To optimally fight tuberculosis (TB) you have to know your epidemic. This means analyzing TB data collected by the National TB Program (NTP) to look at trends, numbers and age- or gender-specific rates, to conduct TB prevalence surveys and drug resistance surveys. Operational and implementation research helps to find solutions and test new tools and strategies. KNCV has wide expertise and experience to help NTPs and other public health institutions to collect and interpret the data they need.

Know your epidemic and testing the solutions

Triaging and treating MDR-TB

In several countries KNCV will assess whether a combination of molecular diagnostic tests can triage TB patients into MDR-TB, pre-XDR-TB and XDR-TB rapidly but sufficiently accurately. Currently, it can take months before the complete drug resistance pattern is known. In the meantime the patient may receive an inappropriate treatment regimen. When the resistance pattern is determined more rapidly, patients can start the most appropriate treatment regimen right away. For MDR- and some pre-XDR-TB patients a shorter treatment regimen can be considered. For other pre-XDR and XDR-TB patients, new drugs (e.g. bedaquiline or delamanid) may be added to the standard MDR-TB regimen to improve treatment outcomes. We will assess the impact of shortened regimens and new drugs on MDR-TB case detection and treatment outcomes, and will support drug safety evaluations through implementation of active pharmacovigilance.

Fighting drug-resistant TB

One of the most important challenges is the spread of multidrug-resistant TB (MDR-TB) and extensively drug-resistant TB (XDR-TB). The causes of this spread vary between countries and settings, from inadequate TB treatment regimens, poor quality drugs or interrupted intake of medication, to uncontrolled transmission of M/XDR-TB due to late diagnosis or poor infection control. Drug resistance surveillance and operational research are vital in order...
Testing the solutions
KNCV tests potential solutions in several countries. Solutions can be new diagnostic tools, new medicines, or new approaches. One example is a project in Chennai, India. The private sector is often the first point of care for people with TB symptoms in India. This pilot project will demonstrate the potential for private health providers to contribute to early detection and successful treatment of TB patients. The pilot will provide health providers and their patients access to free chest x-rays and Xpert MTB/RIF tests at convenient locations. For those diagnosed with TB, the project will provide high-quality, daily therapy to cure the disease, and support to patients to help them complete their full course of treatment. Patients diagnosed with drug-resistant TB will be referred to specialized treatment centers. Results will be used to develop a replicable model for scale-up of involvement of private providers across India and other countries. The project is implemented by REACH, with technical support from KNCV and funding from the Lilly Foundation and United Way Worldwide.

Research confirms policy in Ethiopia
In Oromia Region in Ethiopia it was noted that health care workers were hesitant to follow the policy of decentralizing services to community level. They feared that patients continuing their TB treatment at health posts closer to home would undermine treatment success. We undertook a study of the treatment outcomes of patients treated at the community health post versus those continuing treatment at the health facility. Patients who continued their treatment in the community had comparable outcomes to those at health facility level. Adherence to treatment was even better, with fewer missed doses. These findings confirm the effectiveness of the decentralization of TB treatment services for better access to TB care in rural communities.
to discover trends and causes of M/XDR-TB and to find remedial solutions. Implementation research is important in order to test which of these solutions work best, and how these could be tailored to local circumstances. KNCV helps country programs and partners to ask the right questions and find the data to inform what solutions best improve the outcomes for the patient and eventually the entire program.

**Drug resistance surveillance**

With the increasing challenges in global TB control posed by drug-resistant TB, drug resistance surveillance has become critical. Drug resistance surveillance to measure the burden of MDR-TB and other drug resistance patterns can be done via routine surveillance or via periodic surveys. KNCV has expertise in supporting countries in both. We have provided support to drug resistance surveys in Zimbabwe, Namibia, Vietnam, Tanzania, Kenya, and Malawi.

**Assisting with prevalence surveys**

Annually, the World Health Organization (WHO) estimates the global and national prevalence, incidence and mortality rates for TB. These data are used by the Global Fund and other donors to decide on funding allocations, and by the United Nations to monitor progress towards the Global TB targets and the Sustainable Development Goals. However, for many countries these estimates are largely based on interpretation of indirect data combined with expert opinion and therefore have uncertainties. TB prevalence surveys provide a direct measure to better estimate the TB burden. They also are a rich source of data that can help NTPs adjust their strategies to make a bigger impact. Surveys can identify “hidden” or under-reported patient populations, as well as information on health-seeking behavior and barriers to care. Conducting two prevalence surveys with a 10 year interval enables countries to measure the impact of TB control activities. Conducting a prevalence survey – which requires screening and testing 50,000 to 100,000 people – takes up to three years, from the first preparations to final publication of the results. KNCV has expertise in supporting NTPs in all stages of these surveys: from protocol design, budgeting and planning to implementation, quality monitoring, data analysis and publication. We have supported prevalence surveys in Eritrea, Vietnam, Bangladesh, Pakistan, Tanzania, Rwanda, Ethiopia, and Zambia. KNCV is also involved in strategic discussions on methods, approaches and lessons learned from national TB prevalence surveys for other TB control areas.

**Electronic data collection and management**

Digital systems make data collection and management more efficient and we
Building research capacity

KNCV builds research capacity in countries where this is needed through a comprehensive package of assisting in developing a national research agenda and research programs, operational research courses, supervision of Master and PhD students and mentoring of local researchers. We train people not only to obtain the right data, but also to analyze and interpret them in a systematic way. We also help implement strategies to make sure the data are used properly at all levels, while taking into consideration issues such as confidentiality and research ethics.

Implementation research on Xpert MTB/RIF

Not all doctors are immediately keen on using the new Xpert MTB/RIF test, even though it is praised worldwide for its accuracy and speed. Several research projects, some assisted by KNCV, indicated that doctors often start TB treatment without waiting for the test results because it takes too long to get them back. Moreover, diagnosing TB with Xpert MTB/RIF did not have any effect on treatment outcomes for drug-susceptible TB patients. In contrast, the use of the Xpert MTB/RIF test did lead to increased numbers of patients being diagnosed with MDR-TB. KNCV supported projects also showed a reduction in the time to diagnosis and start of MDR-TB treatment.

With TIBU, a patient can easily complete treatment in another clinic while ensuring that the clinic workers receive all necessary information. In Zambia, KNCV supported the data management of the first fully digital national TB prevalence survey, resulting in much quicker availability of the results, which is commonly the case.