WHITE PAPER

The digital health revolution **will be evidence-led**

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Getting evidence generation right

Today's digital health firms creating next-generation software as a medical device (SaMD) products regularly confront a conflict between rapid software development life cycles and methodical evidence generation procedures. Both processes are vital to successful product development and commercialization, but this conflict cannot be ignored. It can be difficult to manage, especially for firms with little experience running clinical trials or seeking regulatory approvals.

The most effective way to strike a balance between the two processes is to adopt a strategic, integrated approach to evidence generation that aligns the clearly defined phases of clinical research with the milestones of iterative software development. This close alignment between evidence generation and business goals helps forward-thinking firms conduct more valuable studies in less time while using fewer resources, generating evidence that brings greater value to the firm and its potential pharmaceutical and medical technology partners. As healthtech funding shrinks, it's becoming more critical than ever for firms to get evidence generation right. The success of the digital health revolution depends on this.

The conflict between software development and evidence generation workflows

SaMD products have the potential to revolutionize healthcare by delivering life-changing, innovative care. These products can perform complex medical functions such as determining the proper dose of medication, analyzing medical images or determining risk factors for various diseases. Because SaMD products are used for medical purposes, agencies such as the U.S. Food and Drug Administration (FDA) and the European Medicines Agency (EMA) subject them to the same scrutiny as medical devices that administer medications or control heart rhythms. Simply put, SaMD products must be evidence-based and clinically validated before patients can use them.

This scrutiny is necessary to make sure these products are safe and effective. But it also presents challenges to digital health firms that are more familiar with software development than the rigors of clinical trials and regulatory approvals.

Conflicting pressures. Clinical evidence requires a laser focus: For a patient subpopulation with certain symptoms or risk factors, it must be clear that the given intervention delivers a specific outcome. This is a costly, time-consuming process. Because many digital health firms face financial pressures and cannot necessarily afford to delay

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product releases, they may be tempted to answer several questions at once in a clinical study. Unfortunately, this approach adversely affects the quality of a study and often results in a need for additional research—adding more time and strain on their finances.

Timeline balancing acts. Certain aspects of the SaMD product, such as decision support algorithms, need to be fully developed and locked in place prior to a clinical trial. As a result, software teams need to adopt a different approach to development that involves elements that are untouchable, as well as versioning that needs to be maintained for the period of a trial. This is often a contrast to today's software development cycle, during which engineering teams routinely release product updates.

Downstream uncertainty. When evidence generation processes aren't closely linked to product development timelines, firms may find it difficult to demonstrate clinical and financial value to potential investors, payer and provider customers, or to their pharma and medtech partners. This lack of alignment also adversely affects regulatory application workflows, as the ripple effect of poor product and evidence coordination can lead to costly release delays for other products in the planned portfolio.

Missing expertise. Similar to other medical devices, SaMD products require formal human factors investigations to meet regulatory requirements, while consumer, wellness or enterprise software products do not. Digital health firms with a software development background may not have the in-house expertise to conduct their own human factors studies or clinical studies. Acquiring the necessary talent with this expertise is cost prohibitive and causes further delays to study design—yet clinical studies need to be conducted for an increasing percentage of SaMD solutions in different markets around the world.

Lack of transparency. Firms suffer when evidence generation occurs in a vacuum. There's a clear and unmet need to provide evidence generation plans and insights to product teams on a regular basis. Doing so better aligns product development and research workflows to each other and to overall business goals. This results in fewer surprises for the firm, its partners, regulators and ultimately, the patients who benefit from the timely release of proven SaMD products.

It's clear that several factors can make or break SaMD products and the companies that develop them. This points to a critical need for firms to invest in advanced planning—and to look for external expertise when necessary to ensure that planning stays on track.

The case for integrating evidence planning and product development

Integrated evidence planning offers digital health firms the opportunity to provide the necessary alignment between evidence generation, product development workflows and long-term business objectives. The goal is to get the most out of the valuable but scarce resources that are required to conduct proper, evidence-based clinical research.

What integrated evidence planning looks like

At its core, integrated evidence planning is a holistic look at the studies that a firm has completed, has in its pipeline and has in the early design stages—keeping the firm's product development, regulatory and investment timelines in mind. Planning occurs on an ongoing basis so that firms are better able to set priorities **before** committing resources to new research. In doing so, a firm may see that a current trial design could expand to study another objective or endpoint, eliminating the need for a second similar trial.

Taking a 30,000-foot view allows firms to plan for and apply a more systematic, multidisciplinary approach to evidence generation.

Integrated evidence planning is **more systematic** because it casts aside the piecemeal approach to completing studies in a siloed environment where research teams act independently. Each study is conducted as part of a firmwide strategy to generate evidence that meets a specific business

The digital health client's perspective

"Our devices are used for screening and monitoring patients, aimed at the development of new therapies. One of the key challenges in clinical studies is enrolling and recruiting the appropriate patients. Often, we run into situations where principal investigators, eager to find patients, will recruit a patient into a study although that patient is borderline for a symptom or criteria. The sponsor may see results in early studies, but then they will fail to replicate that effect in larger studies. Digital tools are essential to the science, ensuring that we are able to screen and stratify patients appropriately. In Parkinson's disease, there are many subpopulations with different disease causes. If we can't appropriately classify and stratify these subpopulations, clinical trial data risks becoming homogenized. Only through the application of proper screening and diagnostics can we assess appropriate metrics that will lead to tailored treatments and medications."

Dustin Heldman, President, Great Lakes NeuroTechnologies

goal. Not only do research teams know what their counterparts are working on, but they also have access (where appropriate) to the evidence that has been generated when data is managed from a centralized repository. Researchers, especially those independent of the company, can be guided to focus on the most important questions as their investigations begin.

A systematic approach helps firms do more with less, as it dramatically reduces (if not outright eliminates) the number of parallel studies being conducted with nearly identical patient subpopulations or targeted endpoints. This approach also helps to capture more value from each study and to develop a body of evidence that collectively demonstrates product efficacy from studies conducted by both the company and its independent researchers. When studies are designed with the big picture in mind, they're better able to generate evidence of interest to multiple stakeholders as opposed to solely testing for clinical efficacy, care costs, safety and so on.

Integrated evidence design is **more multidisciplinary** because regulatory, clinical and design experts all need to sit at the same table if a firm intends to meet the varying requirements of disparate stakeholders seeking evidence of digital health or connected health product effectiveness. Additionally, this roundtable of experts will help ensure that a study includes the right patient subpopulations and has been designed to meet their needs. This includes but is not limited to populations that need accommodations for vision, hearing or mobility impairment; populations with less experience using consumer-facing digital products; and diverse and non-English-speaking populations that are traditionally excluded from the clinical trial process. This work can take time, but it results in studies that are far more likely to ask the right questions—and far less likely to require a scramble to get the right answers while facing a looming deadline that could make or break the business. Designing more inclusive clinical trials from the start also helps achieve health equity goals by developing products that are more effective for underserved populations than what's available to them today.

The power of integrated evidence planning. When digital health firms engage in integrated evidence planning, they have a much better understanding of what they currently know about their SaMD product, what they need to know to gain regulatory approval or market acceptance and how they can best close that evidence gap. Here are six important ways that firms using integrated evidence planning can gain a competitive advantage:

Meet the right evidence needs for the right audience. Different external stakeholders demand different evidence. Regulators require proof of safety and quality, providers seek proof of improved clinical outcomes and different payers have slightly different expectations for what it will take to allow reimbursement. One problem is that many companies run ahead with studies, assuming what they measure will meet everyone's expectations, only to find out that their studies are inadequate or not optimal. Knowing at a high level which stakeholders are expecting which evidence and when helps firms do two things: Identify which evidence may have already been gathered in a previous investigation and, as a result, prioritize the generation of evidence that isn't yet available.

Streamline regulatory approvals. Beyond providing the proper evidence to regulators, firms must match submission application deadlines with their own internal timelines that drive investment and spending decisions. Discussions with agencies such as the FDA and EMA offer a gateway to commercialization, because knowing that a study is likely to pass muster with regulators is a telltale sign that a company can move ahead with its research. When regulatory pre-submission conversations are part of the evidence generation timeline, firms are better equipped to move ahead at the right time—and they reduce the risk of delays from pursuing studies that aren't able to meet regulatory requirements.

Reduce costs where possible. When resources are scarce, integrated evidence generation allows firms to do more with less because it emphasizes a thorough examination of the goals of each clinical study based on the firm's overall priorities. This big-picture perspective helps a firm's leaders determine whether, for example, a decentralized clinical trial in a different geography would provide the necessary evidence for a study at a fraction of the cost.

Build better investigator relationships. For startups, crafting relationships with clinicians is critically important. Investigators based in large health systems or teaching hospitals sometimes struggle to work with digital health firms that have workflows and research outputs that vary from one study to another. Because an integrated approach to evidence generation is much more systematic, investigators have a clearer view of how a firm's research will benefit their own work, improving the likelihood of longer-term collaboration. This also applies to researchers in smaller institutions who are looking for interesting research opportunities and may be eager to connect with firms working on novel digital solutions and offering research dollars.

Explore additional commercial opportunities. When digital health firms can easily view—and share—their full body of study data, they become attractive partners to pharma and medtech companies. These enterprises benefit greatly from patient experience data, pharmacovigilance data and other evidence of how products truly work in the real world. These enterprises constantly seek new indications or subpopulations they can target with existing, approved products. In both cases, digital health firms are well positioned to provide this evidence—and demonstrate their value as a development partner. Finally, as pharma and medtech increasingly embrace integrated evidence planning as a business practice, digital health firms that have done the same will stand out from competitors that haven't.

"Noble International has been developing educational solutions to improve adherence to and use of medications. Depending on the stakeholders you are talking to, whether it's patients or healthcare providers or payers, the need for evidence is seen very differently. As digital technology rapidly changes, it is important to give these stakeholders a perspective that will support an aggregated point of view for different types of value. This requires insights and understanding of what levers will influence this space and drive impact with this audience."

TIM MCLEROY
Executive Director of Marketing and Patient Services
Noble International

Publish results at the optimal time. Aligning the clinical research process with the publication calendars of leading medical journals helps get papers published at the right time. This is difficult or impossible to accomplish when research happens on an ad hoc basis. Integrated evidence planning ensures that an organization knows how long it will take for a high-impact publication to review, accept and publish its research. With these timelines in mind, the company can build plans to promote the product release and the journal publication hand in hand, maximizing exposure and building momentum for customer conversations.

The benefits of partnership for integrated evidence planning

Digital health firms that are serious about bringing evidence-based and clinically validated SaMD products to market tend to maintain a steadfast focus on product development and commercialization. This is both worthwhile and necessary, as bringing a safe and effective product to market is vital to the survival of the business.

The downside of such a singular focus is that it makes it difficult for firms to prioritize integrated evidence planning. That's where an experienced, connected and trustworthy partner can help firms align evidence generation with product development and business planning.

Partnership lets digital health firms fill two critical skills gaps:

- The expertise needed to design and execute clinical trials is difficult to find, expensive to hire and takes time to build. It's even harder to learn on the fly. At the same time, given the requirements of regulators and expectations of the healthcare and life sciences industries, cutting corners is a nonstarter.

- Evidence planning takes a level of discipline that's difficult for digital health firms to do on their own, especially while balancing the necessities of software release cycles. It also requires expertise in setting business priorities based on an understanding of the varying needs of regulatory agencies, payer and provider customers, and pharma and medtech companies.

"More digital health innovators are coming to us with the end in mind and asking, 'What do we need to do to get reimbursement?' What they should really be asking is, 'What evidence package do we need to get reimbursed, distributed and adopted?' There are layers to designing and generating that evidence package, but a systemic approach has massive benefits over the current sequential and siloed approach: shorter time frames, lower unit cost, richer evidence and stronger research teams."

AHMED ALBAITI
Principal, Digital and Connected Health
ZS

Help standing up an evidence platform. An integrated evidence planning partner can help a digital health firm stand up a platform for collecting evidence that's integrated with but independent of the SaMD they're developing. This is a critical but often overlooked step. The SaMD, of course, is the firm's intellectual property. On the other hand, firms benefit tremendously from making their evidence readily available to pharma and medtech partners, payer and provider customers, regulators and patient advocacy organizations. With the right infrastructure in place, firms can share their evidence with the desired entities while maintaining full control over their product.

Support for commercialization. While pharmaceutical research and development follows a set process that is often uninfluenced by commercial teams until a product has been approved, digital health and SaMD products are different. Commercialization plans for moving from pilots to scaled launches are ideally part of a single, integrated process. The right integrated evidence generation partner should be able to understand, support and provide strategic direction for commercial launches, not just R&D. In other words, the approach to research should support, and in turn be informed by, the program as a whole.

Connections with industry partners. Finally, partners are well positioned to help digital health firms make inroads into connecting with possible pharma and medtech partners. A single startup, acting alone, faces an uphill battle to have the right conversation with the right decision-maker in a multinational company with tens or hundreds of thousands of employees. Even a personal connection with someone inside a company isn't a guarantee that an introduction will ever happen. A partner already working directly with multiple pharma and medtech companies will know exactly where a digital health firm should start, make an introduction and guide a firm through the process of building a long-term and mutually beneficial relationship.

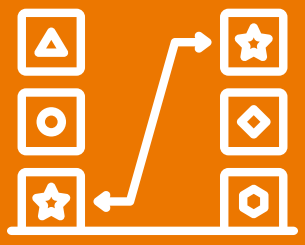
Embrace a holistic approach to evidence generation

Digital health firms face a struggle to collect evidence methodically but release products regularly. As this push and pull affects all parts of the business—not to mention the bottom line—it's clear that firms benefit from a more systematic and integrated approach to evidence generation. It may not be second nature for digital health firms to build evidence generation into their cycles, but it's necessary to their survival and success. When building an integrated evidence strategy into their business, turning to a partner with deep expertise in this area will make a difference.

Looking holistically at what data is needed for which stakeholders at what time not only ensures that firms get the most out of the evidence generation process. It also lets firms see the big picture of what additional value they can extract from their data, both for themselves and for pharma and medtech partners—helping them build longstanding and mutually beneficial relationships.

Integrated evidence planning requires specific expertise to align research workflows with both the software development life cycle and the expectations of regulatory bodies and industry partners.

Contact ZS to advance evidence generation and achieve commercial success.



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Let's bring life to digital

ZS's digital health practice is a global digital innovation consulting and technology group that provides full life cycle strategic services and digital solution development, supported by proven solution platforms. Since 2006 we have worked with more than 500 industry leaders on digital innovation, digital strategy, design, solution architecture, development and evidence generation projects. Together, we can improve outcomes for clinical trials, digital therapeutics and care management by connecting a fragmented digital health ecosystem.

www.zs.com/solutions/digital-health

About ZS

ZS is a management consulting and technology firm focused on transforming global healthcare and beyond. We leverage our leading-edge analytics, plus the power of data, science and products, to help our clients make more intelligent decisions, deliver innovative solutions and improve outcomes for all. Founded in 1983, ZS has more than 12,000 employees in 35 offices worldwide. To learn more, visit www.zs.com or follow us on Twitter and LinkedIn.

Digital health's second wind will be evidence-led

By Ahmed Albaiti,
Principal, Digital and
Connected Health, ZS

No less a digital health authority than David Benshoof Klein—the man who literally coined the phrase "digital therapeutics" in 2012—has declared the ascension of digital therapeutics (DTx) as the standard of care for chronic conditions not just likely but inevitable. I agree—but only if digital health companies adopt a strategic, integrated approach to evidence generation that aligns the clearly defined phases of clinical research with the milestones of iterative software development.

This is a perennial challenge for digital health because the demands of clinical evidence generation exist in tension with the traditional demands of software development, namely: speed, agility and flexibility. Generating regulatory-grade evidence, meanwhile, requires laser focus on specific patient sub-populations and locking in product features pre-clinical trial—requirements that are at odds with the need for speed, agility and flexibility.

Overlooking integration of evidence generation activities into product development cycles, however, frequently leads to costly release delays and products that do not gain traction. This is compounded by product developers either failing, or being unable to, demonstrate sufficient clinical and financial value to investors, distributors and customers. Effective integrated evidence planning takes a holistic, multidisciplinary approach to evidence generation—by looking at all past, current and future studies and aligning them with the firm's product development, regulatory and investment timelines.

Three critical benefits of this approach:

1. It ensures all studies align with the firmwide strategy and that evidence serves specific business goals.
2. It reduces the number of parallel studies targeting the same or similar patient sub-populations and clinical endpoints.
3. It allows companies to generate diverse evidence—of clinical efficacy, safety and business value, for instance—simultaneously.

The implications and opportunities cannot be understated.

Evidence generation cost reduction. Since digital health funding is nothing if not finite, deploying an integrated evidence approach allows companies to do more with less by eliminating duplicative studies and ones that don't align to the overall business strategy.

Investigator relationship enrichment. Clinical investigators inside large health systems and teaching hospitals are critical stakeholders for digital health—both during evidence generation and at launch. Taking an integrated approach to study design ensures workflows and outputs are consistent across studies, making for low-friction collaboration and a clear picture of how a firm's research can benefit investigators in their own work.

Partnership acceleration and viability. When digital heath firms can easily access (and share) their full body of study data—especially patient experience and pharmacovigilance data—it's extremely attractive to potential pharma and medtech development partners.

Medical community engagement. Publishing clinical research in leading medical journals can be key to slipping through often-narrow windows of opportunity for new classes of digital therapies. When companies conduct ad hoc research, it's exceedingly hard to nail the timing. Integrated evidence planning makes it possible.

While success depends on building evidence generation into product development cycles, many digital health firms will struggle to pull it off on their own. We recommend companies at least consider bringing on a partner whose expertise in evidence generation fills their own gaps, simultaneously helping to build their evidence collection platform while freeing up firms to concentrate on what they truly care about in the first place: building innovative digital solutions that help create a healthier world for all.

What comes next for digital health?

The “easy money” era in digital health and healthtech is behind us. So, how will the next wave of companies bring their innovations to market in this more austere environment? We share our perspective on why this is good news for companies that absorb key lessons from a decade’s worth of trial and error.

Let’s look toward the future together and bring life to digital health.

Take 5 tangible actions