WHITE PAPER

Incorporating patient burden assessments into clinical trial feasibility and planning

By the ZS Clinical Feasibility Consortium

Across the industry, feasibility and clinical operations leaders increasingly recognize easing patient burden as not only an ethical responsibility, but also a vital way to improve recruitment, retention and timelines. Approaches to assess and act on patient burden remain inconsistent, however.

This situation is driving the ZS Clinical Feasibility Consortium to identify emerging frameworks, best practices and organizational enablers for translating patient burden insights into trial design and planning decisions. The ZS Clinical Feasibility Consortium comprises ZS and leaders from 15 pharmaceutical sponsors.

The Consortium recognizes that in a landscape defined by intense competition for patients, rising costs and delayed timelines, understanding and reducing patient burden is essential to aligning stakeholders and creating more patient-centric, efficient trials. Fragmented assessment methods have made it difficult to quantify burden's true impact, prompting the ZS Clinical Feasibility Consortium to convene in 2024 and 2025 to establish a standardized approach for incorporating patient burden into trial design and operational planning.

Building on that groundwork, the Consortium has shifted its focus toward identifying the tactics and operating models that most effectively integrate burden insights into real-world decision-making across sponsors.

Defining patient burden

The Consortium first saw a need to establish a common definition for patient burden in the context of clinical research. Working with a patient advocacy group, the Crohn's & Colitis Foundation, the Consortium highlighted key patient factors including:

- Emotional factors such as fears, anxiety and mistrust
- Relational factors such as family considerations
- Time commitments and cost to patients
- Physical factors such as invasive procedures, placebos, concomitant medications and location
- Communication factors such as language barriers
- Systemic factors such as standard of care costs and racism

The Clinical Feasibility Consortium eventually aligned on a common definition of patient burden:

Patient burden in a clinical trial refers to the anticipated and experienced, objective and subjective impact of participating in the trial, beyond the standard of care activities for their condition.

– The Clinical Feasibility Consortium

This common definition enabled us to align on a common goal for clinical trial sponsors: minimizing avoidable patient burden in the clinical trials they design and conduct. Reducing burden is not simply an ethical consideration—it's central to optimizing clinical trial design, patient engagement and operational efficiency. Reducing burden requires a holistic approach across three key elements: tools, processes and governance, and people.

FIGURE 1:

The three key elements of a holistic approach to reducing patient burden

When these three elements are misaligned, the true impact of patient burden isn't appreciated, and trial performance suffers. But when these elements are coordinated, they enable more efficient, patient-centered operations, ultimately resulting in improved operational trial outcomes. The Consortium is aiming to connect these elements to show where sponsors can intervene to meaningfully reduce burden and drive operational impact.

Tools: Our patient burden framework

Integrating patient insights into burden-focused decision-making is critical to ensure mitigation strategies are patient-centered and optimized.

Roughly 90% of sponsors in the Consortium have established a foundational approach to improve patient burden. They often apply versions of the patient burden framework developed by ZS and Tufts University to systematically assess visit schedules, procedure frequency and logistical demands. We'll refer to this ZS/Tufts framework, originally published in 2020, as the patient burden 1.0 framework.

This framework has enabled sponsors to benchmark study designs and identify protocols with disproportionate participant demands. However, as these assessments have become more routinely implemented, several shortcomings have surfaced in the patient burden 1.0 framework:

- Incomplete representation and quantification of the full set of factors that contribute to patient burden.
- A limited ability to consistently link patient burden assessment outputs to key clinical performance outcomes—such as recruitment rate and duration—at scale.
- Insufficient mechanisms to evaluate and communicate trade-offs between patient burden and other key study drivers, including scientific value, quality, cost and resource impact.
- Challenges in operationalizing the tool outputs to inform and drive organizational decision-making.

Given these limitations, the Consortium established an updated patient burden framework that includes key factors that contribute to patient burden. The example in Figure 2 illustrates the framework in action by comparing an example trial with analogous benchmark trials and patients' burden tolerance.

FIGURE 2:

The updated patient burden framework

Patient input opportunities

How can the patient voice be incorporated into the burden assessment?

1 Burden assessment parameters

- Understand the factors that matter most to trial participants
- Demonstrate the levers and trade-offs between patient burden and other metrics, such as site burden, trial length and trial cost

2 Trial design objectives

- Understand patient willingness and tolerance for trial design factors
- Center trial design around minimizing patient burden instead of meeting benchmarked averages

3 Qualitative patient insights

- Bring in qualitative patient insights to enhance holistic communication of patient burden impacts
- Focus on achieving directionality (minimized burden) vs. precision through patient burden assessment

The patient factors in black represent factors that were commonly considered by Consortium members. The patient burden factors in orange are additions to the patient burden framework to address gaps in the patient burden 1.0 framework. These additions were informed by patient input via the Consortium's collaboration with the Crohn's & Colitis Foundation and sponsor experience.

The Consortium added factors such as compensation and emotional and mental factors that were previously left off sponsor patient burden assessment tools. Compensation was incorporated into the updated framework because it meaningfully influences a patient's ability to participate in a trial. Emotional and mental factors were added to capture aspects of participation that are less tangible but nonetheless have a significant impact on the patient experience.

These factors acknowledge stress, uncertainty and cognitive load that can shape willingness to enroll and remain in a trial. They help ensure our updated framework reflects the full spectrum of burden patients face.

The legend in Figure 2 describes the common approach of visually comparing how a given trial stacks up against analogous benchmarked trials. Understanding and adding the patients' perspective in the form of a patient tolerance measure for each of the key patient burden factors would further strengthen and support trial optimization efforts.
For example, patients often judge trial burden by the most demanding visits in the schedule of assessments, rather than by the trial's total burden.

Differences between patient and sponsor perspectives may seem small, but they're important to account for when addressing patient burden. With so many factors shaping the trial experience and limited opportunities to mitigate them, understanding where those perspectives diverge is critical.

The Consortium's findings underscore the importance of adopting holistic, patient-centric approaches to trial design that integrate both qualitative and quantitative insights.
This ensures clinical trials are more inclusive, efficient and aligned with patient needs.

The process and governance: How organizational structures shape decision-making

It's clear to the Consortium that translating patient burden insights into practice depends as much on the process of decision-making—where and how decisions are made—and overall governance as it does on the tools used to generate these insights. In some organizations, burden ownership sits within clinical operations, where feasibility, logistics and patient experience drive decisions. In others, burden considerations are managed within clinical development, where scientific and regulatory priorities are paramount and funding or protocol governance decisions hold greater weight.

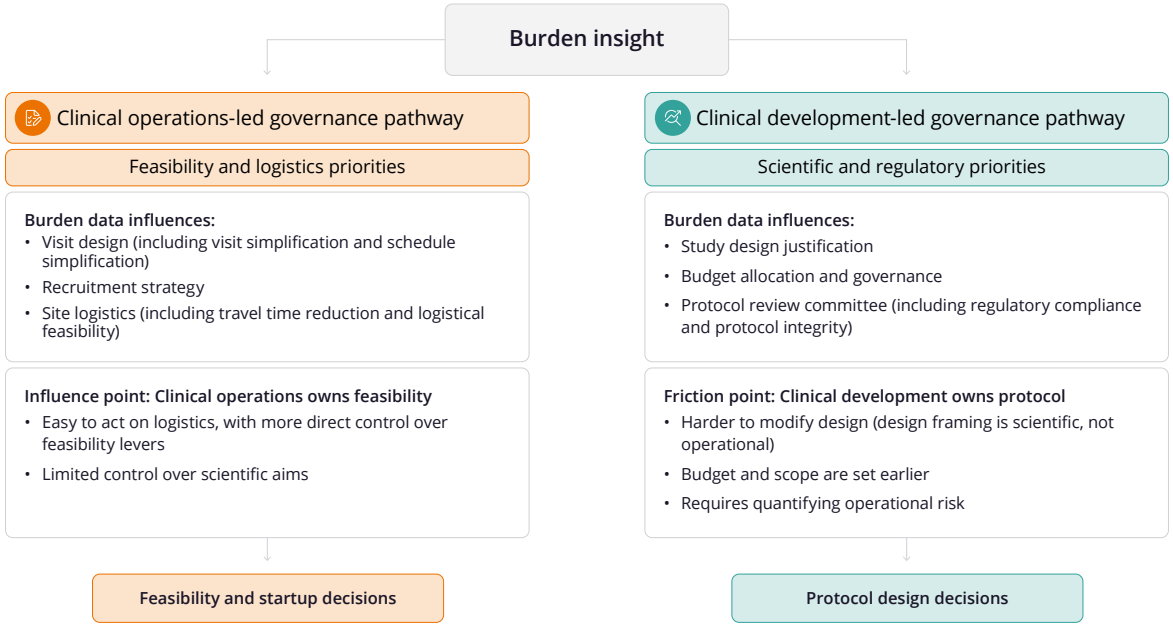
Each of these approaches presents unique strengths and limitations.

- When burden-informed decisions sit in clinical operations, decision-makers often have stronger alignment with patient feasibility optimization implications (including recruitment duration and impact on recruitment rate) and less direct control over protocol design.
- When burden-informed decisions sit in clinical development, burden is more likely to be deprioritized in favor of scientific objectives—unless its operational impact, such as enrollment delays or dropout risk, can be explicitly quantified quickly before program and trial funding decisions.

The trade-offs between these two approaches reinforce the need for an integrated governance approach that ensures burden metrics and insights are visible and actionable when protocol design decisions are being made. Figure 3 shows how burden input travels differently in clinical operations and clinical development-led organizations. The figure highlights where friction or influence occurs, as well as the unique barriers to decision-making impact in each approach.

FIGURE 3:

Translating burden insights into action depends on where governance sits



Consortium members shared compelling strategies for using burden data to persuade governance decision-makers with differing priorities.

- **Clinical operations-driven strategy:** Implications for patient enrollment—such as a particular visit schedule keeping patients from joining the study—resonate with clinical operations stakeholders. Consortium members said concerns about overall trial performance have the greatest impact when raised by clinical operations stakeholders.

- **Clinical development-driven strategy:** Benchmarking the protocol at hand with similar trials in the industry that have been simplified or optimized for patient burden resonates with clinical development decision-makers. Their concerns about scientific integrity and regulatory alignment can be quelled by sharing similar, more patient friendly industry examples that passed regulatory scrutiny.

In both strategies, burden insights gained traction when they were presented in a way that directly aligned with governance and decision incentives specific to the audience in question. While standardization matters when presenting patient burden insights, consistently integrating patient burden considerations into the process itself is equally important for adoption.

For example, when study teams and governance committees consistently see patient burden insights presented in a clear, accessible format that aligns with their priorities, they are more likely to engage and act on the findings. Consortium members have achieved greater success in optimizing patient burden when they incorporate burden considerations in early decision-making, such as at the indication clinical development plan (CDP) or program level. Given that patient burden remains an emerging priority, early exposure is a critical introduction mechanism for study teams and governance decision-makers. Early exposure helps build the familiarity needed to incorporate patient burden insights into decisions made during the final stages of trial design and planning.

People: Patient burden in clinical trial decision-making

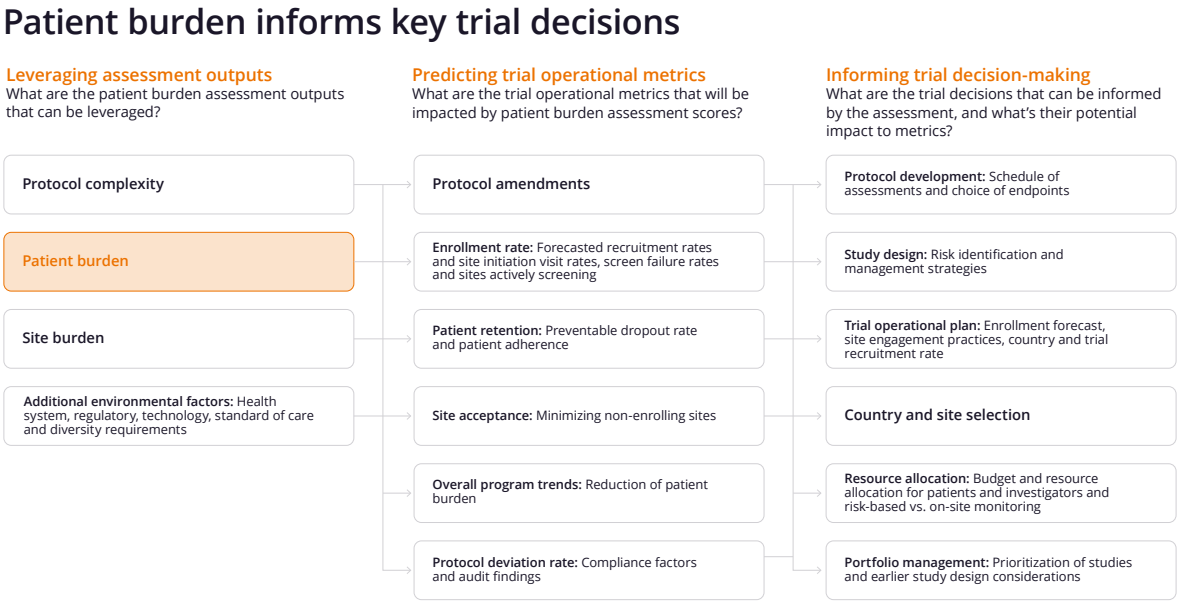
Nearly all Consortium members said they use patient burden assessment methodologies and associated analytics to inform their clinical trial design and operational plans. Yet many acknowledge a common struggle in reducing patient burden.

Effectively addressing patient burden in clinical trials requires more than patient burden analytics—it also necessitates turning data and analysis into actionable insights and building trust-based collaboration among stakeholders to support adoption. The Consortium has identified the essential components for effective adoption by focusing on the people who use patient burden analytics in decision-making. Standardization, tracking and trust-building serve as foundational elements.

Sponsors that successfully integrate burden data into decision frameworks can then translate it into metrics that matter—including time, cost and quality—and are relevant to clinical development stakeholders. For clinical scientists and clinical operations leads, these metrics help connect patient experience data to scientific and operational trade-offs. Figure 4 shows how burden analytics can inform decisions that shape protocol design and operational planning.

FIGURE 4:

Linking protocol optimization assessments, key outcome metrics and decisions



How can patient burden insights effectively inform decision-making? Sponsors need standardized communication of impact, consistent tracking and trust among stakeholders and decision-makers.

Across organizations, the decision-makers who determine how patient burden insights translate into protocol design span clinical development and clinical operations. Each has unique value propositions.

- For clinical scientists and medical directors, the most compelling arguments frame burden insights through the lens of study integrity and scientific trade-offs. These leaders respond to evidence that demonstrates how design simplification can maintain or even strengthen data quality—for example, showing that reducing a visit or replacing an in-clinic assessment with a remote measure wouldn't compromise endpoint validity or regulatory defensibility.
- For clinical operations leaders and study teams, the conversation centers on executional feasibility: whether the protocol can realistically enroll and retain participants on time and within budget. Here, burden insights gain traction when expressed in operational metrics—for example, "a 15% reduction in visit burden correlates with a projected two-month improvement in enrollment timelines."

Ultimately, the key to operationalizing patient burden data is tailoring the message to what each stakeholder values most: scientific rigor, operational feasibility and study success. Sponsors are already seeing success with this approach and are scaling it to develop a rigorous, repeatable framework.

Patient burden optimization in practice

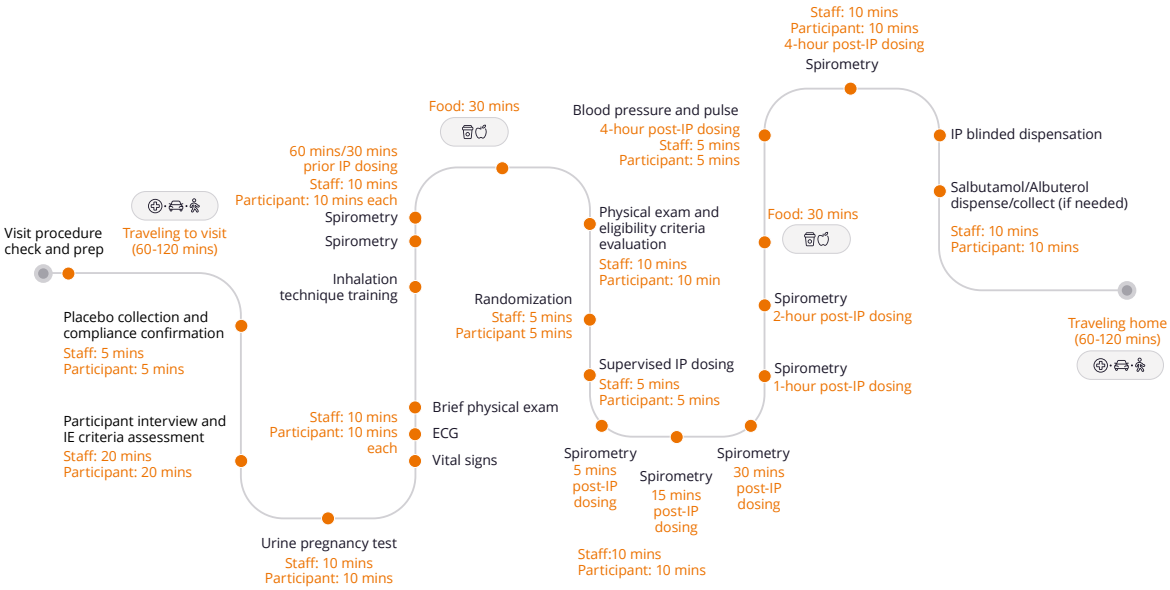
Despite the variability in their respective governance structures, Consortium members aligned on the core characteristics of tools that meaningfully influence decision-making:

- **Digestible and decision-oriented:** Clear visual outputs that translate complex burden scores into intuitive insights for cross-functional teams are critical, ensuring the level of burden is tangible in important and relatable terms, such as time and degree of invasiveness.
- **Embedded in governance workflows:** Burden results are reviewed alongside scientific and operational metrics within protocol review committees or feasibility assessments.
- **Adjustable in real time:** The ability to modify inputs during protocol design sessions and visualize burden impact dynamically is needed. The most effective tool for Consortium members adjusts outputs in real time.

These traits allow burden tools to evolve from static scoring mechanisms into living decision aids that support ongoing dialogue between operations and development stakeholders. Figure 5 below illustrates the Participant Burden Navigator tool, developed by one Consortium member's organization. It's an effective burden optimization tool that systematically assesses and incorporates patient burden considerations into trial design and planning.

FIGURE 5:

Illustration of the Participant Burden Navigator



The Participant Burden Navigator enables the dynamic visualization of patient burden across a study's schedule of assessments. By inputting a draft study design, users—typically within clinical functions—can evaluate protocol adjustments interactively to observe how changes affect total visit time and overall participant impact. This interactive functionality cultivates more informed discussions during trial planning and review, fostering collaboration across teams. In the future, similar visualization approaches could support patient engagement conversations to enhance transparency and engagement during trial participation discussions.

Consortium members explored several examples and agreed that the Participant Burden Navigator was one of the more successful patient burden optimization tools.

Consortium members also shared examples of successful governance. Figure 6 below outlines an optimization summary, which illustrates how effective governance enables patient burden insights, operational data and cross-functional priorities to translate into concrete, high-value design decisions.

FIGURE 6:

Example of an optimization summary for effective governance

Trial ID: AAA-999A; PROTOCOL OPTIMIZATION SUMMARY
Tumor Type A; Phase X; Country of origin = US; Patients planned: XX; Countries: YY

Dimension	Key recommendations	Money saved
Burden for patient and site	**Consider reducing the frequency of comprehensive hematological laboratory assessments.** This recommendation would help bring the patient burden down by 16%. • CPT 80047 Basic metabolic panel; CPT 80051 electrolyte panel	$400,000
	Consider reducing the frequency of physical exams from two timepoints per visit to one timepoint per alternate visit. This would bring the site burden down by 11%.	Physical exams are integral to patient safety and endpoints. Cannot be reduced
	Consider reducing the frequency of questionnaires. Refer to industry benchmarks for similar malignancies.	$160,000
	Reduce invasive biopsies. Despite a low count per quarter, a reduction of one or two total biopsies would impact patient burden significantly and improve patient retention rate by 23%.	N biopsies are SOC
Operational complexity	**Reduce number of countries from 25 to approximately 19** • Remove Japan, Thailand and Taiwan • Retain only South Korea in Asia region, as it will be good representation of the countries removed above. This will reduce operational complexity by 19%.	$500,000
Electronic data capture	• **Consider data collection via remote telehealth portal ABC,** for multiple physicians associated with blinded studies. And enable better collaboration. This would reduce site burden and costs associated with manual data entry	To be determined
	Reduce total CRF pages per patient from 600 to approximately 400-450 to reduce site burden	$400,000 in reduced monitoring costs
	Total savings	**$1,460,000**

In this example, burden reduction opportunities were systematically evaluated across procedures, operational complexity and data collection requirements. They were then escalated through an established governance pathway that balanced scientific rigor, patient feasibility and cost impact. Importantly, each recommendation was assessed not only for its potential to reduce burden but also for scientific acceptability (such as maintaining safety-critical assessments), operational feasibility (such as right-sizing country footprint) and financial implications.

Decisions such as reducing comprehensive lab frequencies, streamlining questionnaires and optimizing case report form (CRF) pages achieved meaningful reductions in both patient/site workload and monitoring costs. And governance appropriately rejected changes that would compromise safety or endpoint integrity. The outcome in this example—$1.46 million

in projected savings while maintaining scientific viability—demonstrates how integrated governance frameworks can align diverse stakeholder incentives, ensure data-driven trade-offs and ultimately make patient-centric design both actionable and sustainable.

This governance model succeeded because it created clear decision rights and aligned incentives across functions, while grounding every recommendation in objective evidence. Clinical development, clinical operations and data management teams each had defined roles in evaluating scientific relevance, operational feasibility and cost implications. This ensured no decision was made in isolation.

The result was a set of design optimizations that protected scientific integrity, improved patient and site experience and generated meaningful operational savings. This demonstrates the power of a governance structure that integrates data, incentives and cross-functional accountability.

Closing the loop: From insights to organizational impact

Successfully adopting burden insights requires intentional change management beyond just developing and refining the patient burden tool itself. It must be centered on tools, governance and processes, and people. Consortium members identified several key levers to enable adoption:

- **Burden champions:** Designate advocates within operations and development who can ensure burden is represented in governance conversations.
- **Embedded KPIs:** Incorporate performance indicators into patient burden insights—such as avoidable amendments and recruitment rates—that inform governance decision-making. This reinforces their operational relevance.
- **Feedback loops:** Enhance the evidence base for patient burden assessments so that they link to clinical trial performance outcomes through systematic statistical analysis.

These levers show that institutionalizing patient burden-informed decision-making is as much a cultural transformation as a technical one, requiring new incentives, communication norms and accountability mechanisms. The shift from theoretical burden measurement to actionable decision integration represents a major step forward for Consortium members. Sponsors that succeeded did so by aligning tools, governance and incentives, ensuring burden insights were discussed at the right time and by the right people.

These adjustments directly strengthen alignment with emerging regulatory expectations under the U.S. Food and Drug Administration's final E6(R3) Good Clinical Practice (GCP) guidelines, which emphasize participant-focused design, operational feasibility and proactive risk management. By integrating burden insights into governance, KPIs and cross-functional decision cycles, sponsors can create traceable evidence showing that patient experience and operational risks were systematically assessed during protocol development. This approach is consistent with R3's principles of quality-by-design. And it not only supports compliance but also streamlines regulatory interactions by demonstrating that study design decisions are data-driven, justified and grounded in real-world feasibility.

We look forward to testing these models against real-world performance metrics as we further the Consortium's mission of transforming patient burden from a measurement exercise into a strategic organizational capability that drives smarter, more patient-centered trial design.

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