The national scale up of antiretroviral therapy in Malawi is based on a public health approach, with principles and practices borrowed from the successful World Health Organization "DOTS" tuberculosis control framework. The scale up of antiretroviral therapy was underpinned by a very strong monitoring and evaluation system, which was used to audit the scale up approach and conduct operational research to answer relevant questions. Examples of research included: i) access to antiretroviral therapy, populations and social groups served, and how the different groups fared with regard to outcomes; ii) determining whether the quality of data at antiretroviral therapy sites was adequate and whether external supervision was needed; iii) finding feasible ways of reducing the high early mortality in patients starting treatment in both Malawi and the sub-Saharan African region; iv) the causes of loss-to-follow-up, what happened to patients who transferred out of sites and whether transfer-out patients had outcomes comparable to those who did not transfer; and v) the important question of whether antiretroviral therapy scale up reduced population mortality. The answers to these questions had an important influence on how treatment was delivered in the country, and show the value of this work within a programme setting. Key generic lessons include the importance of i) research questions being relevant to programme needs, ii) studies being coordinated, designed and undertaken within a programme, iii) study findings being disseminated at national stakeholder meetings and through publications in peer-reviewed journals and iv) research being used to influence policy and practice, improve programme performance and ultimately patient treatment outcomes.