

ADHERENCE IN HYPERTENSION

PART 2: ADHERENCE – THE SCIENTIFIC EVIDENCE

Through the CAT's eye: seeing non-adherence clearly

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Non-adherence: the Oldest Problem in Medicine

"Keep a watch on the faults of the patients, which often make them lie about the taking of things prescribed," wrote Hippocrates. Two and a half millennia later, the sentiment remains painfully relevant. Despite the availability of safe, effective antihypertensive drugs, **non-adherence persists in 30–50% of patients**, contributing to a **twofold higher cardiovascular risk** and a **fourfold increase in stroke**.

As C. Everett Koop, the former U.S. Surgeon General, put it bluntly: "Drugs don't work in patients who don't take them."

Why Is Adherence Still So Poor?

We clinicians are trained to diagnose and prescribe – but not necessarily to ask. In a multinational survey of more than 3,000 primary care professionals, only half routinely asked about adherence.¹ Even when they did, responses were often unreliable. Some patients genuinely believe

they take their medication correctly; others may feel embarrassed to admit lapses.

Traditional approaches – pill counts, refill checks, or self-reports – are **imprecise and often misleading**. The result? Escalation of therapy, unnecessary investigations, and mutual frustration.

The challenge is simple to describe but hard to solve: **how do we know whether a patient is truly taking their medicine?**

A New Lens: The Chemical Adherence Test (CAT)

In 2014, we developed a new way to see adherence objectively – the **Chemical Adherence Test (CAT)**. This laboratory test uses **liquid chromatography–tandem mass spectrometry (LC-MS/MS)** to detect traces of prescribed cardiovascular drugs in a simple spot urine sample.

CAT can currently detect around 60 commonly used medications with high sensitivity and specificity. It is relatively inexpensive (about £45



per sample), robust, and practical – samples can even be mailed to the testing centre. Today, the **National Centre for Adherence Testing (NCAT)** in Leicester, UK, receives specimens from more than 50 centres across the UK and Europe.

When and How to Test

Adherence testing is especially valuable for:

- **Patients with apparent resistant hypertension:** non-adherence increases in a near-linear manner with the number of prescribed medications and reaches around 30–40% in those on three drugs.
- **Unexpected treatment failure**
- **Within the first few months of treatment change**
- **Younger patients** as they are more likely to be non-adherent
- **Clinical trials**, where verifying medication exposure strengthens validity

Testing is straightforward. We obtain verbal consent, explaining that the test is now part of routine assessment for patients on multiple drugs. The urine sample is collected on the same day, and results are typically available within days.

Discussing the Results

This is the crucial moment- and the one that often worries clinicians, especially as we are not formally trained in this area. But with the right framing, CAT results can enhance trust rather than undermine it.

A simple opening line that we use and which has worked well is: “Your urine test did not detect some of your medications. It’s difficult for all of us to remember pills every day – does that happen with you?”

Such an approach invites honesty rather than defensiveness. The next step is to explore barriers and provide tailored interventions:

- **Forgetfulness or disrupted routines:** Use dosette boxes, reminder alarms, and involve family members or partners.
- **Side effects or complex regimens:** Consider switching medications or using fixed-dose combination pills, which are effective but still underused.

- **Lack of understanding:** Often, the term hypertension is misinterpreted as “tension” or stress, and patients are unaware that lifelong treatment may be necessary.
- **Cost or access issues:** Identify and address financial or logistical barriers.

Understanding Behaviour: The COM-B Model

Adherence is not just a pharmacological issue; it’s a behavioural one. We use the **COM-B model of behaviour change**, proposed by Michie et al.⁶

- **Capability** – Does the patient have the knowledge and skills to adhere?
- **Opportunity** – Are medications accessible and affordable?
- **Motivation** – Does the patient see a clear reason to continue long-term therapy?

By addressing these dimensions, clinicians move from blame to collaboration – helping patients succeed.

What the Evidence Shows²⁻⁵

Real-world observational data demonstrate CAT’s power to clarify uncertainty:

- Non-adherence was identified in approximately 25% of referred patients.
- Guided interventions improved clinic systolic blood pressure by about 20 mmHg and avoided unnecessary drug escalation.
- CAT pinpointed which agents were most often omitted, enabling targeted counselling.
- High rates of non-adherence were seen among patients attending TIA, renal, diabetes, and heart failure clinics.
- A single CAT measurement predicted long-term adverse outcomes.
- The test is cost-effective, saving approximately £500 per patient with apparent resistant hypertension.

Beyond routine care, CAT has strengthened major clinical trials – **PATHWAY-2**, **ORBITA**, and **RADIANCE-HTN** – by objectively verifying that participants were truly taking their assigned medications.

Limitations and Lessons Learned

No test is perfect, and CAT has its limitations:

- **Trust:** Some worry that objective testing could erode the doctor–patient relationship. In practice, most patients appreciate the clarity and respond positively when the discussion is handled with empathy.
- **Pharmacokinetics:** Drug half-life and timing of the last dose can affect detection, but studies show minimal impact overall.
- **Accessibility:** CAT currently requires LC-MS/MS equipment and trained personnel. A useful guide for those looking to try up the method is our paper by Lane D, et al.⁷ Efforts are under way to automate analysis and reduce costs tenfold.
- **Evidence gap:** While observational data are strong, randomised trials proving that CAT improves adherence and outcomes remain limited.

The Way Forward: Making Adherence Testing Routine

Hypertension care should include adherence assessment just as naturally as we measure blood pressure, kidney function, or lipids. Integrating CAT or other objective adherence checks can transform care pathways, guiding rational therapy and avoiding unnecessary polypharmacy.

Other priorities include greater clinician awareness and training and embedding adherence checks into digital health systems and remote monitoring

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Take-Home Message

Treating hypertension without checking adherence is like treating anaemia without measuring haemoglobin. Let's make adherence conversations as routine and compassionate as any other part of care, and remember to:

Ask – Check – Chat

- Ask about adherence
- Check with pharmacy records or CAT
- Chat about barriers, without judgement

Through the CAT's eye, we can finally see the unseen – and give our patients the best chance to benefit from the therapies we prescribe.

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