Written evidence submitted by MRC CTU at UCL

Summary

1. This response is on behalf of the MRC Clinical Trials Unit at UCL.

2. DFID have contributed funding to two large randomised controlled trials that have examined whether expensive laboratory tests are required to monitor patients who are on antiretroviral therapy: the DART trial for adults, and the ARROW trial for children.

3. DFID's support for these two trials (DART and ARROW) demonstrate their interest in building a robust evidence base for cost-effective strategies that may enable low-income countries to expand access to treatment.

4. Following on from these trials, DFID has funded the Lablite project, which is looking at how to implement the findings of DART and ARROW in lower-level health facilities, to help increase access to HIV treatment. Lablite is working with Ministries of Health in Malawi, Uganda and Zimbabwe to support the roll-out of antiretroviral therapy to primary health facilities in rural areas. This step is crucial, as the results of the trials alone have not been enough to convince national government to change policy, because of concerns about whether the trial results are generalisable to 'real-life' lower-level health facilities. There are very few international funders for implementation research projects like this, so DFID's support has been vital.

5. The DART and ARROW trials have helped to ensure a better balance between rural and urban healthcare by showing that HIV treatment can be delivered without the use of routine laboratory tests.

6. Lablite is building on this by showing how rural health facilities can safely deliver HIV treatment. This is vital if Universal Access to Antiretroviral Therapy is to be achieved in countries with a high prevalence of HIV in sub-Saharan Africa.

7. The impact of DFID's investment in randomised controlled trials such as DART and ARROW is limited by other major donors and guideline developers promoting approaches that have been shown to be of little benefit and not cost-effective. DFID could perhaps use its position to try to influence other donors and international organisations to adopt an evidence-based public health approach, prioritising interventions that have been proven to be effective and cost-effective.

Background

1. This response is on behalf of the MRC Clinical Trials Unit at UCL. We conduct research into a range of health conditions that are relevant to low-income countries, particularly HIV and tuberculosis. In recent years we have been the recipient of funding from DFID and joint MRC-DFID schemes for a number of research projects that are of relevance to this inquiry.

DFID's support for evidence-based, cost-effective health interventions

2. DFID have contributed funding to two large randomised controlled trials that have examined whether expensive laboratory tests are required to monitor patients who are on antiretroviral therapy: the DART trial for adults, and the ARROW trial for children. Both these trials were conducted in Uganda and Zimbabwe. These trials showed that routine laboratory tests for side-effects provided no benefit (and were therefore not cost-effective). They also showed that routine CD4 tests (that monitor the health of a person's immune system) could provide a small benefit over clinical monitoring alone, particularly after the first 2 years of treatment, but that the costs of these tests are currently so high that the intervention is not cost-effective [1-3].

3. Laboratory tests for side-effects and CD4 monitoring are expensive, and in many places in sub-Saharan Africa facilities to carry out these tests are not available. Requiring these tests as part of routine care for patients on antiretroviral therapy uses scarce resources that could be better spent getting more people onto treatment. It also acts as a barrier to treatment for people who live in rural areas where laboratory facilities are not available.

4. DFID's support for these two trials (DART and ARROW) demonstrate their interest in building a robust evidence base for cost-effective strategies that may enable low-income countries to expand access to treatment.

5. Following on from these trials, DFID has funded the Lablite project, which is looking at how to implement the findings of DART and ARROW in lower-level health facilities, to help increase access to HIV treatment. Lablite is working with Ministries of Health in Malawi, Uganda and Zimbabwe to support the roll-out of antiretroviral therapy to primary health facilities in rural areas. This step is crucial, as the results of the trials alone have not been enough to convince national government to change policy, because of concerns about whether the trial results are generalisable to 'real-life' lower-level health facilities. There are very few international funders for implementation research projects like this, so DFID's support has been vital. www.lablite.org

6. The Lablite project is still ongoing, but is already having an impact on how Ministries of Health train health workers in delivering ART, through innovative approaches such as the use of video case-studies to support mentoring of health workers in primary facilities by those in higher-level facilities.

Ensuring programmes can be sustained once funding has ended

7. DFID encourage research programmes to work in collaboration with key national stakeholders, such as Ministries of Health. Lablite has pursued this approach, and the Ministries of Health in all three countries have been closely involved at all stages of the project. This will help increase the likelihood of the findings of the project being implemented more widely, and sustained once funding for the research is over.

8. DFID also encourage capacity strengthening as part of their research programmes. Working on the DART and ARROW trials has strengthened the capacity of clinicians and other healthcare professionals based in Uganda and Zimbabwe to carry out research. They are now taking an active role in developing new research projects, and promoting high-quality clinical practice.

9. As part of DART, ARROW and Lablite new tools have been developed to train healthworkers in how to treat people with HIV. These tools include a clinical manual, checklist job aid, and video case studies. These training approaches are now being considered by Ministries of Health for wider use in Uganda, Malawi and Zimbabwe, which will help to ensure the sustained impact of these projects.

Ensuring a better balance between rural and urban healthcare & supporting the poorest countries to achieve Universal Access to antiretroviral therapy

10. The DART and ARROW trials have helped to ensure a better balance between rural and urban healthcare by showing that HIV treatment can be delivered without the use of routine laboratory tests.

11. Lablite is building on this by showing how rural health facilities can safely initiate and deliver HIV treatment. This is vital if Universal Access to Antiretroviral Therapy is to be achieved in countries with a high prevalence of HIV in sub-Saharan Africa.

12. Equity data collected so far by the Lablite project indicates that people treated at the lower-level rural health facilities now have less far to travel to access treatment, and have lower transport costs.

Factors limiting the impact of DFID's investment

13. The impact of DFID's investment in randomised controlled trials such as DART and ARROW is limited by other major donors and guideline developers promoting approaches that have been shown to be of little benefit and not cost-effective. DFID could perhaps use its position to try to influence other donors and international organisations to adopt an evidence-based public health approach, prioritising interventions that have been proven to be effective and cost-effective.

References

1. Kekitiinwa, A., et al., *Routine versus clinically driven laboratory monitoring and first-line antiretroviral therapy strategies in African children with HIV (ARROW): a 5-year open-label randomised factorial trial.* Lancet, 2013. **381**(9875): p. 1391-403.
2. Medina Lara, A., et al., *Cost Effectiveness Analysis of Clinically Driven versus Routine Laboratory Monitoring of Antiretroviral Therapy in Uganda and Zimbabwe.* PLoS One, 2012. **7**(4): p. e33672.
3. Mugyenyi, P., et al., *Routine versus clinically driven laboratory monitoring of HIV antiretroviral therapy in Africa (DART): a randomised non-inferiority trial.* Lancet, 2010. **375**(9709): p. 123-31.