

Professor Rob Horne

University of London

| COMPETING INTEREST OF FINANCIAL VALUE \geq £1,000: | |
|--|---|
| Speaker Name | Statement |
| Prof Rob Horne | Received lecture and consultancy fees from AbbVie, Boehringer Ingelheim, Bristol-Myers Squibb, Gilead Sciences, Glaxo-Smith Kline, Janssen and Merck, Sharp & Dome. He is a shareholder in Spoonful of Sugar. |
| 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



With thanks to:



SUPA Research Team

Elizabeth Poliquin
Paulina Bondaronek
Kathryn King
Sarah Jane Besser
Rosemary Mullett



*National Institute for
Health Research*



SUPA Management Group

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Behaviour is a rate-limiting step between effective treatments and health gain

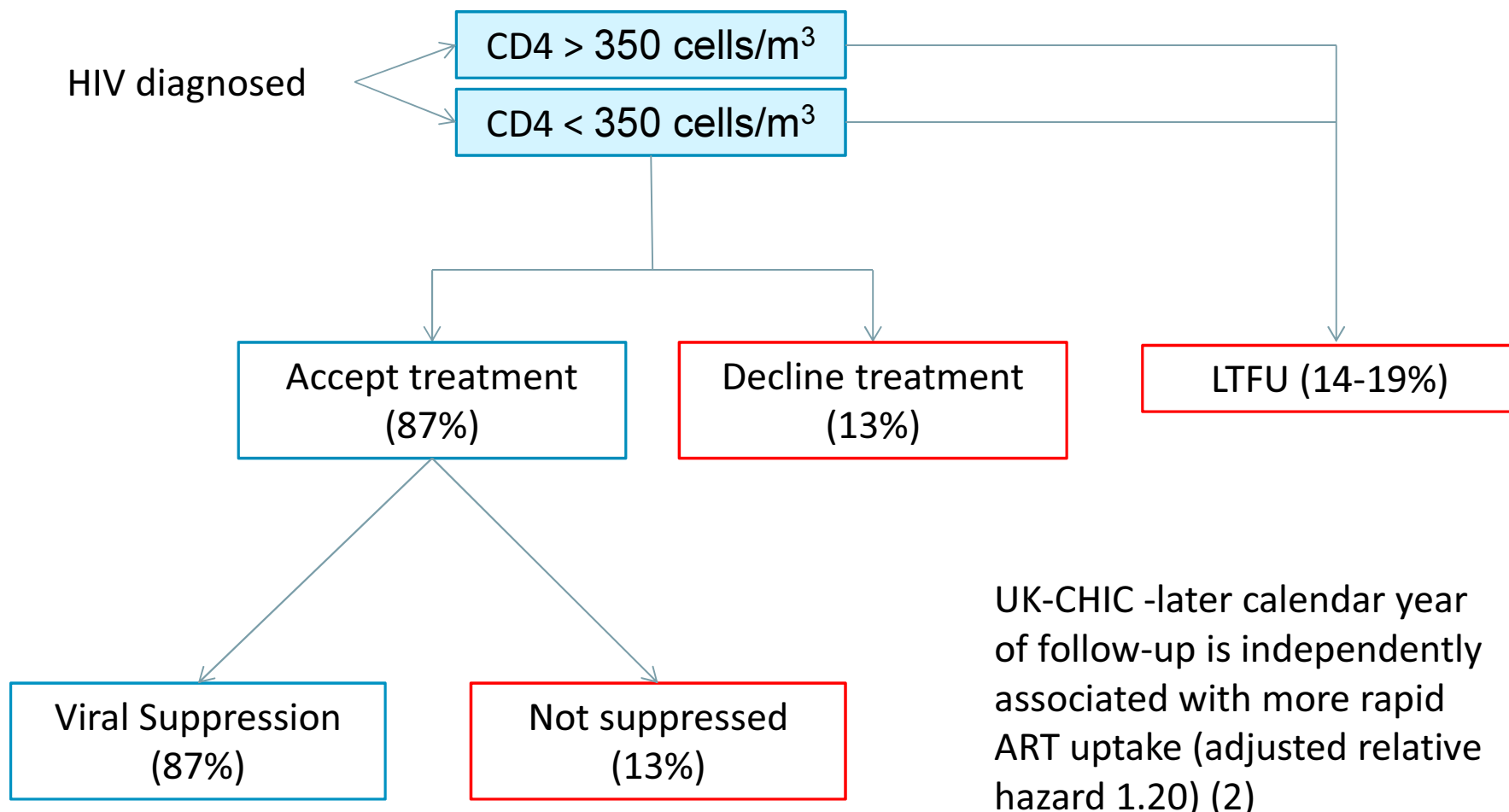


Effective ART

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

Optimum outcomes

Is delayed ART uptake and nonadherence still an issue?

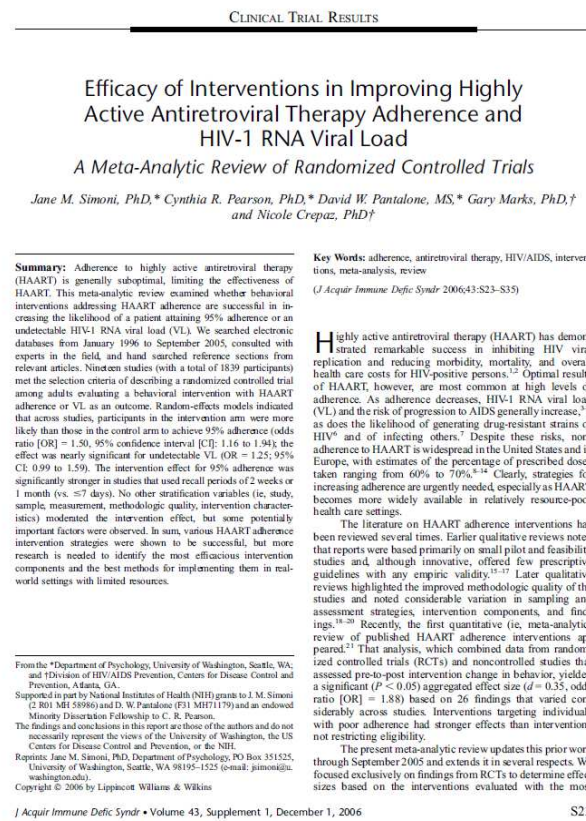


UK-CHIC -later calendar year of follow-up is independently associated with more rapid ART uptake (adjusted relative hazard 1.20) (2)

HPA (UK). (2012). *HIV in the UK: 2012 Report*

(2) Kober, C., Johnson, M., Fisher, M., Hill, T., Anderson J., Bansi L., *et al.* (2012). Non-uptake of highly active antiretroviral therapy among patients with a CD4 count < 350 cells/ μ L in the UK. *HIV Medicine*, 13, 73-78..

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:
 - $\geq 95\%$ adherence (18 studies)
 - undetectable viral load (14 studies)

Findings (Simoni et al., 2006)

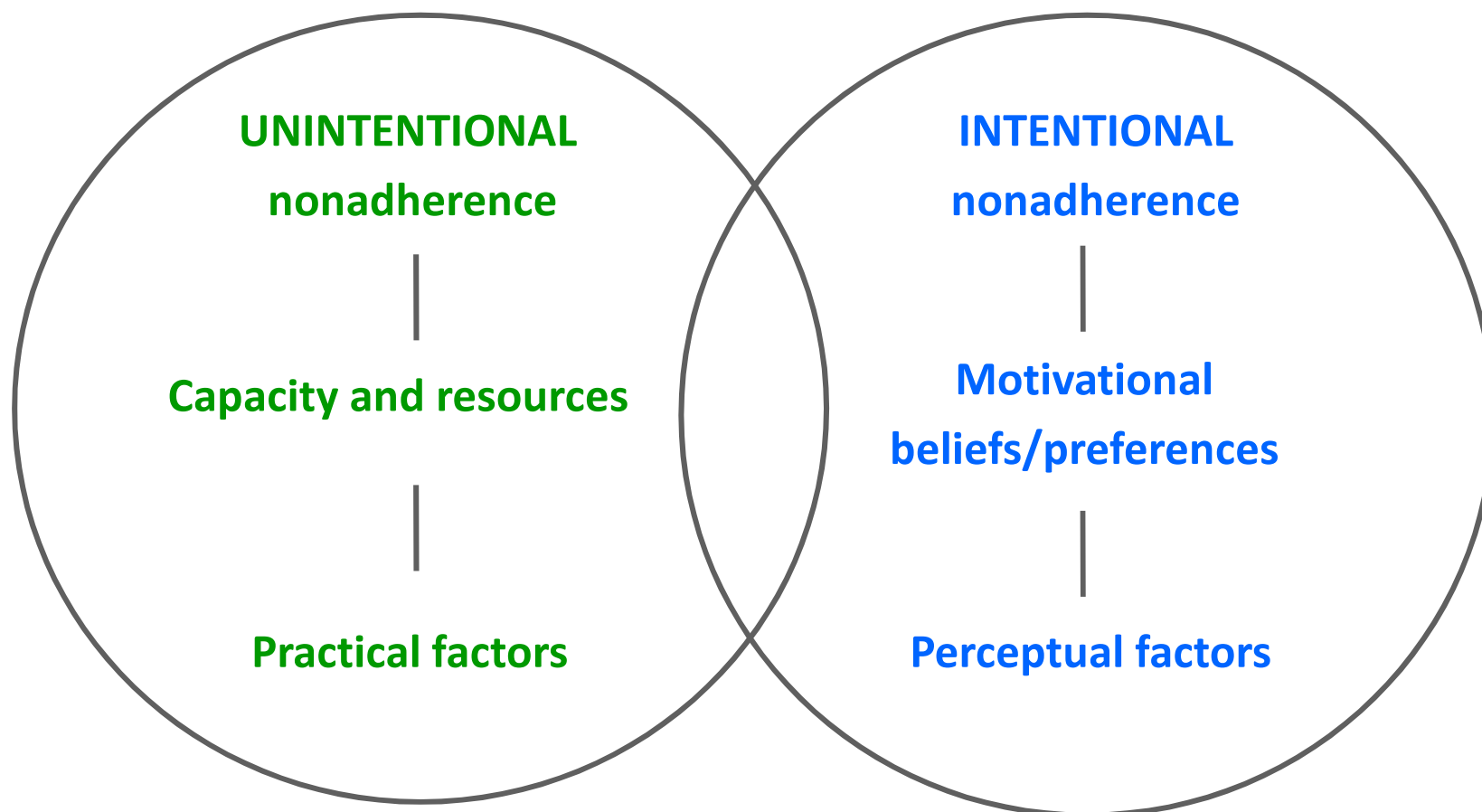
| Measure | Intervention | Control | Effect size |
|-------------------------|--------------|---------|---|
| Adherence | 62% | 50% | OR = 1.50, 95% CI: 1.16 to 1.94; N=1633 (significant) |
| Undetectable viral load | 62% | 55% | OR = 1.25, 95% CI: 0.99 to 1.59; N=1247 (marginally significant) |

- 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

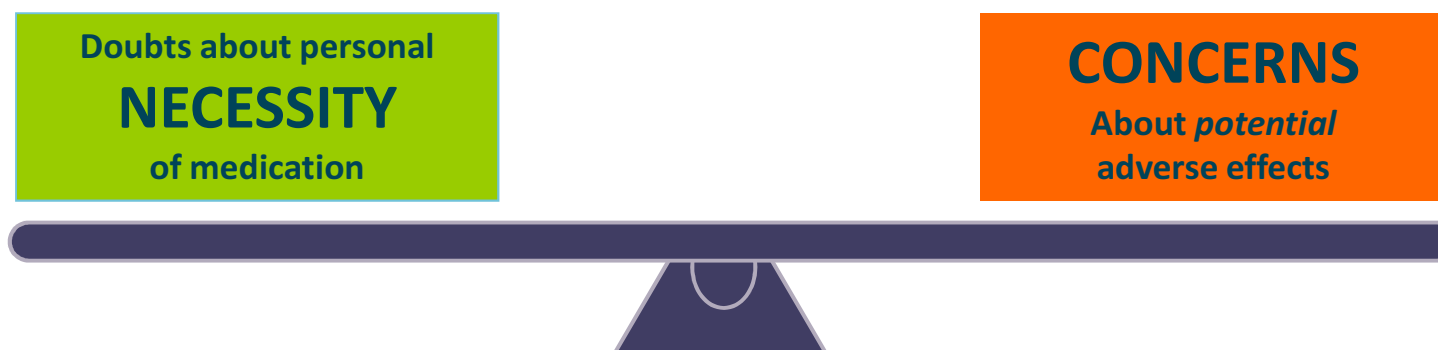
Perceptions and Practicalities Approach (PAPA)



The Necessity-Concerns Framework

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

Low adherence



META-ANALYSIS¹

93 studies covering 24,864 patients across 18 countries

23 different long-term conditions

Necessity $OR = 1.918, p < 0.0001$ Concerns $OR = 0.476, p < 0.0001$

¹Horne, Chapman, Parham, Freemantle, Forbes & Cooper, (in press) *PLOS One*. Understanding patients' adherence-related beliefs about medicines prescribed for long-term conditions: a meta-analytic review of the Necessity-Concerns Framework.

Beliefs about Medicines Questionnaire (BMQ)

BMQ-S11_G8

Project Number

YOUR VIEWS ABOUT MEDICINES PRESCRIBED FOR YOU

- We would like to ask you about your personal views about medicines prescribed for you.
- These are statements other people have made about their medicines.
- Please show how much you agree or disagree with them by ticking the appropriate box.

**There are no right or wrong answers.
We are interested in your personal views**

| | Views about MEDICINES PRESCRIBED FOR YOU: | Strongly Agree | Agree | Uncertain | Disagree | Strongly Disagree |
|-------|--|----------------|-------|-----------|----------|-------------------|
| BMQ1 | My health, at present, depends on my medicines | | | | | |
| BMQ2 | Having to take medicines worries me | | | | | |
| BMQ3 | My life would be impossible without my medicines | | | | | |
| BMQ4 | I sometimes worry about long-term effects of my medicines | | | | | |
| BMQ5 | Without my medicines I would be very ill | | | | | |
| BMQ6 | My medicines are a mystery to me | | | | | |
| BMQ7 | My health in the future will depend on my medicines | | | | | |
| BMQ8 | My medicines disrupt my life | | | | | |
| BMQ9 | I sometimes worry about becoming too dependent on my medicines | | | | | |
| BMQ10 | My medicines protect me from becoming worse | | | | | |
| BMQ11 | These medicine give me unpleasant side effects | | | | | |

YOUR VIEWS ABOUT MEDICINES IN GENERAL

- These are statements that other people have made about medicines in general.
- Please show how much you agree or disagree with them by ticking the appropriate box.

| | Views about MEDICINES IN GENERAL | Strongly Agree | Agree | Uncertain | Disagree | Strongly Disagree |
|------|---|----------------|-------|-----------|----------|-------------------|
| BMQ1 | Doctors use too many medicines | | | | | |
| BMQ2 | People who take medicines should stop their treatment for a while every now and again | | | | | |
| BMQ3 | Most medicines are addictive | | | | | |
| BMQ4 | Natural remedies are safer than medicines | | | | | |
| BMQ5 | Medicines do more harm than good | | | | | |
| BMQ6 | All medicines are poisons | | | | | |
| BMQ7 | Doctors place too much trust on medicines | | | | | |
| BMQ8 | If doctors had more time with patients they would prescribe fewer medicines | | | | | |

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Specific beliefs

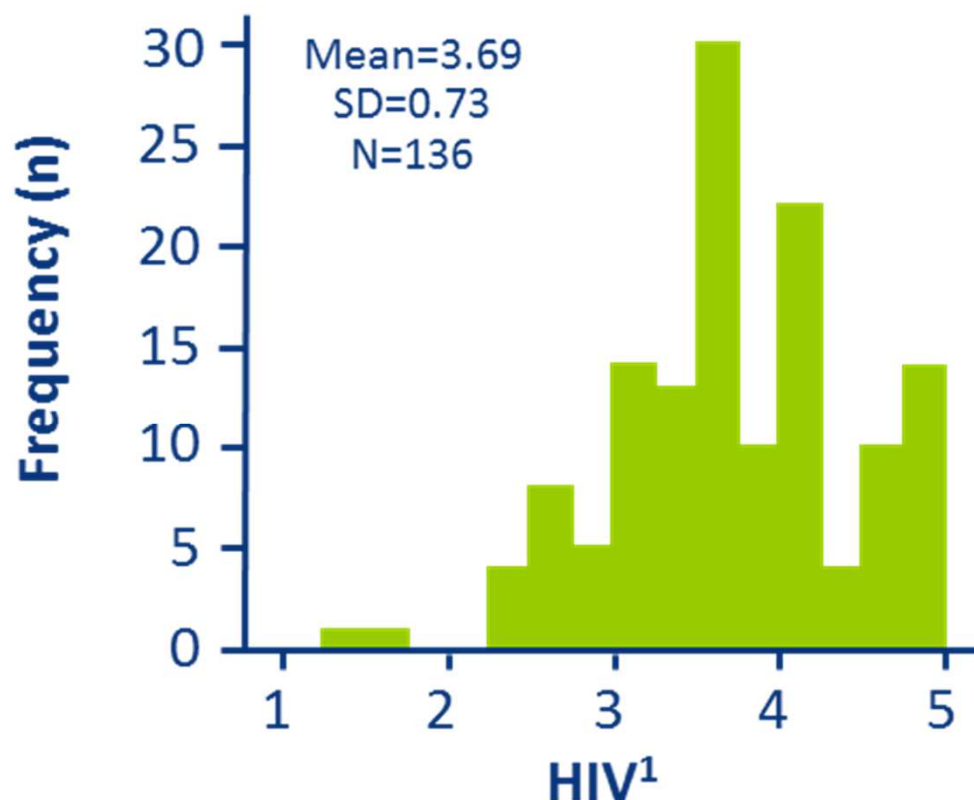
about medicines prescribed for a particular illness

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)

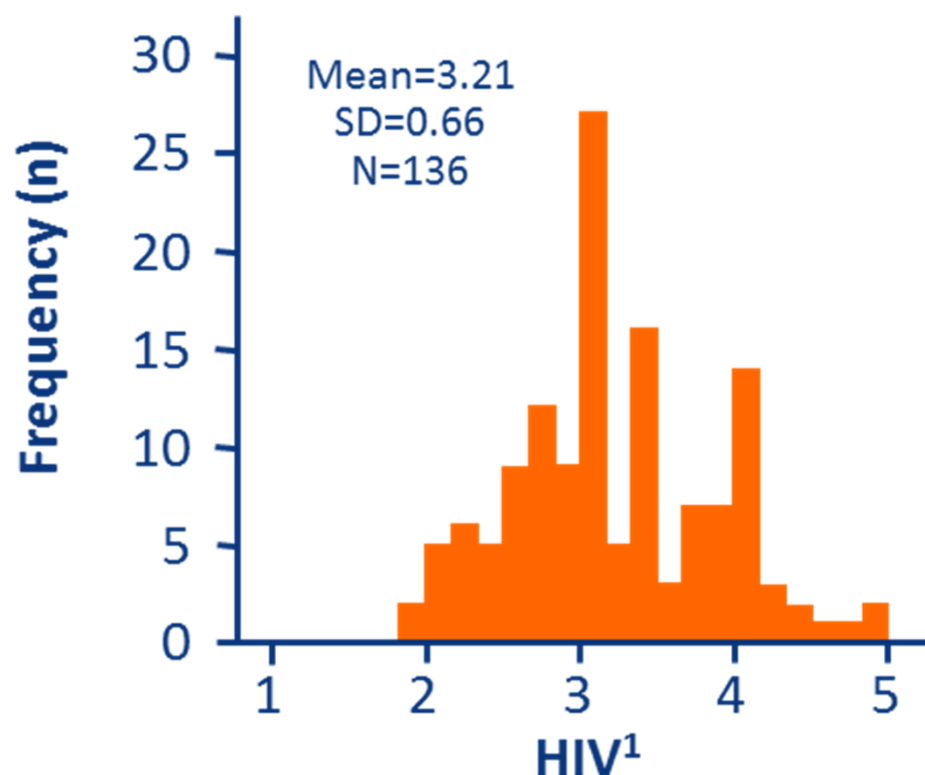


Scores of 5 indicate full endorsement by the patient of their personal need for ART to maintain health now and in the future

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)

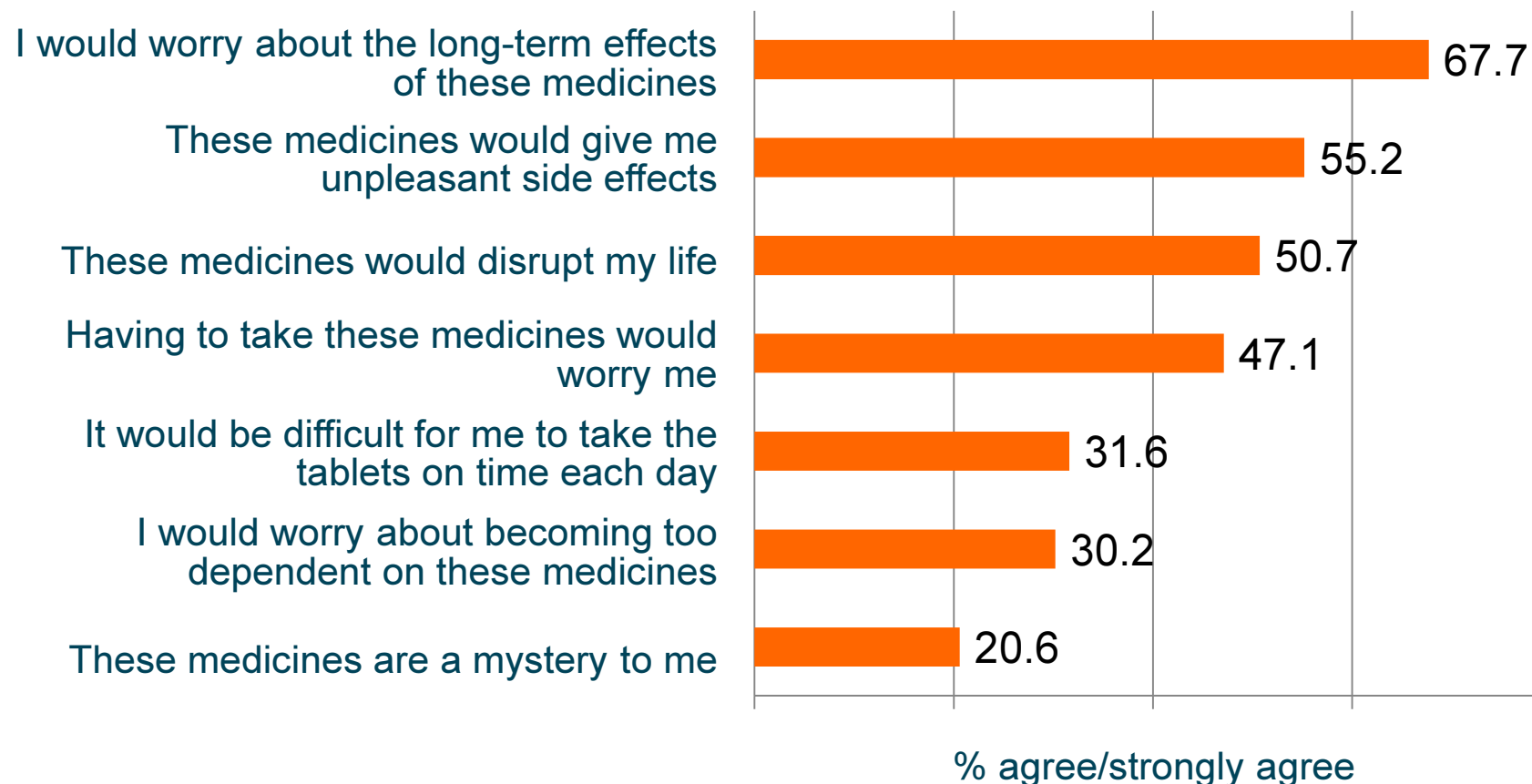


High scores = high CONCERN about ART

NB These concerns are 'pre-treatment'

Over a third of the sample had strong concerns about ART

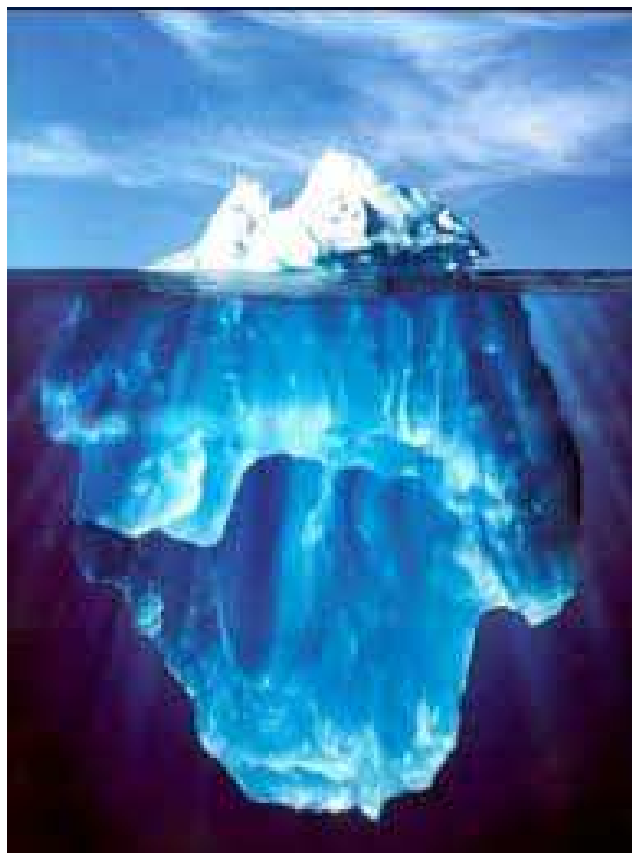
Concerns about HAART at time of treatment offer



Data on file Study design and main findings published in:

Horne R., Cooper, V., Gellairty, G., Leake Date, H & Fisher M. (2007), Patient's perceptions of highly active antiretroviral therapy in relation to treatment uptake and adherence: the utility of the necessity concerns framework, *JAIDS*, 45:334-341.

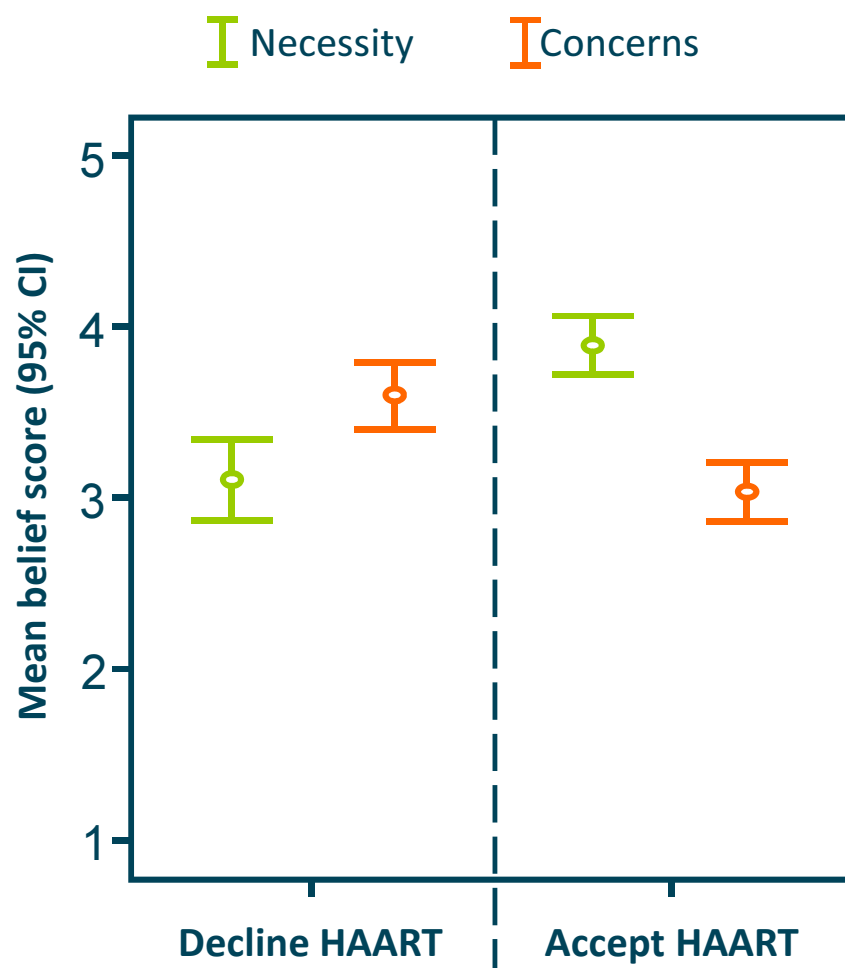
Medication beliefs and nonadherence: a hidden issue



- Doubts about medication and nonadherence are often hidden
- Clinicians assume ‘not my patients’¹
- 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

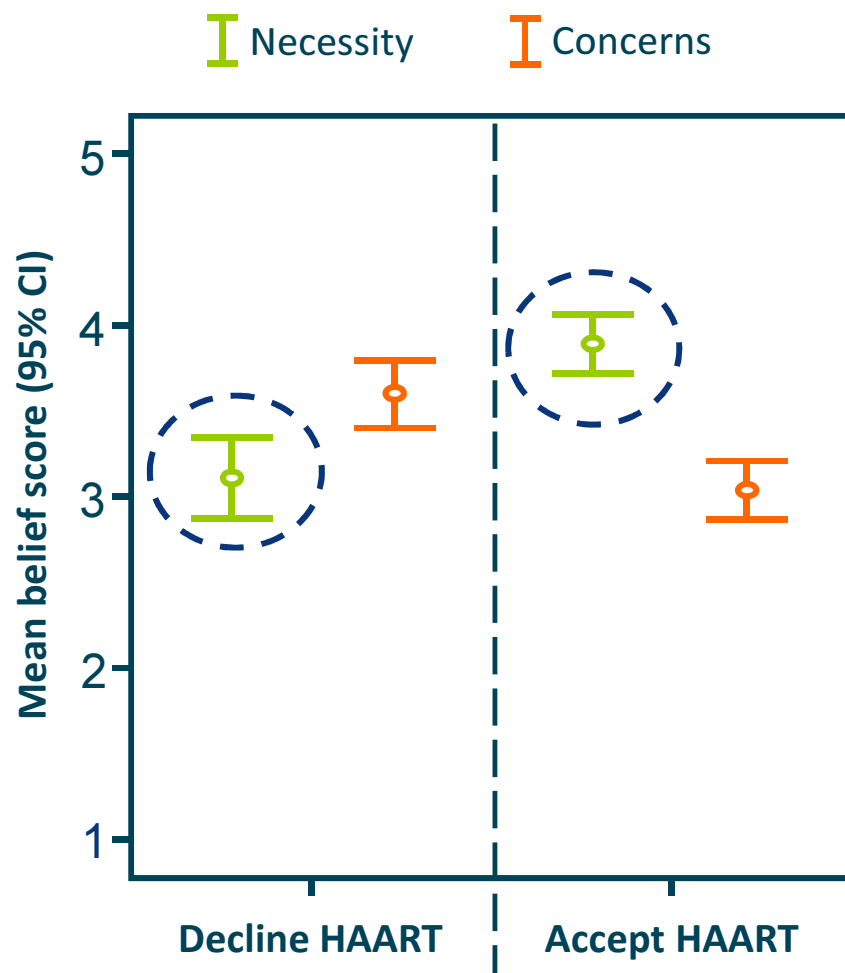
1) National Institute for Health and Clinical Excellence (2009). Medicines Adherence: Involving patients in decisions about prescribed medicines and supporting adherence (CG76): NICE Guideline 76

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



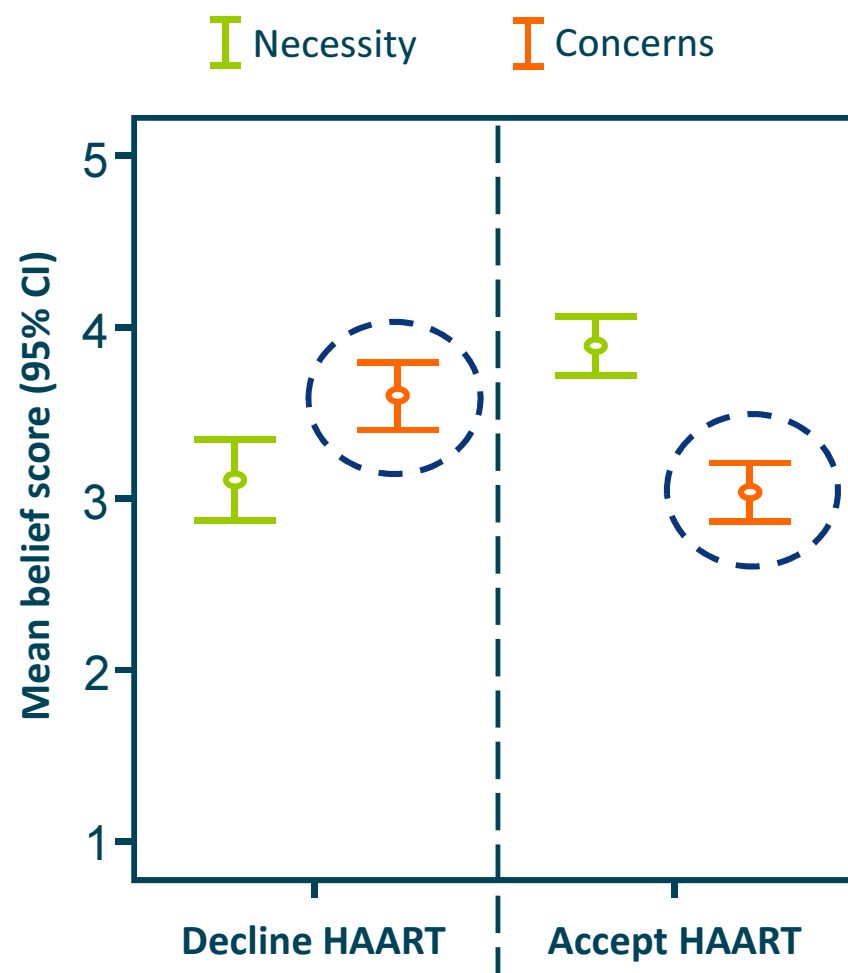
- Declining ART (n=38, 28%) was associated with:
 - Doubts about **necessity** (OR=7.41, CI=2.84–19.37, p<0.001)
 - **Concerns** about potential adverse effects (OR=0.19, CI=0.07–0.48, p<0.001)
- These relationships were independent of negative effect (depression) and clinical variables (CD4 count, viral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

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



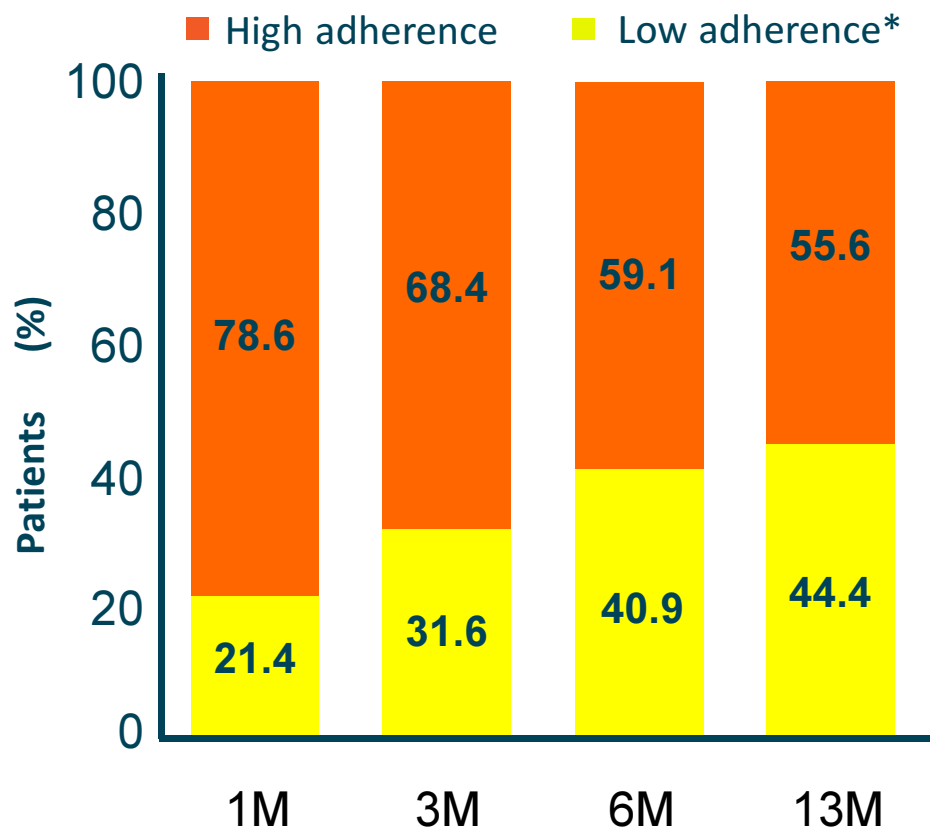
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ART adherence diminishes over time^{1, 2} (N=120 UK patients accepting ART)



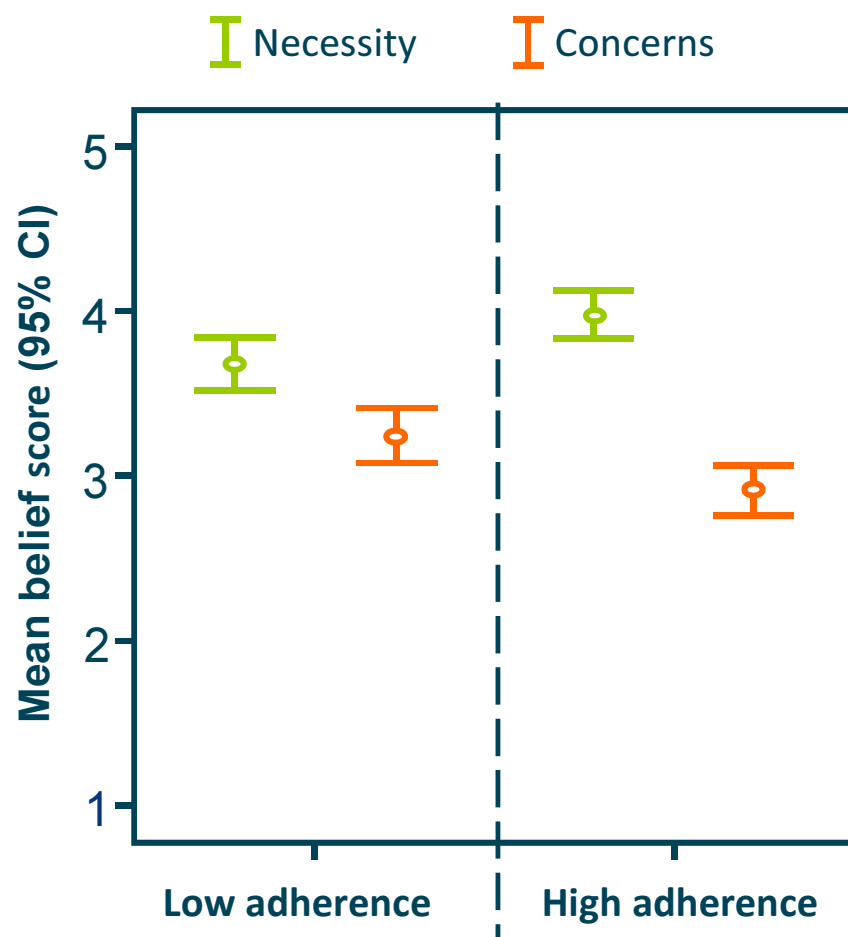
- There was a significant increase in the number of participants reporting low adherence over follow-up (Cochran Q=38.9, df=3, p<0.001)
- Patients in the low-adherence group were significantly less likely to have an undetectable viral load at 6 months (Chi square=10.9, df=1, p=0.001)

* Low adherence = average self-reported (MASRI²) adherence <95% of prescribed dose over previous month and/or unilateral decision to stop

1. Horne R, *et al.* *JAIDS* 2007;45:334–341.

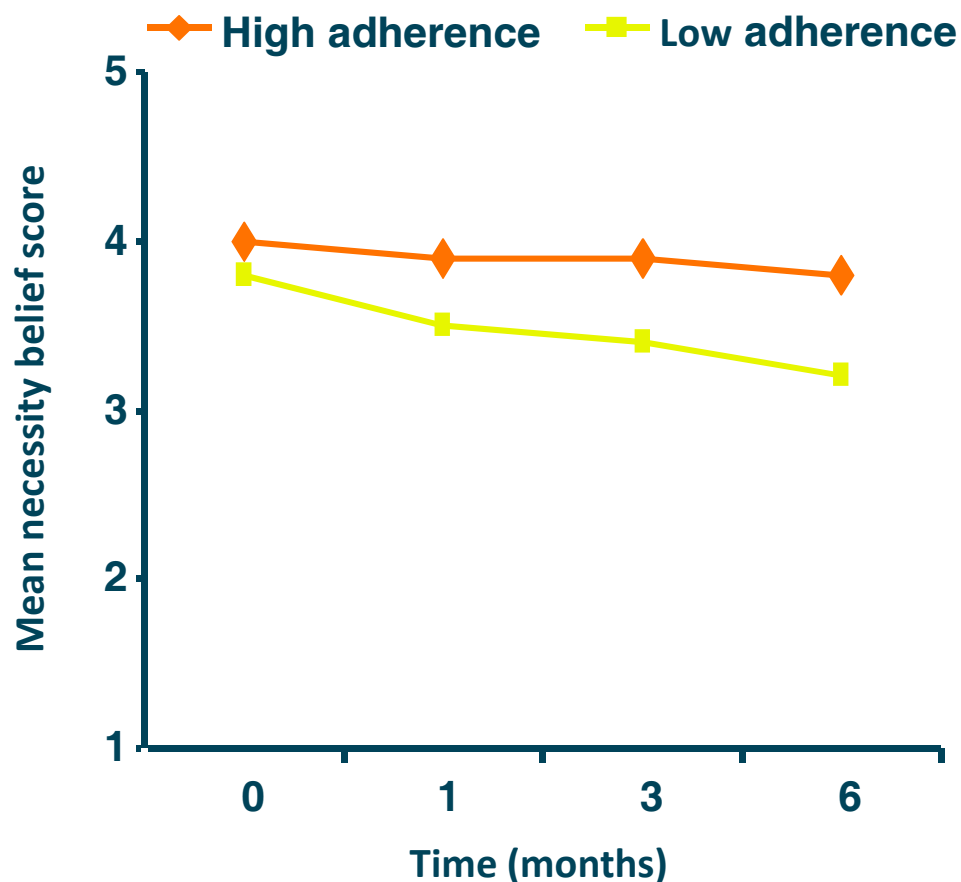
2. Walsh J., Mandalia S. & Gazzard, B. (2002). Responses to a one month self-report on adherence to antiretroviral therapy are consistent with electronic data and virological treatment outcome. *AIDS*; 16(2):269-277.

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)

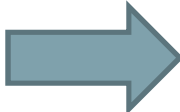
Relationships remained significant when controlling for depression and anxiety

ARE THESE ISSUES RELEVANT NOW?.....



RP PG 010910047

- Supporting Uptake 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


Current
stage

| WS | Study | Title |
|----|-------|--|
| 1 | 1 | Identifying new barriers to ART uptake and adherence |
| | 2 | Refining measures of perceptual and practical barriers to ART |
| | 3 | Development of intervention manuals and materials |
| 2 | 5 | RCT to assess the efficacy of the intervention |
| 3 | 6 | Assessment of cost utility and cost effectiveness of the interventions |
| 4 | 7 | Preparing for NHS implementation |

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 Men¹.

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}



1. Horne, R. & Weinman, J. (2002) Self-regulation and self-management in asthma: exploring the role of illness perceptions and treatment beliefs in explaining non-adherence to preventer medication, *Psychol Health*, 17:17–32.
2. Hall, S., Weinman, J., & Marteau, T. M. (2004). The motivating impact of informing women smokers of a link between smoking and cervical cancer: the role of coherence. *Health Psychology*, 23(4), 419-424.

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

Horne R & Weinman J. *Psychol Health* 2002;17:17–32.

Halm, E. A., Mora, P., & Leventhal, H. (2006). *Chest*, 129(3), 573-580

Leventhal H, et al. (1997) Illness representations: Theoretical foundations. In *Perceptions of health and illness: Current research and applications*. Edited by KJ Petrie & J Weinman. London: Harwood Academic

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.

(F, 40, Zimbabwean, asymptomatic)

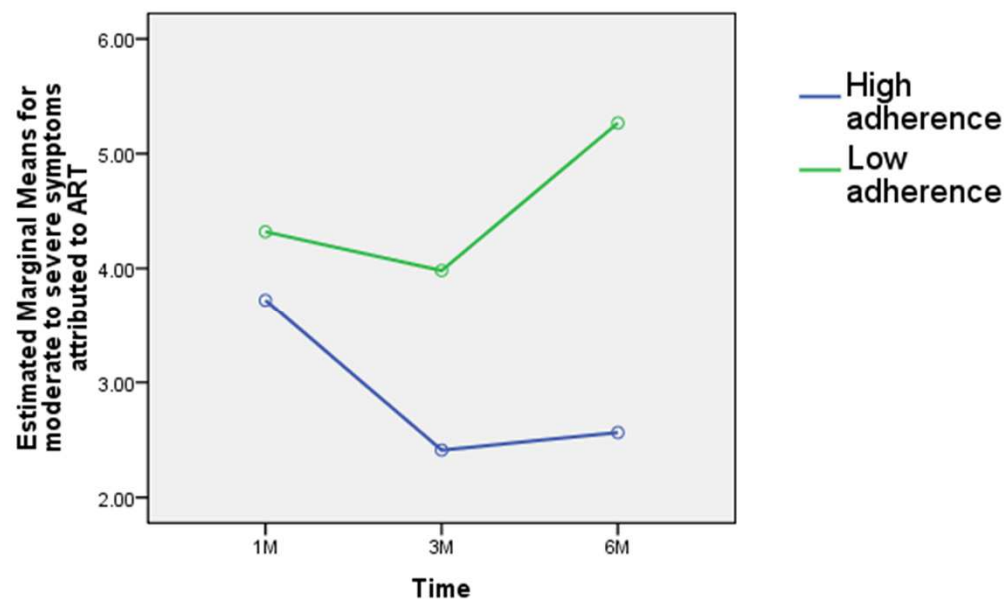


(M, 45, Zambian, symptomatic)

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.

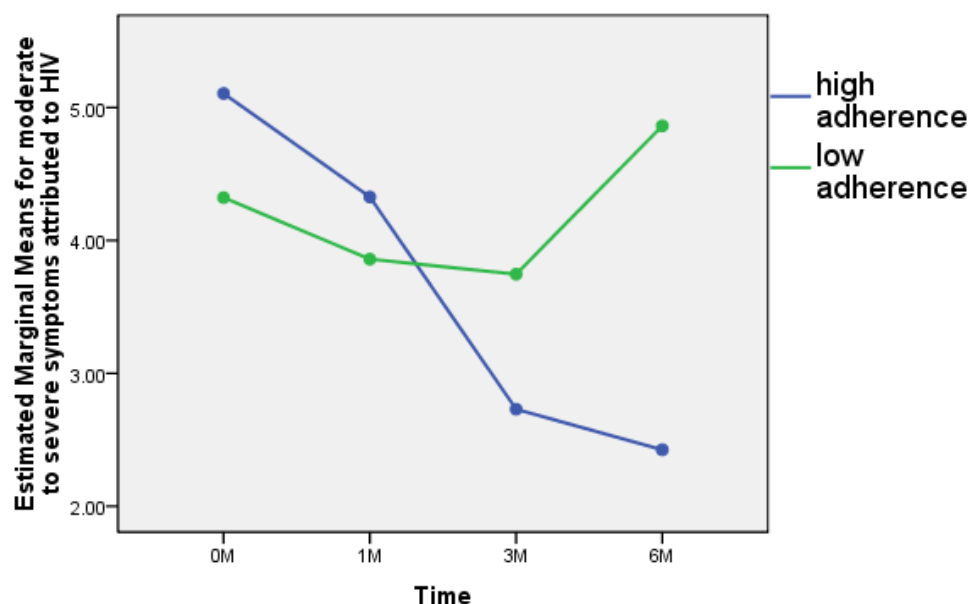
Increase in HIV-related symptoms associated with a decrease in necessity ($r=-0.22$, $p<0.05$)

80 HIV+ patients receiving antiretroviral treatment in Brighton, UK

Cooper, V., Horne, R., Gellaitry, G., Hankins, M. & Fisher, M. (2009) *AIDS Care*, Apr 21 (4), 520-8.

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

($r = -0.22, p < 0.05$)

ART CONCERNS PREDICT ART SIDE EFFECTS

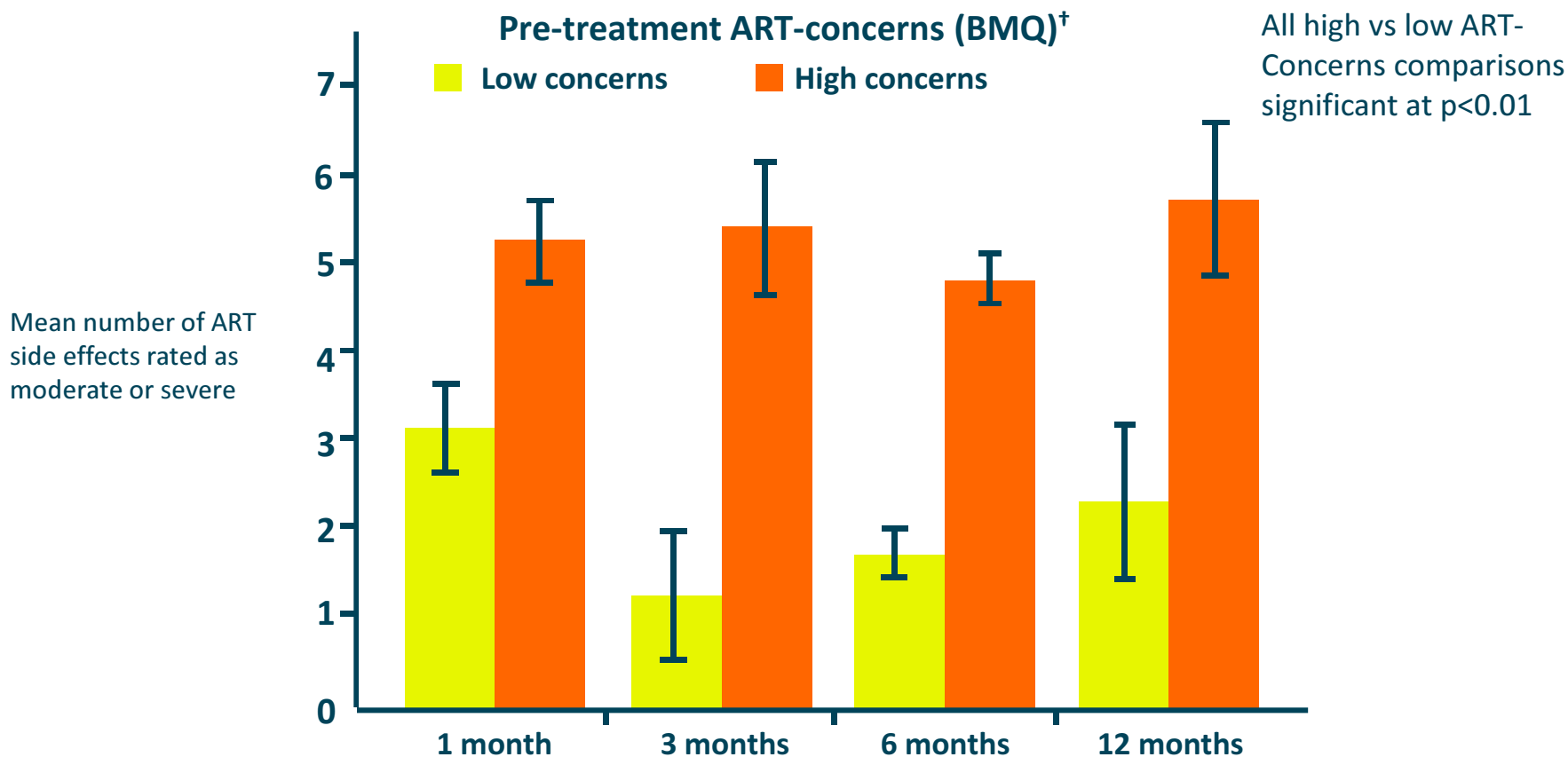
Copyright 2003 by Randy Glasbergen.
www.glasbergen.com

Prescriptions



**“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



Horne R , Cooper V., Chapman, S. (2011). *6th International Conference on HIV Treatment and Prevention Adherence*; Abstract 70058 .

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



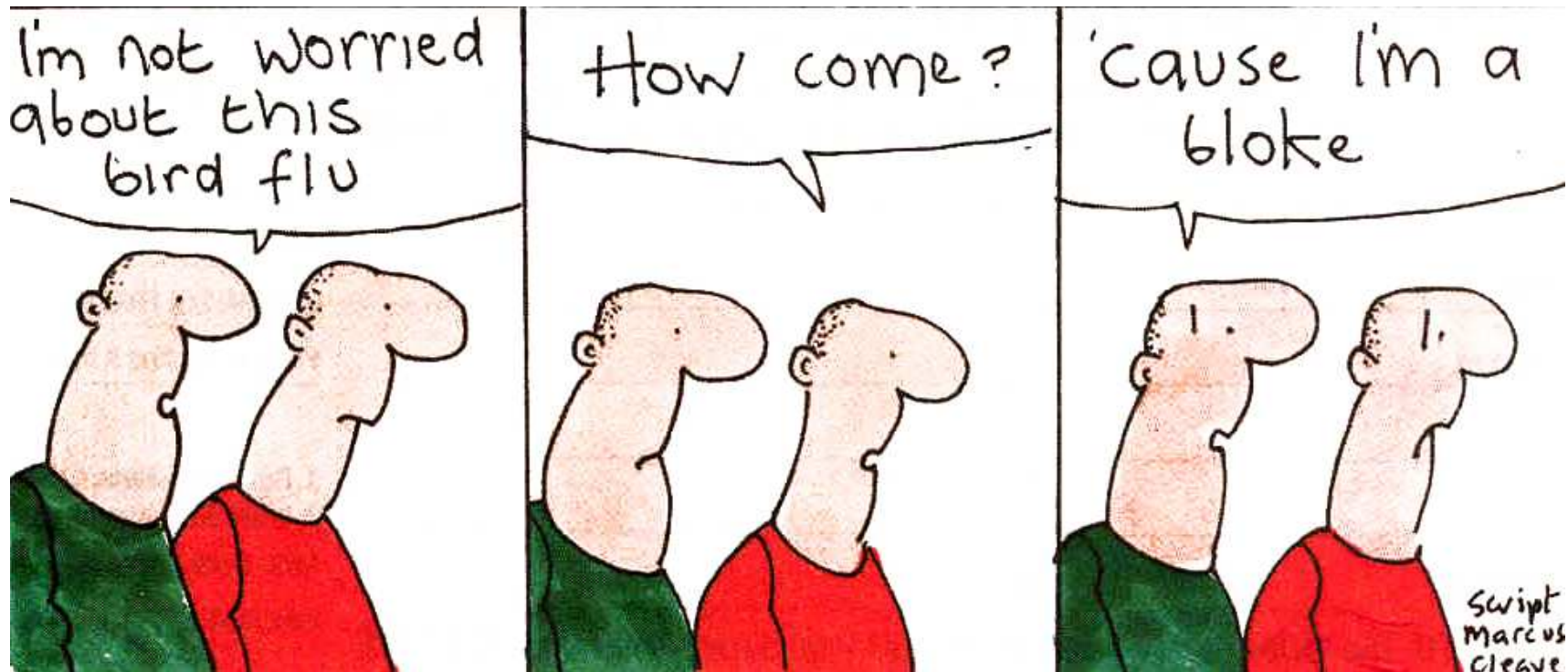
DISEASE STEREOTYPES

- 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'.....*

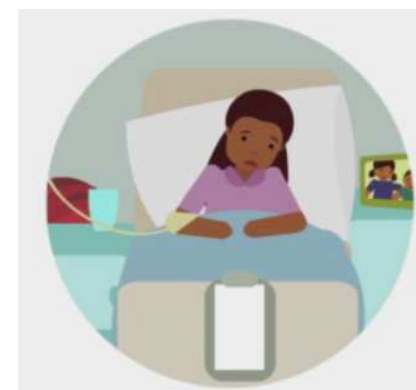


Additional insights: Difficulty in simultaneously accepting the diagnosis and ART

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)



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*

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:

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

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)



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

Doubts about necessity and ART Concerns were often based on misconceptions eg :

(F, 46, DRC,
symptomatic
)

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

(M, 40, Ugandan,
asymptomatic)



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.

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

(F, 35, Jamaican, symptomatic)

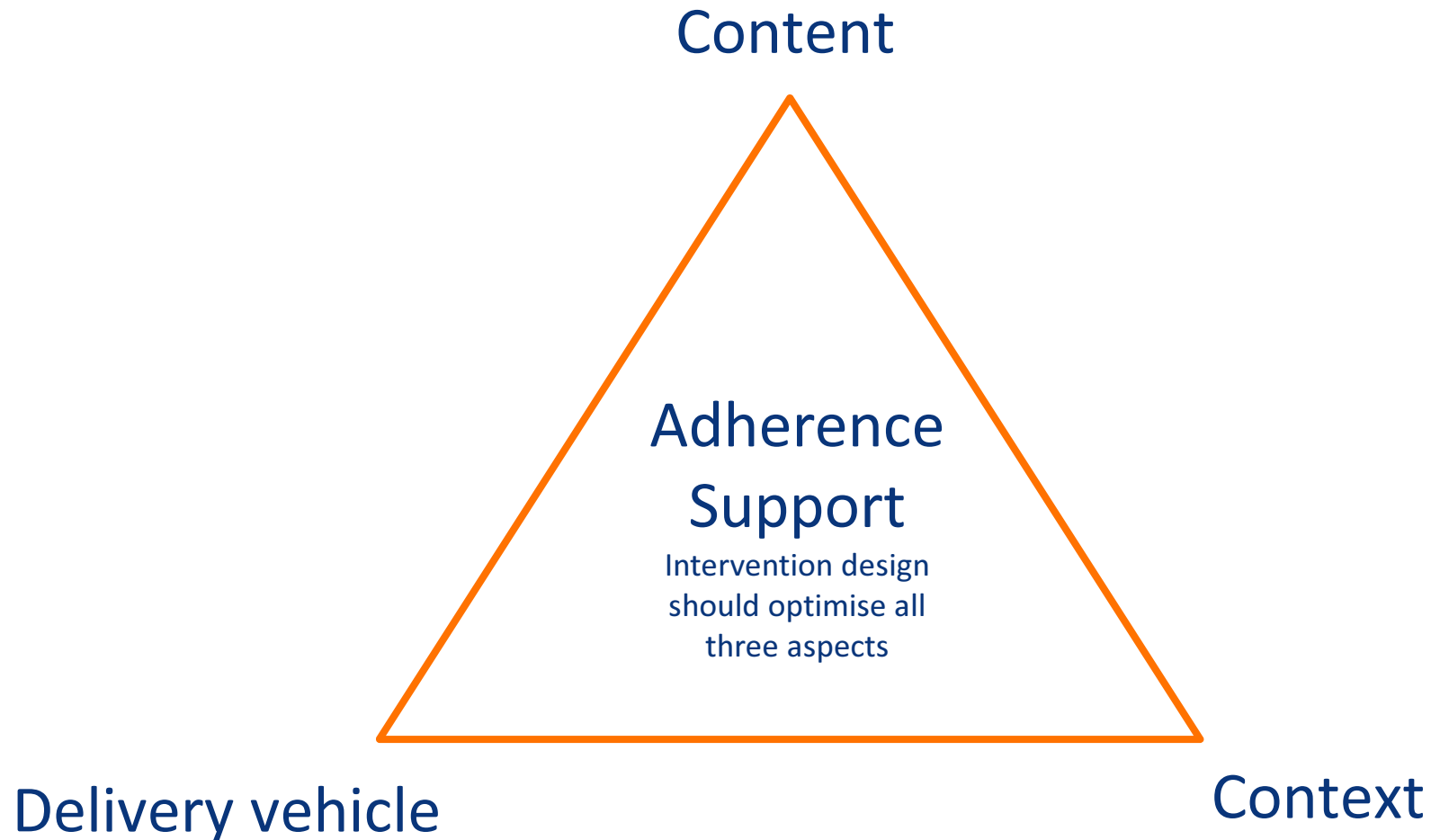


Your main worry is not about my life has been cut short, no. It's now about the quality of life you are leading in terms of medication all the time so it's a catch 22. Do you lead a long life which you're not happy with or do you lead a short quality life?

(M, 45, Zambian, symptomatic)

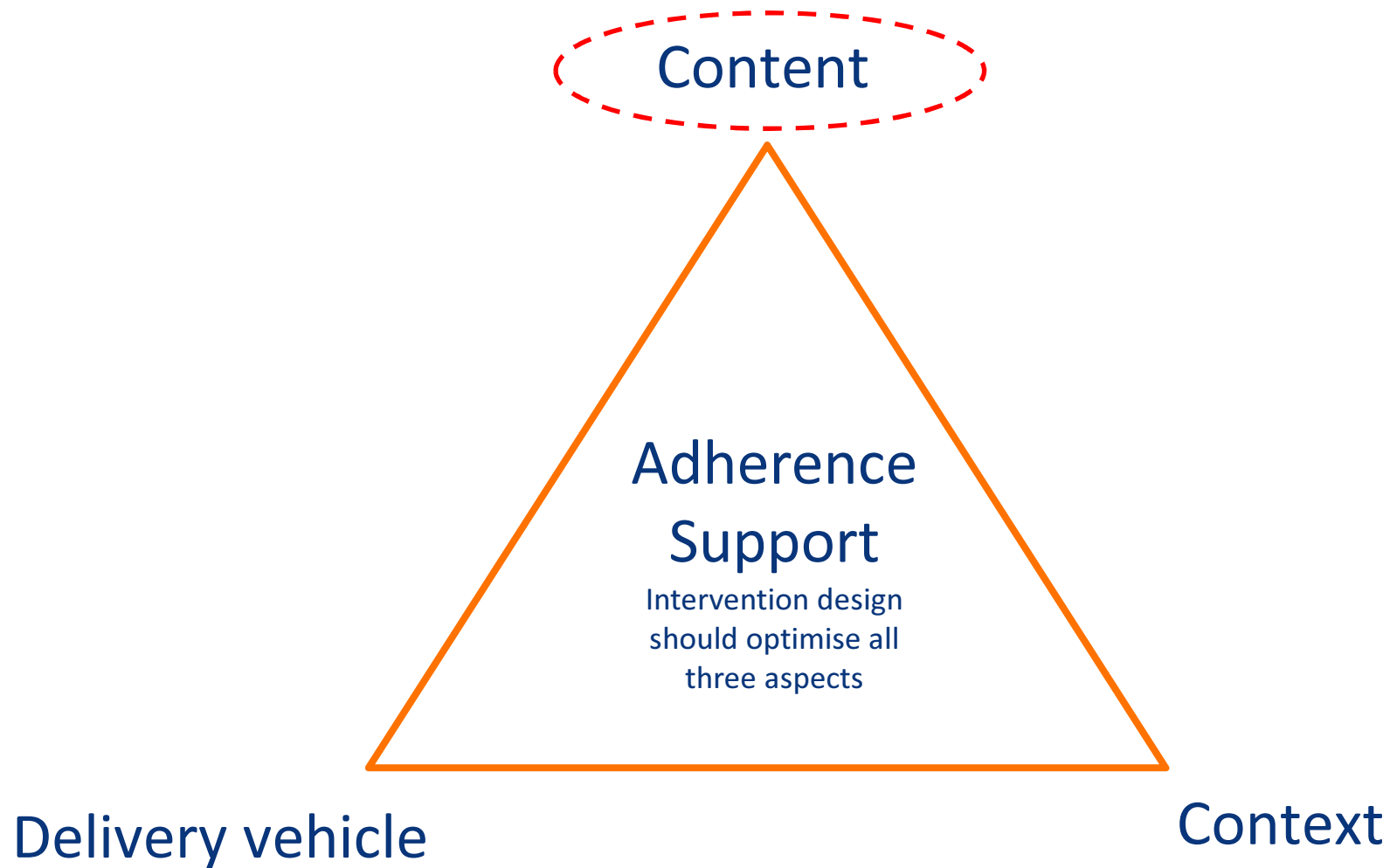
Implications for interventions to support ART uptake and adherence

Adherence support: the need for intelligent design at all three points of the triangle

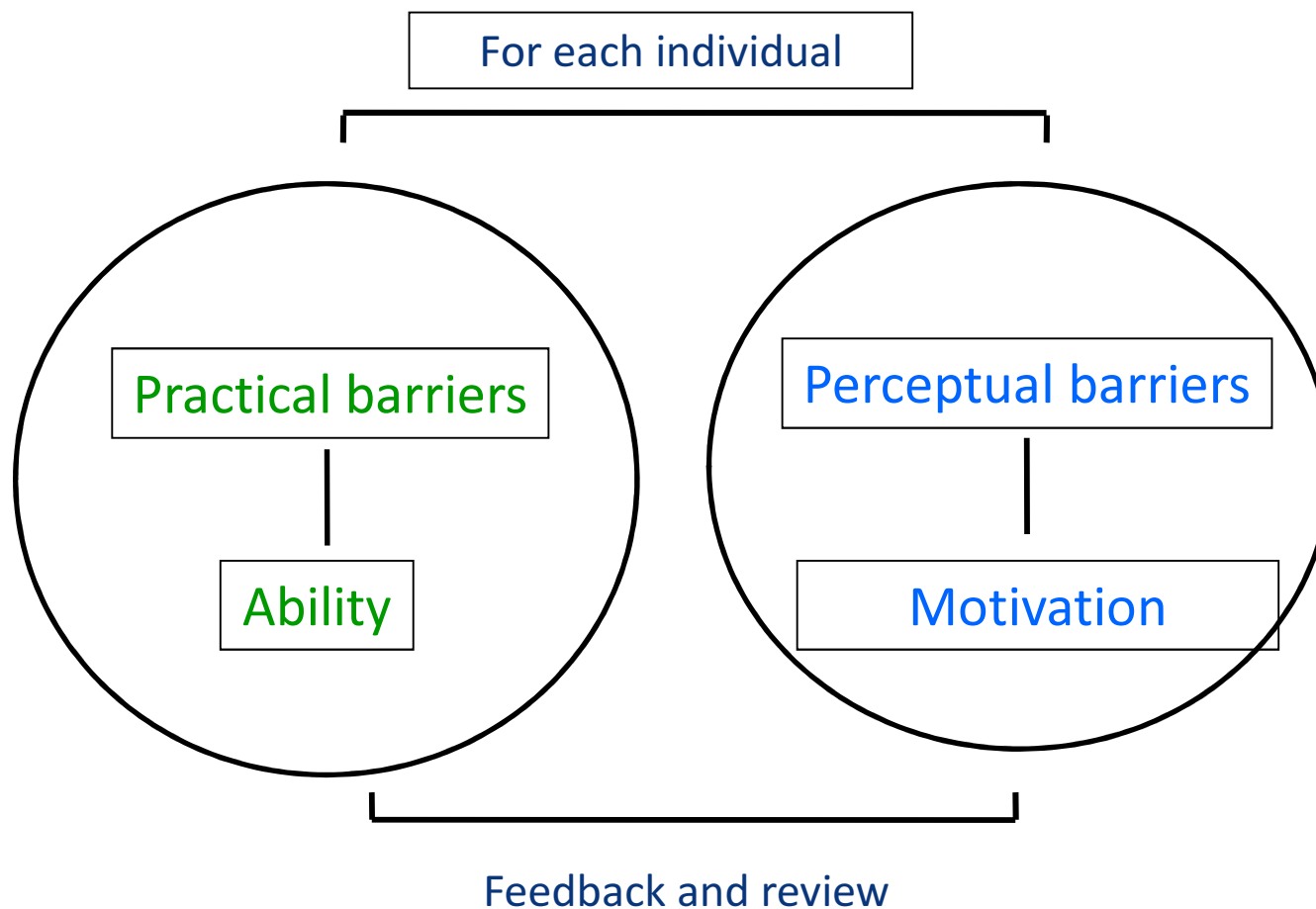


Horne, R. & Clatworthy, J. (2010). Adherence to Advice and Treatment. In D. French, K. Vedhara, A.A. Keptein, J. Weinman (Eds.), *Health Psychology* (pp. 175-188).

Considerations for intervention development



The Perceptions and Practicalities Approach



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 reources



North Middlesex



PI: Dr. Johnathan Ainsworth

**Pharmacist:
Kirstin Knonyongwa**

Homerton



PI: Prof. Jane Anderson

**Pharmacist:
Richard Castles**

Kings college



**PI: Dr. Frank Post
Pharmacist:
Shema Doshi**

Q.E, Woolwich



PI: Dr. Stephen Kegg

**Pharmacist:
Karen Buckberry**



Ancillary studies

Chelsea & Westminster

PI: Dr. Mark Nelson

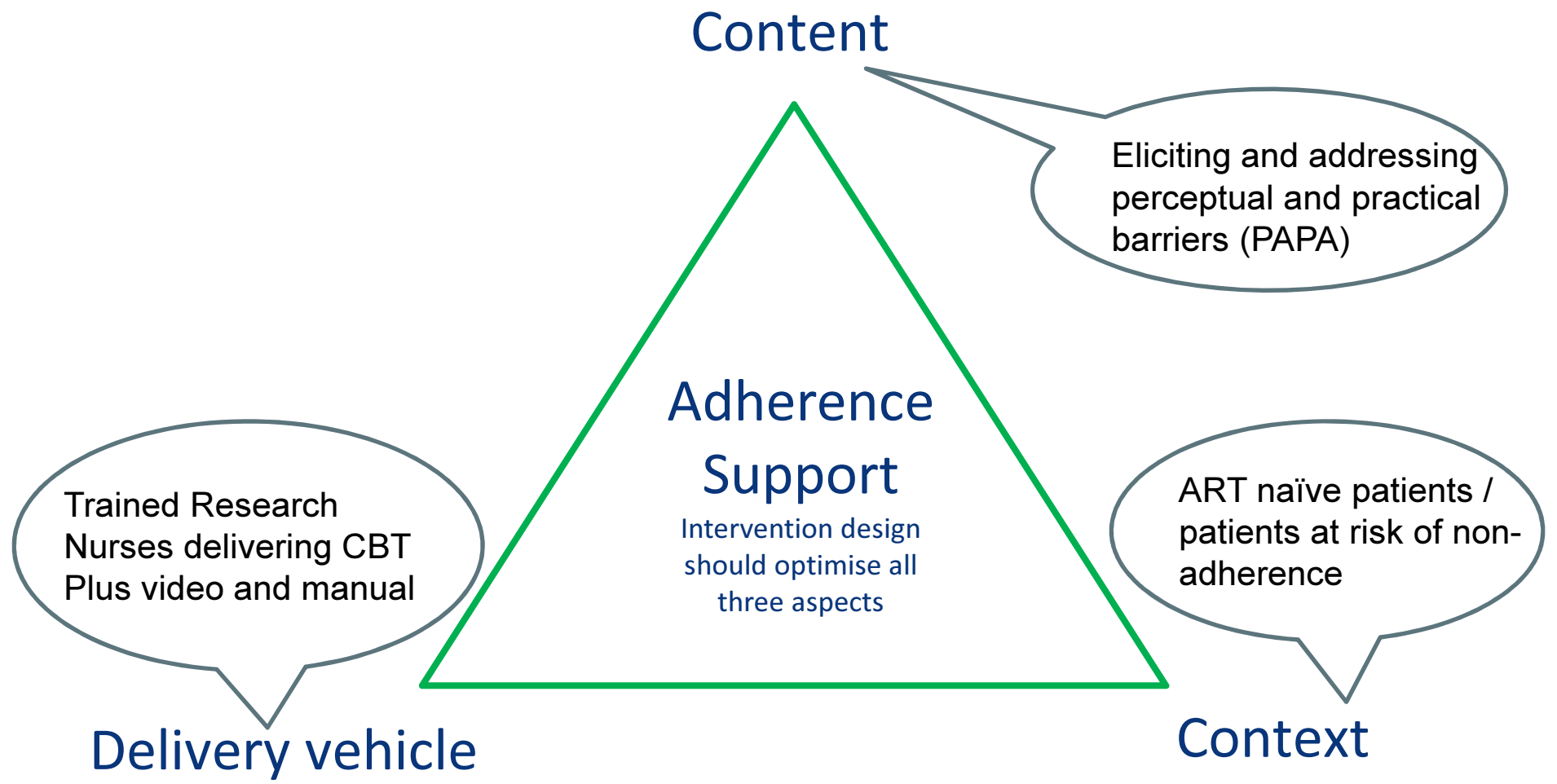


Brighton

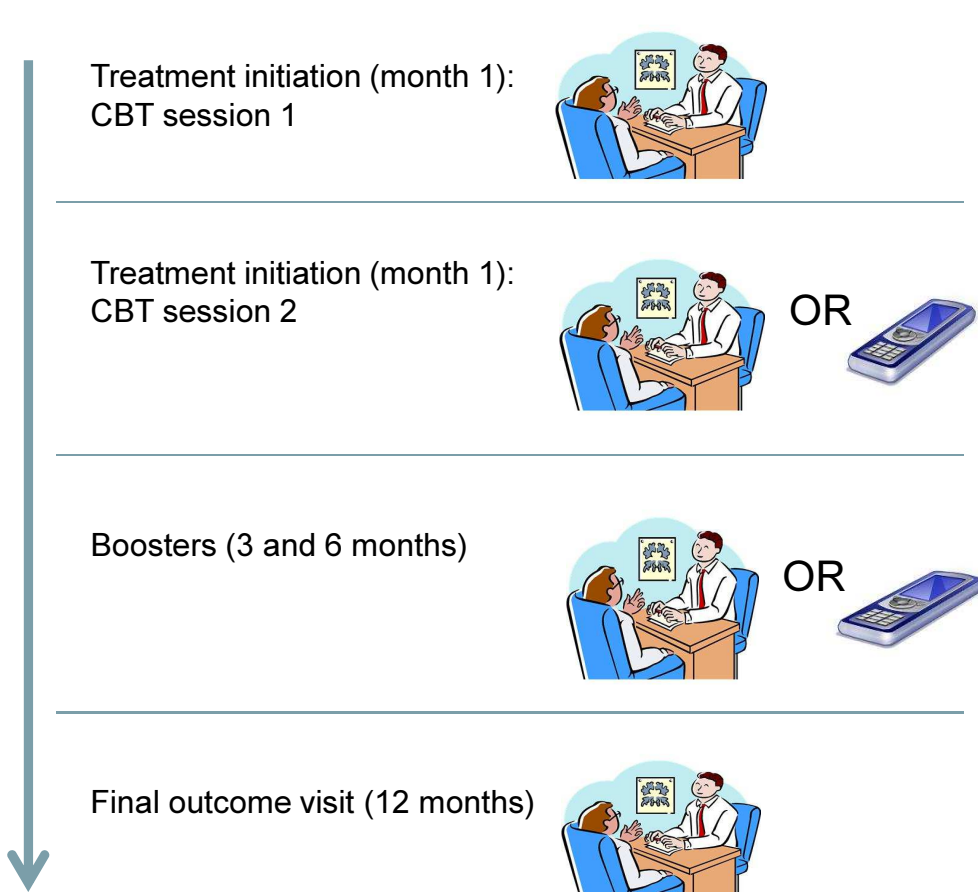
**PI: Prof. Martin Fisher
Pharmacist: Heather Leake-Date**



SUPA Intervention



Intervention



- 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.

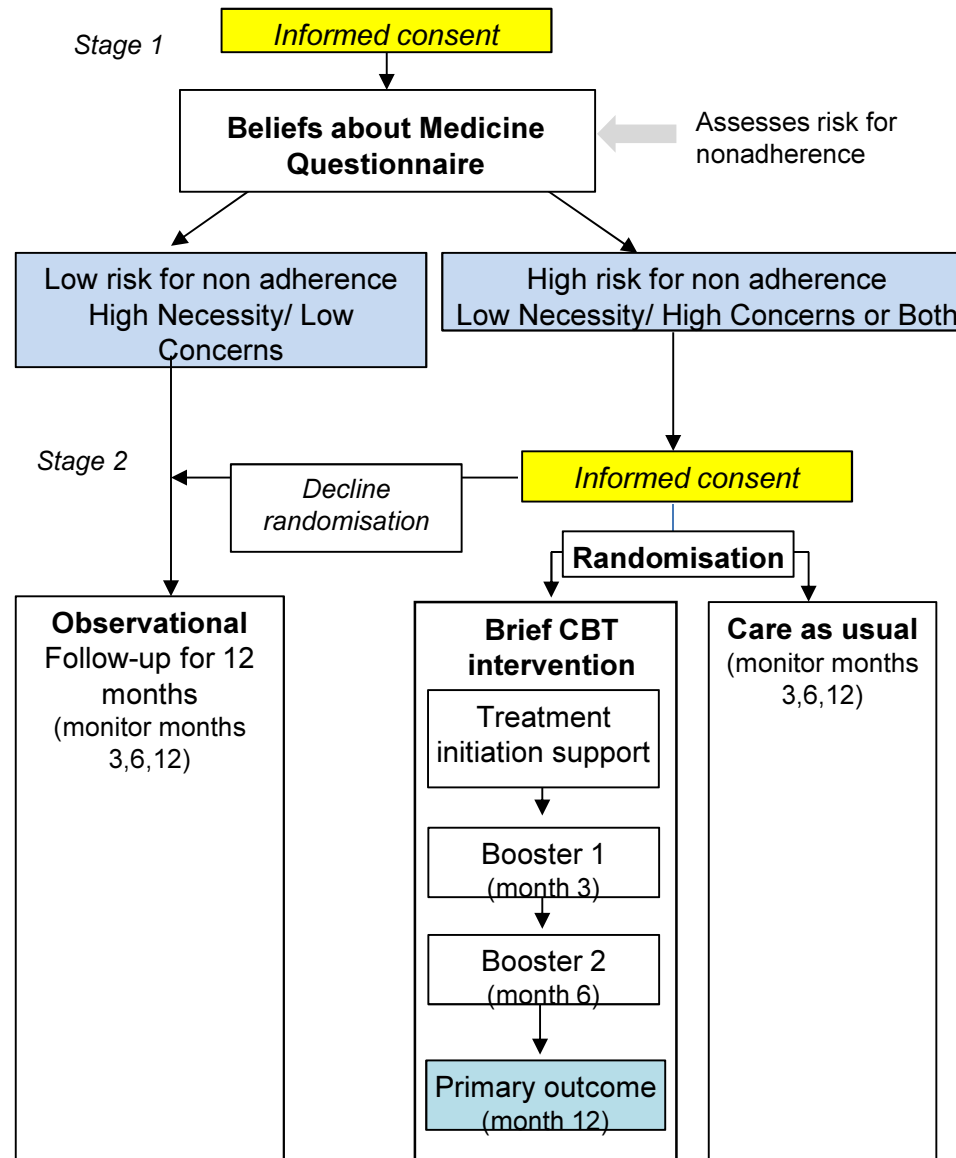
- MEMs will measure adherence rates

Trial design

Start date: January 2014

Observational Outcomes:

BMQ
Treatment failure
Disengagement from care at 12 months



Intervention Primary outcomes:

- Proportion of months under follow-up where adherence $\geq 90\%$

Intervention Secondary Outcomes:

At 12 months:

- 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

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.....