Bayesian Guidance & ClinicalTrials.gov Reporting: Closing the gap

Alignment of ClinicalTrials.gov reporting with FDA draft guidance on Bayesian methods

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Agenda

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02 FDA Guidance

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Introduction

Introduction

What the guidance covers?

- FDA recommendations on the appropriate use of Bayesian methods in clinical trials supporting drug and biologic approvals.
- Focused primarily on Bayesian methods used for primary inference of efficacy and safety.

How a Bayesian trial works?

- Applies the **Bayesian theorem** to assess treatment effect.
- Bayesian methods start with what we already know (**prior evidence**), combine it with new study results (**likelihood**), and then calculate an updated estimate (**posterior probability)** of how likely (**credible interval**) a treatment is to help or harm patients.

KEY CONCEPTS

1. **Prior evidence**
   Existing knowledge, historical or external data
2. **Likelihood**
   Evidence contributed by the observed trial data
3. **Posterior probability**
   Updated probability of treatment benefit or risk
4. **Credible interval**
   The range in which the effect lies, with stated probability

ClinicalTrials.gov results posting form currently lacks the dedicated data fields to report the key parameters based on Bayesian analysis.

*Source: Embracing Bayesian Methods in Clinical Trials: FDA's Long-Awaited Draft Guidance | Regulatory Agencies | JAMA | JAMA Network

Advantages of Bayesian guidance over other approaches

Flexibility in adaptive designs

Arms, doses and sample size can be adjusted based on accumulating data.

Efficient use of external data

Historical and registry data can be borrowed through the prior.

Enhanced interim decisions

Posterior probabilities give a direct basis for stopping rules.

More intuitive inference

Results stated as the probability that a treatment works.

Reduced sample size

Borrowing and adaptation can lower enrolment in some settings.

FDA Guidance for Reporting Bayesian Studies

FDA Guidance for Reporting Bayesian Studies

Pre-specification	Bayesian methods must be pre-specified before the trial begins.
Justified priors	Prior distributions must be scientifically justified and built in a clear, systematic way.
Defined criteria	Sponsors must define success criteria, operating characteristics, borrowing methods, p-value thresholds and sensitivity analyses.
Early FDA dialogue	Early discussion with FDA is strongly encouraged for complex Bayesian designs.

These expectations set the benchmark against which current ClinicalTrials.gov reporting was assessed.

Objectives and Methods

Objectives and Methods

RESEARCH QUESTION

How closely does ClinicalTrials.gov results reporting align with FDA recommendations for Bayesian trial design and analysis?

Sources

- Interventional studies posted on ClinicalTrials.gov that used Bayesian methods.
- FDA draft guidance on Bayesian methodology.

Search criteria

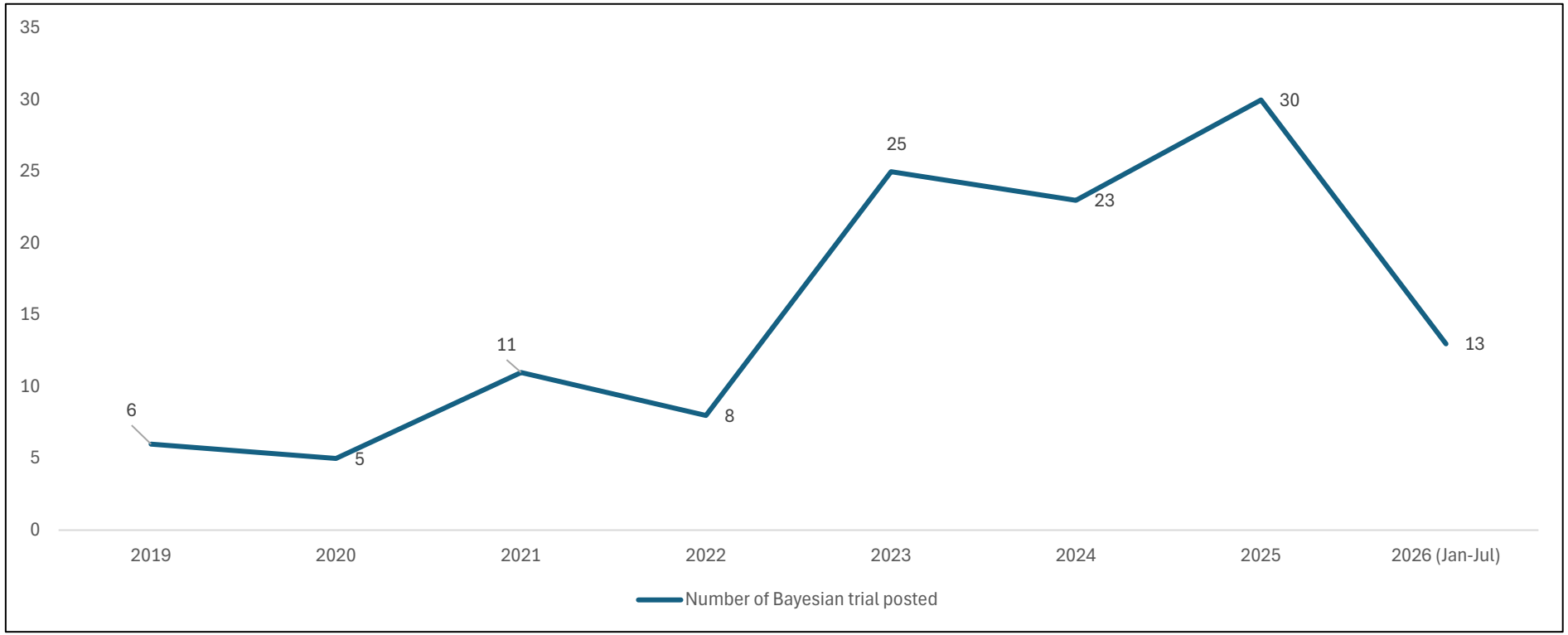
- Study type: Interventional
- Other artifact: Bayesian analysis
- Date first registered: between January 2016-July 2026 (~10 years).
- Trial with Results: Yes

10	years of data reviewed	**900**	registered trials with Bayesian analysis	**121**	with posted results (evaluable)	**50**	random studies reviewed

Observations

Observations: Annual reporting trend

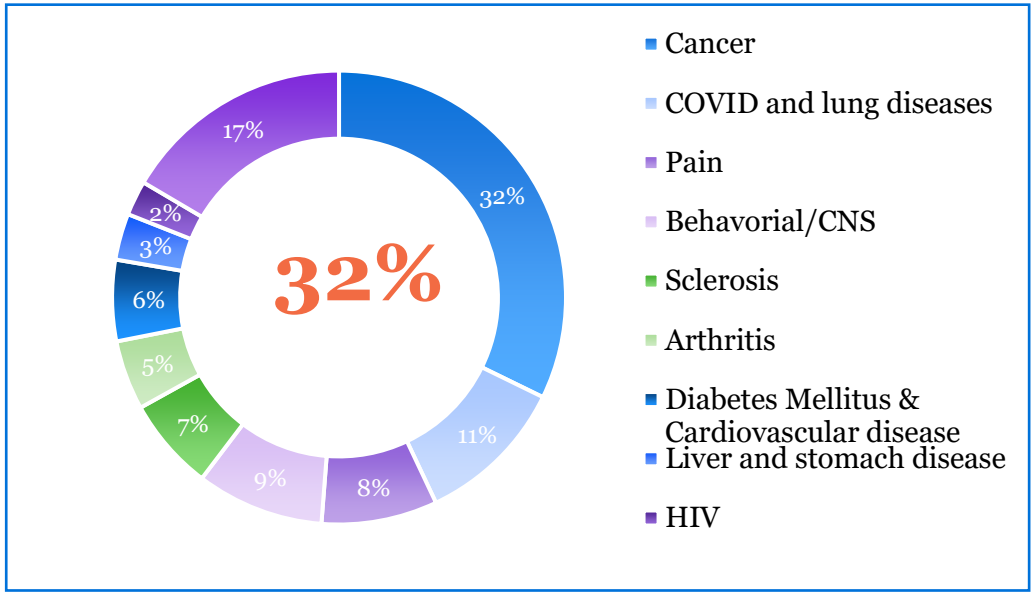
There has been an increase in the number of studies with Bayesian design reported on clinicaltrials.gov.



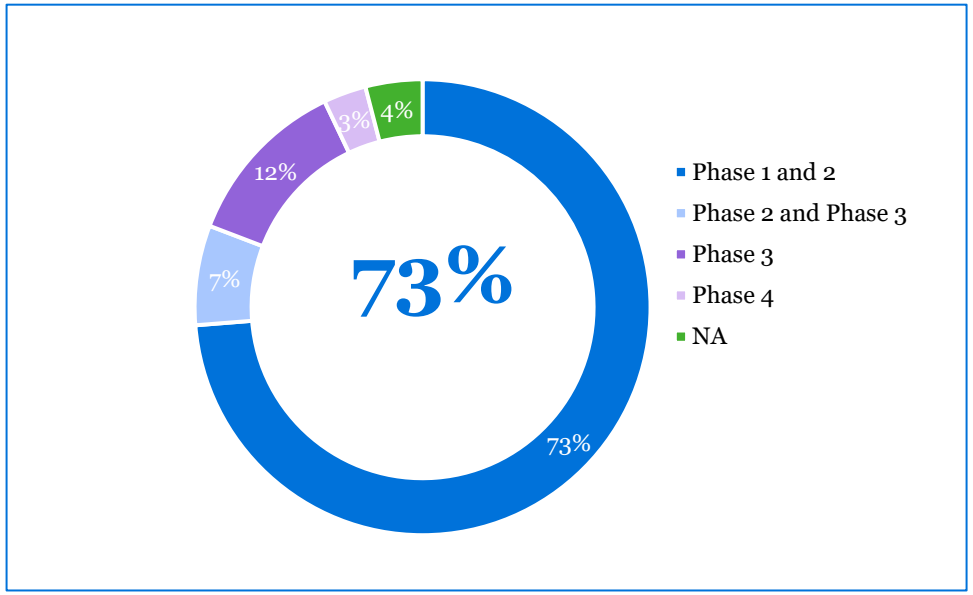
Note: Data is collected for trials results with Bayesian analysis posted on clinicaltrials.gov in the last 10 years.

Observations: Study conditions and Phase

Study conditions



Study phase



Increased adoption of Bayesian designs in early-phase and oncology trials — especially in trials using adaptive designs and complex scenarios, such as those lacking effective alternatives and with challenging patient recruitment*.

*Source: [Use of Bayesian approaches in oncology clinical trials: A cross-sectional analysis - PMC]

Observations: Gap analysis with PRS data fields

Bayesian FDA recommended element	Available Structured Field/Option in ClinicalTrials.gov?	Current reporting style
Bayesian model	No	Reported using OM description or statistical analysis comments free text field
Credible interval	No	
Prior distribution	No	
P (effect > δ)	No	
Posterior mean / median	No	Entered as Mean; estimation parameter used to report 'posterior mean difference'

⚠ ***While Bayesian information is documented within descriptive text fields, the lack of dedicated structured PRS fields drives variability in reporting practice.***

Bayesian results in posted studies: Current practice

EXAMPLE 1

Posterior mean difference and credible interval placed in estimation comments.

Ref: NCT03515824 (Merck Sharp & Dohme LLC)

Statistical Analysis 2	
Statistical Analysis Overview	
Comparison Group Selection	Part A: MK-1697 65 mg
Comments	[Not Specified]
Type of Statistical Test	Other
Comments	Bayesian posterior credible interval
Method of Estimation	
Estimation Parameter	Pooled-adjacent-violator algorithm
Estimated Value	0.0
Confidence Interval	(2-Sided) 80% 0.0 to 33.1
Estimation Comments	[Not Specified]

EXAMPLE 2

Bayesian mixed model and 95% credible interval embedded in the outcome description.

Ref: NCT04530552 (National Cancer Institute (NCI))

1. Change in Prostate Specific Antigen (PSA) Levels

Type: Primary | Time Frame: Baseline to end-of-intervention (mean 4.8 weeks; up to 9 weeks)

Description	The proportion of participants with >= 25% decline in PSA levels (from baseline to end-of-intervention) will be reported along with the 97.5% credible interval for the response rate based on the posterior distribution of the response rate derived from a non-informative prior for the response rate, which is consistent with the Bayesian approach.

Statistical Analysis 1	
Statistical Analysis Overview	
Comparison Group Selection	Cohort 1
Comments	Posterior probability of observing a response rate ≥ 50%
Type of Statistical Test	Other
Comments	[Not Specified]
Method of Estimation	

The information is present—but not consistently structured for retrieval or comparison.

Source: ClinicalTrials.gov screenshots reproduced from PHUSE Poster_Draft 5

Bayesian results in posted studies: Current practice

EXAMPLE 3

Posterior probabilities are mentioned in the OM description.

Ref: NCT04529096 (Eli Lilly)

Outcome Measures

Expand all / Collapse all

1. Change From Baseline for Average Pain Intensity as Measured by the NRS

Type: Primary | Time Frame: Baseline, up to Week 8

Description	The NRS was used during the preliminary data entry period and daily throughout the study to describe pain severity. Participants were asked to describe their average pain over the past 24 hours, on a scale of 0 to 10: 0 = no pain, and 10 = pain as bad as you can imagine. Posterior mean change from baseline, 95% credible interval (CrI) was derived using Bayesian mixed model repeated measures. The Bayesian analyses include posterior probabilities instead of p-values, and 95% credible intervals instead of 95% confidence intervals
Time Frame	Baseline, up to Week 8

EXAMPLE 4

Priors used are mentioned in statistical analysis comments.

Ref: NCT05838742 (GSK)

Statistical Analysis 1

Statistical Analysis Overview

Comparison Group Selection	Placebo, GSK3858279 - 60 mg Weekly
Comments	[Not Specified]
Type of Statistical Test	Other
Comments	Analysis performed using a Bayesian mixed model repeated measures adjusting for treatment, week, baseline, region and the treatment by week and baseline by week interactions using vague priors.

The information is present—but not consistently structured for retrieval or comparison.

Source: ClinicalTrials.gov screenshots reproduced from PHUSE Poster_Draft 5

Discussion

Discussion

- Use of Bayesian methods in registered clinical trials has increased substantially.
- Key Bayesian reporting elements such as prior distributions, posterior probabilities, credible intervals, and sensitivity analyses are inconsistently represented in ClinicalTrials.gov.
- Lacking structured fields may create reporting gap and indirectly limit transparency and reproducibility.

Recommendations

- *ClinicalTrials.gov could introduce structured templates specifically designed for Bayesian trials.*
- *PRS could be updated to include Bayesian based key parameters in existing relevant dropdowns*

Acknowledgements

Thanks to our colleagues Ridhima Mehra, Shalini Dwivedi, Pooja Phogat and Stuart Donald for their guidance and expertise on this presentation.

References

- Use of Bayesian Methodology in Clinical Trials of Drug and Biological Products | FDA
- Embracing Bayesian Methods in Clinical Trials: FDA's Long-Awaited Draft Guidance | Regulatory Agencies | JAMA | JAMA Network
- Use of Bayesian approaches in oncology clinical trials: A cross-sectional analysis - PMC
- Study Details | NCT03515824 | Study of MK-1697 in Participants With Advanced Solid Tumors (MK-1697-001) | ClinicalTrials.gov
- Study Details | NCT04530552 | Testing the Effects of Low Dose Apalutamide on Prostate-Specific Antigen (PSA) Levels in Men Scheduled for Removal of the Prostate Gland | ClinicalTrials.gov
- Study Details | NCT04529096 | Chronic Pain Master Protocol (CPMP): A Study of LY3016859 in Participants With Chronic Low Back Pain | ClinicalTrials.gov
- Study Details | NCT05838742 | A Dose-Finding Study to Evaluate the Efficacy and Safety of GSK3858279 in Adults With Knee Osteoarthritis (OA) Pain | ClinicalTrials.gov

Thank You

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Krystelis — Clinical Trial Transparency

Questions & discussion