SMART TRIALS: ASSESSMENT OF AT-HOME SAMPLING AND DIGITAL HEALTH TECHNOLOGIES IN A CLINICAL PILOT TRIAL

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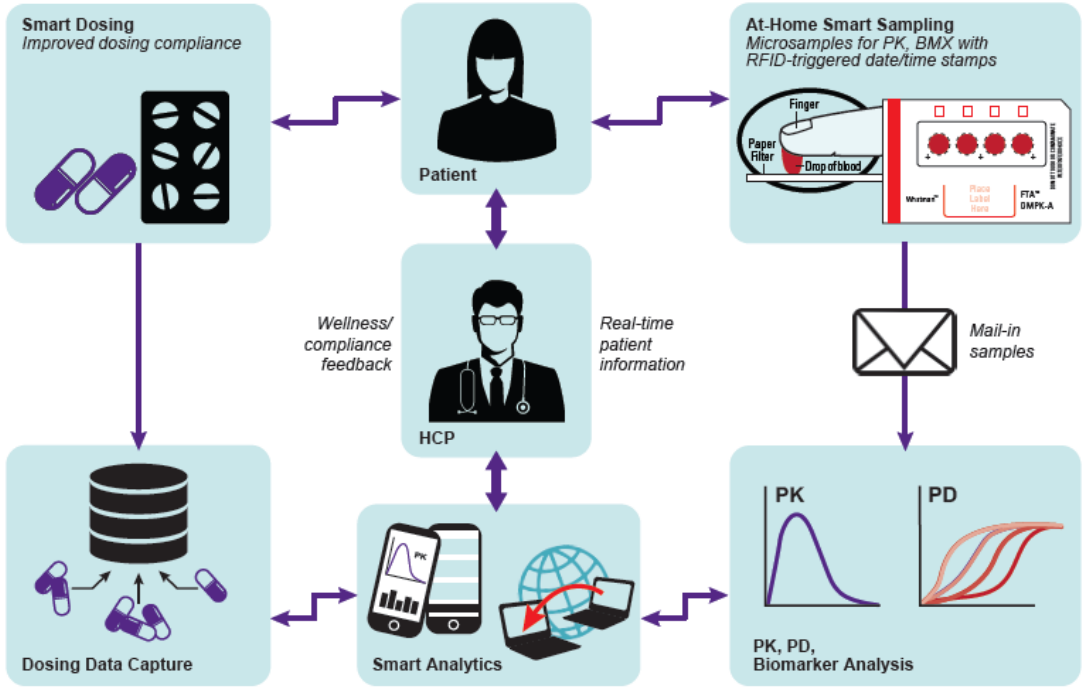
Smart Trials: A Patient Centric Approach to Enriching Clinical Trial Data

Smart Trials is a cross-functional, multi-year innovation project at Merck & Co., Inc. aimed at **enriching clinical trial datasets** and enabling more **rapid and informed clinical decisions** through a **patient-centric approach**

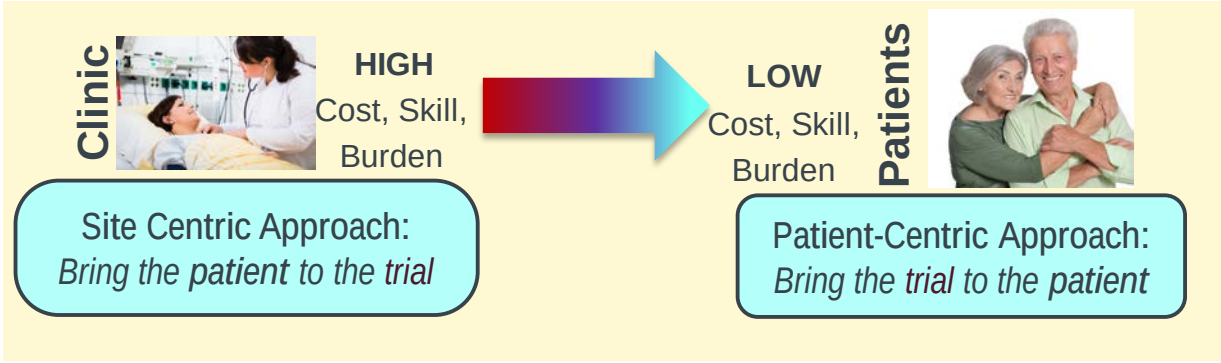
Smart Dosing: mobile technologies to accurately monitor dosing information (i.e. if and when the patient took the drug)



Smart Sampling: technologies for use in the outpatient setting to collect PK, PD, or biomarker samples coupled with date/time stamps

Smart Analytics: technology options to collect, integrate, and visualize data and make it available in real time

Disclaimer: These are just a few examples of the technologies and not an endorsement of any product.



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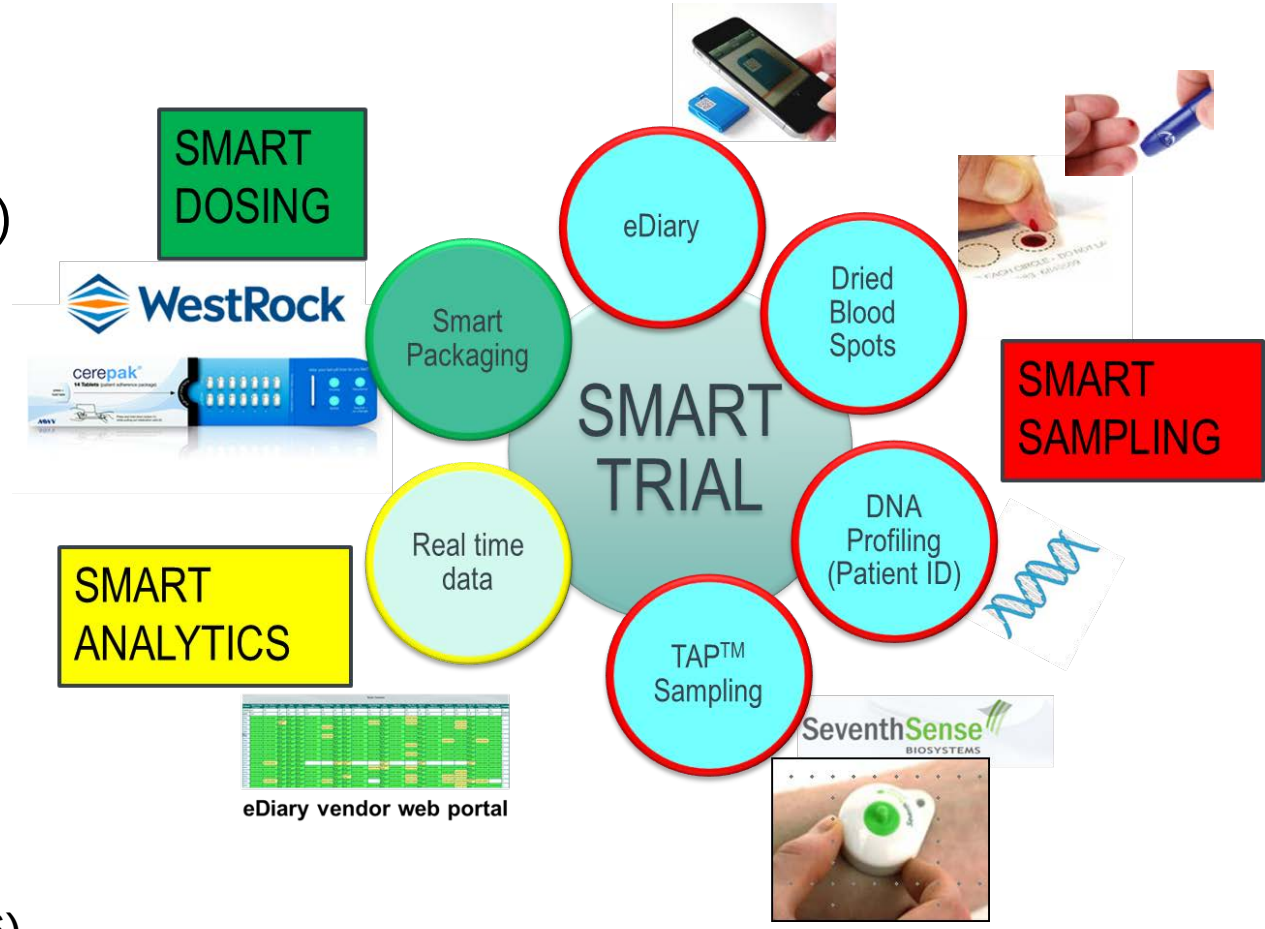
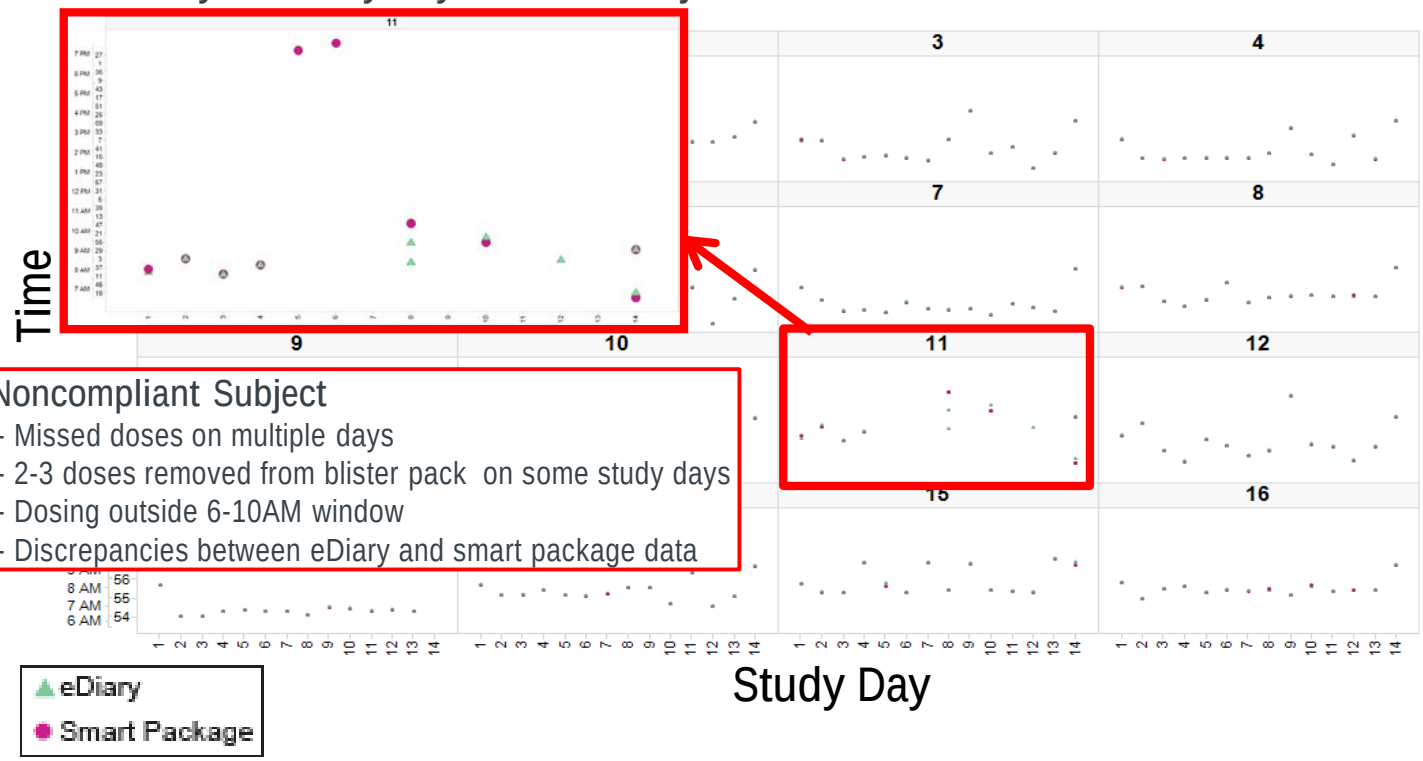
Clinical Pilot Study Design

- 2 period, fixed sequence study
- 100 mg QD sitagliptin administered to 16 healthy subjects
- Period 1 – “Smart” dosing & sampling (Days 1-14)
  - In-clinic training
  - Dosing date/time captured via smart packaging (passively) and eDiary (patient-reported)
  - In-clinic PK sampling (Days 1,14)
  - At-home PK sampling on (Days 5, 8, 10, 12)
  - eDiary for date/time capture of PK samples
  - In-clinic blood collections via TAP™ (Days 1, 14)
- Period 2 – “Traditional” dosing & sampling (Days 15-16)
  - Traditional packaging
  - In-clinic dosing (Days 15-16) and sampling (Day 16), with date/time captured by clinic staff
- Questionnaire for subject feedback



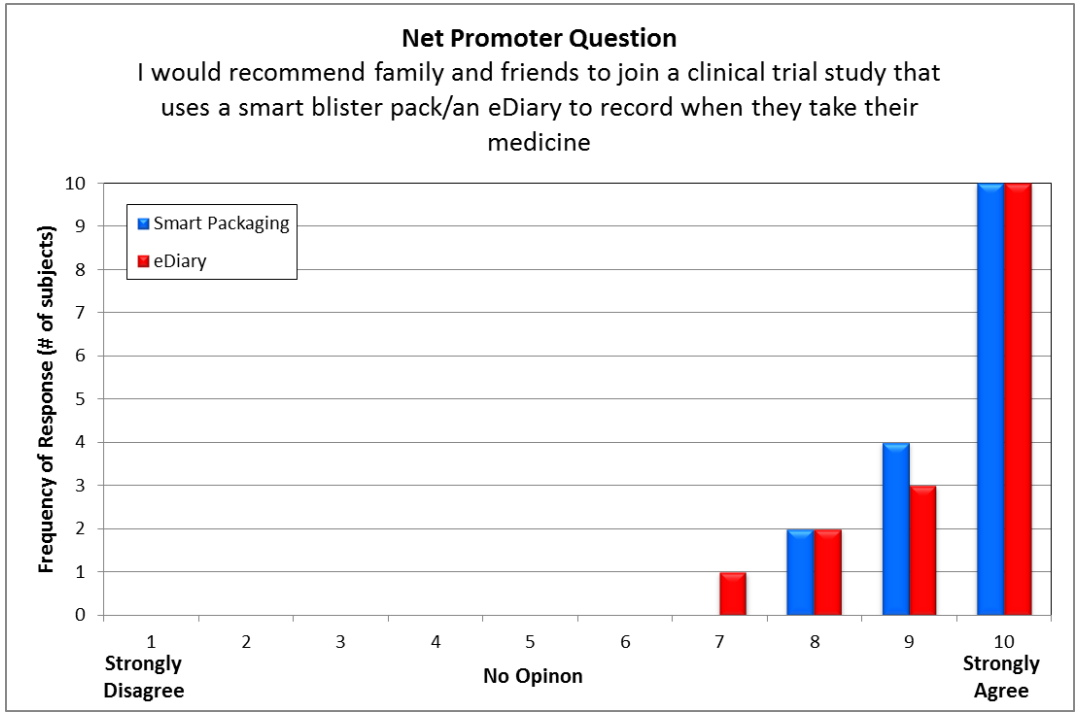
Smart Dosing Results

Dosing Times in Period 1 Captured by Smart Packaging and Self-Reported in eDiary vs. Study Day for Each Subject



Noncompliant Subject
- Missed doses on multiple days
- 2-3 doses removed from blister pack on some study days
- Dosing outside 6-10AM window
- Discrepancies between eDiary and smart package data

Subject Questionnaire Results



- Noncompliant subject highlights importance of collecting this type of data
- Most subjects were strong supporters of the smart packaging and eDiary technologies and found the technologies easy to use
- Data from this pilot trial support future use of smart packaging in clinical trials

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Note: Four data points between 11 AM and 9 PM are not shown in above figure (3 from Smart Package and 1 from eDiary)

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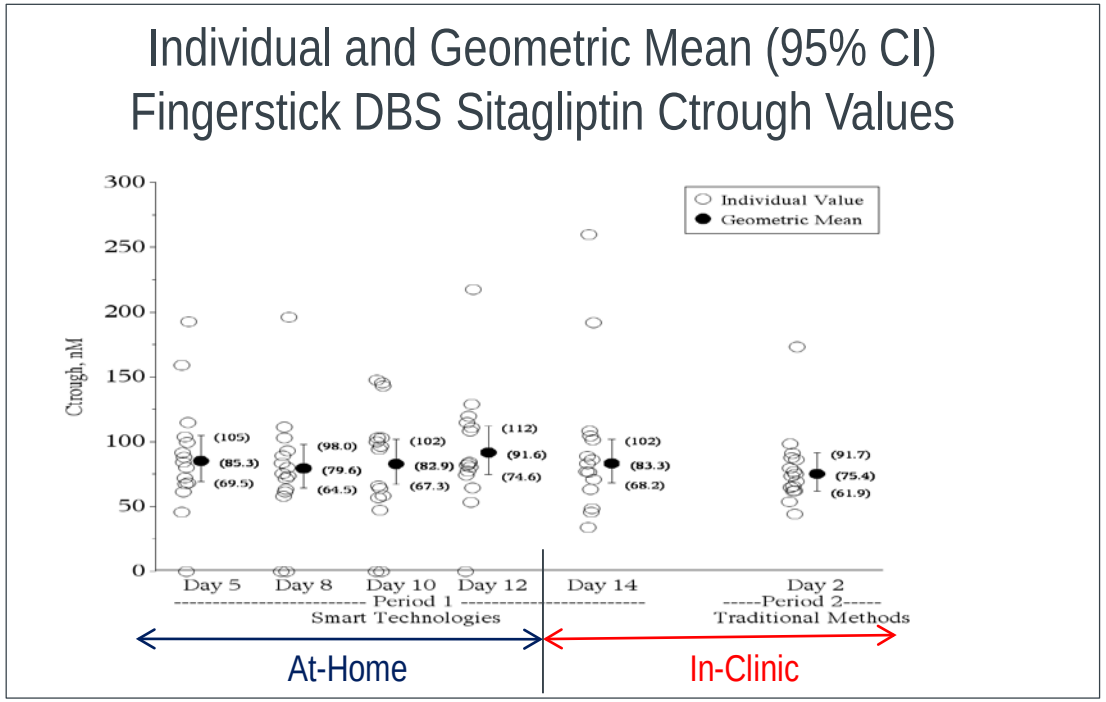
Smart Sampling Results

PK Data:



- **eDiary data:** Two subjects had missing eDiary entries for collected PK samples
- **Comparison of PK & Dosing Data:** Undetectable sitagliptin concentrations for at-home samples collected from 2 subjects, despite reported dosing via Smart Packaging & eDiary
  - In one case, DNA profiling confirmed subject ID → potentially dispensed dose without ingestion
  - In another case, DNA profiling did not confirm subject ID → suggests samples collected by someone else

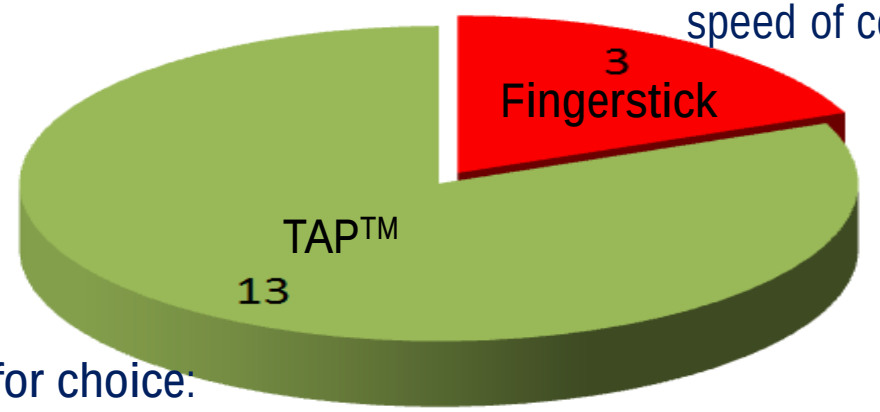
- Sitagliptin concentrations from samples collected at-home were generally similar to those collected in-clinic
- Missing eDiary data highlight importance of adding automated date/time stamps
- Smart Packaging is an improved yet imperfect indicator of adherence
- DNA profiling can be a useful tool as a means of confirming patient ID and sample disambiguation

Smart Sampling Questionnaire Results

TAP™ device

- Minimally invasive, micro-needle based sampling via push-button
- Painless, no sharp exposure
- This trial used TAP™ for limited in-clinic sampling (performed by clinic staff) to get subject feedback

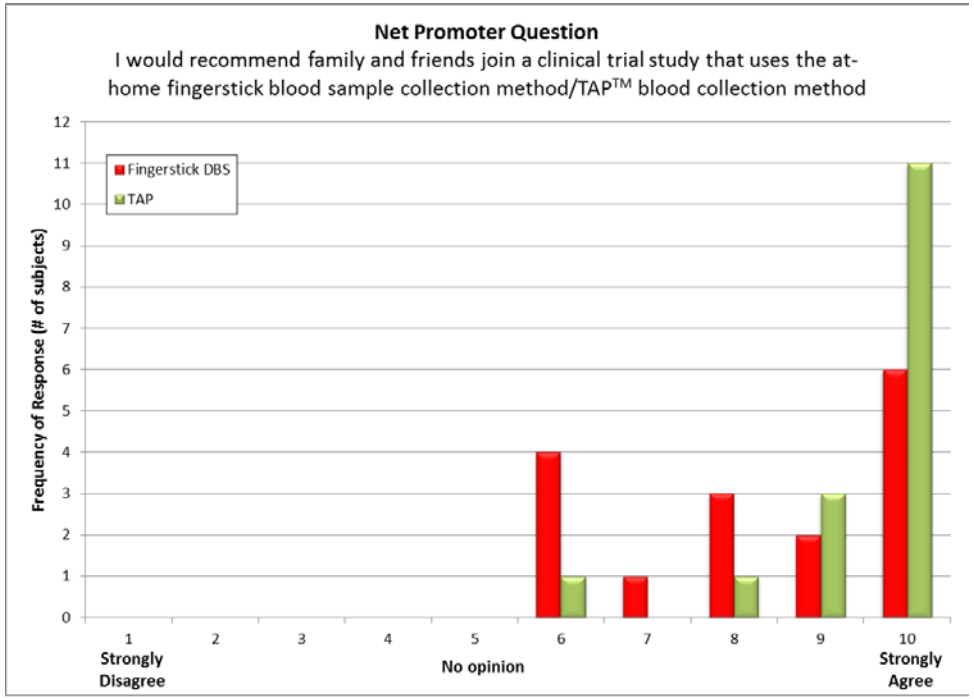
If you had a choice, which would you choose to use in a future clinical trial?



Rationale for choice:
speed of collection

Fingerstick via lancet

Rationale for choice:
less painful



Less painful methods of sampling may be beneficial in driving subject preference for at-home sampling

Conclusions and Future Directions

- Smart Trials is aimed at modernizing clinical trials in order to improve data quality, enrich data sets, and drive a more patient-centric approach
- Results of this study have demonstrated the feasibility and subject acceptance of digital health and outpatient sampling technologies for future clinical trial use and identified areas of focus for further investigations (e.g. automated date/time stamps for sampling, painless methods of sampling, more streamlined data integration)
- Clinical pilot such as the one presented here provide the types of data and experiences that will be necessary to enable the transition to patient-centric trials. Cultural change management to shift organizational thinking is another key part of this transition.
- Future directions:
  - Continue evaluating digital health technologies & outpatient sampling approaches in pilot trials to enable readiness for implementation in clinical development programs
  - Inclusion of Smart Trials approaches into clinical development programs

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