Evaluation of non-continuous temperature monitoring practices for vaccine storage units: A Monte Carlo simulation study

Supplemental Material

Appendix A. Methods

Using the R software program, we developed a simulation model. The structure of the simulation model was primarily determined by the type and the availability of data from the DDL Pilot Project. We used only data obtained from combination refrigerator units, as opposed to pharmacy-grade refrigerators, stand-alone refrigerators, dorm-style refrigerators, or any type of freezer unit. We did this to constrain the scope of our study while also maximizing the potential relevance of our results. In the simulation, storage unit temperature events are simulated at a 5-minute time-step over a total time period of 90 days, or 25,920 five-minute increments. In the primary analysis, the simulation model was run 500 times for each group of simulations. We targeted specific levels of possible cumulative excursion time to represent the median, 70th percentile, and 90th percentile of excursion time in storage units in our data. In addition to these three simulation groups, a fourth simulation group was constructed to provide a worst-case context, where cumulative excursion time was allowed to vary up to 90% of simulation runtime.

<u>Model</u>

The model is constructed using two vectors, the storage unit temperature vector, represented by y_t^h, and the temperature excursion vector, represented by x_n^h. Storage unit temperature status, represented by y_t^h, is equal to 0 if the storage unit is operating at normal temperatures and is equal to 1 if the storage unit is experiencing a temperature excursion. The direction of the temperature changes are indicated by h, so that if $h = high$ the temperature is above the normal range (a high temperature excursion) and if $h = low$ the temperature is below the normal temperature range (a low temperature excursion). The subscript t represents the time-step, from the start of the simulation, $t = 0$, to the end of the simulation, $t = T$.

The temperature excursions are represented by x_n^h. The duration of the temperature excursion is captured by the value of x. The excursions are indexed by n, where N_x is total number of excursions and, as with y_t^h, the superscript h represents the direction of the temperatuer excursion. The cumulative length of time for all excursions, no matter the type, is represented by D. The cumulative length of time for either high or low temperature excursions represented by D^h, with $h = high$ and $h = low$ for high and low excursions, respectively.

Cumulative temperature excursion time

The total amount of time the storage unit experiences an excursion in any given simulation can be expressed in terms of the temperature status of the storage unit and in terms of the set of excursions:

[1] $$D^h = \sum_n^N x_n^h = \sum_t^T y_t^h \text{ , } \forall\, h$$

Which states, the cumulative length of time for high or low excursions in a given simulation iteration is equal to the sum of the temperature excursion vector for high or low excursions, which is also equal to the sum of the storage unit temperature vector for high or low excursions.

For each of the 500 simulation iteration, the first step is to select the target level of the cumulative time the storage unit experiences within any excursion state, represented by $\widetilde{D}$. The target cumulative excursion time is uniformly distributed between 0 and the maximum cumulative excursion time for a given simulation group. The total excursion time $\widetilde{D}$ is subdivided into either a low temperature or high temperature excursion time, represented as $\widetilde{D}^h$. We assign the portion of $\widetilde{D}$ that is either high or low temperature based on a uniformly random value between 0 and 1.[2]

[2] $\widetilde{D} \sim u(0, \phi^D)$

[3] $\widetilde{D}^{h=high} \sim \widetilde{D} * u(0,1)$

[4] $\widetilde{D}^{h=low} = \widetilde{D} - \widetilde{D}^{h=high}$

Individual temperature excursions

The length of individual temperature excursions are generated sequentially until the constructed vector of temperature excursions contains a cumulative excursion time that is sufficiently close to the target cumulative excursion time for each temperature direction, i.e., cumulative excursion time is required to be less than ρ units difference from the target.

[5] $D^h > \widetilde{D}^h - \rho^h, \forall\, h$

For computational convenience, we set ρ equal to the median value from the distribution of the lengths of individual temperature excursions.

All of the characteristics of a given temperature excursion (both the temperatures and the duration) are uniformly sampled (or bootstrapped) from temperature excursions recorded during the DDL pilot project. We represent the vector of excursions recorded in the DDL pilot project by z_m^h for the duration of the temperature excursion and d_m^h for excursion direction. We define M_z, $M_z^{h=high}$, and $M_z^{h=low}$ as, respectively, the total number of excursions, the total number of high excursion, and the total number of low excursions found in the data. When we draw an excursion from the data to populate the simulations excursion vector, we assign that observation's duration and temperature to the simulation's excursion vector to maintain full correlation between temperature and length of excursion.

[6] $\widetilde{m}_n^h \sim u\left(0, M_z^h\right), \forall\, n, h$

The previous equation randomly selects the index of an excursion from the data that will be inserted into the simulation. The next equations store the duration ($z_{m=\widetilde{m}_n^h}^h$) of the randomly selected temperature excursion from the data in the temperature excursion vector (x_n^h).

[7] $x_n^h = z_{m=\widetilde{m}_n^h}^h, \forall\, n, h$

These features allow the temperature excursions to be parameterized by data observed by DDLs that have operated in practice. Once x_n^h is populated, each excursion is randomly inserted into the storage unit

[2] We considered using data to parameterize the subdivision of $\widetilde{D}$ into high or low. Data from the DDL pilot project suggested the portion of excursion time due to low excursions was 0.6. Our selection of uniform distribution between 0.0 and 1.0 seems reasonable.

temperature vector, such that no excursions overlap and there is at least a 5 minute interval between excursions.

Temperature monitoring practices

Once y_t has been populated with excursions, the temperature monitoring practices are evaluated. Each temperature monitoring practice is associated with zero, one, or two daily readings of the current temperature and zero, one, or two daily readings of the min/max temperature. We evaluate many combinations of these potential practice options. The min/max temperature readings captures the minimum and maximum temperatures that have occurred since the previous, or most recent, min/max temperature reading occurred. In this way, a single min/max reading can detect at most 2 temperature excursions, one high excursion (the max for the previous window exceeds the acceptable range) and one low excursion (the min for the previous window also exceeds the acceptable range). A single min/max reading combined with a current temperature reading can detect at most 3 temperature excursions. This would occur if the current temperature is out of range, but at a less extreme position than the min or max reading. In practice, a temperature monitor would have a difficult time assessing if the current out of range temperature was a part of a different excursion from the min or max out of range temperature. In such a case, the current temperature could conceivably be a point along the temperature trajectory of a single excursion (where the min or max is the apex or nadir of the excursion). Given this study utilizes simulated data, and the simulation program has, in a sense, full knowledge of individual excursion counts and lengths, our analysis did not account for this ambiguous situation.