A FOCUSED REVIEW ON THE UPCOMING INTRODUCTION OF PREP ACROSS ENGLAND

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CONTEXT

An investigation into the impact pre-exposure prophylaxis (PrEP) will have on patients at high risk of the sexually transmitted Human Immunodeficiencey Virus (HIV) infection, across England. **91.5%** of current HIV care in the UK is in England (1) ; however, patients don't have access to pre-exposure care outside of clinical trials. This report comes as the Government's Department of Health and Social Care's (DHSC) recently announced to make PrEP available on the National Health Service (NHS) in England (2).

AIMS

To provide a general overview of what is currently known regarding PrEP including a review on clinical trials and a discussion on the health impact and financial implications of therapy.

HYPOTHESIS

The preliminary hypothesis for this investigation is that PrEP has led to reduced rates of HIV seroconversion amongst participants, but it is also hypothesised that PrEP has led to an increase in sexually transmitted infections (STIs) and 'risky sexual behaviour'.

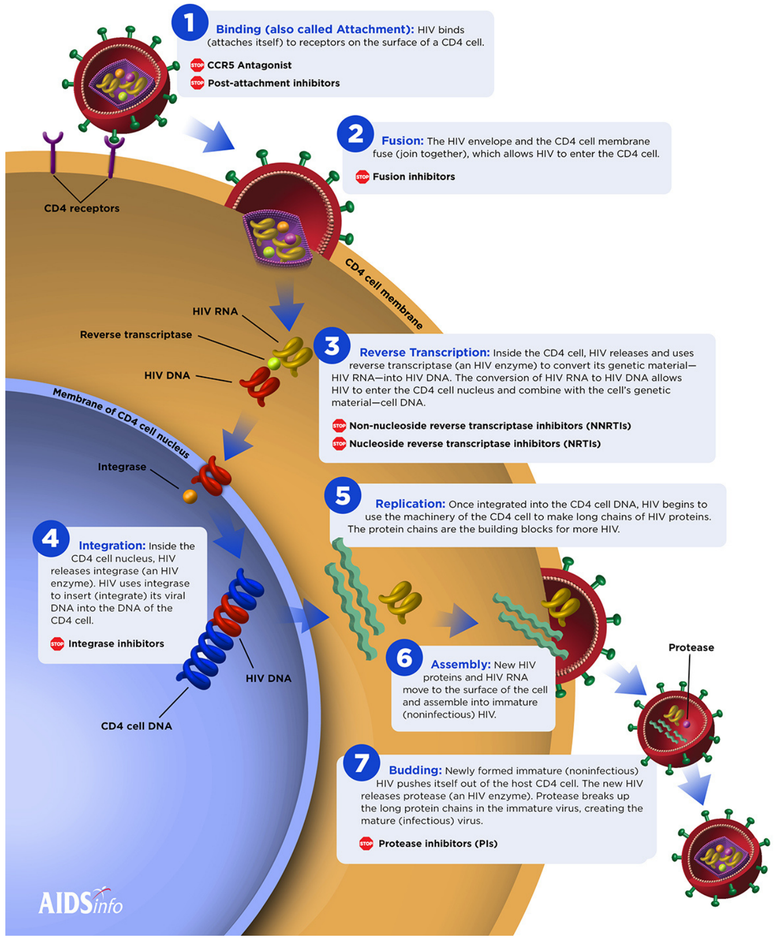

Figure 1. The HIV life cycle, from the point of viral invasion of a CD4 cell to the release of new viral material; is illustrated and explained in steps in his diagram. The points where HIV preventative drugs intervene with these stages are also labelled. (3)

WHAT IS HIV

- HIV is an infection caused by the Human Immunodeficiency Virus. Shown in figure 1, it targets and infects the immune systems T-cells or lymphocytes that are involved in protecting the body against pathogenic invasions (4).
- The reduction in CD4+ cell leaves the body unable to neutralise opportunistic infections taking advantage of the impaired immune system. At the advanced stage of HIV infection, a patient may develop acquired immune deficiency syndrome (AIDS) (4).
- Aside from post-exposure prophylaxis, there are no effective vaccines preventing HIV transmission and there is currently no cure.

WHAT IS PREP

- PrEP is a daily oral antiretroviral medication taken prior to exposure to HIV, by people who are at high risk of catching the virus (5), to stop the risk of HIV seroconversion.
- Contains a combination of two Nucleoside reverse transcriptase inhibitors (NRTIs) - emtricitabine and tenofovir disoproxil fumarate (6).
- Shown in Figure 1, NRTIs target the reverse transcription of viral RNA into DNA.

CLINICAL ANALYSIS OF DATA

- The PROUD trial found across 243 participants receiving immediate treatment, only 1% developed HIV. This suggested PrEP was 99% effective in preventing HIV (7) .
- 9% of individuals deferred treatment by a year developed HIV, which suggests PrEP conferred a higher level of protection against those without treatment.
- Another preceding clinical trial across a much larger cohort of 2499, showed a reduction in HIV contraction by 75% in participants taking PrEP daily (8).
- Public Health England highlight a 29% decline in newly diagnosed HIV cases as of 2015, which can be argued is due to increased PrEP use, as the introduction of clinical trials runs across this timeline (9).
- A 6% fall from 2017 to 2018 is particularly significant since this period represents the first year of the IMPACT trial – the government's latest trial on PrEP use in England, and so this figure accounts for thousands taking PrEP.

HEALTH IMPLICATIONS

- Short-term side effects can include diarrhoea, headache, tiredness, nausea and vomiting (10); whilst guidelines suggest long term side effects can be lactic acidosis and severe hepatomegaly with steatosis (11).
- Side effects can prevent adherence to therapy, especially with PrEP, which is only effective when taken daily. Poor adherence can lead to treatment failure, as skipping doses can put a mild selective pressure on pathogens to mutate and become resistant.
- The PROUD trial found 28 adverse effects that led to an interruption in following the course of therapy (7). Other studies counteracted this with findings that side effects diminished over time and instead suggest adherences were due to 'stigma, rumours, and relationship difficulties due to being perceived as HIV positive were prevalent' (12).

RISK BEHAVIOUR

- PrEP might lead to increased risk behaviour; such as sexual behaviour change, increased number of sexual partners and decreased condom use that may all contribute to an increased rate of STI rates.
- Sexually active gay, bisexual and men who have sex with men are already considered at a high risk group for catching STIs (13).
- Globally, WHO found that 72% of individuals who continued taking PrEP in their research were diagnosed with chlamydia, gonorrhoea or syphilis within a year (14), but research focused in England like the PROUD study found no difference in the number of sexually transmitted infections for individuals on PrEP (7).

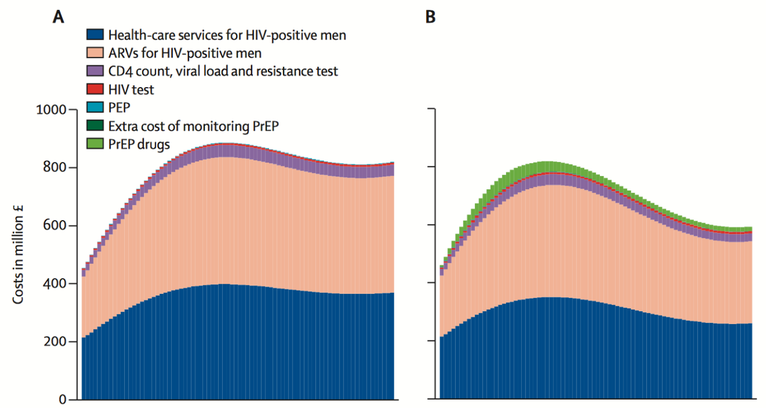

Figure 2. Financial models on the undiscounted HIV budget impact across 80 years; (A) if PrEP is not introduced (B) if PrEP is introduced. Both figures treat the cost of antiretroviral medications as unchanged across this period. Compared to (A), the smaller distribution of the curve in (B) indicates a reduction in spending (15)

FINANCIAL IMPLICATIONS

- PrEP therapy costs the NHS an estimated cost of £4,331 per person per year (15). This is greater than the price of post-exposure prophylaxis at £677.50 for a 28-day course of therapy (16), and even against a clinic box of 144 male condoms at £10.76 (17).
- PrEP is available privately at £20-50 (18); however, patients might not be able to afford this. Not funding PrEP opens the door to the production and sale of black market PrEP, which is illegal, unregulated and unsafe.
- A recent financial model found that therapy would result in a total saving of £1.0 billion discounted, a drop from £20.6 billion to £19.6 billion per annum, shown in figure 2. This is already against the lifetime cost of treating one HIV infected person in the UK already standing at around £400,000 (15).

CONCLUSION

- Funding pre-exposure prophylaxis therapy would be a financially beneficial strategy for the NHS.
- Cost-effectiveness of PrEP outweighs the cost of providing HIV treatment, and there is limited evidence suggesting the introduction of PrEP should affect rates of STIs and harmful changes in sexual behaviour amongst individuals.

REFERENCES