Panel Discussion Innovative Measures
Ingestion Sensor Based Technology

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Disclosures

• No commercial disclosures
Definition of Adherence

• The extent to which a person’s BEHAVIOUR .... coincides with medical or health advice -- Haynes, 1979

• Drug dosing history defined by size of doses, time-intervals between doses & duration of treatment.

• Satisfactory Medication Adherence is achieved when the gaps between a patients dosing history and the prescribed dosing regimen have little or no effect on therapeutic outcome. (John Urquhart/Terry Blaschke)
Dominant 21st Century Technology

• We are all ‘wired’, carrying cell phones
• ‘Wired’ means real-time data transfer
• Optimal Adherence System? Accurate measurement of medication ingestion to provide dosing history, utilizing WiFi/Cellular networks to relay real-time data
DHFS incorporating edible ingestion sensor technology developed by Proteus Digital Health (PDH), Redwood City, CA.

First technology that allows date- and time-stamping of actual ingestions of oral medications.

Designed as a self-management tool.

Allows remote viewing of ingestion data in near real-time.

Digital Health Feedback System
Edible Sensor

- Microchip, 1 x 1 x 0.45 mm, coated with very thin layers of commonly ingested excipients (minerals and metals)
- The active layers are thin films of magnesium and cuprous chloride with a gold under-layer that acts as current collector
the sensor

proteus
Patient Set Up
Patients Change Patch and Follow Progress
Clinical Safety and Approvals

No adverse events occurred in relation to sensor from >20,000 human ingestions

Some self-limited skin rashes at patch site (<10%)

July 2015 FDA cleared for the measurement of adherence.

FDA approval for Abilify Mycite (apiprazole tablets with sensor)

Oct 2017
Digitizing Medications: combination with edible sensor

a) Edible sensor-in-Tablet Assembly ‘Abilify Mycite’

b) Edible sensor-on-Tablet Assembly using transparent excipients for attachment.

c) Co-Encapsulation
Co-encapsulation

- Repackaging evaluated by randomized cross-over PK (Rifamate, Isoniazid)\(^1\)
- Dissolution and/or PK (Rifinah, Genvoya, Truvada, Descovy, Tivicay, Odefsey)\(^2\)
- Dissolution (multiple)\(^3\)
- No difference in co-encapsulated and native drug.


Report for 11 Weeks
21st Jun 2015 - 5th Sep 2015

PATCH SENSED

Medication Adherence

- **All Medications**
  - 100% On Time
  - 128 Pills

- **Rifamate 150 / 300mg**
  - 100% On Time
  - 128 Pills

- **Proteus Pill**
  - -- On Time
  - 1 Pill

Steps
- **3,994 Steps**
  - Daily Average

Activity
- **0 hr 46 min**
  - Daily Average

Rest
- **11 hr 12 min**
  - Daily Average

Heart Rate
- **81 bpm**
  - Daily Average

Blood Pressure
- **-- / -- mmHg**
  - Daily Average

Weight
- **-- lb**
  - 30 Aug 2015
Captures longitudinal drug dosing patterns
Can support medication adherence
TB: ‘Wirelessly Observed Therapy’

**WOT VS DOT**

- 75 Active TB patients in continuation phase
- The Positive Detection Accuracy of WOT 98.4% (CI 97.5-99%) \(^1\)
- WOT outperformed DOT in randomized study \(^2\)

<table>
<thead>
<tr>
<th>7 days</th>
<th>Total number of confirmed doses/ prescribed doses</th>
<th>DOT</th>
<th>WOT</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Mean 62.3 %</td>
<td>2372/3808</td>
<td>7326/7574</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median percent (%) of confirmed doses for each subject (95% CI)(^a)</td>
<td>63.6 (58.3, 67.6)</td>
<td>97.7 (95.5, 98.3)</td>
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</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>5 days</th>
<th>Total number of confirmed doses/ prescribed doses</th>
<th>DOT</th>
<th>WOT</th>
<th>P-value</th>
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</thead>
<tbody>
<tr>
<td></td>
<td>Mean 87.2%</td>
<td>2372/2720</td>
<td>5263/5436</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Median percent (%) of confirmed doses for each subject (95% CI)(^a)</td>
<td>89.9 (82.2, 95.2)</td>
<td>97.9 (95.7, 98.8)</td>
<td></td>
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</tr>
</tbody>
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Notes: \(^{a}\) Percent calculated at the subject level (total number of confirmed doses/total number of prescribed doses for each subject) CI = confidence interval

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2. Browne SH et al. CROI Boston 2018
Ongoing Studies

- TB Treatment
- HIV Treatment
- PrEP
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