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Rapid Antiretroviral Therapy Scale-Up In Hubei Province, China

An international partnership to train and mentor local health care workers in HIV prevention and care raised physicians’ competence levels and dramatically reduced annual AIDS mortality rates.

by Renslow Sherer, Xien Gui, Faxian Zhan, Caroline Teter, Diana Liu Ping, and Randolph F. Wykoff

ABSTRACT: In 2003, physicians in China were unprepared to care for people with AIDS. Project HOPE partnered with Hubei Province health authorities to train and mentor doctors and build capacity for HIV care. From 2004 to 2006, seventy-eight Chinese “master trainers” were trained, who then trained and mentored 8,759 health workers. During this period, as the free antiretroviral therapy period began, measures of physician competence in HIV care improved significantly, and annual mortality from AIDS fell from 49 percent to 8.8 percent. This international partnership created a sustainable capacity for effective HIV prevention and care that could be replicable in other settings. [Health Affairs 27, no. 4 (2008): 1140–1147; 10.1377/hlthaff.27.4.1140]

In the central Chinese provinces of Henan, Hubei, Anhui, Shanxi, and Shandong, HIV transmissions increased dramatically, after improper plasma donation procedures in the 1990s, to an estimated 250,000 former plasma donors. As a result, the HIV epidemic began in rural villages and townships, far removed from urban and university-based medical centers. By July 2004, 617 people with AIDS were reported in Hubei Province, most of whom were former plasma donors, and secondary spread to spouses and children was observed. Hospitals and clinicians in Hubei Province were poorly equipped to manage AIDS-related opportunistic infections, as evidenced by the reported AIDS mortality rate of 49 percent in 2002, and to prescribe antiretroviral therapy (ART) when it became available in 2003 and 2004.

Of the sixty-nine million residents of Hubei Province, 80 percent are rural farmers. The province contains 32 cities, 347 counties, 4,467 townships, 91,000 villages, and an estimated 73,000 doctors, of whom 4,300 work at the township level and 67,000 work at the village level. The provincial public health authority is the Hubei Province Center for Disease Control and Prevention (CDC), which manages clinics...
at each level. The Hubei CDC is responsible for surveillance and communicable disease reporting, prevention, screening, and treatment, including TB, sexually transmitted infections (STIs), and HIV.3

The Division of Treatment and Care (DTC) in the National Center for AIDS/STD Control and Prevention, China CDC, was established in 2001 to oversee national HIV care and treatment. The DTC began the China Comprehensive Response Program (China CARES) to distribute ART in 2003 as part of the Four Frees and One Care policy. The DTC convened a panel of Chinese and international HIV experts in July 2004 to set the care standards for the use of ART.4

In Hubei Province, the Board of Health and its CDC initiated an ambitious effort in November 2003 to build local capacity for HIV prevention and treatment by training county, township, and village-level health care workers. The principal partners were Project HOPE, Wuhan University, and Zhongnan Hospital. This report summarizes the experience of this training and mentoring program.

The HIV Prevention And Treatment Program

- **Record keeping.** The Hubei CDC maintained provincial records of the gradual scale-up of ART and HIV care starting in 2003–04. County CDCs distributed and monitored ART as it became available. Local CDCs also maintained treatment outcome data, such as CD4 cell counts and mortality, and monitored clinicians’ performance in HIV care through the completion of standardized clinical data collection forms at local clinics, with regular reports sent by fax to provincial and national CDCs.

- **Training and mentoring.** Project HOPE led the training and mentoring program. The partners convened a Senior Technical Advisory Group (SenTAG) of Chinese and international HIV experts in early 2004 at Wuhan University. SenTAG defined the training agenda, the curriculum, the evaluation plan and tools, and the plans for ongoing support and mentoring of the master trainers and the trainees. A cascading Training of Trainers (TOT) program followed from July 2004 to December 2005. Four groups of senior Chinese trainees—for a total of seventy-eight master trainers—were selected by the Hubei CDC and the local county CDCs to be master trainers, based on their clinical skills and experience working with HIV-infected patients. In July 2004, seventy-five physicians chosen by the Hubei CDC met for a five-day training session. Morning didactic lectures were followed by afternoon small-group patient encounters, role playing, and case discussions led by the master trainers. In subsequent training sessions, the master trainers assumed greater responsibility for presentations, case discussions, and ongoing mentoring. The newly developed Chinese CDC Free ART Manual (July 2004) was adapted for use by county-level health care workers. Trainees received manuals and a compact disc of all presentations, materials, and care tools in Chinese and English.

- **Knowledge assessments.** Short-term knowledge improvement was measured by pre- and posttraining knowledge assessments. Mentoring of clinicians and continuous quality improvement were initiated in parallel with training activities. Activities included direct patient encounters, structured chart reviews, case discussions, and assessment of compliance with China’s Free ART Guidelines to assess long-term gains in clinical competence. Monitoring and evaluation were based on test scores, participants’ satisfaction surveys, qualitative and quantitative mentoring outcomes, and standard HIV clinical outcomes such as mortality, retention in ambulatory care, change in CD4 cell count, and maintenance on ART. Finally, the partners conducted a follow-up mentoring and assessment process in the highest-incidence counties in 2006 with local staff, the master trainers, and visiting HIV experts.

Results Of The Program

From January 2002 to August 2006, the Hubei CDC reported that 3,063 people with HIV, most of whom were former plasma donors, were diagnosed and entered into care.
From July 2003 to August 2006, 1,143 patients were started on ART. Of these, 55 percent were male, 77 percent were plasma donors, and 54 percent had an AIDS-defining opportunistic infection (Exhibit 1). Of 751 patients for whom data were available, the mean baseline CD4 cell count was 102 cells/ml. As of August 2006, 62 of 347 counties were administering ART, and the majority of patients with HIV lived in one of five counties or one city (Exhibit 1). Of patients started on ART, as of August 2006, 122 (10.6 percent) patients died and 13 (1.1 percent) were lost to follow-up. Of 1,021 living patients on ART, 848 (83 percent) remained on ART for an average of eighteen months of follow-up. CD4 cell counts were not uniformly available; in 751 patients for whom baseline data were available, an average CD4 cell in-

| EXHIBIT 1 |
| Baseline Characteristics Of Patients With HIV Infection Enrolled In Antiretroviral Therapy Program, Hubei Province, China: 2002–August 2006 |

| Sex | Male | 625 (54.68%) |
|     | Female | 518 (45.32%) |
| Age in years, mean (range) | 39.3 (1–66) |
| HIV risk behavior | Plasma donor/blood transfusion | 76.96% |
|     | Heterosexual | 17.24 |
|     | Men who have sex with men | 0.97 |
|     | Intravenous drug users | 0.97 |
|     | Other | 3.86 |
| Year of enrollment | 2002 | 1 |
|     | 2003 | 262 |
|     | 2004 | 282 |
|     | 2005 | 352 |
|     | 2006 (Aug) | 246 |
| Total | 1,143 |
| AIDS opportunistic infections | Number of patients | 616 |
|     | Percent of patients | 53.89% |
| Mean CD4 cell count (range) among 751 patients for whom data are available | 0–50 cells/ml | 102 (0–597 cells/ml) |
|     | 51–100 cells/ml | 250 (33.29%) |
|     | 100–200 cells/ml | 160 (21.31%) |
|     | >200 cells/ml | 264 (35.15%) |
| County of origin | Suizhou | 224 |
|     | Xishui | 170 |
|     | Badong | 73 |
|     | Daye | 55 |
|     | Wuhan City | 52 |
|     | Dawu | 19 |
|     | Other | 550 |

SOURCE: Hubei Province Center for Disease Control and Prevention.
NOTE: N = 1,143.
crease of 136 cells/ml was seen after twelve to eighteen months. All-cause mortality declined from 49 percent in 2002 to 14 percent in 2005 and to 8.8 percent by August 2006 (Exhibit 2).

- **ART regimens.** The most common initial ART regimen was generic zidovudine, didanosine, and nevirapine. Didanosine was first available in the powdered formulation, leading to high rates (30–50 percent) of gastrointestinal side effects and initial patient dissatisfaction with ART. This problem was mitigated initially by traditional herbal anti-nausea preparations and later by the introduction of didanosine in tablet form and the addition of lamivudine to the national Free ART Formulary in 2005.

- **Training participants.** At all levels of care, 8,759 health care workers—including 2,822 physicians in CDC-run clinics and Board of Health hospitals, 1,940 registered nurses, 1,446 laboratory technicians, and 2,551 administrators—participated in one or more of 85 training sessions and 262 half-day workshops. Seventy-eight master trainers received intensive training as trainers and subsequently conducted broad training sessions at the county, township, and village levels involving an average of fifty health care workers, including a nucleus of physicians on the HIV care team in their clinic or hospital. All participants received pocket ART guides and ongoing mentoring and support from the master trainers and from Project HOPE and partner clinical staff.

- **Community education and counseling.** The partners also conducted community education regarding HIV prevention and treatment, patient and family adherence assessments, and stigma reduction activities in parallel to the clinical training efforts that reached 12,658 youth and 1,997 community members. Ninety-eight percent of people living with HIV reported participation in adherence counseling in the previous three months. In CDC surveys of 138 and 192 patients on ART in 2005 and 2006, respectively, 86 percent of respondents reported 95–100 percent adherence to medications over the past three days.

- **Knowledge scores of trainees.** Mean-training participant scores on posttraining knowledge assessments showed improvement, with an average increase of 28 percent, compared to pretraining test scores. Trainees’ satisfaction levels were a mean 9.6 on a scale of 1 (least satisfied) to 10 (most satisfied). Significant improvement in trainees’ knowledge and clinical competence was observed in standardized instruments of conformity with the Free ART Manual.

- **Assessment of clinicians’ skills.** Conversely, deficiencies in physician skills were identified that persisted over time, including the lack of ability to synthesize and present clinical cases and engage in complex clinical

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**EXHIBIT 2**
All-Cause Mortality Among People With HIV/AIDS In Hubei Province, China, By Year Of Diagnosis, 2002–August 2006

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**SOURCE:** Hubei Province Center for Disease Control and Prevention.
reasoning and differential diagnosis and knowledge of the use of diagnostic tests and treatments that were unavailable in China. Additionally, each master trainer was observed and mentored in the presentation of HIV lectures and answering questions.

Finally, 143 CDC physicians with experience with five or more patients participated in the follow-up mentoring and assessment of clinicians' performance in 2006 in the six highest-incidence counties. Proficiency in the implementation of the Free ART Guidelines was assessed by the performance on five indicators of clinical care, including the appropriateness of ART initiation, adherence counseling, lab monitoring, hepatitis B screening, and management of nevirapine rash. Physician participants demonstrated 81–93 percent adherence to the Chinese guidelines on these indicators.

Clinical oversight. Two infectious disease physicians from Wuhan University, one nurse, and one Project HOPE HIV clinician expert provided on-site clinical oversight of the program with the master trainers. Program administration for the training sessions was provided by a senior administrator and supporting administrative staff at Project HOPE, and the Hubei CDC was led by the AIDS program director under the Hubei CDC director.

Discussion

This is the first report of a provincewide effort to scale up ART in China. Our experience suggests that rapid scale-up of HIV care and treatment, including ART, using existing health care worker capacity and a cascading TOT methodology is feasible and effective in rural areas of China. Improvements in clinical knowledge and competence contrast sharply with an anonymous survey of basic HIV knowledge among 1,400 Chinese health care workers in eleven provinces conducted in 1999, which found a very low level of knowledge of HIV/AIDS among them (that is, the frequency of correct responses to HIV knowledge and treatment questions ranged from 3 percent to 68 percent). The observation of rates of adherence above 95 percent in 86 percent of rural residents with HIV at this early point in the epidemic compares favorably with the reported experience in Hunan Province in mid-2006, in which 80 percent of 308 rural patients reported taking 90 percent or more of their prescribed doses in the previous week.

High ART adherence rates. Similarly, the observation of rates of adherence above 95 percent in 86 percent of rural residents with HIV at this early point in the epidemic compares favorably with the reported experience in Hunan Province in mid-2006, in which 80 percent of 308 rural patients reported taking 90 percent or more of their prescribed doses in the previous week.

Satisfactory treatment outcomes. Finally, satisfactory ART treatment outcomes were observed in more than two-thirds of treated patients, characterized by increases in CD4 cell counts of an average of 138 cells/ml and the declining mortality rate. These outcomes compare favorably with the outcomes in eighteen ART scale-up programs in developing countries in Asia, Africa, and South America, in which the median CD4 cell increase was 103 cells/ml after six months and declining mortality rates were reported. In those programs, the loss-to-follow-up rates were 12–19 percent.

Declines in mortality. While provincewide mortality data from other provinces are not available for comparison, our finding of an 82 percent decline in mortality in 3.6 years in Hubei Province and a mortality rate of 8.8 percent in 2006 compare favorably with available HIV mortality survey data reported by the national China CARES Center. Zhang reported an 11 percent overall mortality in 2006 and a 76 percent decline in mortality from 28.8 per 100 patient-years in 2002 to 6.8 per 100 patient-years at the end of 2006.

Overall Evaluation And Future Directions

Three important features of the capacity-building program were the development of HIV expertise in local CDC staff as Chinese master trainers, the triage of the effort to coun-
ties with the highest HIV burden, and the on-
going mentoring and consultation from both an on-site American expatriate Project HOPE expert and a leading Chinese HIV expert to the master trainers. The role of the expatriate resident clinical expert was essential to this program, a conclusion also reached in the small pilot ART program in Jilin Province. These practices may be of value to the effort to reform the current Chinese medical education system and, in particular, to establishing an effective medical care network in rural settings.

The Hubei CDC linked this training program to the rapid expansion of HIV prevention and testing centers, and thus increased the likelihood that people who tested positive would be able to obtain ART and receive well-informed health care. The aggressive and enlightened central government HIV policies in 2001 (creation of the DTC and the China CARES Program as part of the Four Frees and One Care initiative) were essential drivers and creative stimulants of these actions in Hubei Province.

Contributions of the partners. Each partner provided services that were critical to the training and mentoring program. The Hubei CDC selected the master trainers and the trainees, enabled ongoing mentoring at the CDC clinics, and maintained clinical records. Wuhan University contributed expert clinician time and training space, and Zhongnan Hospital provided training space at the Zhongnan Hospital HIV Training Center. Project HOPE contributed the TOT training methods, state-of-the-art training materials in Chinese and English, program resources and administration, training records, and resident expatriate expert clinical faculty for the duration of the program.

Value of the TOT approach. The TOT approach in this program gradually elevated local physicians and other health care providers to an adequate level of knowledge and skills over time through mentoring conducted by Chinese physicians under the guidance and oversight of expert clinicians. Thus, the project nurtured a cadre of Chinese master trainers with HIV knowledge and clinical skills combined with the critical operational knowledge caring for people with HIV in Hubei Province. These activities strengthened the durability of the program’s outcomes and the sustainability of high-quality care for people living with HIV in Hubei Province.

Training in other provinces. Scant information is available regarding HIV training in other provinces. By June 2005, only 700 physicians nationally were reported to have received five-day training sessions conducted by the China CARES Program, and another 520 physicians participated in a two-month residency. The Pangaea Global Health Foundation conducted week-long training sessions in Yunnan and Anhui Provinces in preparation for HIV clinical care centers and shared methods, faculty, and training materials from Project HOPE. Although the outcomes are as yet unknown, these projects also placed an emphasis on a resident expatriate HIV expert to ensure longitudinal mentoring of local clinicians, rather than relying on single, short-lived training sessions.

Obstacles along the way. Major obstacles were encountered during the implementation of this program. For example, rural physicians had the equivalent of an eighth-grade education in the United States, followed by five years of medical school, in which a passive “apprenticeship” approach was used for clinical training. As a result, physicians demonstrated low competence in medical case presentation, clinical reasoning and differential diagnosis, and treatment planning. Supplemental modules to develop these skills were introduced, but this obstacle will need to be addressed at the level of health professional schools in China as part of their planned medical education reform.

Regular longitudinal follow-up for medical problems was unfamiliar to physicians and patients in China. To address this challenge, the Hubei CDC used home visits and patient visits to special community centers known as “warm houses,” and the project emphasized the guideline requirement for regular follow-up. Similarly, rural physicians were not experienced in the principles of early diagnosis and
disease prevention. Thus, the stigma of HIV testing was not offset by any perceived health benefit of early treatment, and the uptake of HIV testing was slow—a problem that persists today.

The project jointly trained local CDC and hospital physicians to develop care linkages with some success, but reform at the national level will be necessary to address the impact of privatization, decentralization, and underfinancing of public health services. Central government programs to provide US$1,000 stipends for each patient with AIDS and to provide health insurance have offered partial relief, and the goal of national health reform is to provide basic medical services to the entire population by 2020.13

**Dealing with stigma.** Although stigma toward people with HIV improved over time, it remains a potent obstacle to effective prevention and care.14 Health care workers and hospitals that serve people with AIDS commonly suffered secondary discrimination. The leadership of the CDC was essential to ensure physicians’ participation in the project by making it mandatory.

**Deficiencies in rural health care.** Systemic deficiencies in health care in rural China posed additional obstacles, many of which persist today. CD4 cell counts and other important diagnostic tests were not widely available until 2005, and many medications for opportunistic infections, such as gancyclovir and rifabutin, were either too expensive or unavailable. Viral load testing was unavailable and is only in limited use currently, resulting in prolonged periods of viremia in failing patients and a high level of ART resistance in 17 percent of patients with detectable viremia.15 Even with greater availability of viral load testing, cost considerations may limit their regular use.

**Future directions for HIV care.** Our findings reinforce lessons for the future direction of HIV and health care in China.16 The partners encountered insufficiently trained staff, inadequate technical resources, and a fragmented health system with no incentive to support hospital care for people with HIV. The same enlightened pragmatism that led the national CDC to expand methadone clinics and harm reduction to reduce the spread of HIV among intravenous drug users will be necessary to address the persistent obstacles in rural health care that we encountered in Hubei Province. Expanded efforts to reduce stigma are needed to enable the identification of HIV-infected people and safely enroll and retain them in care. Ensured access to high-quality health care that includes coordinated hospital and ambulatory care is an urgent national priority for those unable to afford health care. China has the resources to invest in the rural health infrastructure, but bolder steps than limited health insurance and stipends to special populations may be required.

To achieve high-quality care in rural settings, our experience suggests that reform of the medical education system will be required. Needed are curriculum content that meets international standards and is regularly updated, as well as training and mentoring methods that nurture the independence and clinical decision making of doctors in training and reward service at the county, township, and village levels. Mechanisms for postgraduate placements in community medicine clinics that merge opportunities for service and research at the county and township levels, and mechanisms for adequate reimbursement for physicians and hospitals may be useful to jump-start this process. The recent memory of the effectiveness of China’s “barefoot doctors” could be an effective tool to use in motivating practitioners and moving public opinion behind such an effort, if the economic rewards and academic incentives are sufficient.
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NOTES
11. “China to Pilot Medical Reform Plan This Year” (Editorial), Chinese Medical Journal 121, no. 3 (2008): 199.