

Study Structure

- N=12 Moderate asthmatic patients aged 18-55
- 28 days on study
- Measurements expected:
 - 2 Mobile spirometry readings per day
 - 5 in-clinic spirometry readings at scheduled visits

Three Big Questions

- Compliance
 - Are patients generating mobile spirometry readings?
- Validity
 - How do mobile and in-clinic spirometry readings compare?
- Reliability
 - How noisy are at-home readings compared with in-clinic readings?

Validating Remote FEV₁ Monitoring in Moderate Asthmatics to Increase Study Power

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GOAL
eliminate the challenges of mobile lung function measurement and increasing the frequency of data collection while subjects are at home



VISION
Enable early phase studies powered to detect effect using at-home spirometry

In-clinic spirometry is quite reliable

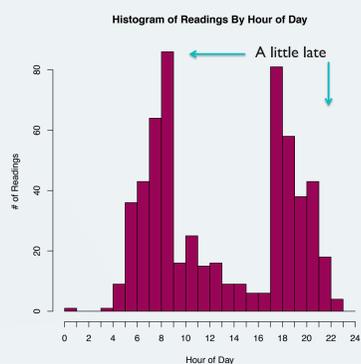
- Patients provide spirometry readings at all study visits
- ICC = 0.94
 - LMM fit for measurements from 12 patients
 - Higher indicates better consistency
- Residual SD = 0.20 L
 - Expected standard error of the difference = 0.28 L

Compliance By Subject

Subject	Readings	Days	Readings/Day
1	52	29	1.9
2	45	29	1.6
3	39	28	1.4
4	45	29	1.6
5	43	29	1.5
6	33	29	1.2
7	29	29	1.0
8	29	28	1.1
9	55	29	2.0
10	19	29	0.7
11	19	30	0.7
12	51	29	1.8
Total n = 12	527	347	1.4

Patients are expected to provide:
One morning reading (6 a.m. – 10 a.m.)
One evening reading (6 p.m. – 10 p.m.)

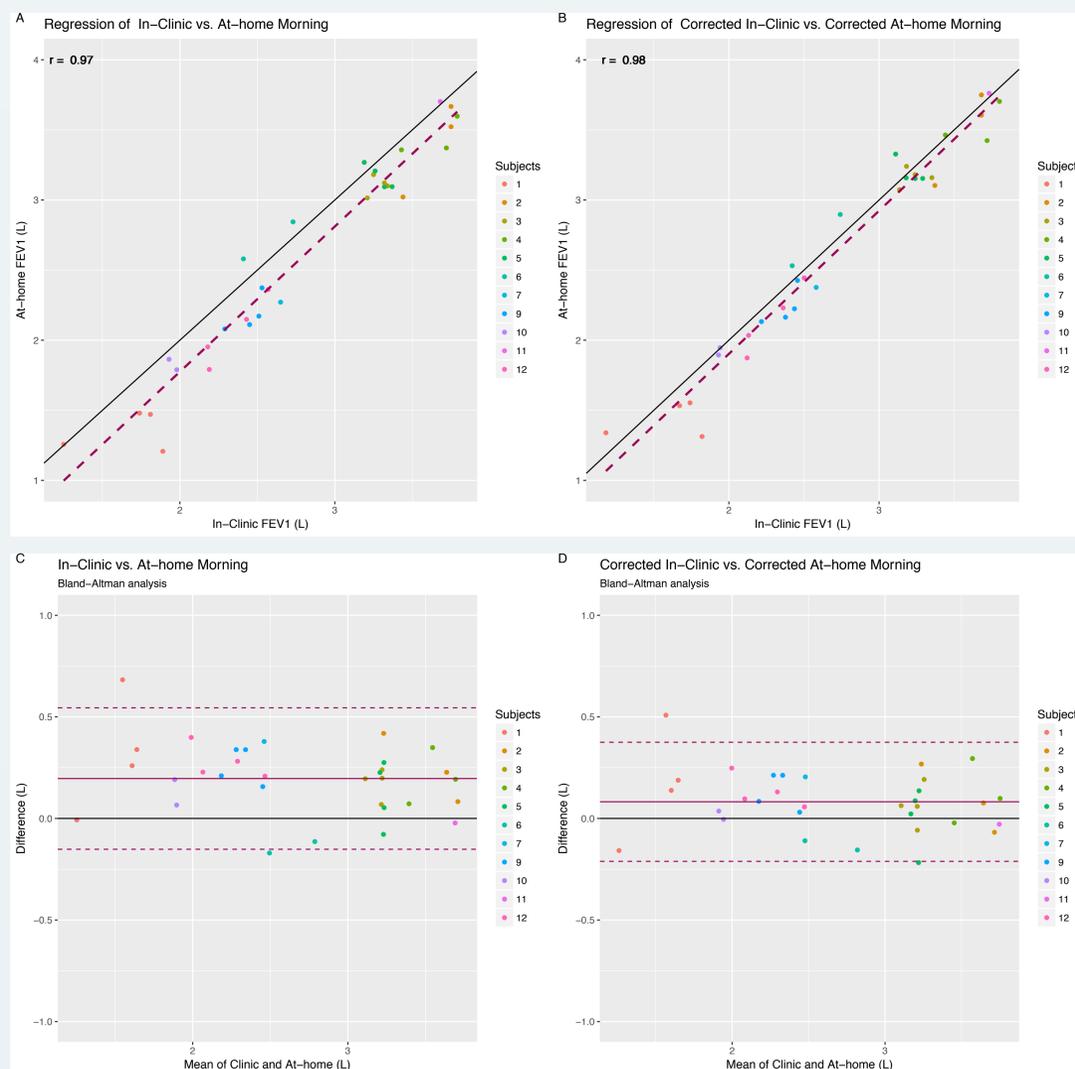
Compliance at a Glance



Compliance Take Home Message

- Patients are generating a tens of measurements over multiple weeks
- Compliance rates vary across patients
 - Improved/Increased reminders may help some patients continue to generate readings

Comparison of In-Clinic Spirometry Measures to At-home measures



Validity Take Home Message

- Mobile measurements show strong correlation with in-clinic measurements
- Regression of mobile measurements against in-clinic measurements is consistent with proper calibration
- Bland-Altman analysis indicates
 - Significant mean difference (0.20 L) when comparing morning at-home and in-clinic measurements
 - Bias removed when hour-of-day is accounted for
 - Overall this is consistent with proper calibration in the context of diurnal effects

Mobile Spirometry is As Reliable

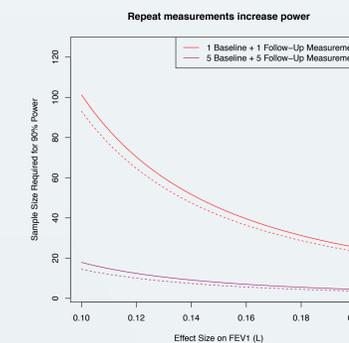
- Patients provide mobile spirometry measurements throughout study
- ICC = 0.93
 - Fit LMM for 527 measurements and 12 patients
- Residual SD = 0.19
 - Expected standard error of the difference = 0.27
- Do real world phenomena impact measurements in the “wild”?
 - Results suggest this is not a major concern

Note: ICC Estimated using LMM with patient-specific random effects

Repeat measures substantially reduce variability

- In-clinic spirometry
 - Endpoint: Follow-Up – Baseline
 - SD(FEV1 Visit 2 – FEV1 Visit 6) = 0.31
- Remote spirometry
 - Endpoint: Average(Follow-Up) – Average(Baseline)
 - SD(Average(First 5) – Average>Last 5)) = 0.13
 - Equivalent to ~4x increase in sample size
 - From only 5 measurements
 - Further improvement possible

Powerful studies. Fewer samples.



Reliability Take Home Message

- Mobile measurements are equivalently reliable to in-clinic measurements
- More measurements means fewer samples
 - 5x more measurements = 4x fewer samples