (PAPA)

UNINTENTIONAL nonadherence

Capacity and resources

Practical factors

INTENTIONAL nonadherence

Motivational beliefs/preferences

Perceptual factors

http://www.sdo.nihr.ac.uk/sdo762004.html.
The Necessity-Concerns Framework

Common-sense evaluations of prescribed medication influence our motivation to start and continue with treatment

Low adherence

Doubts about personal NECESSITY of medication

CONCERNS
About potential adverse effects

META-ANALYSIS¹
93 studies covering 24,864 patients across 18 countries
23 different long-term conditions
Necessity OR = 1.918, p < 0.0001 Concerns OR = 0.476, p < 0.0001

Beliefs about Medicines Questionnaire (BMQ)

**Specific beliefs**
about medicines prescribed for a particular illness

**General beliefs**
about medicines as a whole – pharmaceuticals as a class of treatment

Variations in ART Necessity beliefs

BMQ Specific Necessity Scores (Likert scale of 1–5, where 1 is low and 5 is high)

Scores of 5 indicate full endorsement by the patient of their personal need for ART to maintain health now and in the future.

Scores < 5 indicate an element of doubts with doubt increasing as the scores get lower.

Variations in ART Concerns

BMQ Specific Concerns Scores (Likert scale of 1–5, where 1 is low and 5 is high)

High scores = high CONCERN about ART

NB These concerns are ‘pre-treatment’

Over a third of the sample had strong concerns about ART

Concerns about HAART at time of treatment offer

I would worry about the long-term effects of these medicines: 67.7%
These medicines would give me unpleasant side effects: 55.2%
These medicines would disrupt my life: 50.7%
Having to take these medicines would worry me: 47.1%
It would be difficult for me to take the tablets on time each day: 31.6%
I would worry about becoming too dependent on these medicines: 30.2%
These medicines are a mystery to me: 20.6%

% agree/strongly agree

Data on file Study design and main findings published in:
Medication beliefs and nonadherence: a hidden issue

- Doubts about medication and nonadherence are often hidden
- Clinicians assume ‘not my patients’
- Patients often reluctant to express doubts, concerns or nonadherence, because they fear this will be interpreted by the clinician as a ‘doubt in them
- Patient may trust the clinician BUT not the treatment

Baseline beliefs about ART independently predict uptake (N=136)

- Declining ART (n=38, 28%) was associated with:
  - Doubts about necessity (OR=7.41, CI=2.84–19.37, p<0.001)
  - Concerns about potential adverse effects (OR=0.19, CI=0.07–0.48, p<0.001)
- These relationships were independent of negative effect (depression) and clinical variables (CD4 count, viral load, years since HIV diagnosis)

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ART adherence diminishes over time\textsuperscript{1, 2} (N=120 UK patients accepting ART)

- There was a significant increase in the number of participants reporting low adherence over follow-up (Cochran Q=38.9, df=3, p<0.001)

- Patients in the low-adherence group were significantly less likely to have an undetectable viral load at 6 months (Chi square=10.9, df=1, p=0.001)

* Low adherence = average self-reported (MASRI\textsuperscript{2}) adherence <95% of prescribed dose over previous month and/or unilateral decision to stop

ART adherence (6 and 12 months) predicted by baseline (pre-treatment) beliefs

- At 12 months, 44.4% of patients were classified as low adherence
- Low adherence predicted by BASELINE:
  - Doubts about necessity (F [1,115] = 7.7, p<0.01)
  - Concerns about potential adverse effects (F [1,115] = 8.4, p<0.005)
- These relationships remained significant after controlling for age, previous experience of ART and depression

Mean necessity belief scores for high- and low-adherence groups over 6 months of taking ART

- Significant decline in ART-necessity beliefs over time (F [3,74] = 7.5; p<0.001)
- Significant interaction between necessity and adherence (F [1,76] = 5.8; p<0.01)
- Relationships remained significant when controlling for depression and anxiety

ARE THESE ISSUES RELEVANT NOW?.............
• **Supporting U**P**t**ake and Adherence to Highly Active Anti-Retroviral Therapy
• Applying the Medical Research Council guidance to evaluate an intervention to support uptake and adherence to antiretroviral therapy for HIV
• NIHR Funded 5 Workstreams programme

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<thead>
<tr>
<th>WS</th>
<th>Study</th>
<th>Title</th>
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<td>1</td>
<td>1</td>
<td>Identifying new barriers to ART uptake and adherence</td>
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<td>2</td>
<td>5</td>
<td>RCT to assess the efficacy of the intervention</td>
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<td>3</td>
<td>6</td>
<td>Assessment of cost utility and cost effectiveness of the interventions</td>
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<td>4</td>
<td>7</td>
<td>Preparing for NHS implementation</td>
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Workstream 1: Exploring patients’ beliefs about ART

Aimed to explore
- Patients’ experience of being HIV positive
- Patients’ perspectives on treatment

Inclusion
- >18
- On ART > 12 months
- Having experienced virological failure according to BHIVA guidelines during treatment
- First generation black African or black Caribbean

Sample
- Recruited from King’s College and Homerton Hospitals
- 52 adults living with HIV
- 45 UKBA, 7 UKBC; 37 female, 15 male
- 31 symptomatic, 21 asymptomatic
- 40 average age, range 20-55
Overview of the findings

Necessity
- Inclination to let HIV take its natural course without HAART
- Preference for non-pharmacological methods of controlling HIV

Concerns
- Concerns about side effects
- Concerns about long-term effects
- Perceived negative effect on quality of life
- Perceived negative effect on sense of self

Practical barriers
- Forgetting
- Difficulty integrating into routine
- Difficulty swallowing

Additional insights
- Being overwhelmed
- Stigma (self-stigma)
- The role of God in treatment
- Medical mistrust

- The study findings support the Necessity-Concerns Framework, and provide additional insights about the experience of taking treatment.

- Many of the themes were common with our findings with previous qualitative work with Men who have sex with Men.

1Cooper et al. (2010). Perceptions of HAART among gay men who declined a treatment offer: Preliminary results from an interview-based study. AIDS Care, 14(3), 319-328.
Common-sense origins of medication necessity beliefs
Treatment necessity: common coherence between representations of illness and treatment \(^1, \, ^2\)


Judging personal need for maintenance treatment (MT) without symptoms

Taking MT does not make you feel better (contrast with ‘as needed’ meds)

Missing doses may not immediately make you feel worse

Potentially reinforcing perception that MT does not matter to me

– Many patients do not have a clear ‘common-sense’ rationale for why MT is necessary...‘no symptoms, no problem’
– Contrast between short- and long-term consequences

Doubts about necessity: Incongruous symptom experience and need for ART

Some patients’ experiences (of feeling fine) did not match their common-sense beliefs about when ART would be necessary.

If you have headache you say let me take paracetamol to make the headache stop. And okay you are told you have HIV yeah? But you don’t have symptoms, you are not sick from it and you are told “take medication”. I don’t have headache and they are giving me medication to stop the headache.

I think when I feel a little bit worse like I’ve got thrush on my throat or something, I’ll go back and restart the medication.
Symptom experiences predict non-adherence to ART

1. Symptoms attributed to ART side effects

Patients’ attributions that symptoms were due to ART between 1M month and 6M associated with lower adherence at 6M. \( (F(1,66)=4.1, \ p<0.05) \)

This was independent of adherence and 1M and 3M.

Increase in HIV-related symptoms associated with a decrease in necessity \( (r=-0.22, \ p<0.05) \)

80 HIV+ patients receiving antiretroviral treatment in Brighton, UK
Symptom experiences and interpretations predict non-adherence to ART

2. Symptoms attributed to HIV

Patients’ perceptions of improving symptoms attributed to HIV between baseline and 6M associated with higher adherence at 6M. (F(1, 66) = 5.0, p<0.05)

This was independent of adherence and 1M and 3M.

Increase in HIV-related symptoms associated with a decrease in necessity (r=-0.22, p<0.05)

80 HIV+ patients receiving antiretroviral treatment in Brighton, UK
ART CONCERNS PREDICT ART SIDE EFFECTS
"I’ve been taking this medication for 50 years and I’m going to sue! The side effects made me wrinkled, fat and bald!"
Pre-treatment concerns about ART predict side effects at 1, 3, 6 and 12 months

Mean number of ART side effects rated as moderate or severe

Pre-treatment ART-concerns (BMQ)†
- Low concerns
- High concerns

All high vs low ART-Concerns comparisons significant at p<0.01


Number of symptoms rated by patient as moderate or severe
ART-Concerns Dichotomized at scale midpoint ie, low = 1–3; high = ≥3.01
Disease Prototypes and Stereotypes inform medication necessity beliefs

DISEASE PROTOTYPES

- People have pre-existing models of common illnesses
- Influence *how* and *when* we act if experiencing symptoms or receiving health advice

DISEASE STEREOTYPES

- What sort of person gets this disease?
- How much do I resemble them?

Prototypic and stereotypic ideas about illness may be mistaken BUT logical.

They influence the perceived salience of health messages. ‘Does this apply to me’......
**Additional insights:** Difficulty in simultaneously accepting the diagnosis and ART

Patients commonly felt so overwhelmed by the diagnosis they found it difficult to simultaneously accept the diagnosis and commit to life-long treatment:

*It was like having a death sentence hanging over you and the shock, the despair [...] what’s the point of using it, the medication, because you’re going to die. It’s not curable, something will happen. It was a lot to cope with, with the scare, the futility.*

(40, F, Nigerian, asymptomatic)

Poliquin et al (*in preparation*)
Negotiating the role of God in treatment

ART highlights dilemmas regarding the role of God in treatment. Some patients doubted the necessity for ART, believing that only God could control one’s life course:

“You are just human beings, you are doctors, we are all created by God ... You cannot say when I will die, you can’t because you did not create me, it is God that created me and He is the one who will say when I will die.”

F, 29, Nigerian, symptomatic

This was particularly strengthened by having witnessed a testimony:

“I have seen testimonies, I have seen people cured from prayer from a Nigerian man of God, they are made whole, they are healed.”

(F, 42, Nigerian, symptomatic)

Poliquin et al (*in preparation*)
Common-sense origins of medication concerns
**Additional insights: Risk of disclosure through visibility of ART**

Patients felt that ART (often large and colourful), made their HIV status visible:

"I’ve had a friend come around say, ‘oh what are you doing with all these big, big, big, big tablets, what’s wrong with you? Because it seems to be the kind of tablet for a big problem."

(F, 40, Nigerian, symptomatic)

The cost of status disclosure could have severe social and economic consequences including ostracism and homelessness:

"I don’t have a house, so I was sleeping with friends... I can’t take the medication because maybe they will start talking about me and maybe they would refuse me sleeping in their house."

F, 37, Nigerian, symptomatic

Poliquin et al (*in preparation*)
Doubts about necessity and ART Concerns were often based on misconceptions eg:

- I find personally that if I can afford to eat well, I don’t need to take medication. (French translation)

- This new one are they reducing it now because you only take it once a day and I was saying, are they reducing it down because I’m taking it too long? I wonder if I’m going to dead soon because they’re reducing it down.

(M, 40, Ugandan, asymptomatic)

(F, 46, DRC, symptomatic)

Poliquin et al (in preparation)
Necessity-Concerns dilemma:

**Balancing need and harm**

**Misconceptions about the meaning of treatment and treatment changes**

I was still in denial. I would say I don’t really need these tablets, I don’t see what they’re doing for me, all they’re doing they’re just making me feel worse.

Your main worry is not about my life has been cut short, no. It’s now about the quality of life you are leading in terms of medication all the time so it’s a catch 22. Do you lead a long life which you’re not happy with or do you lead a short quality life?

(F, 35, Jamaican, symptomatic)

(M, 45, Zambian, symptomatic)

Poliquin et al (*in preparation*)
Implications for interventions to support ART uptake and adherence
Adherence support: the need for intelligent design at all three points of the triangle

Considerations for intervention development

Content

Adherence Support
Intervention design should optimise all three aspects

Delivery vehicle

Context
The Perceptions and Practicalities Approach

For each individual

Practical barriers
- Ability

Perceptual barriers
- Motivation

Feedback and review

Perceptions and Practicalities Approach to facilitate informed engagement with medication

Perceptual

1. Communicate a ‘common-sense rationale’ for why the treatment is needed – taking account of the patients perceptions of HIV and symptom expectations

2. Elicit and address CONCERNS about potential adverse effects of the treatment – including support with side-effect management

Practical

3. Make the regimen as convenient and easy to take as possible and address limitations in capacity and resources
SUPA Intervention

Adherence Support

Intervention design should optimise all three aspects

Content

Eliciting and addressing perceptual and practical barriers (PAPA)

Delivery vehicle

Trained Research Nurses delivering CBT Plus video and manual

Context

ART naïve patients / patients at risk of non-adherence
Treatment initiation (month 1): CBT session 1

OR

Treatment initiation (month 1): CBT session 2

OR

Boosters (3 and 6 months)

OR

Final outcome visit (12 months)

• Treatment support sessions will utilise a Cognitive Behavioural Therapy (CBT) approach.

• Sessions will communicate:
  1) a rationale for the personal necessity of medication
  2) elicit and address concerns (practical/physical/emotional/cognitive) about medication
  3) problem-solve potential perceptual and practical barriers to adherence.

If patients delay/decline ART, they will remain in study. Treatment support will continue to focus on barriers to starting treatment, rather than provide ongoing support with adherence.

• MEMs will measure adherence rates
Trial design

**Start date: January 2014**

**Observational Outcomes:**
BMQ
- Treatment failure
- Disengagement from care at 12 months

**Informed consent**

**Beliefs about Medicine Questionnaire**

- Low risk for non adherence
  - High Necessity/ Low Concerns
- High risk for non adherence
  - Low Necessity/ High Concerns or Both

**Assesses risk for nonadherence**

**Stage 1**

**Randomisation**

**Informed consent**

**Stage 2**

**Brief CBT Intervention**
- Treatment initiation support
- Booster 1 (month 3)
- Booster 2 (month 6)
- Primary outcome (month 12)

**Care as usual**
- (monitor months 3, 6, 12)

**Intervention Primary outcomes:**
- Proportion of months under follow-up where adherence ≥ 90%

**Intervention Secondary Outcomes:**
- Treatment failure
- Change in perceptual & practical barriers
- Disengagement in Care
- Ratings of depression/ anxiety
- Referral out of intervention
- Health & Social Service Use
- QoL
- Rate of ARV switching

**Observational Follow-up for 12 months**
- (monitor months 3, 6, 12)
Take Home Messages

In order to support uptake of and adherence to HAART, we need to tailor support to the needs of the individual addressing the perceptual and practical factors influencing motivation and ability to start and continue with treatment by:

1. Providing a ‘common-sense’ rationale for the necessity of ART, even in the absence of symptoms

2. Eliciting and addressing individual concerns about potential adverse effects of ART

3. Identifying and addressing relevant practical barriers to adherence

This approach is also relevant to co-infection, where uptake and adherence to treatment may also be a significant challenge
Thank you for listening.....