

ChatGPT-4o Summary

A convenient way to see the numerical link between iCGM measurement error and the resulting shift in Time in Range (TIR) is to compare “true” glucose values to the iCGM’s reported values and track how often readings cross the 70 mg/dL or 180 mg/dL boundaries. In short, even when an iCGM meets 21 CFR 862.1355 accuracy standards (e.g., $\pm 15\%$ in the 70–180 mg/dL range), the resulting difference between “true” TIR and “sensor-reported” TIR is usually on the order of a few percentage points (often 1–5%). Below is a distilled look at how to express that relationship numerically and why it tends to stay within a small range.

1. A Basic Formula for TIR Error

Let:

- True TIR = fraction of time the actual (true) glucose is between 70–180 mg/dL.
- ICGM TIR = fraction of time the iCGM readings are between 70–180 mg/dL.

We can break down ICGM TIR into two pieces:

1. The sensor reports “in-range” when glucose really is in-range (true positives).
2. The sensor reports “in-range” when glucose is actually out-of-range (false positives).

Formally:

Then the error or “bias” in TIR is:

- If this is positive, the sensor-based TIR is higher than reality (it’s overcounting in-range time).
- If this is negative, the sensor-based TIR is lower than reality (under-reporting in-range time).

1. Why iCGM Error Usually Translates to $<5\%$ TIR Difference

A. FDA Accuracy Criteria Limit Large Misclassifications

Under 21 CFR 862.1355, an iCGM must meet certain accuracy cutoffs. For example, in the 70–180 mg/dL range, at least 70% of readings must lie within $\pm 15\%$ of the reference. That level of accuracy makes massive boundary-crossing errors (e.g., reporting 180 when you’re actually at 140) much less frequent.

B. Most Glucose Values Aren’t Right on the Edge

Most people’s glucose values aren’t perched exactly at 70 or 180 mg/dL all the time. Errors matter most when the true glucose is near a boundary:

- True ≈ 70 mg/dL but the iCGM reads 65 or 75.
- True ≈ 180 mg/dL but the iCGM reads 175 or 185.

If a large chunk of time is spent right near 70 or 180 mg/dL, you get more “borderline misclassifications” that can shift TIR. If not, the effect on TIR is smaller.

C. Typical Simulation: $\sim 1\text{--}5\%$ TIR Shift

One modeling approach (shown in the PDF you shared) uses error distributions aligned with the FDA's minimum requirements plus a plausible glucose profile (e.g., 70% time in range, 10% below 70 mg/dL, 20% above 180 mg/dL). In that example, the net TIR difference came out to about 1–2 percentage points—and under more extreme assumptions, the difference might approach 5%. Generally, real-world devices exceeding the minimal standards see TIR biases in the 1–3% range for many patients.

1. Example Calculation

Suppose a person's true glucose distribution is:

- 70% in 70–180 mg/dL,
- 10% <70 mg/dL,
- 20% >180 mg/dL.

A simplified model might assume:

- When true <70 mg/dL, there's a ~15% chance the sensor drifts \geq 70 mg/dL (a "false in-range").
- When true 70–180 mg/dL, there's a ~25% chance it drifts out of range (a "false out-of-range").
- When true >180 mg/dL, there's a ~25% chance it drifts into 70–180 mg/dL (a "false in-range").

Then the sensor-reported TIR (ICGM TIR) is:

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ICGM TIR
= (0.75 × 0.70) + (0.25 × 0.70)* for false out-of-range
  (chance sensor
   says in-range
   when true in-range) (chance sensor
                        says in-range
                        when true out-of-range)
≈ 0.70 × 0.75 + 0.30 × 0.25
= 0.525 + 0.075
= 0.60 (60%)
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(Values 0.75 and 0.25 used just as an example to illustrate the method.)

If the True TIR is 70%, but the sensor-based TIR is 60%, the difference is –10 percentage points in this toy example. In practice, actual iCGM performance is better than this hypothetical scenario, and real-world differences typically fall below 5%. But this is the basic arithmetic behind how to link measurement error probabilities to TIR shifts.

1. Bottom Line: Expect a Few-Point Difference in TIR

- Typical Range: With iCGMs meeting 21 CFR 862.1355, the TIR discrepancy from true TIR is often 1–5 percentage points in real-world use.
- Worst-Case Scenarios: If a person's glucose distribution clusters near 70 or 180 mg/dL and if the iCGM exhibits a consistent bias or larger random swings, TIR deviation can approach that upper bound (~5% or slightly more).
- Best-Case Scenarios: If most values lie comfortably within the range (e.g., 100–150 mg/dL), the TIR difference might be only 1–2% because misclassifications near the boundaries are rare.

Hence, there isn't a single "universal" formula that says "X% sensor error \Rightarrow Y% TIR difference," but empirical and simulation-based data suggest that the performance standards in 21 CFR 862.1355 typically keep TIR misestimates to within a few percentage points for most users.