# Feasibility and Performance of a Continuous Ketone Monitoring Sensor

**Shridhara Alva, Ph.D.**

**Divisional Vice President, Clinical Affairs**

**Abbott Diabetes Care**

# Conflicts of Interest

*Shridhara Alva is an employee of Abbott Diabetes Care.*

*The work presented here is supported by Abbott Diabetes Care.*

# Diabetic Ketoacidosis and Type 1 Diabetes

DKA is a leading cause of death among children and adults with diabetes[1]

## • Prevalence

**Annual DKA prevalence among T1D adults across countries[1]**

***3-10%***

## • High risk T1D populations



- Youth and adults with suboptimal insulin management



- Patients using insulin pumps

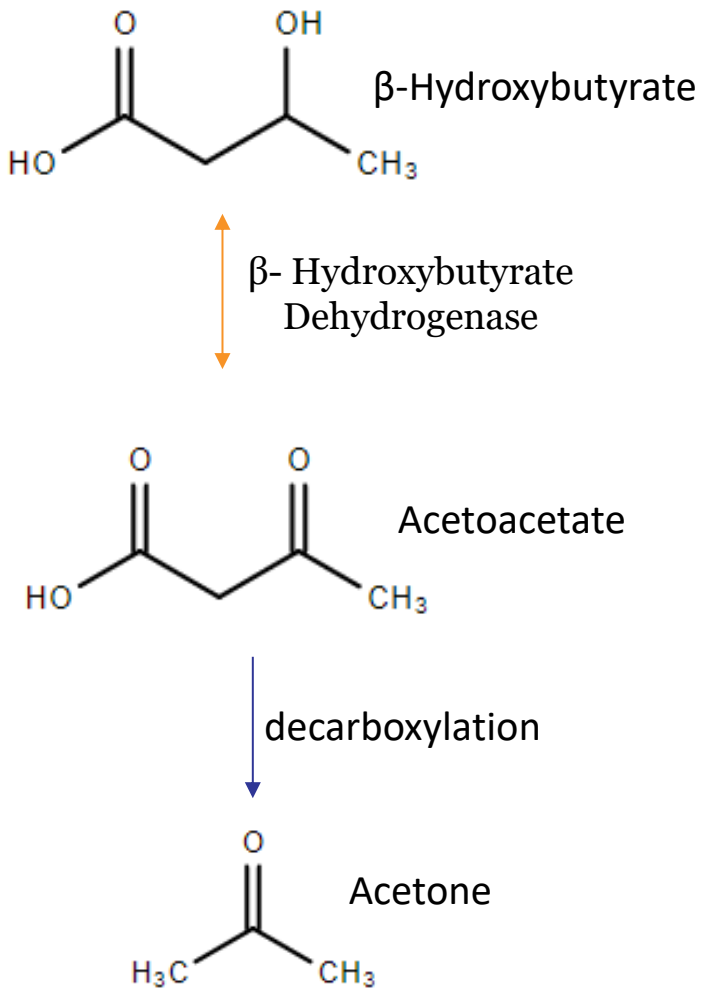


- Patients using SGLT2 therapies

1. Nguyen et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211042656

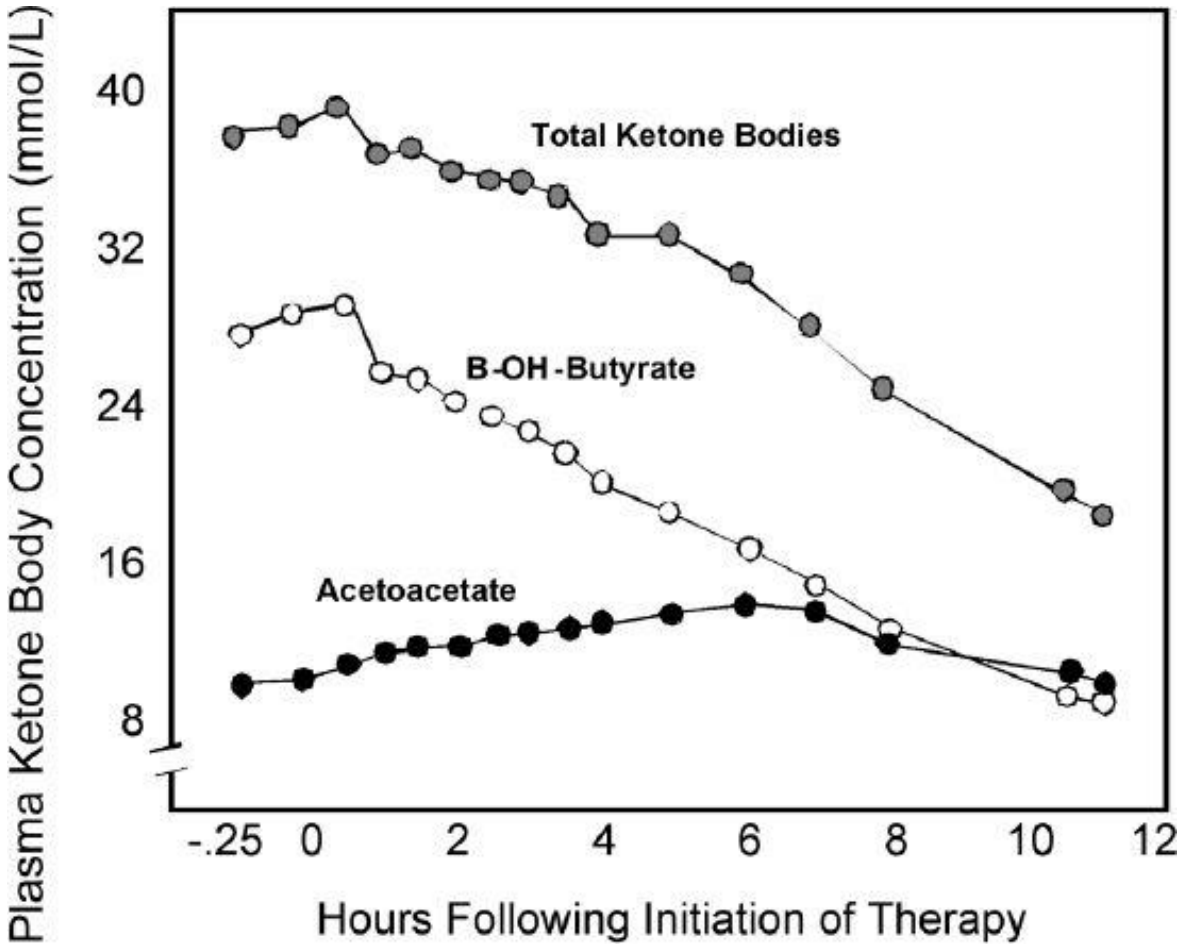
# Ketone Bodies and Ketone Assays

- Urine ketone
  - Compare color after 30 – 60 sec with color chart
  - Urine ketone (acetoacetate) is 2-4 hours behind blood values
- Blood Ketone - laboratory
  - Laboratory Assay using Nitroprusside test
  - Measures Acetoacetate
- Blood ketone – Point of Care/Home Test
  - Whole blood test
  - Measures β-hydroxybutyrate




Misra & Oliver, *Diabetes Medicine* (2015): https://doi.org/10.1111/dme.12604

# Clearance of Ketone Bodies Following Initiation of Therapy




- Upon initiation of therapy
  - B-hydroxy butyrate level drops steadily
  - Acetoacetate level increases initially and stays elevated for much longer period
  - Persistent urine ketonuria despite resolution of blood ketonemia

Laffel, L *Journal of Diabetes Science & Technology* (2007): https://doi.org/10.1177/193229680700100122

# Ketone Monitoring is inconvenient and ineffective.

## Limitations of Current Ketone Monitoring




Urine Testing



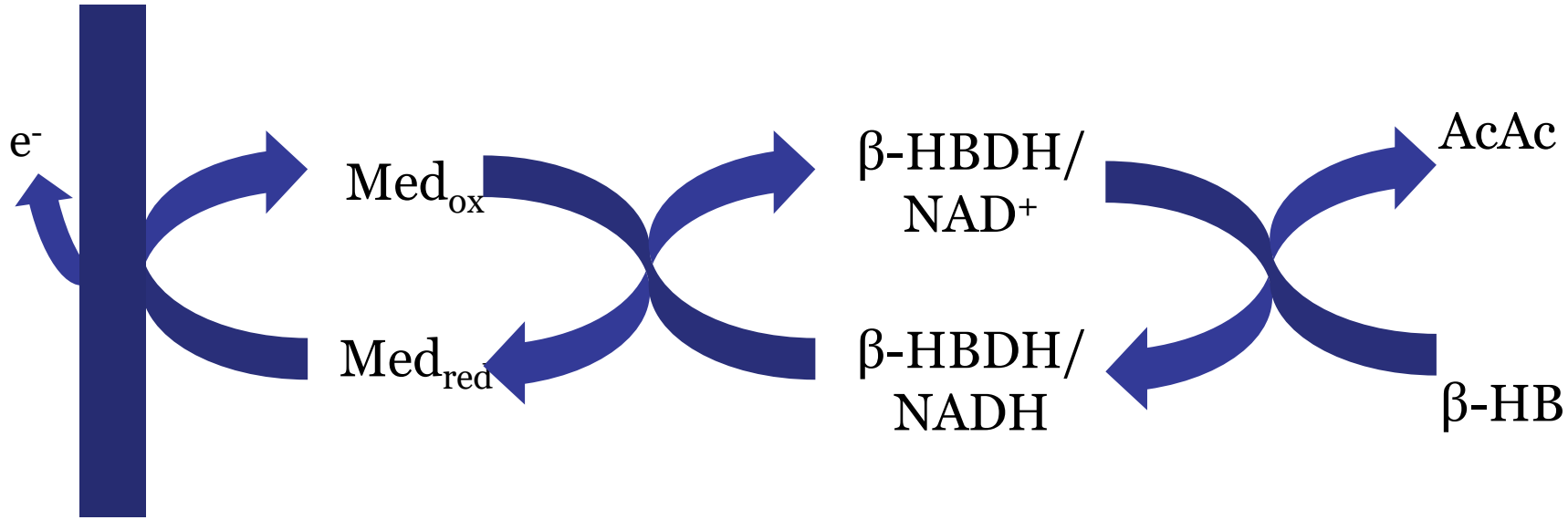

Blood ketone testing

- Current ketone monitoring confirms ongoing DKA versus detecting its onset
- Patients rarely check their ketone levels as recommended due to cost and burden[1]
  - Only 20% own home ketone monitoring[2] and 33% of patients own out-of-date strip[3]
  - Patients avoid fingerprick blood testing[1]


1. Nguyen et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/1932296821104265
2. Foster et al, *Journal of Diabetes Technology and Therapeutics* (2019): https://doi.org/10.1089/dia.2018.0384
3. Larsson et al, *Internal Medicine Journal 2018):* https://doi.org/10.1111/imj.13798

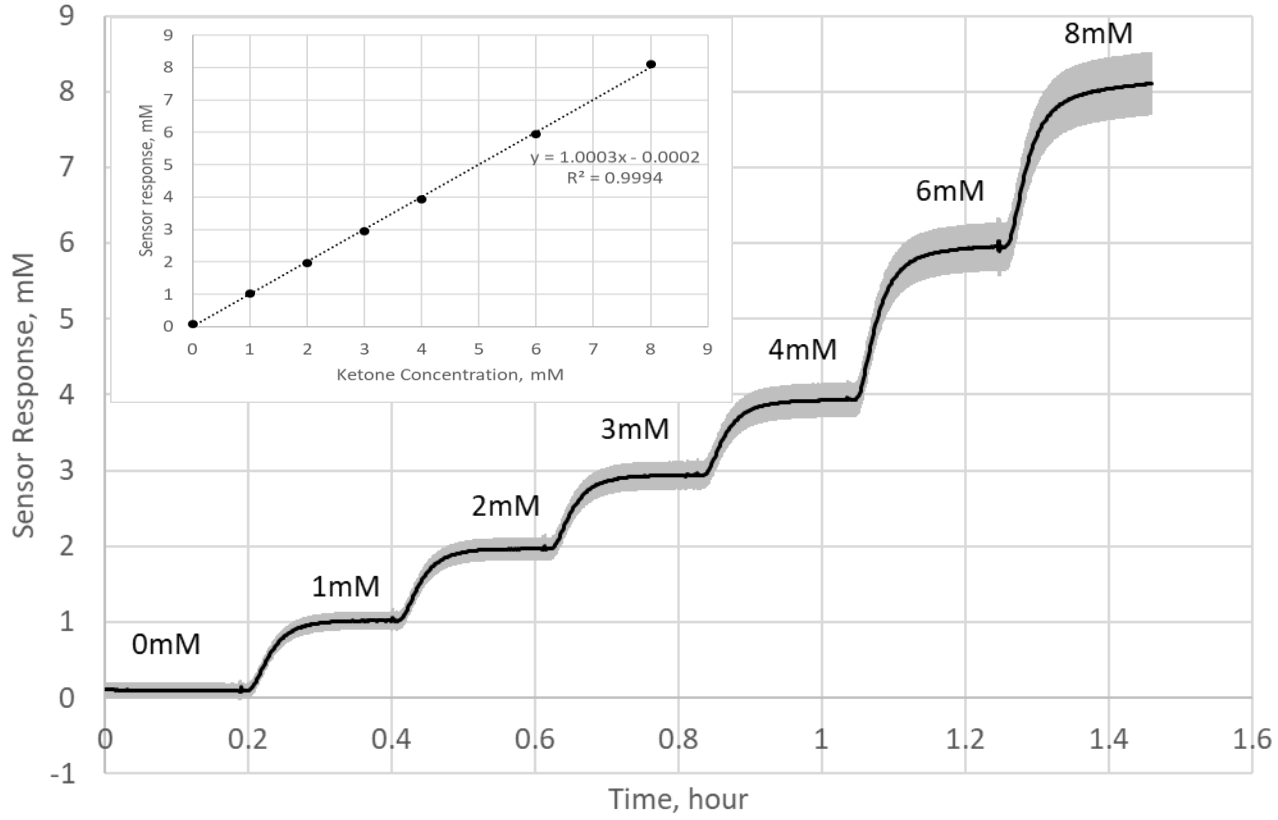
# Continuous Ketone Monitoring – *In Vitro* Data

- Sensor structure and dimensions similar to FreeStyle Libre Sensor with ketone specific chemistry
- $NAD^+$ dependent β-HBDH and a proprietary redox mediation chemistry containing Osmium complex




Alva et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211008185

# *In vitro* Performance Across Ketone Range




Alva et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211008185

# First Human Continuous Ketone Monitoring

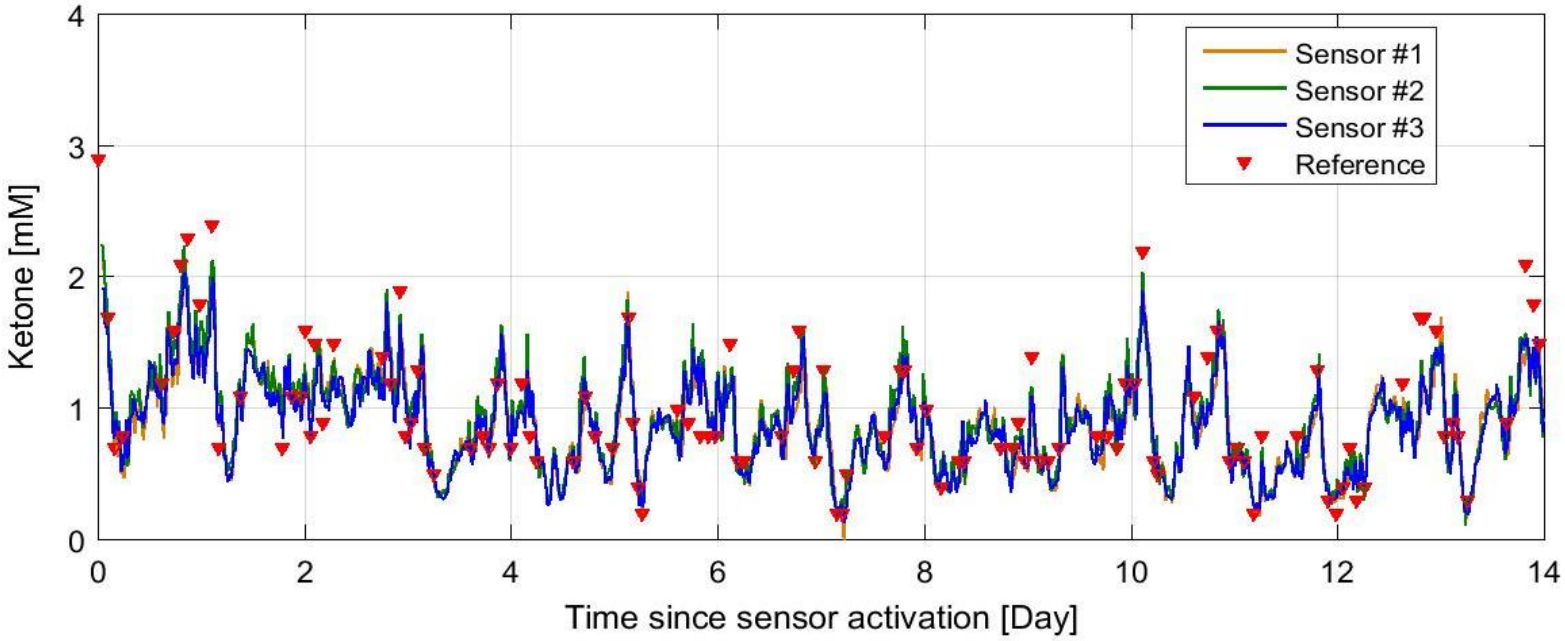
- First human study of Continuous Ketone sensor reported in 2021
- Study involved 12 participants practicing low carbohydrate diet
- Sensor in the FreeStyle Libre 2 form factor was used in the study
- Data reported with a single retrospective calibration of the sensor
- Demonstrated that ISF ketone levels track capillary ketone levels and can be measured over a 14-day period with these sensors

Alva et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211008185

# *In vivo* Performance Over 14 Days

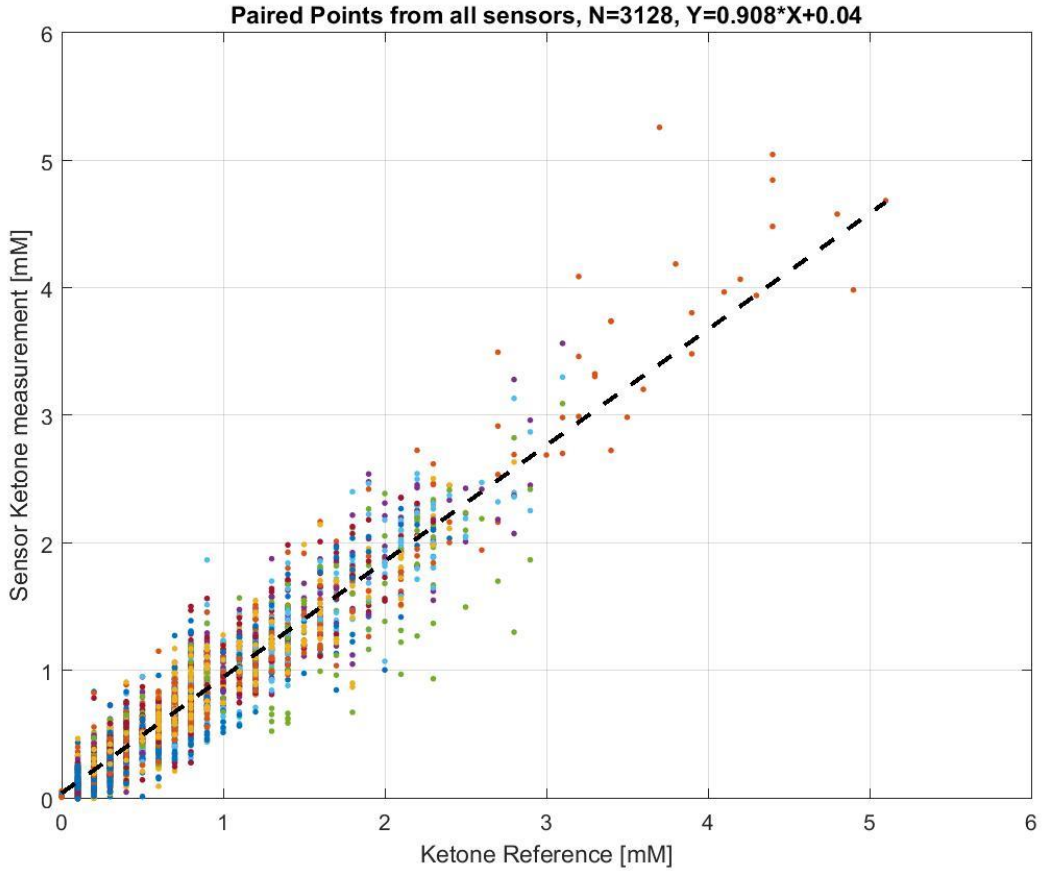
three sensors simultaneously worn by one subject

Capillary ketone reference




Alva et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211008185

# *In vivo* Performance: Correlation with Capillary Ketone




| Range | Percentage Within 0.3mM/ 30% | Mean MAD/ MARD | Paired Data Points |
|---|---|---|---|
| <1.5mM | 91.7% | 0.129 mM | 2724 |
| >= 1.5 mM | 89.7% | 14.4% | 408 |
| Combined | 91.4% | | 3132 |

No adverse events reported

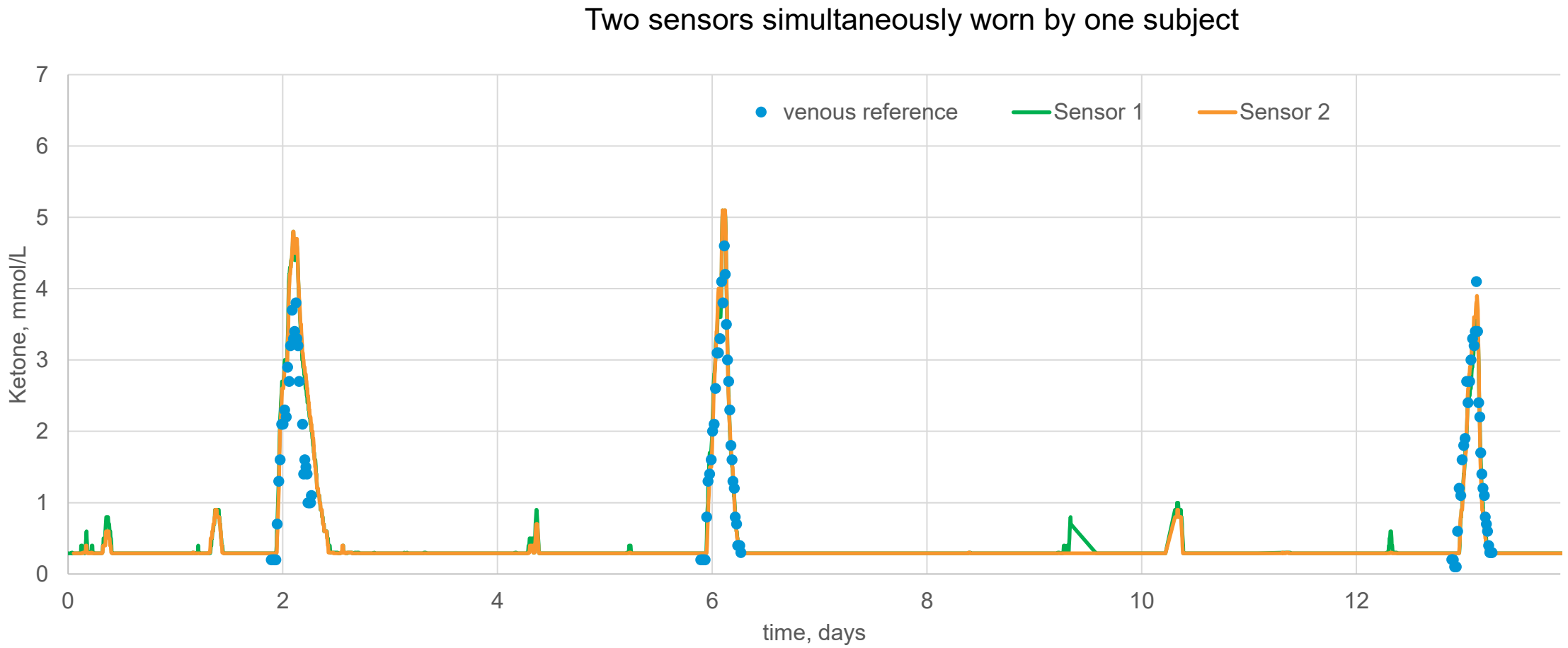
Alva et al, *Journal of Diabetes Science & Technology* (2021): https://doi.org/10.1177/19322968211008185

# *In vivo* Performance – Factory Calibration

- Study enrolled 36 participants with or without low carbohydrate diet
- Sensor in the FreeStyle Libre 2 form factor was used in the study
- Data collected with three unique factory calibration of the sensor lots
- Study participants consumed exogenous ketone to generate elevated ketone levels in a clinic setting
- Reference measurements with ketone strips were performed using venous blood using Precision Xtra ketone strip.

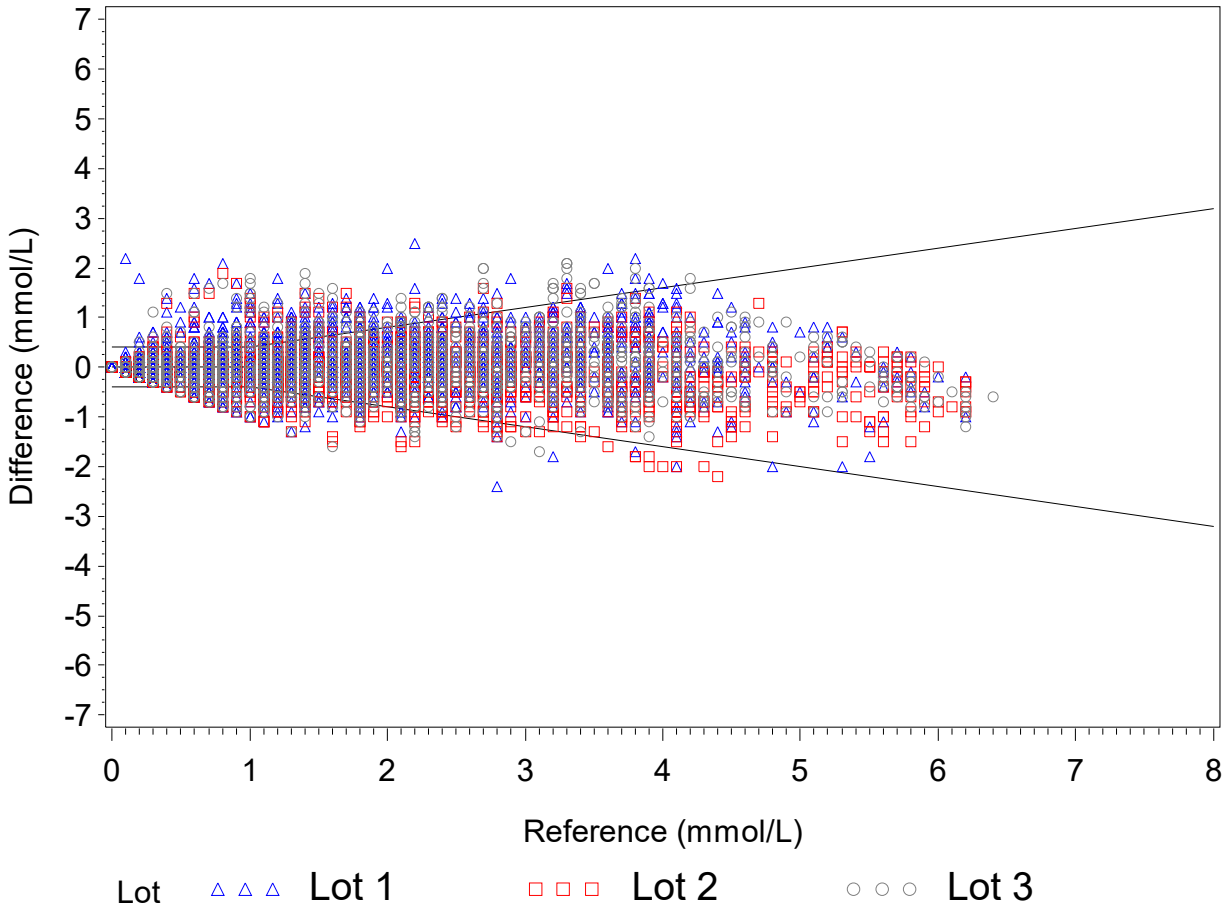
Data on file

# *In vivo* Performance with Exogenous Ketone




Data on file

# Sensor Performance against Venous Strip Reference




| Percentage Within 0.3mM/ 30% | Percentage Within 0.4mM/ 40% | Mean Absolute Difference, mmol/L | Paired Data Points |
|---|---|---|---|
| 85.0% | 91.1% | 0.30 ± 0.32 | 8922 |

Lag time is ~4 mins

No serious adverse events

3 mild application site symptoms
(pain and bruising)

Data on file

# Integrated Continuous Glucose and Ketone Monitoring System




## Integrated Continuous Glucose and Ketone Monitoring

- Designed to continuously monitor glucose and ketones levels every minute without scan
- Provide alarms for elevated and high ketone levels
- Leverages FreeStyle Libre 3 form factor
- Achieved US FDA breakthrough designation

Integrated continuous glucose and ketone monitoring system under development. Smartphone imagery for illustration purposes only. Not real patient data.

# Current Status and Next Steps

- Ability to measure β-hydroxybutyrate in ISF has been demonstrated with good correlation between the sensor and blood ketone levels
- Sensor is stable over the wear duration
- The sensor can be factory calibrated and responds quickly to changing ketone concentrations.