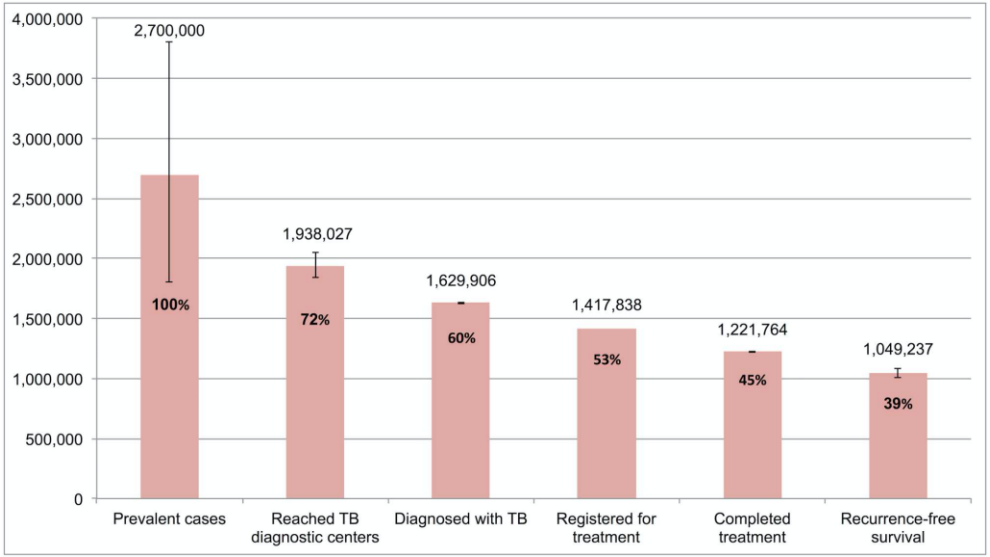
Tackling TB In The Time of COVID-19

Digital Adherence Technologies and Other “Ready-Now” Tools To Facilitate More Differentiated and More Virtual Care For Persons Affected By TB

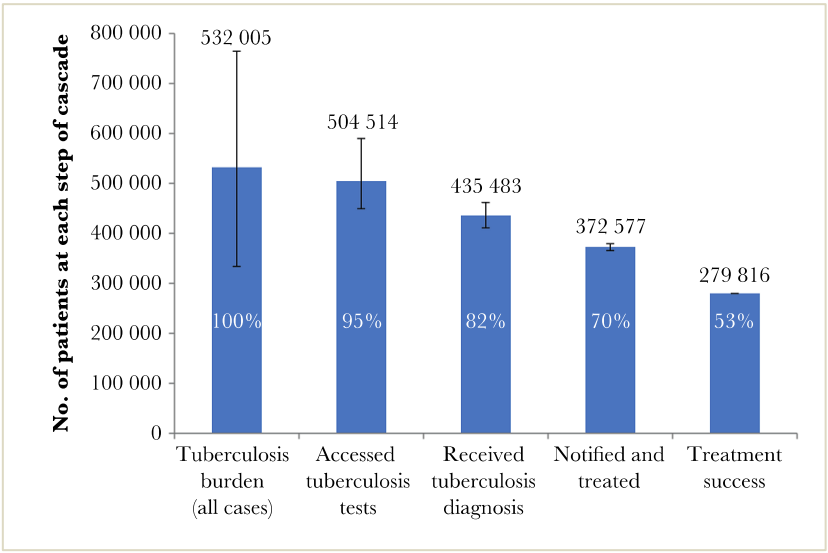
TB IS A TREATABLE AND CURABLE DISEASE, AND YET . . .

In Many High Burden Regions Health Outcomes Remain Suboptimal

All Forms of TB – RNTCP in India



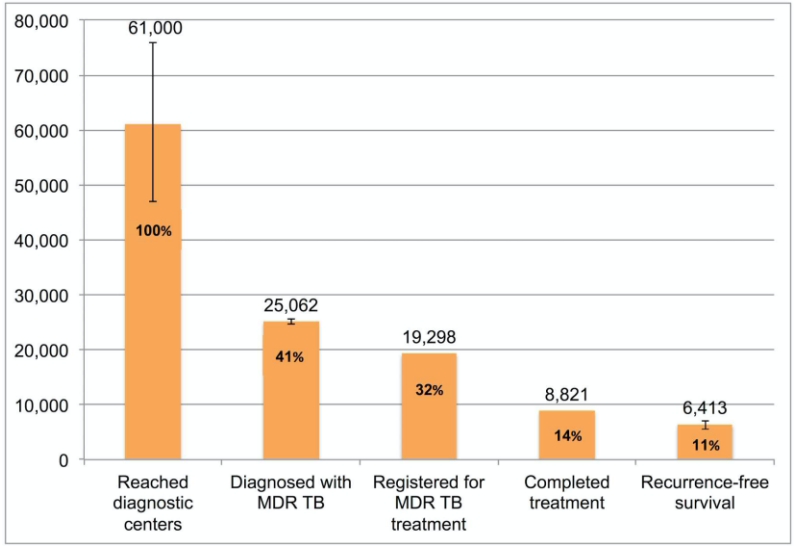
All Forms of TB – South Africa



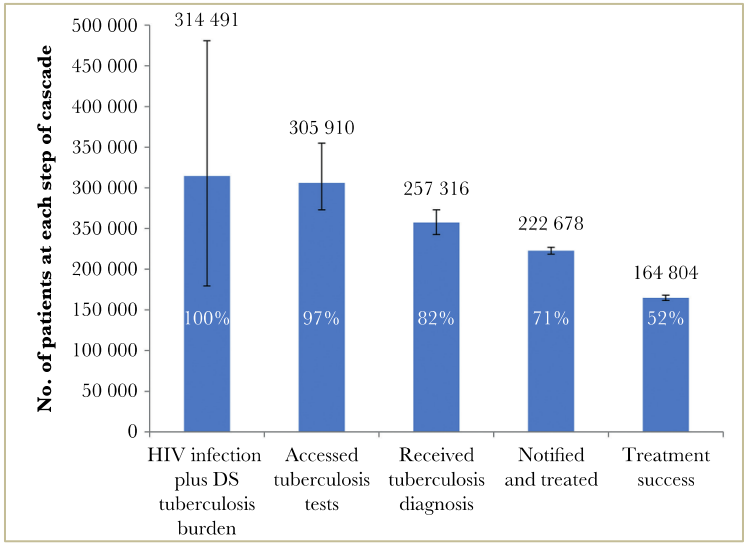
* Subbaraman R, Nathavitharana RR, Satyanarayana S, Pai M, Thomas BE, et al. (2016) The Tuberculosis Cascade of Care in India's Public Sector: A Systematic Review and Meta-analysis. PLOS Medicine 13(10): e1002149. https://doi.org/10.1371/journal.pmed.1002149

FOR MDR-TB AND TB/HIV-AFFECTED PEOPLE, THE SITUATION IS EVEN WORSE

MDR-TB Patients – RNTCP in India



TB/HIV Patients – South Africa



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AND COVID-19 HAS MADE THINGS WORSE*

- Fewer people tested and treated for TB
  - An 18% reduction in 2020 compared to 2019
- Fewer people treated for MDR-TB and for XDR-TB
  - Persons on MDR-TB treatment declined by 19%
  - Persons on XDR-TB treatment declined by 37%
- Fewer HIV-positive TB patients treated for HIV and TB
  - Persons on ARV and TB treatment declined by 16%

Overall, Around 1,000,000 Fewer Persons Affected By TB Were Treated In 2020 Compared To 2019

* Results Report 2021, The Global Fund

PARADOXICALLY, COVID-19 HAS ACCELERATED THE SCALED ADOPTION OF SOME OF THESE NEW TOOLS

- Care for persons affected by TB was already moving away from pure facility-based care (e.g., DOT to SAT). Health facility access challenges during COVID-19 have accelerated that "medication custody" shift.

- Health facility access challenges also have forced TB programs to rely on alternative options, such as digital adherence and tele-health technologies, to bring required TB services to the people and communities affected by TB.

"COVID-19 has catalyzed a multitude of innovations across all three diseases, such as multi-month dispensing of TB and HIV drugs; using ***digital tools to monitor TB treatment or enhance prevention interventions***; and introducing patient-centered diagnostic approaches, such as co-testing for HIV, TB and COVID-19. Many of these innovations will outlast the crisis and strengthen our fight against HIV, TB and malaria." (emphasis supplied)

Results Report 2021, The Global Fund, Letter From The Executive Director

ADHERENCE TO TB TREATMENT IS ESSENTIAL

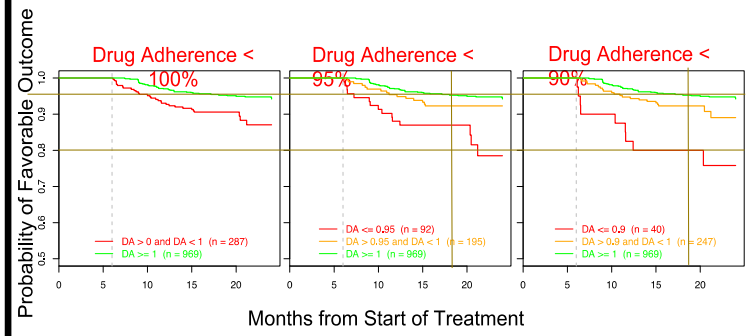
We Also Know That Baseline Adherence Is Poor

- Adherence Is A Multi-Factor Behavioral Issue That Changes Over Time
- Some of The Reasons for Poor Adherence:
  - Long, complicated regimens,
  - Dosing confusion,
  - Side effects,
  - DOT, which is:
    - burdensome on patients
    - inconsistent with patient lifestyle
    - stigmatizing

Severity of non-adherence (in patients who "completed treatment")	TB recurrence rate, 18 months after completing treatment
"Regular" adherence (Complete treatment within 8 months)	9%
"Irregular" adherence (Complete within 10 months)	15%
"Very irregular" adherence (Complete treatment within 12 months)	25%

Study of 534 smear + patients in India found a strong relationship between adherence and post-treatment TB recurrence.

Source: Thomas et al. Int J TB Lung Dis 2005; 9(5): 556-61[6]



TB patients taking HRZE with <90% adherence had 5.6 times increased risk of TB recurrence in a meta-analysis of the OFLOTUB, REMox, and Rifaquin trials.

Source: Nature Medicine, 2018, Volume 24, Number 11, Page 1708, Marjorie Z. Imperial, Rada M. Savic, et al.

There Is Now Real Hope For Better, Shorter Regimens
In The Interim, We've Developed Tools To Improve Treatment Outcomes By Mitigating **THESE** Challenges To Treatment Adherence

INTEGRATED DIGITAL ADHERENCE TECHNOLOGIES

Everwell

sureAdhere

wisepill

Three Independent Entities Have Collaborated to Create One Integrated System Providing Technology **CHOICES** To Patients and Providers

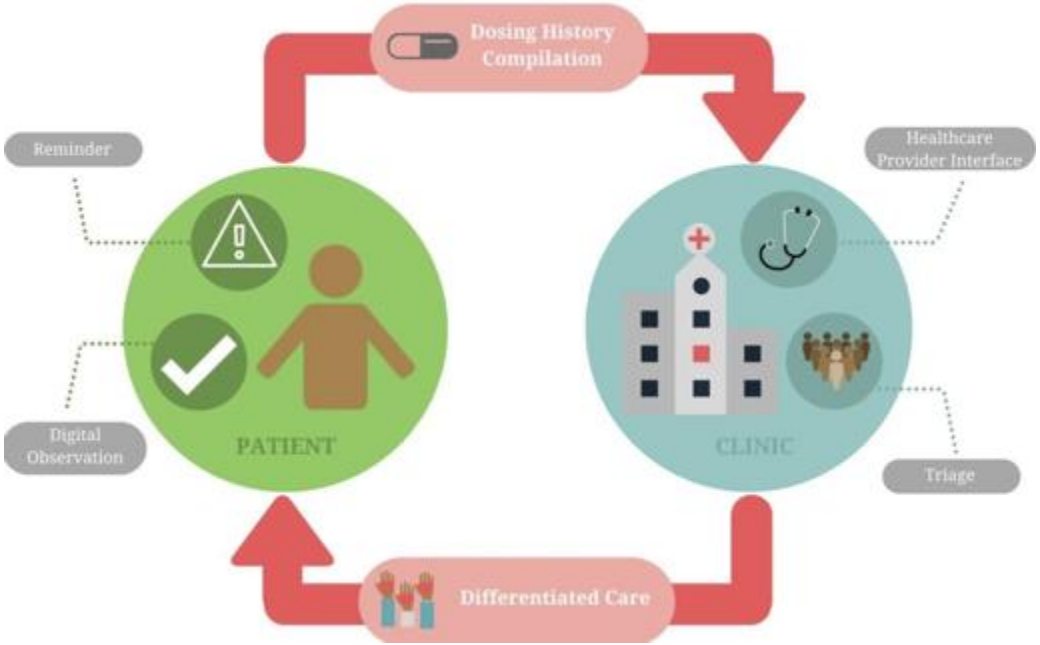
99DOTs: Uses augmented packaging to reveal codes as a person takes their medication. Users report their dose adherence through a toll-free call or SMS.

VOT/ VDOT: Video-observed therapy allows for people to share videos of them taking their medication. Nurses or healthcare workers can review the videos to understand adherence.

evriMED/ MERM/ Smart Pillboxes: All these terms refer to an electronic pillbox which holds medications in a box with reminders and alerts. When the box is opened, the device sends a signal reporting adherence.

The Everwell Hub: An open-source digital platform that allows providers to register patients and allocate them to any of the three DATs using a web-based dashboard, or Android mobile application. Behind secure logins, providers can also review historical adherence, task lists, and other data.

DAT – TOWARD DIFFERENTIATED AND VIRTUAL CARE



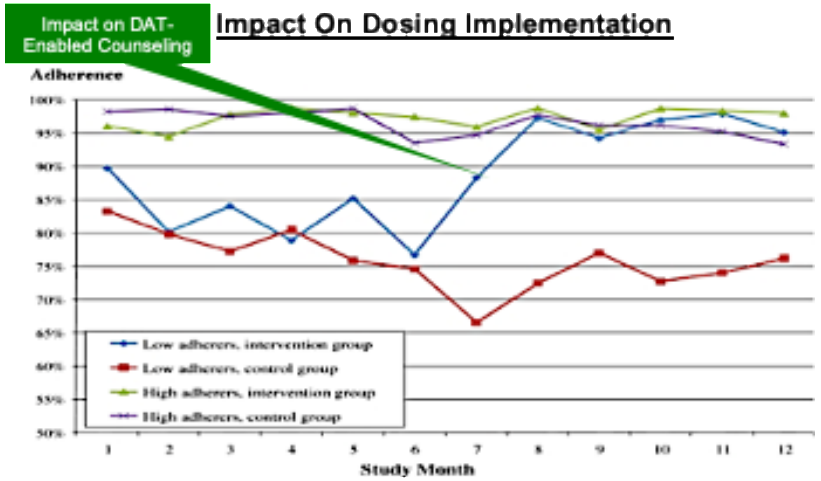
* Subbaraman R, de Mondesert L, Musiimenta A, et al Digital adherence technologies for the management of tuberculosis therapy: mapping the landscape and research priorities. BMJ Global Health 2018;3:e001018.

DAT-Enabled Differentiated Care – How It Works:

1. DATs provide self-administering patients with reminders or other **dosing assistance** – medication organizers, pictograms, labels
2. DATs **electronically observe/verify daily dosing** and deliver detailed dosing histories to health systems
3. Applying evidence-based escalation protocols, dosing histories are used to **continuously triage patients** and identify patients who are problematically non-adherent
4. Those non-adherers are **prioritized for engagement** by providers to understand and to address reasons (side effects, refill required, asymptomatic) for poor adherence

WHY THIS APPROACH?

- **Low patient burden** -- Patients are left alone unless they are demonstrably having adherence issues
- **Transparent** -- Both patients and providers can see the patient's dosing history – promoting trust and transparency
- **Just Another "Vital Sign"** – like BP, weight
- **Behavioral Insights** -- Dosing histories highlight specific non-adherence patterns unique to each patient
- **Enables/Informs Patient-Provider Discussions:**
  - of the specific adherence challenges each patient is experiencing,
  - of specific steps the patient can take to address their specific adherence challenges
- **It's WHO Approved --** Based On Favorable Results from A Range Of Trials Conducted In US, EU, and High Burden Regions



"... a simple intervention involving monthly adherence counseling based on DAT feedback significantly improved mean adherence among Chinese ART patients. **We found an impact on adherence that was both very high — above the 95% threshold — and sustained**, with mean adherence above 95% throughout the 6-month intervention period." Sabin et al. AIDS Behavior, 2010.

PROGRESS MADE THROUGH SPRING, 2020

Supportive Guidance for DAT from WHO Issued

Catalytic Innovation Phase	Proof of Concept Phase	Early Implementation Phase	Transition to Scale Phase	Continued Innovation Phase
Everwell wisepill		TB REACH —WAVE 6—	Unitaid	GH+ Labs
Early catalytic funding from BMGF developed the core DAT tool kit – MERM device, 99DOTS, and Everwell Hub (Nikshay)	China deploys and rigorously evaluates MERM technology and approach, and India deploys and evaluates IDAT approach and Nikshay platform.	TB REACH grantees deploy and evaluate DAT in 13 projects across 11 countries. 	UNITAID funds "transition to scale" grant to a consortium (KNCV, Aurum, PATH, LSH&TM) to scale-up DAT to 70,000+ patients (DS, DR, and LTBI), in 5 countries. The Global Fund Beginning in 2020, Global Fund supports and facilitates inclusion of DAT in country program requests for multi-year funding. Approximately 13 countries applied for DAT support	GH Labs leading innovation to develop new and improved DAT for DS and DR-TB, based on implementation lessons learned. BILL & MELINDA GATES MEDICAL RESEARCH INSTITUTE Gates MRI uses DAT in TB clinical trials, creating adherence "closed loop" across clinical trials and clinical practice

Over 400,000 People Using DATs In Clinical Trials And Clinical Practice Across More Than 25 Countries

KEY INSIGHTS, AND HOW COVID-19 HAS "HELPED"

- DATs are relatively affordable, readily scalable, and well accepted by patients and providers
- If health care professionals don't engage, patients disengage
- Escalation-based task lists generated for each provider facilitate patient engagement and follow-up
- **Patients see their DAT as a connection with their provider and want the DAT tools to facilitate and leverage that connection:**
  - **E-prescribing and refill**
  - **Questions about facility locations, hours of operation, etc.**
  - **Questions about dosing**
  - **Questions about side effects**
  - **Questions about direct benefit transfer**
  - **Desire for more "virtual care"**

Because facility access has been challenging during COVID-19, there has been tremendous focus on enhancements that facilitate "at home" and more "virtual care"

The DAT Toolkit Has Evolved To Support That Model*

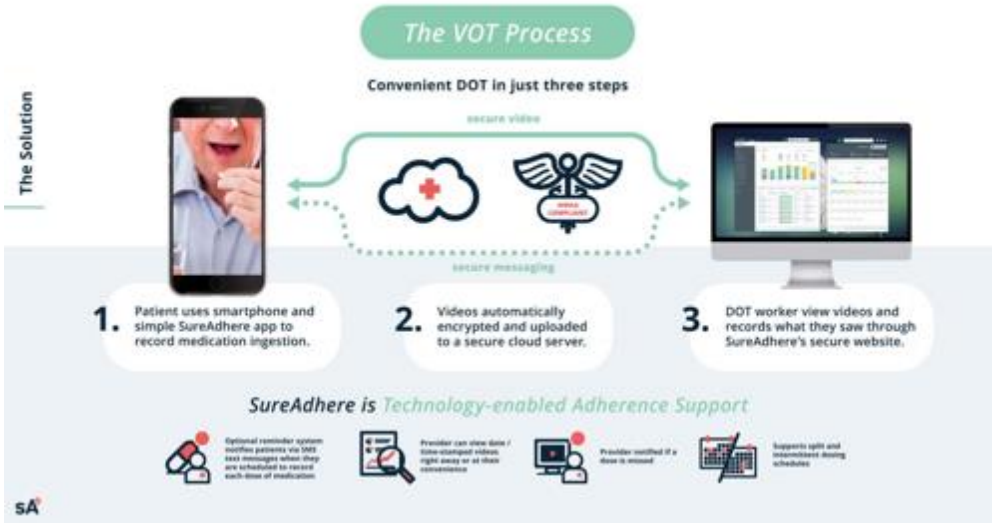
* For a comprehensive listing of other digital tools helping to "re-imagine TB care," visit the website of the Re-Imagining TB Care Project at **www.reimaginingtbcare.org**

RECENT PROGRESS IN PATIENT ENGAGEMENT/VIRTUAL CARE

Everwell Hub partner application to support better citizen and patient engagement, review and manually indicate adherence, and **reach out to providers for virtual care**.

India's Nikshay partner application to deliver health information, **identify symptoms**, **locate facilities**, review and indicate adherence and **view direct benefit payments**.

VIDEO OBSERVATION TECHNOLOGY: NO LONGER JUST DOSE MONITORING



HOW ASYNCHRONOUS VOT WORKS

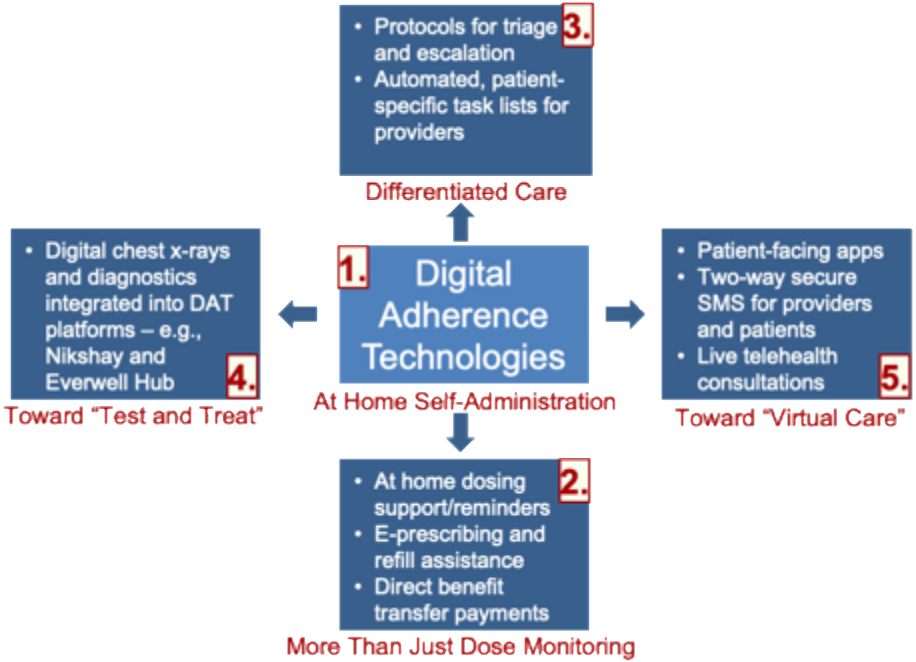
Some Of The Real-World Advantages of An Asynchronous Approach:

- 'Check-in' videos may be recorded according to personal schedules;
- Videos can be be recorded with or without a network signal;
- Video upload process is fully automated to prevent mistakes or tampering;
- Provider may view videos when convenient and follow up as required.

- SureAdhere's VOT can operate as a stand-alone system or can be part of an "integrated" DAT approach via the Everwell Hub
- SureAdhere (and other VOT solutions) can be used in clinical trail as well as clinical practice-programmatic settings:
    - For clinical trials, these technologies provide complex regimen support and pill-by-pill dosing histories
- In clinical practice-programmatic setting and driven by the facility access challenges of COVID-19, several "virtual care" features have been added:
    - **Two-way secure SMS between provider and patients** facilitates engagement around issues such as dosing confusion and side effects,
    - Soon, SureAdhere's VOT will enable **Zoom interaction to enable "live" teleconsultation** if and as required

CONCLUSION – COVID HAS ACCELERATED A SHIFT TOWARD LARGELY "AT HOME CARE" FOR PERSONS AFFECTED BY TB

- COVID-19 has created unprecedented willingness to consider changes in traditional facility-based care and tools
- During this time, existing digital adherence technologies have been leveraged to move toward a more "at home care" model:
  - **Step 1** – self-administering patients remotely monitored
  - **Step 2** – self-administering patients receive dosing and other support
  - **Step 3** -- dose history-informed differentiated care
  - **Step 4** – integrated diagnostics move us toward a "test and treat" model
  - **Step 5** – patient-provider engagement moves toward more virtual care



COVID-19 Has Moved TB Care To More Of An "At Home" Model. The Toolkit Has Evolved To Support That Model. Let's Not Go Back To Largely Facility-Based Care!

* This More "Virtual Care" Toolkit Is Being (i) Widely Used In TB Drug Development Trials, (ii) Scaled Up In Programmatic Settings In India, (iii) Rigorously Evaluated by ASCENT, and (iv) Demonstrated in 10-12 Other Global Fund Countries.