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Implementing parallel spreadsheet models for health policy decisions: The impact of unintentional errors on model projections

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Abstract

Background

Spreadsheet software is increasingly used to implement systems science models informing health policy decisions, both in academia and in practice where technical capacity may be limited. However, spreadsheet models are prone to unintentional errors that may not always be identified using standard error-checking techniques. Our objective was to illustrate, through a methodologic case study analysis, the impact of unintentional errors on model projections by implementing parallel model versions.

Methods

We leveraged a real-world need to revise an existing spreadsheet model designed to inform HIV policy. We developed three parallel versions of a previously validated spreadsheetbased model; versions differed by the spreadsheet cell-referencing approach (named single cells; column/row references; named matrices). For each version, we implemented three model revisions (re-entry into care; guideline-concordant treatment initiation; immediate treatment initiation). After standard error-checking, we identified unintentional errors by comparing model output across the three versions. Concordant model output across all versions was considered error-free. We calculated the impact of unintentional errors as the percentage difference in model projections between model versions with and without unintentional errors, using +/-5% difference to define a material error.

Results

We identified 58 original and 4,331 propagated unintentional errors across all model versions and revisions. Over 40% (24/58) of original unintentional errors occurred in the column/row reference model version; most (23/24) were due to incorrect cell references. Overall, >20% of model spreadsheet cells had material unintentional errors. When examining error impact along the HIV care continuum, the percentage difference between versions



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with and without unintentional errors ranged from +3% to +16% (named single cells), +26% to +76% (column/row reference), and 0% (named matrices).

Conclusions

Standard error-checking techniques may not identify all errors in spreadsheet-based models. Comparing parallel model versions can aid in identifying unintentional errors and promoting reliable model projections, particularly when resources are limited.

Introduction

Systems science approaches are increasingly used to inform health policy decisions and the allocation of scarce resources [1]. While a variety of frameworks exist to represent a system, model implementation is often complex and unclear, hindering acceptance of model results.

To promote the uptake of model findings into practice, the health-related literature and international guidance on best modeling practices emphasize two model characteristics: accessibility (i.e., ease of model use and reliance on widely available software) and transparency (i.e., clarity in the methods used to develop and implement models) [2–7]. Model implementation using spreadsheet software can improve both. Spreadsheet software allows for clear presentation of a model's structure or health states, values for the data used to populate the model, and mathematical relationships between the health states and data. Spreadsheet model calculations are immediately accessible, as is the impact of changes in the input data on the model's projected outcomes, all in real time to reflect local needs and with minimal training. The inherent transparency of spreadsheet models thus promotes model credibility, which is valued highly by decision makers [7].

Spreadsheet-based models, while transparent and accessible, are cumbersome and prone to implementation error [8]. These errors can have profound policy implications [9–11], particularly in contexts with constrained resources and limited technical capacity. While best practice guidelines on error identification approaches do exist (e.g., assessment of model performance, double-programming) [4, 7], practical, straightforward, and evidence-based guidance is limited on approaches to identify errors beyond standard error identification techniques and for settings with limited resources. Capitalizing on a real-world need to make policy-relevant updates to an existing spreadsheet-based model, the HIV Policy Model [12, 13], we aimed to illustrate, through a methodologic case study analysis, the impact of unintentional errors on model projections by implementing parallel model versions.

Materials and methods

Study design

We conducted a methodologic case study analysis in order to demonstrate the feasibility of the proposed method—i.e., implementation of parallel model structures—in identifying unintentional errors for spreadsheet models developed and updated in real-world settings. The analysis was designed to demonstrate the method's practical potential by illustrating the substantial impact that unintentional errors can have in informing policy decisions.

We emphasize that this methodologic demonstration was intended to bridge the gap between academia and practice by addressing the need for practical, timely solutions for avoiding unintentional model errors in real-world settings [2]. Modeling guidelines recommend, among other well-established model verification techniques, use of double-programming, in which multiple trained programmers independently implement models [4]. However, implementation of this approach may not be feasible due to lack of technical capacity, time, or financial resources [7]. In the context of increasing interest from decision makers from a variety of resource-limited settings (such as state health departments and ministries of health) in generating evidence to inform their decisions [14, 15], practical new approaches are necessary. Broadly, this methodologic demonstration involves mimicking real-world conditions (i.e., a single programmer) and demonstrating that during model revision, unintentional errors can occur, can be identified, and have the potential for substantial policy impact. As importantly, we demonstrate that this practical, straightforward solution can be implemented and used to identify errors that might otherwise go unnoticed.

Existing spreadsheet model: The HIV Policy Model

The HIV Policy Model is a multi-cohort, state-transition model of treated and untreated HIV disease, originally developed for Haitian decision makers to examine the number of deaths averted by earlier antiretroviral therapy (ART) initiation and scale-up. The model employs a conceptually simple structure and is implemented using widely available spreadsheet software (Microsoft Excel, Redmond, WA, USA). The original deterministic model includes 13 main health states, subdivided to characterize the nuances of disease progression and care engagement for a total of 48 health states. These health states are captured in approximately 1,100 spreadsheet cells over a 15-year policy-relevant time horizon. Successive, hypothetical cohorts of HIV-positive individuals enter the model annually and progress through three mutually exclusive, collectively exhaustive stages of untreated disease that are defined according to immunologic status (i.e., CD4 cell count). The stages of untreated disease are: Asymptomatic (corresponding to CD4 count >350 cells/ μ L), Intermediate (CD4 count 200–350 cells/ μ L), and AIDS (CD4 count <200 cells/ μ L). Within each disease stage, fractions of a cohort remain out of care, enter pre-treatment care, initiate ART, become lost to follow-up, or die. Transition probabilities are derived from local patient-level clinical data from three observational cohorts and a randomized trial of early versus delayed ART [16-22], conducted over more than twenty years by the Haitian Study Group for Kaposi's Sarcoma and Opportunistic Infections clinic that provides comprehensive HIV testing, treatment, and related services in Port-au-Prince, Haiti. The model's performance is assessed systematically and iteratively through face validity checks, examining model behavior (e.g., logic checks, identification of implementation errors), testing internal validity, and corroborating model projections using external data sources [4, 7, 13]. Additional details on the model structure, data used to parameterize the model, and model calibration and validation process, as well as findings from policy analyses, are available elsewhere [12, 13].

Parallel model versions

We developed the initial HIV Policy Model to be compact, with all transition probabilities to a given health state characterized in a single cell formula and, following best practices, relying primarily on the use of cell names [23]; we refer to this version as <u>Single Name</u>. We compared two additional versions: <u>Single Cell</u> retained the same structure and format but used column/ row cell references (e.g., A1), instead of cell names. <u>Matrix</u> used transition probability matrices, with health state transitions occurring across multiple cells and relying on cell names (for transition probability matrices) and cell references (for matrix multiplication). Prior to revisions described below, Matrix had approximately 37,000 cells versus the 1,100 in the other versions. However, for ease in error identification and impact calculation across model versions, we also presented Matrix output in the same compact structure as Single Name and Single Cell.

Model revisions

Across all versions, we assessed three policy-relevant revisions to evaluate unintentional errors and their impact on model projections (Fig 1). The first revision, <u>Re-entry into Care</u>, reflected realistic clinical care engagement practices by incorporating new transitions from existing health states: patients lost to follow-up in the Intermediate or AIDS health states could return to care. The second, <u>Universal ART</u>, allowed for immediate initiation of ART upon diagnosis, regardless of stage of disease progression and in line with the global debate then surrounding guidelines for antiretroviral initiation in low-income settings [24–26]. The third, <u>Guideline-based ART</u>, incorporated new health states allowing for antiretroviral initiation in line with new guidelines at the time of model revision [27]; this accommodated antiretroviral initiation. International guidelines for ART initiation changed twice during model development, requiring model revisions to remain up-to-date. One programmer implemented all revisions. For each model revision, fidelity to the revision specification was enhanced via written documentation of the planned revision, detailed graphical representations of the planned revisions, comprehensive logs outlining all model updates, and comparison of the revised model to the revision plan.

Analytic approach and policy impact

To identify errors, we implemented a given revision across all three model versions, conducted standard debugging techniques following best practices for systems modeling [4], and

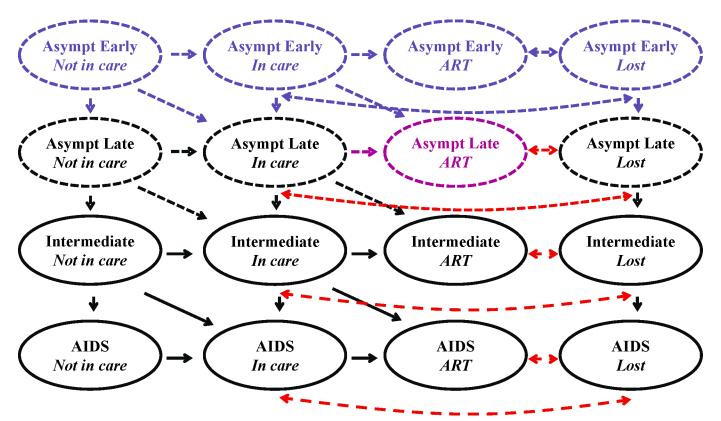


Fig 1. Schematic of revisions to the HIV Policy Model. Shown is a simplified schematic of the HIV Policy Model. Each oval represents a main health state and the arrows represent transitions between health states. Dotted lines reflect new health states or transition probabilities, while colors indicate the implemented model revision. Red represents the Re-entry into Care revision, purple the Universal ART revision, and blue the Guideline-based ART revision. Death from AIDS-or non-AIDS-related causes is not shown.

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compared output for all three model versions simultaneously to identify remaining unintentional errors. Standard error identification approaches included: face validity checks (e.g., simple checks of output reasonableness), negative output tests (i.e., functionality checks to confirm that the model does not project negative output), extreme value analysis (e.g., mortality risk for a given value at either 0 or 1), alternative assumptions about the model's initial cohort distribution across health states (e.g., the initial cohort is in a single health state), and tracking of the size of a single cohort over time [4, 7, 28]. To detect unintentional errors, we identified discrepancies in output across model versions, assuming that models free of unintentional errors should project identical output. Specifically, for each revision, an error was detected when the difference in the projected number for a given spreadsheet cell between two model versions was not zero (Eqs 1–3):

r

r

$$n_{c, SN} - n_{c, SC} \neq 0 \tag{1}$$

$$n_{c, SN} - n_{c, M} \neq 0 \tag{2}$$

$$n_{c,SC} - n_{c,M} \neq 0 \tag{3}$$

where *n* is the projected number in spreadsheet cell *c* for a given model (*SN*: Single Name, *SC*: Single Cell, *M*: Matrix). This process is depicted visually in Fig 2 and is shown in tabs Diff (SN-SC), Diff (SN-Matrix), and Diff (SC-Matrix) in S1 File, S3 File and S5 File. The identification process for unintentional errors was complete when we corrected all identified unintentional errors and found no discrepancies in output across versions. That is, for each corresponding cell across model versions:

$$n_{c, SN} - n_{c,SC} = 0 \tag{4}$$

Haalth state	Model version	Year										
Health state	woder version	2010	2011	2012	2013							
Asympt Early, Not in Care	Single Name	25,833	24,960	24,407	24,056							
	Single Cell	25,833	24,960	24,407	30,025							
	Matrix	25,833	24,960	24,407	24,056							

Fig 2. Example of unintentional errors detected by comparing model projections. This figure is a snapshot of projections from all three model versions (Single Name, Single Cell, Matrix) for the Guideline-based ART revision. Each cell in this snapshot shows the number of people living with HIV projected to be in a given health state (Asymptomatic Early stage of disease, Not engaged in care) between 2010 and 2013, after standard debugging. The figure shows that model output for this health state is identical across the three model versions for 2010, 2011, and 2012, indicating no unintentional implementation errors. However, in 2013, the projected output for this health state differs across the three model versions (Single Name: 24,056, Single Cell: 30,025, Matrix: 24,056). In this example of an unintentional error, the principle error was due to an incorrect cell reference in the Single Cell model version, was propagated over an additional 10 health states, and took 10 minutes to identify and correct. Full model projections for the Guideline-based ART revision with unintentional errors are available in tabs Model (SN), Model (SC), and Model (Matrix) in S5 File.

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$$\boldsymbol{n}_{c, SN} - \boldsymbol{n}_{c, M} = 0 \tag{5}$$

$$n_{c, SC} - n_{c, M} = 0 \tag{6}$$

where *n* is the projected number in spreadsheet cell *c* for a given model (*SN*: Single Name, *SC*: Single Cell, *M*: Matrix). This process was performed separately for each model revision (Re-Entry into Care, Guideline-based ART, and Universal ART) and is shown in tabs Diff (SN-SC), Diff (SN-Matrix), and Diff (SC-Matrix) in supplementary files S2 File, S4 File, and S6 File.

We classified and characterized unintentional errors identified in Eqs <u>1</u>–<u>3</u>. Unintentional errors were classified as due to: incorrect cell names, incorrect cell references, incorrect range (s) in a formula, incorrectly copied formulae, overwritten formulae, and misuse of built-in functions [29]. For each revision, we also examined: number, type, and location of errors; time required to implement each revision and correct errors; and error rate—the number of errors per total time spent implementing revisions and corrections. Employing the "original sin" rule, we counted errors only in the original cell where the error occurred [30]. However, we also tracked propagated errors, which were repeated with incorrectly copied formulae or when original errors resulted in errors in dependent cells.

To examine the impact of unintentional errors, we compared projections for models with versus without unintentional errors. We first identified our gold standard comparator, which was the corrected model fulfilling Eqs 4-6. For a given spreadsheet cell in each model version, we then calculated the percentage difference between the revised (but incorrect) model version and the subsequent revised, gold-standard model that was error-free to our knowledge [10] (Eqs 7–9):

$$\frac{n_{c, SN, errors} - n_{c, SN, no errors}}{n_{c, SN, no errors}} \times 100 = \% \text{ difference}_{c, SN}$$
(7)

$$\frac{n_{c, SC, errors} - n_{c, SC, no errors}}{n_{c, SC, no errors}} \times 100 = \% \text{ difference}_{c, SC}$$
(8)

$$\frac{n_{c, M, \text{ errors}} - n_{c, M, \text{ no errors}}}{n_{c, M, \text{ no errors}}} \times 100 = \% \text{ difference}_{c, M}$$
(9)

where *n* is the projected number in spreadsheet cell *c* for a given model (SN: Single Name, SC: Single Cell, or M: Matrix) that either has unintentional errors (denoted as *errors*) or has no known unintentional errors (denoted as *no errors*). These calculations are shown in detail in <u>S7 File</u>. Our threshold for error seriousness was 5%, a threshold for an error to be considered material [31].

We also assessed the impact of errors for outcomes along the HIV care continuum (i.e., total number HIV-infected, diagnosed and linked to care, receiving ART, retained in care prior to ART and retained in care when receiving ART), a policy-relevant lens for evaluating HIV programs [32, 33]. To do so, we calculated the percentage difference in the number in each step along the care continuum by 2023 between model versions with and without unintentional errors, similar to Eqs 7–9. Model versions with and without unintentional errors for each of the three revisions are available as supporting information in S1–S7 Files.

Results

Types of unintentional errors and unintentional error rate

Across all revisions and versions, 58 original unintentional errors occurred, with most due to incorrect cell references (69%) or names (28%) (Table 1). The 58 original unintentional errors occurred in a total of 2,208 new or revised model spreadsheet cells (736 changed cells / model version x 3 model versions = 2,208), with approximately 3% of changed model cells having an

Version Revis	Revision	Unintent	ional errors (nur	nber)	Model cells		Unintenti errors / m (%)		Time (h	nours)		Unintentional error rate (number / hour)		
		Original	Туре	Propagated	Total	New or revised model cells	Total model cells	Original errors / changed cell	Total errors* / model cell	Revise model	Identify, correct errors	Total	Original†	Propagated‡
	1	Incorrect cell name (1)	146	147	76	1,360	1%	11%	0.7	<0.1	0.7	1.5	213.7	
	Universal	7	Incorrect cell references (4); Incorrect cell name (3)	851	858	220	1,640	3%	52%	0.9	0.6	1.5	4.8	580.2
	Guideline	e 10 Incorrect co reference (7 Incorrect co name (3)		1178	1188	440	2,140	2%	56%	1.6	0.6	2.2	4.7	547.9
	Subtotal:	18		2173	2193	736	5,140	2%	43%			4.3	4.2	505.8
Cell Unive	Re-entry	0	_	-	0	76	1,360	0%	0%	0.8	-	0.8	-	-
	Universal	17	Incorrect cell references (17)	841	858	220	1,640	8%	52%	1.1	3.3	4.4	3.8	190.4
	Guideline	7	Incorrect cell reference (6); Logic (1)	752	759	440	2,140	2%	35%	3.1	0.6	3.7	1.9	204.2
	Subtotal:	24		1593	1617	736	5,140	3%	31%			8.9	2.8	179.0
Matrix	Re-entry	0	-	-	0	76	1,360	0%	0%	0.7	-	0.7	-	-
	Universal	7	Incorrect cell reference (6); Typographical error (1)	409	416	220	1,640	3%	25%	1.8	0.7	2.4	2.9	168.1
	Guideline	9	Incorrect cell name (9)	154	163	440	2,140	2%	8%	3.1	1.1	4.2	2.1	36.4
	Subtotal:	16		563	579	736	5,140	2%	11%			7.3	2.2	76.9

* Total errors are defined as the sum of original and propagated errors.

† Original error rate: original unintentional errors (column 3) per total time spent revising the model and identifying and correcting unintentional errors (column 12).
‡ Propagated error rate: propagated unintentional errors (column 5) per total time spent revising the model and identifying and correcting unintentional errors (column 12).

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original unintentional error. The number of original unintentional errors per changed cell was similar across model versions (2%, Single Name; 3%, Single Cell; 2%, Matrix), although was as high as 8% for the Universal model revision. Across all model versions and revisions, we identified 4,331 propagated errors arising from the original unintentional errors, resulting in an overall unintentional error rate of 28% ([58 original errors + 4,331 propagated errors] / [5,140 total model cells / model version x 3 model versions] * 100% = 28%). The most original unintentional errors (24 errors) occurred in Single Cell, which also required the most implementation time (8.9 hours; 2.8 original unintentional errors/hour). While the least time (4.3 hours) was spent revising and correcting Single Name, it had the most propagated unintentional errors; 4.2 original unintentional errors and highest unintentional error rate (2173 propagated unintentional errors and the lowest error rate.

Impact of unintentional errors on model output

We examined the impact of unintentional errors on model output (Table 2, Fig 3). Across all models and revision, 22% of model spreadsheet cells had model output differences of >5%, the threshold for an error to be considered material (3,373 material unintentional errors / [5,140 total model cells / model version x 3 model versions] * 100% = 22% [31]. However,there was wide variation across model versions and revisions in the percentage of cells with material errors, ranging from 0% to 51% (Single Name), 0% to 43% (Single Cell), and 0% to 8% (Matrix). Some of the differences in model output arising from material unintentional errors were substantial: Overall, 6% of spreadsheet cells with material unintentional errors more than doubled model output across all model versions and revisions (Summary Table tab in S7 File). However, the greatest model output differences generally occurred in the more complex revision (e.g., Guideline-based ART) for the Single Name and Single Cell versions. At times, there were major differences in model output arising from unintentional errors. For example, in the Matrix model version (Guideline-based ART revision), 11 spreadsheet cells, or approximately 7% of spreadsheet cells with material unintentional errors, increased model output for a particular cell by more than eight times. Detailed information on the magnitude of error impact, by model and revision, is available in S7 File; for example, in the Re-entry, SN tab, Panel 1 shows the model output with unintentional errors, Panel 2 shows the model output with errors corrected, Panel 3 shows the percentage difference between the uncorrected and corrected models, and Panel 4 provides a summary of error magnitude.

In assessing the impact of unintentional errors on key steps along the HIV care continuum, we found wide variation in the percentage difference in model output for versions with and

	Frequency (percentage)† of spreadsheet cells																	
								ingle Cell						Matrix				
Type of error*	Re-entr	-entry Universal Guideline		Re-entry Universal			Guideline		Re-entry		Universal		Guideline					
No error	1,213	(89)	782	(48)	952	(44)	1,360	(100)	782	(48)	1,381	(65)	1,360	(100)	1,224	(75)	1,977	(92)
Non-material error	147	(11)	150	(9)	91	(4)	0	(0)	147	(9)	187	(9)	0	(0)	285	(17)	9	(0)
Material error	0	(0)	708	(43)	1097	(51)	0	(0)	711	(43)	572	(27)	0	(0)	131	(8)	154	(7)

Table 2. Frequency and percentage of error type.

*A non-material error is defined as an error for which the percentage difference is \leq 5% for model output in a given spreadsheet cell from model with errors versus the model without known errors. Errors with >5% difference for model output in a given spreadsheet cell were considered material errors.

† The total number of spreadsheet cells for the Re-entry revision is 1,360, for the Universal revision is 1,640, and for the Guideline revision is 2,140. Shown are column percentages for each revision in each model version. The overall percentage of spreadsheet cells with errors reported in the text is based on the sum of all errors or all material errors divided by the sum of all spreadsheet cells (15,420). Column percentages may not add to 100% due to rounding.

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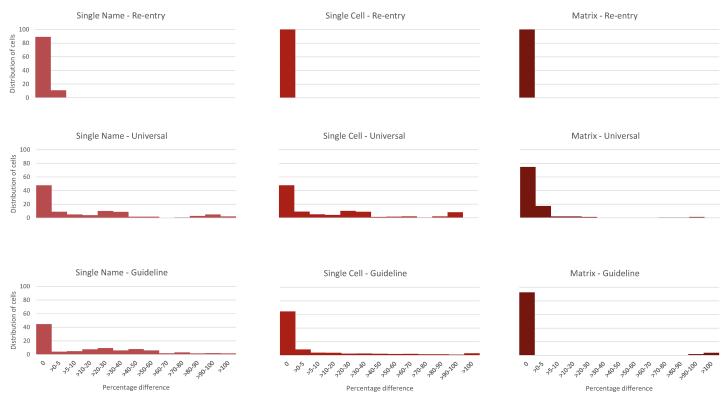


Fig 3. Distribution of the percentage difference in model output due to implementation errors, by model version and revision. This figure shows the distribution of the size of unintentional errors for each cell in the spreadsheet model. The horizontal axis shows the percentage difference in model projections for models with unintentional errors compared to the revised, gold-standard model without unintentional errors. The vertical axis shows the percentage of spreadsheet cells. Panels are organized from least complex model revision to most complex (top to bottom). A percentage difference of 0% indicates no unintentional error. No unintentional errors occur in the Re-entry revision of the Single Cell–Re-entry model version. However, nearly half of cells in the more complex Universal revision of the Single Cell model version produced a >5% difference between model projections with versus without unintentional errors.

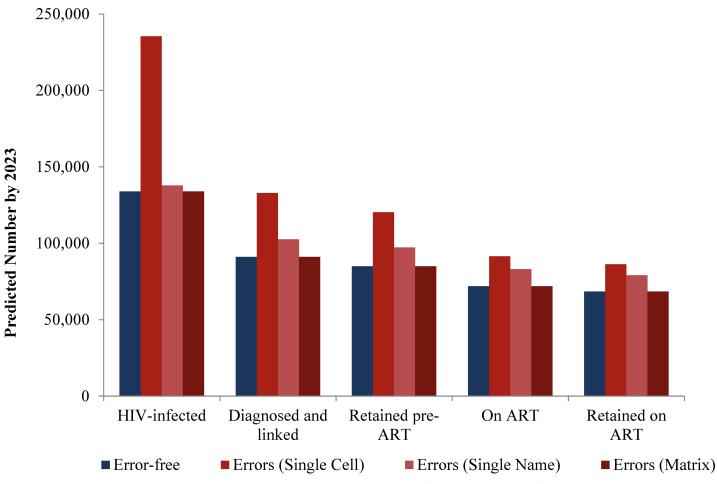
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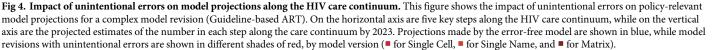
without unintentional errors, with more complex revisions generally resulting in larger projection differences. For example, differences in model output for less complex revisions ranged from 0% (Re-entry) to -17% (Universal ART) across all model versions. The most complex revision implemented, Guideline-based ART, yielded projection differences ranging from 3% to +16% (Single Name), +26% to +76% (Single Cell), and 0% (Matrix) across the HIV care continuum (Fig 4).

Discussion

Across all model versions, this methodologic case study analysis finds that implementation of model revisions generally results in unintentional errors. This demonstration also suggests that at times, unintentional errors can result in substantial policy implications, with near doubling of projections along one step in the HIV care continuum. While our demonstration cannot assess the extent to which unintentional errors may be due to random variability or propensity for larger errors in some model types, our results do illustrate the range of possible outcomes that might occur in the real world: unintentional errors may not materially affect projections, or they could change a study's policy conclusions.

While there is no 'best' model structure, using multiple versions of the same model to validate results may be one way, in additional to traditional debugging approaches, to reduce unintentional errors in spreadsheet models that may be used to inform policy decisions. Our





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study corroborates recent findings emphasizing the importance of cross-model validation and use of multiple model versions to identify implementation errors and assess model assumptions [34]. While this process may be time consuming and potentially expensive, it is crucial for identifying unintentional errors. This approach can be relatively easily and routinely implemented for simple deterministic model structures with analytical solutions, as well as for more complex model structures (e.g., Monte Carlo simulation) by using fixed seeds for the generation of random numbers.

This approach could be especially valuable in settings with limited resources and technical capacity. Analysts with limited training are especially in need of simple, validated ways to verify model outputs in simple forecasting models they may have developed to inform local policy. High-quality evidence, including systematic and thorough model validation efforts, thus becomes a critical step not only in model implementation but in allocating scarce resources [35]. Given the potential for this method of error-checking to prevent policy mistakes, decision makers in resource-limited settings may find this approach of parallel model comparisons to be worth the resource investment.

This study's findings contribute to an increasing literature on systems science model performance assessment, including error identification, in the health context. Best practice guidelines highlight the importance of debugging (i.e., error elimination), transparency, and broader model performance assessment processes [4, 36], as well as the importance of reporting these methods (e.g., see the CHEERS checklist [37]). Much of the existing literature addresses specific model validation and calibration approaches [38-45] or focuses on demonstrating adequate model performance for existing disease-specific models [34, 46-52]. Emerging work by Caro has introduced an approach to integrate different decision analytic modeling approaches both to improve usability of these methods for decision makers and to increase model transparency [53]. A much smaller health-related literature addresses a key domain of model performance—error identification—and focuses mainly on describing error taxonomy and current approaches to error identification in spreadsheet models. Recent work by Chilcott and colleagues describes errors in health technology assessment models and provides qualitative insights into defining modeling errors, avoiding these errors, and identifying them [7]. Tappenden and Chilcott extend this work by developing a formal taxonomy of errors, including those related to model implementation, that can undermine model credibility [28].

The current analysis thus extends existing knowledge in several key ways: First, we introduce an additional approach, beyond standard error identification techniques, to identify unintentional errors. Because standard debugging techniques are well-suited for identifying errors that can be identified in extreme conditions (e.g., extreme value analysis, negative output tests), the current method offers an additional approach for identifying material errors that may otherwise go unnoticed. Indeed, this is among the first studies in the health modeling literature that contributes empirical evidence on the frequency and impact of unintentional errors. Second, we explicitly adopt a material error threshold with which to evaluate potential implementation errors, thresholds that are largely lacking in the health-related literature. While some existing work has referenced error thresholds in the context of assessing internal validity [13, 54] or performing cross-model validation [34], we are among the first, to our knowledge, to explicitly examine unintentional errors within a defined threshold. Finally, in an illustrative example, we highlight the potential impact of failing to identify material unintentional errors on policy decisions. Although such evidence exists outside the health sector [55–57], evidence quantifying how unintentional errors could influence health decision making is scant.

Our work has several limitations. First, we used a model representing clinical engagement for a single disease and the model's simple conceptual structure may not be applicable to all clinical policy questions. Second, mimicking constraints similar to resource-limited conditions, we conducted a methodologic case study analysis rather than a more rigorous experimental design, which suggests that our findings should be interpreted with caution. Specifically, one individual implemented model revisions and only one time, which did not allow us to assess measures of central tendency or random variability in our projections. Further, the single programmer implementing the model versions and revisions was knowledgeable about the model, which may have served to underestimate the number, and therefore the impact, of potential unintentional errors as well as the total time taken to implement model revisions, identify unintentional errors, and correct them. Similarly, an approach relying on a single programmer to implement multiple model versions (versus multiple programmers implementing a single model version [4]) may have resulted in repeated programming errors, thereby overestimating unintentional errors and their impact. However, despite these limitations, our findings suggest that unintentional errors occur when implementing spreadsheet models, that they can be identified, and that they could have significant policy implications.

This type of timely and practical solution for identifying unintentional errors is crucial for resource-limited settings that may rely on internal spreadsheet-based models to inform their policy decisions, such as health departments or Ministries of Health.

Third, we did not have available a single gold-standard, error-free model with which to identify implementation errors and make model projection comparisons. Because each model revision was made concurrently across model versions, we instead adopted an alternative approach: identification and correction of unintentional errors for each model version, resulting in an error-free model to our knowledge, which could be used as a comparator to its corresponding model with errors. We chose this approach to more thoroughly test the model's behavior, and future work on comparative approaches for unintentional error identification is warranted. We also did not compare projections from a parallel model implemented in a different software platform, an approach that may provide additional opportunities to identify unintentional errors [7]. Regardless of the software used for model implementation, however, findings from this work emphasize the importance of internal model validation as a means to confirm model implementation. In addition to the error identification approach described in the current analysis, a more comprehensive systematic, iterative model performance assessment process is also critical, particularly one that examines both internal and external validity [13]. Yet even comprehensive model validation efforts cannot ensure that a model reflects reality. Finally, while we found substantial differences in model projections using model versions with unintentional errors versus without, it is unclear whether a given policy decision would have changed as a result of unintentional errors as we lack additional economic cost or budget data as well as empirical data on how decision makers use model projections to inform policy.

Conclusions

In this research, we provide evidence that developing parallel model versions aids in identifying and resolving unintentional errors when revising spreadsheet models. This work suggests that standard error identification techniques may not identify all spreadsheet model errors and that unintentional errors can have a profound impact on model projections. Standard debugging techniques and modeling best practices are always recommended, but in some contexts, limited resources may preclude the use of standard but resource-intensive error identification techniques. As systems science approaches are scaled and begin to reach a variety of consumers, including decision makers who are well-positioned to respond to model findings, care should be taken to identify unintentional errors and promote reliable model projections. Implementation of parallel model versions during model development and revision is one means to do so.

Supporting information

S1 File. Re-entry_errors. This file contains the three model versions for the Re-entry into Care model revision, before identification of unintentional implementation errors. (XLSX)

S2 File. Re-entry_errors_corrected. This file contains the three model versions for the Reentry into Care model revision, after identification and correction of unintentional implementation errors. (XLSX)

S3 File. Universal ART_errors. This file contains the three model versions for the Universal ART model revision, before identification of unintentional implementation errors. (XLSX)

S4 File. Universal ART_errors_corrected. This file contains the three model versions for the Universal ART model revision, after identification and correction of unintentional implementation errors.

(XLSX)

S5 File. Guideline-based ART_errors. This file contains the three model versions for the Guideline-based ART model revision, before identification of unintentional implementation errors.

(XLSX)

S6 File. Guideline-based ART_errors_corrected. This file contains the three model versions for the Guideline-based ART model revision, after identification and correction of unintentional implementation errors.

(XLSX)

S7 File. Magnitude of unintentional errors. This file contains model output for a given model revision and version *with* unintentional errors, model output for a given model revision and version *without* unintentional errors, calculation of the error magnitude (defined as the percentage difference in model output for each spreadsheet cell for models with versus without unintentional errors), and the distribution of error magnitude. (XLSX)

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References

- Mabry PL, Olster DH, Morgan GD, Abrams DB. Interdisciplinarity and Systems Science to Improve Population Health: A View from the NIH Office of Behavioral and Social Sciences Research. American journal of preventive medicine. 2008; 35(2 Suppl):S211–24. https://doi.org/10.1016/j.amepre.2008.05.018
 PMID: 18619402
- Alistar SS, Brandeau ML. Decision making for HIV prevention and treatment scale up: bridging the gap between theory and practice. Medical decision making. 2012; 32(1):105–17. https://doi.org/10.1177/ 0272989X10391808 PMID: 21191118
- 3. Weinstein MC, Toy EL, Sandberg EA, Neumann PJ, Evans JS, Kuntz KM, et al. Modeling for health care and other policy decisions: uses, roles, and validity. Value in health: the journal of the International Society for Pharmacoeconomics and Outcomes Research. 2001; 4(5):348–61.
- Eddy DM, Hollingworth W, Caro JJ, Tsevat J, McDonald KM, Wong JB. Model Transparency and Validation: A Report of the ISPOR-SMDM Modeling Good Research Practices Task Force–7. Medical Decision Making. 2012; 32(5):733–43. https://doi.org/10.1177/0272989X12454579 PMID: 22990088
- 5. Kimmel AD, Schackman BR. Considerations for Developing Applied Health Policy Models: The Example of HIV Treatment Expansion in Resource-Limited Settings. In: Zaric GS, editor. Operations

Research and Health Care Policy. International Series in Operations Research & Management Science. 190: Springer New York; 2013. p. 313–39.

- 6. Rahmandad H, Sterman JD. Reporting guidelines for simulation-based research in social sciences. System Dynamics Review. 2012; 28(4):396–411. https://doi.org/10.1002/sdr.1481
- Chilcott J, Tappenden P, Rawdin A, Johnson M, Kaltenthaler E, Paisley S, et al. Avoiding and identifying errors in health technology assessment models: qualitative study and methodological review. Health technology assessment (Winchester, England). 2010; 14(25):iii–iv, ix-xii, 1–107.
- 8. Kruck SE, Sheetz SD. Spreadsheet accuracy theory. J Information Sys Educ. 2001; 12(2):93–108.
- 9. Kruck SE. Testing spreadsheet accuracy theory. Information Software Technol. 2006; 48(3):204–13. https://doi.org/10.1016/j.infsof.2005.04.005
- Powell SG, Baker KR, Lawson B. Impact of errors in operational spreadsheets. Decision Support Systems. 2009; 47(2):126–32.
- Hill SR, Mitchell AS, Henry DA. Problems with the interpretation of pharmacoeconomic analyses: a review of submissions to the Australian Pharmaceutical Benefits Scheme. Jama. 2000; 283(16):2116– 21. PMID: 10791503
- Kimmel AD, Charles M, Deschamps MM, Severe P, Edwards AM, Johnson WD, et al. Lives saved by expanding HIV treatment availability in resource-limited settings: the example of Haiti. Journal of acquired immune deficiency syndromes (1999). 2013; 63(2):e40–8. https://doi.org/10.1097/QAI. 0b013e3182918875 PMID: 23535289
- Kimmel AD, Fitzgerald DW, Pape JW, Schackman BR. Performance of a Mathematical Model to Forecast Lives Saved from HIV Treatment Expansion in Resource-Limited Settings. Medical Decision Making. 2015; 35(2):230–42. https://doi.org/10.1177/0272989X14551755 PMID: 25331914
- Uneke CJ, Ezeoha AE, Ndukwe CD, Oyibo PG, Onwe F. Promotion of evidence-informed health policymaking in Nigeria: bridging the gap between researchers and policymakers. Global public health. 2012; 7(7):750–65. https://doi.org/10.1080/17441692.2012.666255 PMID: 22394290
- Rosenfeld LA, Fox CE, Kerr D, Marziale E, Cullum A, Lota K, et al. Use of computer modeling for emergency preparedness functions by local and state health officials: a needs assessment. Journal of public health management and practice. 2009; 15(2):96–104. https://doi.org/10.1097/01.PHH.0000346004. 21157.ef PMID: 19202407
- Charles M, Leger PD, Severe P, Guiteau C, Apollon A, Gulick RM, et al. Virologic, clinical and immunologic responses following failure of first-line antiretroviral therapy in Haiti. Journal of the International AIDS Society. 2012; 15(2):17375. https://doi.org/10.7448/IAS.15.2.17375 PMID: 22713258
- 17. Deschamps MM, Fitzgerald DW, Pape JW, Johnson WD Jr. HIV infection in Haiti: natural history and disease progression. AIDS (London, England). 2000; 14(16):2515–21.
- Fitzgerald DW, Severe P, Joseph P, Mellon LR, Noel E, Johnson WD Jr., et al. No effect of isoniazid prophylaxis for purified protein derivative-negative HIV-infected adults living in a country with endemic tuberculosis: results of a randomized trial. Journal of acquired immune deficiency syndromes (1999). 2001; 28(3):305–7.
- Leger P, Charles M, Severe P, Riviere C, Pape JW, Fitzgerald DW. 5-year survival of patients with AIDS receiving antiretroviral therapy in Haiti. The New England journal of medicine. 2009; 361(8):828– 9. https://doi.org/10.1056/NEJMc0809485 PMID: 19692699
- Pape JW, Jean SS, Ho JL, Hafner A, Johnson WD Jr. Effect of isoniazid prophylaxis on incidence of active tuberculosis and progression of HIV infection. Lancet (London, England). 1993; 342(8866):268–72.
- Severe P, Juste MA, Ambroise A, Eliacin L, Marchand C, Apollon S, et al. Early versus standard antiretroviral therapy for HIV-infected adults in Haiti. The New England journal of medicine. 2010; 363 (3):257–65. https://doi.org/10.1056/NEJMoa0910370 PMID: 20647201
- Severe P, Leger P, Charles M, Noel F, Bonhomme G, Bois G, et al. Antiretroviral therapy in a thousand patients with AIDS in Haiti. The New England journal of medicine. 2005; 353(22):2325–34. https://doi. org/10.1056/NEJMoa051908 PMID: 16319381
- 23. Spreadsheet Standards Review Board. Best Practice Spreadsheet Modeling Standards Version 7.12003 [28 November 2015]. Available from: http://www.ssrb.org/.
- Gallant JE, Mehta SH, Sugarman J. Universal antiretroviral therapy for HIV infection: should US treatment guidelines be applied to resource-limited settings? Clin Infect Dis. 2013; 57(6):884–7. <u>https://doi.org/10.1093/cid/cit382 PMID: 23759345</u>
- Lundgren J, Wood R. Editorial commentary: universal antiretroviral therapy for HIV infection?. Clin Infect Dis. 2013; 57(6):888–90. https://doi.org/10.1093/cid/cit381 PMID: 23759346
- Richardson E, Grant P, Zolopa A. Evolution of HIV treatment guidelines in high- and low-income countries: converging recommendations. Antiviral Res. 2014; 103:88–93. https://doi.org/10.1016/j.antiviral. 2013.12.007 PMID: 24374148

- 27. World Health Organization. Consolidated guidelines for the use of antiretroviral drugs for treating and preventing HIV infection. Recommendations for a public health approach. June 2013. [17 April 2017]. Available from: http://www.who.int/hiv/pub/guidelines/arv2013/en/.
- Tappenden P, Chilcott JB. Avoiding and identifying errors and other threats to the credibility of health economic models. PharmacoEconomics. 2014; 32(10):967–79. https://doi.org/10.1007/s40273-014-0186-2 PMID: 25027943
- Powell SG, Baker KR, Lawson B. A critical review of the literature on spreadsheet errors. Decis Support Syst. 2008; 46(1):128–38. https://doi.org/10.1016/j.dss.2008.06.001
- Panko RR, Aurigemma S. Revising the Panko-Halverson taxonomy of spreadsheet errors. Decis Support Syst. 2010; 49(2):235–44. https://doi.org/10.1016/j.dss.2010.02.009
- 31. Vorhies JB. The new importance of materiality. Journal of Accountancy. 2005; 199(5):53.
- Bradley H, Hall HI, Wolitski RJ, Van Handel MM, Stone AE, LaFlam M, et al. Vital Signs: HIV diagnosis, care, and treatment among persons living with HIV—United States, 2011. MMWR Morbidity and mortality weekly report. 2014; 63(47):1113–7. PMID: 25426654
- Gardner E, McLees M, Steiner J, Del Rio C, Burman W. The spectrum of engagement in HIV care and its relevance to test-and-treat strategies for prevention of HIV infection. Clin Infect Dis. 2011; 52 (6):793–800. <u>https://doi.org/10.1093/cid/ciq243</u> PMID: <u>21367734</u>
- 34. Jahn B, Rochau U, Kurzthaler C, Paulden M, Kluibenschadl M, Arvandi M, et al. Lessons Learned from a Cross-Model Validation between a Discrete Event Simulation Model and a Cohort State-Transition Model for Personalized Breast Cancer Treatment. Medical decision making. 2016; 36(3):375–90. https://doi.org/10.1177/0272989X15604158 PMID: 26476865
- Brunetti M, Shemilt I, Pregno S, Vale L, Oxman AD, Lord J, et al. GRADE guidelines: 10. Considering resource use and rating the quality of economic evidence. Journal of Clinical Epidemiology. 2013; 66 (2):140–50. https://doi.org/10.1016/j.jclinepi.2012.04.012 PMID: 22863410
- Caro JJ, Briggs AH, Siebert U, Kuntz KM. Modeling good research practices—overview: a report of the ISPOR-SMDM Modeling Good Research Practices Task Force—1. Value in health. 2012; 15(6):796– 803. https://doi.org/10.1016/j.jval.2012.06.012 PMID: 22999128
- Husereau D, Drummond M, Petrou S, Carswell C, Moher D, Greenberg D, et al. Consolidated Health Economic Evaluation Reporting Standards (CHEERS) Statement. Value in Health. 2013; 16(2):e1–e5. https://doi.org/10.1016/i.jval.2013.02.010 PMID: 23538200
- Enns EA, Cipriano LE, Simons CT, Kong CY. Identifying best-fitting inputs in health-economic model calibration: a Pareto frontier approach. Medical decision making. 2015; 35(2):170–82. https://doi.org/ 10.1177/0272989X14528382 PMID: 24799456
- Goldhaber-Fiebert JD, Brandeau ML. Evaluating Cost-effectiveness of Interventions That Affect Fertility and Childbearing: How Health Effects Are Measured Matters. Medical decision making. 2015; 35 (7):818–46. https://doi.org/10.1177/0272989X15583845 PMID: 25926281
- Jackson C, Jit M, Sharples L, DeAngelis D. Calibration of complex models through Bayesian evidence synthesis: a demonstration and tutorial. Medical decision making. 2015; 35(2):148–61. https://doi.org/ 10.1177/0272989X13493143 PMID: 23886677
- Karnon J, Vanni T. Calibrating models in economic evaluation: a comparison of alternative measures of goodness of fit, parameter search strategies and convergence criteria. PharmacoEconomics. 2011; 29 (1):51–62. https://doi.org/10.2165/11584610-000000000-00000 PMID: 21142278
- 42. Kong CY, McMahon PM, Gazelle GS. Calibration of disease simulation model using an engineering approach. Value in health. 2009; 12(4):521–9. https://doi.org/10.1111/j.1524-4733.2008.00484.x PMID: 19900254
- Taylor DC, Pawar V, Kruzikas D, Gilmore KE, Pandya A, Iskandar R, et al. Methods of model calibration: observations from a mathematical model of cervical cancer. PharmacoEconomics. 2010; 28 (11):995–1000. https://doi.org/10.2165/11538660-000000000-00000 PMID: 20936883
- Van Calster B, Vickers AJ. Calibration of risk prediction models: impact on decision-analytic performance. Medical decision making. 2015; 35(2):162–9. https://doi.org/10.1177/0272989X14547233 PMID: 25155798
- Vanni T, Karnon J, Madan J, White RG, Edmunds WJ, Foss AM, et al. Calibrating models in economic evaluation: a seven-step approach. PharmacoEconomics. 2011; 29(1):35–49. https://doi.org/10.2165/ 11584600-000000000-00000 PMID: 21142277
- 46. Ciaranello AL, Morris BL, Walensky RP, Weinstein MC, Ayaya S, Doherty K, et al. Validation and calibration of a computer simulation model of pediatric HIV infection. PloS one. 2013; 8(12):e83389. <u>https://doi.org/10.1371/journal.pone.0083389</u> PMID: 24349503

- Fryback DG, Stout NK, Rosenberg MA, Trentham-Dietz A, Kuruchittham V, Remington PL. The Wisconsin Breast Cancer Epidemiology Simulation Model. Journal of the National Cancer Institute Monographs. 2006;(36):37–47. https://doi.org/10.1093/jncimonographs/lgj007 PMID: 17032893
- Joranger P, Nesbakken A, Hoff G, Sorbye H, Oshaug A, Aas E. Modeling and validating the cost and clinical pathway of colorectal cancer. Medical decision making. 2015; 35(2):255–65. https://doi.org/10. 1177/0272989X14544749 PMID: 25073464
- Kim JJ, Kuntz KM, Stout NK, Mahmud S, Villa LL, Franco EL, et al. Multiparameter calibration of a natural history model of cervical cancer. American journal of epidemiology. 2007; 166(2):137–50. https://doi. org/10.1093/aje/kwm086 PMID: 17526866
- Rydzak CE, Cotich KL, Sax PE, Hsu HE, Wang B, Losina E, et al. Assessing the performance of a computer-based policy model of HIV and AIDS. PloS one. 2010; 5(9). https://doi.org/10.1371/journal.pone. 0012647 PMID: 20844741
- Salomon JA, Weinstein MC, Hammitt JK, Goldie SJ. Empirically calibrated model of hepatitis C virus infection in the United States. American journal of epidemiology. 2002; 156(8):761–73. PMID: 12370165
- Yeh JM, Kuntz KM, Ezzati M, Hur C, Kong CY, Goldie SJ. Development of an empirically calibrated model of gastric cancer in two high-risk countries. Cancer epidemiology, biomarkers & prevention. 2008; 17(5):1179–87. https://doi.org/10.1158/1055-9965.epi-07-2539 PMID: 18483340
- Caro JJ. Discretely Integrated Condition Event (DICE) Simulation for Pharmacoeconomics. PharmacoEconomics. 2016; 34(7):665–72. https://doi.org/10.1007/s40273-016-0394-z PMID: 26961779
- Goldie SJ, Yazdanpanah Y, Losina E, Weinstein MC, Anglaret X, Walensky RP, et al. Cost-effectiveness of HIV treatment in resource-poor settings—the case of Cote d'Ivoire. The New England journal of medicine. 2006; 355(11):1141–53. https://doi.org/10.1056/NEJMsa060247 PMID: 16971720
- Caulkins JP, Morrison EL, Weidemann T. Spreadsheet Errors and Decision Making: Evidence from Field Interviews. Journal of Organizational and End User Computing (JOEUC). 2007; 19(3):1–23. https://doi.org/10.4018/joeuc.2007070101
- 56. Panko RR. What we know about spreadsheet errors. J End User Comput. 1998; 10(2):15–21.
- 57. Powell SG, Baker KR, Lawson B. Errors in operational spreadsheets. Journal of Organizational and End User Computing. 2009; 21(3):24–36.