Background: HIV prevention trials have been conducted assessing a range of approaches to decrease the incidence of HIV infection, including vaccination, circumcision, vaginal and rectal microbicides, oral pre-exposure prophylaxis (PrEP) and treatment as prevention (TasP). Of these, male circumcision, one vaccine combination, 1% tenofovir gel used at the time of sex, oral emtricitabine/tenofovir or tenofovir, and effective treatment resulting in reduced viral load have all been shown to reduce HIV acquisition by 30 to 97%. Scale up of circumcision, which decreases the risk of HIV in men by >50%, has increased globally with the availability of new devices which permit the delivery of this procedure at low cost and high safety. Oral and topical antiretrovirals have emerged as potent tools for the prevention of HIV, and since the approval of emtricitabine/tenofovir by the FDA for prevention of HIV in 2012, a number of programs have been initiated to scale up the availability of PrEP and to explore the public health impact of this intervention. At the same time, there is an increased recognition that adherence to oral and topical PrEP is critical to the success of this approach. The FemPrEP and VOICE trials, which were conducted in populations of young women living in high seroincidence communities in Africa, each reported low levels of adherence to daily products. This factor likely accounted for the lack of reported efficacy in these studies, in contrast to the studies performed in men who have sex with men and HIV serodiscordant couples. Tenofovir gel is in a phase 3 clinical trial among women using a coital rather than daily approach (FACTS-001), and as a rectal microbicide in MSM (MTN-017). For new PrEP agents, strategies are focused on the sustained delivery of ARVs. One example is a vaginal ring which delivers low doses of the NNRTI dapivirine over a month of use, and randomized efficacy trials evaluating this approach are underway. Injectable ARVs are in phase 1 studies, with promising results emerging from animal models. The success of the HPTN 052 study which demonstrated that effective treatment of HIV-infected persons, resulting in virological suppression reduced HIV transmission by 97%, has led to the increased rollout of TasP as a key strategy in the HIV prevention toolbox. Of the HIV vaccines tested to date, only the RV144 HIV vaccine has been successful in reducing HIV incidence. Although the reduction in HIV was 31% with this vaccine and the results of this study likely only apply to those patients with subtype E virus, the study has energized the vaccine field and has led to the development of a vaccine protocol to assess the efficacy of this strategy against clade C HIV in S Africa in a study planned for 2015.