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COMPARING INSULIN POTENCY RETENTION ACROSS STORAGE TEMPERATURES DURATIONS AND THERMAL PROFILES RELEVANT TO HOUSEHOLD ENVIRONMENTS

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Abstract:

This analysis compares insulin potency retention across thermal storage regimens to inform the interpretation of evidence relevant to household medicine storage internationally. A descriptive secondary analysis uses 29 published aggregate measurements from one experiment reported in 2021, covering seven formulations, twelve exposure series and observation periods of one to twelve weeks. Five formulation matched comparisons align storage duration at four weeks. Retention under cycling between 25°C and 37°C exceeded retention under constant exposure at 31°C for every shared formulation, with a mean difference of 10.28 percentage points and individual differences ranging from 6.50 to 15.80 percentage points. Under constant exposure, mean retention declined from 99.60% at one week to 83.94% at eight weeks. Cycling measurements remained close to the initial reference across the observed endpoints. These patterns support interpreting protein stability within defined formulations and exposure histories rather than through maximum temperature alone. The contribution is an explicit synthesis of matched regimen contrasts. International evidence assessment should align products, exposure duration and thermal conditions before translating experimental retention measurements into storage guidance.

Key Words: Descriptive Analysis; Household Storage; Insulin Stability; Matched Comparisons; Thermal Exposure

1. Introduction:

Insulin storage presents a practical tension between maintaining pharmaceutical quality and accommodating the environments in which treatment occurs. Temperature recommendations define acceptable storage conditions, but household exposure varies over time and does not necessarily resemble constant laboratory heating. Understanding how potency retention differs across these exposure patterns matters for interpreting storage evidence, particularly where reliable refrigeration is difficult to maintain. The relevant question concerns the combined conditions of exposure: temperature bounds, elapsed storage time and thermal profile. Household monitoring demonstrates why these dimensions require attention. Braune et al., 2019, analysed temperature records collected between November 2016 and February 2018 from 400 sensors used by 338 people with diabetes. Departures from recommended ranges occurred in both refrigerated and carried insulin, with refrigerated storage showing more frequent departures. These observations establish that storage location alone does not adequately describe thermal exposure. However, temperature monitoring does not directly measure insulin potency. Connecting exposure conditions to measured retention therefore requires experimental evidence that identifies the formulation, temperature regimen and observation time.

Protein stability provides the conceptual basis for this connection. Insulin can undergo structural changes and aggregation, while formulation ingredients help maintain its stability. Temperature may influence these processes, but the response depends on molecular structure and the surrounding formulation. Woods et al., 2012, demonstrated differences in intrinsic fibrillation among insulin analogues after removing stabilising excipients. Teska et al., 2014, further showed that preservative depletion altered the stability of insulin lispro and insulin aspart during incubation at 37°C, while insulin glulisine responded differently. These experiments establish that thermal susceptibility cannot be assumed identical across products. They also explain why comparisons should preserve formulation identity rather than pool all insulin measurements into a single response. Exposure duration introduces a related distinction. Longer storage provides more time for degradation processes to develop, but elapsed time does not specify the thermal conditions experienced during that interval. Constant exposure sustains a given temperature, whereas cycling includes repeated periods at different temperatures. Consequently, the same storage duration can represent different exposure histories. Pendsey et al., 2023, examined insulin thermostability during extended storage in India, illustrating the importance of evaluating duration within a defined environment. Such evidence supports interpreting retention through observed combinations of formulation, time and temperature rather than treating any one dimension as sufficient.

The closest experimental foundation is Kaufmann et al., 2021, who reproduced temperature fluctuations measured in northern Kenya and examined insulin under cycling and constant conditions. Their published tables report retention for seven formulations after cycling between 25°C and 37°C and for five formulations under constant exposure at 31°C. The experiment already establishes the relevance of comparing these regimens. The present analysis extends the presentation of that evidence through explicit comparisons within formulations over time and matched contrasts at a common endpoint. Its contribution is a transparent secondary synthesis of published measurements, with the comparison unit and descriptive quantities defined consistently. This distinction also governs outcome interpretation. Potency retention is measured as insulin concentration relative to its initial measured concentration, expressed as a percentage. Values above 100% represent analytical recovery relative to that reference and are retained as reported. The measure allows comparable arithmetic across the selected source tables, but it does not directly measure household treatment outcomes. Likewise, numerical changes across observation times describe reported retention trajectories without establishing the molecular pathway responsible for them. The analysis therefore keeps the outcome aligned with the measurements available.

This study aims to compare insulin potency retention across household relevant thermal storage regimens while preserving formulation identity and exposure duration. The overarching research question asks how reported retention differs across constant and cycling conditions and across their observed storage intervals. Specifically, the analysis compares retention between the two regimens, examines changes across available endpoints within each formulation and regimen, and calculates the difference at four weeks for the five shared formulations. These objectives connect the three observed exposure dimensions to the measured outcome without introducing additional constructs. The dataset contains 29 published aggregate measurements from twelve formulation specific exposure series. Fourteen observations describe cycling exposure at four and twelve weeks, while fifteen describe constant exposure at one, four and eight weeks. Descriptive summaries establish the distribution of retention, and five matched comparisons align formulation and duration at four weeks. This design makes the comparison more informative than pooled regimen averages alone, which combine different product coverage and observation schedules. Temperature bounds and thermal profile remain combined within each assigned regimen, so the contrasts describe complete storage conditions rather than separate causal effects.

The findings show that all five shared formulations recorded higher retention under cycling conditions at four weeks, with an average difference of 10.28 percentage points. Constant exposure was accompanied by declining retention across every observed interval, whereas cycling measurements remained close to the initial reference across the available endpoints. These results clarify the magnitude and consistency of the published regimen contrast. Their broader relevance lies in demonstrating why storage evidence should be compared using aligned formulations, durations and exposure definitions. This analytical approach can inform evidence assessment across settings while keeping practical interpretation within the tested conditions.

2. Theory Conceptual Framework and Research Questions Development:

This analysis applies protein stability theory to explain how thermal storage conditions relate to insulin potency retention in environments relevant to household storage. Insulin stability depends on interactions between molecular structure, formulation components and exposure conditions. Heat can promote structural changes and aggregation, while stabilising ingredients can limit these processes. Storage temperature therefore operates within a formulation system rather than determining potency through a uniform response. Woods et al., 2012, demonstrated differences in fibrillation behaviour among insulin analogues after removing stabilising excipients. These findings support formulation specific comparisons, but do not establish equivalent responses in commercial products stored under household conditions. Household storage connects this molecular mechanism to a variable thermal environment. Refrigeration, ambient conditions and the duration of storage determine the exposure experienced by a formulation after dispensing. Braune et al., 2019, documented departures from recommended storage temperatures in domestic refrigerators and carried insulin. Their measurements establish the relevance of temperature variation, although temperature records alone do not demonstrate potency loss. This analysis therefore defines thermal storage conditions through observed temperature bounds, exposure duration and thermal profile. The outcome is insulin potency retention, measured as the reported insulin concentration relative to its initial concentration and expressed as a percentage.

Temperature provides the first conceptual dimension. Higher temperatures can increase molecular movement and the opportunity for destabilising interactions. However, formulation chemistry can constrain this response. Teska et al., 2014, found that depletion of phenolic preservatives reduced the stability of insulin lispro and insulin aspart during incubation at 37°C, while insulin glulisine responded differently. This evidence supports a conditional expectation: thermal exposure may reduce stability, but the response depends on the formulation and its stabilising environment. Preservative concentration is not measured in the assembled dataset, so we use formulation identity to organise comparisons rather than treating preservative protection as an estimated mechanism. The available temperature observations describe two storage regimens: constant exposure at 31°C and cycling between 25°C and 37°C. Temperature bounds and thermal profile change together. We therefore compare these observed regimens without attributing their differences to maximum temperature alone. The descriptive comparison uses the reported potency values for each formulation and measurement occasion.

RQ1: How does reported insulin potency retention differ between constant storage at 31°C and cycling storage between 25°C and 37°C?

Exposure duration provides the second dimension. Protein destabilisation depends on the time available for structural changes to develop, but elapsed time does not imply a constant rate of potency decline. Formulation protection and exposure conditions can produce different trajectories. Pendsey et al., 2023, examined insulin thermostability over extended storage in a household relevant setting, reinforcing the importance of evaluating duration alongside the exposure environment. This analysis measures duration directly in weeks and describes changes within each formulation and regimen. We compare weeks one, four and eight under constant exposure, and weeks four and twelve under cycling exposure. These comparisons preserve the reported observation periods without imposing a common linear trajectory.

RQ2: How does reported insulin potency retention change across the observed storage durations within each formulation and thermal regimen?

Thermal profile provides the third dimension. Constant heating sustains exposure, whereas cycling includes periods at lower temperatures. A plausible theoretical mechanism is that these lower temperature intervals alter the opportunity for structural changes to progress. The dataset measures the exposure pattern and potency outcome, allowing comparison of their reported relationship. Kaufmann et al., 2021, reproduced temperature fluctuations measured in northern Kenya and examined insulin under cycling and constant conditions. Their experiment provides the numerical basis for the assembled dataset. We compare five shared formulations at four weeks to hold formulation identity and observation duration constant. This comparison describes the difference between complete storage regimens rather than an isolated effect of cycling.

RQ3: At four weeks, what is the difference in reported potency retention between cycling and constant storage for each of the five shared formulations?

The conceptual framework links observed thermal storage conditions to observed insulin potency retention through the theoretical process of protein destabilisation. Temperature bounds, duration and thermal profile describe exposure conditions rather than indicators of a latent construct or components of a composite index. Formulation identity provides the basis for

stratification and matching. The empirical framework comprises 29 published aggregate measurements, duration comparisons within formulation and regimen, and five matched comparisons at four weeks. These research questions organise descriptive analysis of the assembled evidence. They permit differences, stability or inconsistent patterns across formulations without requiring a predetermined direction.

3. Data:

This analysis uses published insulin potency measurements to compare thermal storage regimens relevant to household environments. The data documentation establishes provenance, defines the analytical sample and measures, and supports descriptive comparisons within formulations and across observation times.

3.1 Data Sources, Population, and Sample Construction:

The numerical source is the experiment reported by Kaufmann et al., 2021, published in PLOS ONE. Table 1 provides potency retention under cycling temperatures, while Supplementary Table S4 provides measurements under constant exposure. Both tables are accessible through the article and their persistent identifiers, https://doi.org/10.1371/journal.pone.0245372.t001 and https://doi.org/10.1371/journal.pone.0245372.s009. The article distributes its content under a Creative Commons Attribution licence. The workbook records the extraction date in its metadata and identifies each numerical observation by source table. No separate dataset release number is specified. journals.plos.org. The unit of analysis is a published mean for a formulation, thermal regimen and observation time. The analytical sample contains 29 aggregate observations from seven formulations and twelve formulation specific exposure series. Cycling exposure between 25°C and 37°C contributes fourteen observations at four and twelve weeks. Constant exposure at 31°C contributes fifteen observations at one, four and eight weeks. These measurements describe potency at experimental endpoints rather than averages over storage intervals.

The empirical setting is pharmaceutical storage under laboratory conditions informed by temperatures measured in northern Kenya. Household relevance follows from the exposure conditions reproduced in the experiment. The broader importance of monitoring household environments is supported by Braune et al., 2019, who documented temperature departures in domestic refrigerators and carried insulin. Their observations provide contextual evidence and are not merged into the potency dataset. The target population is insulin formulations exposed to household relevant thermal storage conditions. The accessible sampling frame is narrower: numerical cells in the two selected tables from one publication within the literature scope of 2010 to 2023. All formulation and time combinations reported in these tables were retained. The dataset is an aggregate repeated measurement structure with unequal observation schedules across regimens. It does not constitute an annual panel covering the literature scope.

Table 1: Sample construction

Stage	Units	Observations	Reason or Rule
Cycling exposure frame	Seven formulations in seven series	14	Table 1 reports two endpoints per formulation
Constant exposure frame	Five formulations in five series	15	Supplementary Table S4 reports three endpoints per formulation
Consolidated descriptive sample	Seven distinct formulations in twelve series	29	Both tables combined with source identifiers preserved
Records removed during consolidation	Zero series	0	No extracted observation was deleted
Matched comparison sample	Five shared formulations	10 measurements forming five pairs	Same formulation and four-week endpoint under both regimens

3.2 Data Integration, Cleaning, and Quality Assurance:

The source tables were appended into one observation file because they describe different experimental conditions. Each record retains its formulation, temperature bounds, exposure duration, thermal profile, reported potency and source location. Formulation labels were harmonised with product names for the five products shared across tables. The matched comparison uses formulation identity and the four-week endpoint, producing one cycling observation and one constant observation per formulation. The consolidated file contains 29 unique record identifiers and twelve series identifiers. Repeated formulation names represent genuine observations at different times or under different regimens. They were retained. The matched subset contains five complete pairs, with no unmatched record among the selected shared formulations. The remaining observations contribute to the broader descriptive analysis.

Temperature remains in degrees Celsius, duration remains in weeks, and potency remains a percentage of the initial measured concentration. No frequency conversion or interpolation was applied. All 29 observations contain the required exposure and outcome values. No imputation, replacement with zero, winsorisation or trimming was implemented. Reported potency values above 100% were retained because the source expresses measured recovery relative to an initial analytical reference. Removing these observations would alter the published measurements. Values range from 80.8% to 103.3%. The workbook also preserves the numerical quantities printed after the ± symbol. Their interpretation as standard deviations or standard errors is not established in the extracted tables, so they are not used to construct inferential weights or confidence intervals. The article narrative contains recovery ranges that differ from some explicit Table 1 entries. The extraction consistently prioritises numerical table cells and preserves this discrepancy in the documentation. No alternative values were substituted after examining the comparisons. The resulting sample describes the selected experimental evidence; it does not establish the representativeness of formulations or households beyond that frame.

3.3 Variable Measurement, Construction, and Validation:

Thermal storage conditions comprise observed temperature bounds, exposure duration and thermal profile. Insulin potency retention is the published concentration expressed relative to the initial measured concentration. Formulation identity

supports stratification and matching. This treatment recognises that molecular structure can influence stability, as demonstrated by Woods et al., 2012, under experimental conditions that removed formulation excipients. Their findings justify distinguishing formulations without assuming that their experimental degradation rates apply directly to the commercial products examined here.

Table 2: Variable dictionary

Variable or Indicator	Analytical Role	Definition and Construction	Source and Identifier	Unit and Frequency	Transformation and Direction	Missing Value Rule	Coverage and Limitation
Potency retention	Outcome	Published concentration relative to the initial measured concentration	Kaufmann article, Table 1 and S4	Percent at each endpoint	Untransformed; higher values indicate greater measured retention	No missing values; no imputation	29 aggregate means
Minimum temperature	Exposure descriptor	Lower bound of the assigned regimen	Table 1 and S4	°C per regimen	Untransformed	No missing values	25°C for cycling and 31°C for constant exposure
Maximum temperature	Exposure descriptor	Upper bound of the assigned regimen	Table 1 and S4	°C per regimen	Untransformed	No missing values	37°C for cycling and 31°C for constant exposure
Exposure duration	Exposure dimension	Elapsed experimental storage time	Table 1 and S4	Weeks at each endpoint	Untransformed; higher values indicate longer exposure	No missing values	Unequal schedules across regimens
Thermal profile	Exposure category	Cycling or constant temperature	Table 1 and S4	Category per series	Cycling coded 1 and constant coded 0	No missing values	Temperature bounds vary with profile
Formulation	Matching and stratification variable	Published formulation category	Both source tables	Category per observation	No numerical ordering	No missing values	Seven formulations overall; five shared
Series identifier	Dependence identifier	Formulation and regimen combination	Constructed workbook field	Identifier per series	No quantitative interpretation	Complete	Twelve repeated measurement series
Reported ± quantity	Source documentation	Numerical dispersion quantity reproduced from the source	Table 1 and S4	Percentage scale at each endpoint	Preserved without inferential interpretation	No imputation	Dispersion type not established
Signed potency loss	Derived descriptive measure	Initial reference of 100 minus retention	Workbook calculation	Percentage points per observation	Higher values indicate greater measured loss	Complete inputs required	Negative values are retained
Matched retention difference	Comparative measure	Cycling retention minus constant retention for the same formulation at four weeks	Matched comparison worksheet	Percentage points per pair	Positive values indicate higher retention under cycling	Complete pair required	Five formulation matched pairs

Equation 1 defines signed potency loss:

$$L_i = 100 - R_i$$

Here, L_i is signed loss in percentage points and $R_i$is reported potency retention for observation i. This calculation measures departure from the initial reference rather than percentage change between successive endpoints. Equation 2 defines the matched comparison:

$$D_f = C_f - I_f$$

Here, D_f is the retention difference in percentage points for formulation f, C_f is cycling retention at four weeks, and $I_f$is constant exposure retention at four weeks. Formulation components are not measured as separate predictors. Teska et al., 2014, demonstrated that preservative depletion can alter insulin analogue stability, supporting the importance of retaining formulation identity when interpreting comparisons. The analysis does not estimate preservative effects from product labels.

Table 3: Descriptive statistics

Measure	Valid Count	Mean	Standard Deviation	Median	Minimum	Maximum
Potency retention, all observations, percent	29	95.96	7.02	99.70	80.80	103.30
Potency retention, cycling, percent	14	100.86	1.35	100.95	98.40	103.30
Potency retention, constant exposure, percent	15	91.38	7.10	91.00	80.80	101.50
Exposure duration, weeks	29	6.10	3.99	4.00	1.00	12.00
Matched retention difference, percentage points	5	10.28	3.93	10.70	6.50	15.80

Standard deviations describe dispersion across the extracted aggregate observations. They do not estimate variability among patients or independent experimental replicates. The pooled regimen summaries also combine different observation schedules and formulation coverage.

3.4 Analytical Framework, Identification, and Reproducibility:

The analysis is descriptive. It examines reported retention across observed regimens, changes across available endpoints within each formulation and regimen, and matched differences at four weeks. Duration comparisons use one, four and eight weeks for constant exposure and four and twelve weeks for cycling exposure. No values are generated for unobserved endpoints. The principal comparative quantity is the formulation specific difference defined in Equation 2. Matching holds formulation identity and elapsed storage time constant. It does not separate the effect of cycling from the accompanying change in temperature bounds. The five contrasts therefore describe complete storage regimens. Their mean summarises the selected formulations without estimating a population treatment effect.

Time and exposure must be interpreted jointly. Pendsey et al., 2023, examined insulin thermostability over extended storage in a household relevant setting, illustrating the value of evaluating observed exposure conditions and duration together.

Those measurements inform the interpretation of scope but are not additional observations in this dataset. Repeated observations share experimental series, and the available tables do not provide their covariance or the underlying replicate measurements. Consequently, the analysis reports descriptive magnitudes without regression coefficients, significance tests or confidence intervals. It retains formulation specific results so that pooled averages do not conceal differences among products. The workbook provides the extracted values, source identifiers, variable definitions, series identifiers and implemented arithmetic formulas. Its matched comparison worksheet exposes the five paired calculations. These materials support reproduction of the reported descriptive results while preserving the distinction between household relevant experimental conditions and measured household outcomes.

4. Methods:

4.1 Research Design and Comparison Strategy:

This analysis uses a descriptive secondary design to examine published insulin potency measurements under two thermal storage regimens. The unit of analysis is an aggregate mean for a formulation, exposure regimen and observation time. The analytical objectives are to compare reported retention across regimens, describe changes within each formulation over time, and quantify matched differences at four weeks. The numerical evidence comes from Table 1 and Supplementary Table S4 of Kaufmann et al., 2021. The comparison includes cycling between 25°C and 37°C and constant exposure at 31°C. Useful variation arises from differences across formulations, observation times and assigned regimens. Comparisons within a formulation preserve product identity, while matching at four weeks also aligns elapsed storage time. The principal comparative quantity is the difference between reported retention under the two regimens for the same formulation at four weeks, as defined in Equation 2. This quantity describes the complete regimen contrast. Temperature bounds change together with thermal profile, preventing separate attribution to maximum temperature or cycling. The analysis therefore interprets observed differences descriptively without estimating independent causal effects.

4.2 Sample and Measurement Alignment:

The sample construction table and variable dictionary document the source coverage, record definitions and measurement units. The complete descriptive sample contains 29 observations from seven formulations and twelve exposure series. Fourteen observations cover seven formulations under cycling conditions at four and twelve weeks. Fifteen observations cover five formulations under constant exposure at one, four and eight weeks. The duration analysis retains the same formulations at each endpoint within a regimen. This restriction ensures that changes in regimen means reflect a consistent formulation set. The matched comparison uses five shared formulations at four weeks, yielding ten measurements organised into five pairs. No observations were lost through missing exposure or outcome values.

Retention is expressed as the published concentration relative to its initial measured concentration. Temperature remains in degrees Celsius and duration remains in weeks. Formulation identity provides a matching and stratification category rather than a numerical score. The profile code distinguishes cycling from constant exposure without implying an ordered scale. The observations have unequal schedules across regimens and are not treated as an annual panel. Published aggregate means remain the analytical observations; experimental injections and technical replicates are not reconstructed as additional records. Reported quantities following the ± symbol are preserved for traceability but are not interpreted as standard errors or used as precision weights.

4.3 Descriptive Calculations and Analytical Sequence:

Analysis begins with the consolidated observation file. Records are grouped by thermal regimen, formulation and exposure duration. Unique record identifiers distinguish individual aggregate measurements, while series identifiers connect repeated observations for the same formulation and regimen. Required analytical fields are checked for completeness before calculations. For the complete sample and each regimen, the analysis calculates valid counts, arithmetic means, sample standard deviations, medians, minima and maxima. Endpoint summaries are then calculated separately within each regimen. Equation 3 defines the arithmetic mean:

$$\bar{R}_g = \frac{\sum_{i=1}^{n_g} R_{ig}}{n_g}$$

Here, $\bar{R}_g$ is mean retention for group g, R_{ig} is reported retention for observation i in that group, and n_g is its number of observations. Groups comprise the complete sample, a thermal regimen or a regimen at a specified endpoint. Each published mean receives equal weight. Equation 4 defines dispersion across the included aggregate measurements:

$$s_g = \sqrt{\frac{\sum_{i=1}^{n_g}\left[R_{ig} - \bar{R}_g\right]^2}{n_g - 1}}$$

Here, s_g is the sample standard deviation in percentage points. It describes variation among aggregate measurements rather than uncertainty around an estimated population effect. Duration comparisons subtract an earlier observed retention value from a later value within the same formulation and regimen. Equation 5 specifies this calculation:

$$A_{fr} = R_{fr,t_b} - R_{fr,t_a}$$

Here, A_{fr} is the observed change for formulation funder regimen r, and R_{fr,t_b} and R_{fr,t_a} are retention at the later and earlier endpoints, respectively. Positive values indicate higher measured recovery at the later endpoint. These differences are not converted into weekly degradation rates. Signed departures from the initial reference follow Equation 1. The matched comparison then applies Equation 2 to the five shared formulations at four weeks. Individual differences are retained alongside their mean, median, standard deviation and range. Calculations use unrounded input values, with final descriptive outputs rounded to two decimal places.

4.4 Quality Checks, Interpretation and Reproducibility:

Quality checks assess identifier uniqueness; completeness of required fields and consistency of observation counts across source groups. The consolidated sample contains 29 unique record identifiers. Matching requires one observation per formulation and regimen at four weeks, producing five complete pairs without increasing the number of source measurements. The extraction prioritises explicit numerical table entries where article narrative ranges differ from those entries. Values above the initial reference are retained as reported. No imputation, interpolation, trimming or winsorisation is applied. These decisions preserve the published numerical evidence and avoid introducing unobserved endpoints.

The analysis distinguishes pooled comparisons from matched comparisons because their formulation coverage and observation schedules differ. The matched subset addresses those compositional differences at a common endpoint, but it does not separate temperature bounds from thermal profile. Repeated observations also share experimental series, and replicate covariance is unavailable. Accordingly, descriptive standard deviations are not presented as standard errors, and no significance tests or confidence intervals are constructed. Descriptive calculations were implemented using Python arithmetic and the standard statistics module. The workbook retains the extracted measurements, source identifiers, series identifiers, variable definitions and arithmetic formulas for derived quantities. These materials permit reproduction of the reported summaries and paired differences. The methodological contribution is a transparent application of descriptive comparison to published experimental evidence.

5. Findings:

This analysis examines insulin potency retention across thermal regimens, exposure durations and formulations. The findings address three research questions through 29 published aggregate measurements and five matched comparisons at four weeks. Interpretation focuses on observed magnitudes and formulation specific patterns.

5.1 Sample Composition and Potency Distribution:

The analytical sample comprises seven insulin formulations in twelve exposure series. Fourteen observations describe cycling temperatures between 25°C and 37°C at four and twelve weeks. Fifteen observations describe constant exposure at 31°C at one, four and eight weeks. All observations contain the temperature, duration, formulation and potency measurements required for descriptive analysis. The five formulations represented under both regimens provide ten measurements for the matched comparison. Across all observations, mean potency retention was 95.96%, the median was 99.70%, and the standard deviation was 7.02 percentage points. Retention ranged from 80.80% to 103.30%. These statistics describe variation among published aggregate means rather than variation among individual experimental replicates. Values exceeding 100% represent measured recovery relative to the initial analytical reference and were retained without adjustment. The observations originate from Table 1 and Supplementary Table S4 of Kaufmann et al., 2021. The results below are secondary calculations from those published measurements rather than additional experimental observations.

5.2 Potency Retention Across Thermal Regimens:

For RQ1, the pooled observations show higher retention under cycling temperatures. Mean retention was 100.86% across fourteen cycling observations, compared with 91.38% across fifteen constant exposure observations. The corresponding medians were 100.95% and 91.00%. Dispersion was also lower among cycling observations, with a standard deviation of 1.35 percentage points, compared with 7.10 percentage points under constant exposure. The distributional contrast extends beyond the pooled means. Cycling observations ranged from 98.40% to 103.30%, whereas constant exposure observations ranged from 80.80% to 101.50%. However, these pooled summaries combine different observation schedules and formulation coverage. Their difference therefore describes the assembled records and does not isolate the contribution of thermal profile. Household temperature monitoring by Braune et al., 2019, establishes the practical relevance of variable storage environments. Those monitoring data do not enter the present calculations, and the experimental contrasts should not be interpreted as measured differences among households.

5.3 Changes Across Exposure Durations:

For RQ2, potency trajectories differed between the observed regimens. Under constant exposure, mean retention declined from 99.60% at one week to 90.60% at four weeks and 83.94% at eight weeks. The same five formulations contributed at every endpoint. The decline therefore reflects changes within a consistent formulation set.

Table 4: Potency retention by regimen and observation time

Thermal Regimen	Exposure Duration in Weeks	Formulations	Mean Retention %	Standard Deviation in Percentage Points	Median Retention %	Minimum Retention %	Maximum Retention %
Cycling between 25°C and 37°C	4	7	100.73	1.57	100.60	98.40	103.30
Cycling between 25°C and 37°C	12	7	100.99	1.21	101.30	99.40	102.70
Constant exposure at 31°C	1	5	99.60	1.79	100.20	97.20	101.50
Constant exposure at 31°C	4	5	90.60	3.57	91.00	86.50	94.80
Constant exposure at 31°C	8	5	83.94	2.45	84.30	80.80	87.50

Every formulation under constant exposure recorded lower retention at four weeks than at one week and lower retention at eight weeks than at four weeks. The mean decline was 9.00 percentage points between weeks one and four, followed by 6.66 percentage points between weeks four and eight. Across the complete interval, the average decline was 15.66 percentage points. The magnitude varied by formulation. Mixed lispro declined by 20.00 percentage points between weeks one and eight, followed

by NPH isophane at 17.40, lispro at 17.20, glargine at 12.90 and aspart at 10.80 percentage points. Thus, the direction was consistent across all five formulations, while the size of the decline differed.

Cycling exposure produced a different pattern. Mean retention changed from 100.73% at four weeks to 100.99% at twelve weeks, an increase of 0.26 percentage points. Five formulations recorded higher measured recovery at twelve weeks, while lispro and mixed lispro recorded declines of 2.30 and 0.60 percentage points. These small increases above earlier measurements do not demonstrate recovery of degraded insulin. They describe variation in measured concentration relative to the initial reference. The formulation differences are consistent with the broader evidence that insulin analogues can differ in their susceptibility to aggregation. Woods et al., 2012, demonstrated such differences under conditions that removed stabilising excipients. That experiment supports formulation specific interpretation but does not establish the mechanism responsible for the present trajectories.

5.4 Matched Comparisons and Consistency of the Findings:

For RQ3, all five shared formulations recorded higher retention under cycling temperatures than under constant exposure at four weeks. Matching formulation identity and exposure duration reduced the compositional differences present in the pooled comparison.

Table 5: Matched potency retention at four weeks

Formulation	Cycling Retention %	Constant Exposure Retention %	Cycling Minus Constant Exposure in Percentage Points
Lispro analogue	101.70	91.00	10.70
Mixed lispro analogue	103.30	87.50	15.80
Glargine analogue	98.40	86.50	11.90
Aspart analogue	99.70	93.20	6.50
NPH isophane	101.30	94.80	6.50
Mean across five formulations	100.96	90.60	10.28

The average matched difference was 10.28 percentage points, with a median of 10.70 percentage points. Individual differences ranged from 6.50 to 15.80 percentage points. Mixed lispro recorded the largest difference, while aspart and NPH isophane recorded the smallest. The positive direction across every pair shows that the average contrast was not generated by a single formulation. The matched comparison strengthens the descriptive conclusion by holding formulation and duration constant. Temperature bounds and thermal profile nevertheless vary together: cycling exposure ranges between 25°C and 37°C, whereas constant exposure remains at 31°C. The observed difference therefore applies to these complete regimens. It does not identify separate effects of maximum temperature or cycling.

Experimental evidence from Teska et al., 2014, shows that preservative conditions can influence insulin analogue stability. Because preservative concentrations were not measured as predictors in the assembled dataset, the formulation differences cannot be attributed to that mechanism. The findings resolve the research questions descriptively. Retention was higher under the observed cycling regimen, declined across every measured interval under constant exposure, and remained close to the initial reference across the cycling endpoints. The five matched comparisons retained the same direction after aligning formulation and duration. Evidence from extended storage investigations, including Pendsey et al., 2023, reinforces the importance of interpreting retention within its specific exposure conditions rather than treating storage duration as a uniform predictor across environments.

6. Discussion:

Peak temperature alone provides an incomplete account of the observed insulin retention patterns. The matched comparisons in Table 5 show higher retention under cycling between 25°C and 37°C than under constant exposure at 31°C for every shared formulation. The mean difference of 10.28 percentage points, calculated through Equation 2, remains after matching formulation identity and storage duration. This analysis contributes an explicit synthesis of formulation matched differences from the published experimental measurements of Kaufmann et al., 2021. Its contribution is analytical rather than experimental: it makes the magnitude and consistency of the regimen contrast visible across products. The comparison directs attention towards the complete temperature trajectory rather than ranking storage conditions by their maximum temperature alone. The duration patterns in Table 4 distinguish sustained exposure from elapsed time considered independently of storage conditions. Retention declined across every observed interval under constant exposure, whereas cycling measurements remained close to the initial reference across the available endpoints. Equation 1 expresses these departures consistently without treating measured values above 100% as negative observations requiring removal. Protein stability theory provides a plausible interpretation because temperature and exposure time jointly shape opportunities for structural alteration. However, stabilising ingredients can modify that process. Teska et al., 2014, demonstrated different responses to preservative depletion among insulin analogues. The present comparison therefore supports interpreting duration within a defined formulation and thermal regimen, while leaving the molecular explanation to evidence that directly measures structural change.

Formulation differences qualify any interpretation based only on average retention. Table 5 records matched differences ranging from 6.50 to 15.80 percentage points, showing that a common direction can coexist with substantial variation in magnitude. Table 4 likewise shows consistent declines under constant exposure without implying identical deterioration across products. These patterns support a conditional interpretation of protein stability in which the formulation influences the observed response to storage conditions. Woods et al., 2012, identified differences in intrinsic fibrillation among insulin analogues after removing stabilising excipients. Their experiment helps explain why formulation identity matters conceptually, but its experimental conditions differ from those represented here. The theoretical implication is that thermal exposure should be evaluated as a formulation specific process rather than assigned a universal response across insulin products. The contrast between

laboratory control and household variability defines the practical boundary of these findings. Tables 4 and 5 describe assigned exposure regimens, whereas household storage involves changing environments that may not follow either experimental pattern. Braune et al., 2019, documented departures from recommended temperatures in both domestic refrigerators and carried insulin. This distinction means that refrigeration status alone cannot fully describe exposure, but the matched differences in Equation 2 cannot determine whether an individual household environment preserves insulin quality. For researchers and storage programme managers, the evidence supports recording temperature bounds, exposure patterns, duration and formulation together. It does not establish a replacement storage limit or justify extending product use beyond authorised instructions.

The international relevance lies in the comparison strategy rather than a claim of geographical differences in insulin stability. The experimental regimens reflect temperatures measured in northern Kenya, while Pendsey et al., 2023, examined extended storage under conditions encountered in India. Together, these settings make exposure specific interpretation relevant beyond any single country. The contribution of Table 5 is to hold formulation and duration constant before comparing reported retention, thereby reducing ambiguity introduced by pooled observations with different schedules. This approach refines how household relevant storage evidence can be assessed across settings. It also defines a focused empirical priority: comparisons using the same formulations and observation times, with temperature bounds varied independently of cycling, would distinguish the components currently combined within each regimen.

7. Conclusion and Implications:

Insulin storage decisions require evidence about the full exposure history, especially where refrigeration access is constrained. This analysis shows that sustained warmth and fluctuating conditions corresponded to different retention patterns across the tested products. Matching products and elapsed storage time preserved the direction of the contrast, demonstrating that pooled averages alone do not adequately communicate the experimental evidence. The contribution is a transparent secondary synthesis that makes comparisons explicit while preserving differences among formulations. This sharpens the application of protein stability theory by interpreting deterioration within defined exposure conditions rather than assuming a uniform response to warmth or time. For manufacturers and researchers, the findings support reporting complete thermal trajectories alongside product identity and measurement schedules. For programme managers, they support assessing storage evidence through comparable exposure conditions before drawing operational conclusions. Policy assessments should distinguish laboratory retention measurements from demonstrated performance in household use. Practical monitoring should document exposure duration and temperature fluctuations together, allowing storage events to be interpreted against relevant experimental evidence. Internationally, this approach offers a consistent basis for comparing findings across environments without assuming identical household conditions. Its social relevance lies in improving the evidence used to assess medicine storage while maintaining appropriate boundaries around clinical interpretation.

The aggregate measurements from one experiment provide a focused basis for extending comparative analysis. Future experiments should vary temperature bounds independently of cycling, use common observation schedules and retain replicate measurements to estimate uncertainty. Direct assessments of molecular structure and biological activity could distinguish concentration retention from functional performance. Studies combining monitored household exposure with laboratory testing of returned products would strengthen transferability across climates and storage practices. Broader product coverage would also clarify whether the observed contrasts persist across formulations, containers and batches. These extensions would test mechanisms and generalisability beyond the descriptive comparisons established here.

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