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Patient and caregiver knowledge as a driver of basic science

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Direct engagement with patients and caregivers can transform basic research by uncovering underrecognized disease features and guiding generation of hypotheses. Integrating structured patient input into early-stage research can help to align biological discovery with clinically relevant questions.

We can now sequence a human genome in hours, yet life-threatening disease symptoms may remain unrecognized for years. This paradox reveals how far biomedical research has advanced technologically while remaining fundamentally disconnected from patient experience. Over the past two decades, research capacity has expanded dramatically; more than 9,000 medicines are in active development and publications in health-related analytics have increased more than 30-fold[1]. At the foundation of this progress lies basic research — the work of scientists investigating disease mechanisms and biological pathways, driven by the aspiration to achieve breakthroughs that lead to cures. However, a crucial question remains unasked in most laboratories: do the hypotheses that emerge from basic research address what matters most to patients?

Patients and their caregivers have rich, experiential knowledge that extends beyond their painful symptoms and burdens. They observe how condition features manifest in daily life, recognize patterns that emerge over time and notice subtle phenomena that remain undetected at clinical visits or in laboratory studies[2]. When integrated thoughtfully, this perspective may reveal new biological signals, complement existing scientific approaches, refine research priorities, and direct basic research towards questions with greater relevance to patient needs. The gap between basic research and tangible patient needs is particularly acute in rare diseases, for which small patient populations limit the explanatory power of traditional quantitative approaches and amplify the consequences of missing information[3]. In these settings, the experience of each patient and caregiver has disproportionate value, yet basic researchers rarely encounter this knowledge directly, relying primarily on literature and accumulated scientific knowledge. For brevity, we use the term patients throughout to refer to both patients and their caregivers.

Listening to patients requires methodology and guidance

In the past few years, the pivotal role of patients in guiding healthcare and research has been increasingly recognized. The principle appears in policies, funding priorities and mission statements. However, patient engagement rarely happens when basic research hypotheses are being formulated. Some might argue that meeting patients is the clinician's role, but clinical interactions are often episodic, time-constrained and focused on immediate symptoms, offering only a partial view of condition burden (Fig. 1). A systematic review found that fear of dismissal, concern about being labelled difficult and medical hierarchy can prevent patients from raising important concerns with clinicians[4]. As a result, crucial information may not always surface in these encounters. Basic researchers rarely engage directly with patients or receive dedicated training for these interactions. Instead, their engagement is typically limited to presenting findings and explaining the biological and molecular mechanisms of disease. The exchange rarely flows the other direction (Fig. 1). Transforming this pattern requires a methodological structure. Semi-structured interview approaches, which are widely used in fields such as product management to understand user needs, can and should be adapted for preclinical and clinical research. These interviews create space for open questions and spontaneous expression, revealing phenomena that predetermined surveys may miss. Using these tools in direct patient engagement, basic researchers may be able to connect patient observations to underlying biology and recognize patterns that suggest molecular mechanisms, ultimately redirecting work towards questions with greater biological relevance. Without this knowledge, years of research efforts may pursue questions that patients could have reframed from the start.

Indeed, a growing body of qualitative engagement studies demonstrates the empirical yield of these methodologies[5,6]. For example, in Kleefstra syndrome, a rare neurodevelopmental condition caused by loss of function of *EHMT1*, semi-structured interviews with caregivers uncovered seven previously unreported features, including atypical developmental regression and dysregulation of the autonomic nervous system[7]. The interviews also revealed daily life challenges experienced by patients, including fatigue, drowsiness and night-time incontinence, that are a considerable burden for caregivers but often remain invisible to clinicians. These findings can now inform the selection of outcome measures and clinical trial endpoints in therapeutic development for this syndrome. However, caregiver reports have an inherent limitation, as they surface clinical features without revealing their underlying biology, leaving novel phenotypes vulnerable to misclassification or misattribution[7]. Integrating basic researchers into this process helps to connect these observations to molecular mechanisms and helps to prioritize features that warrant biological investigation and are meaningful to patients and caregivers.

Renewed motivation and more innovative science

Of note, the benefits extend beyond identifying overlooked symptoms or refining research priorities. Direct engagement with patients and caregivers grounds otherwise abstract laboratory work in the lived experiences of those who are affected by the condition. Researchers report that such encounters increase motivation, work efficiency and their sense of purpose within the laboratory[8]. This connection matters because translation from basic discovery to patient benefit may take years or not occur during a researcher's career. Witnessing how their

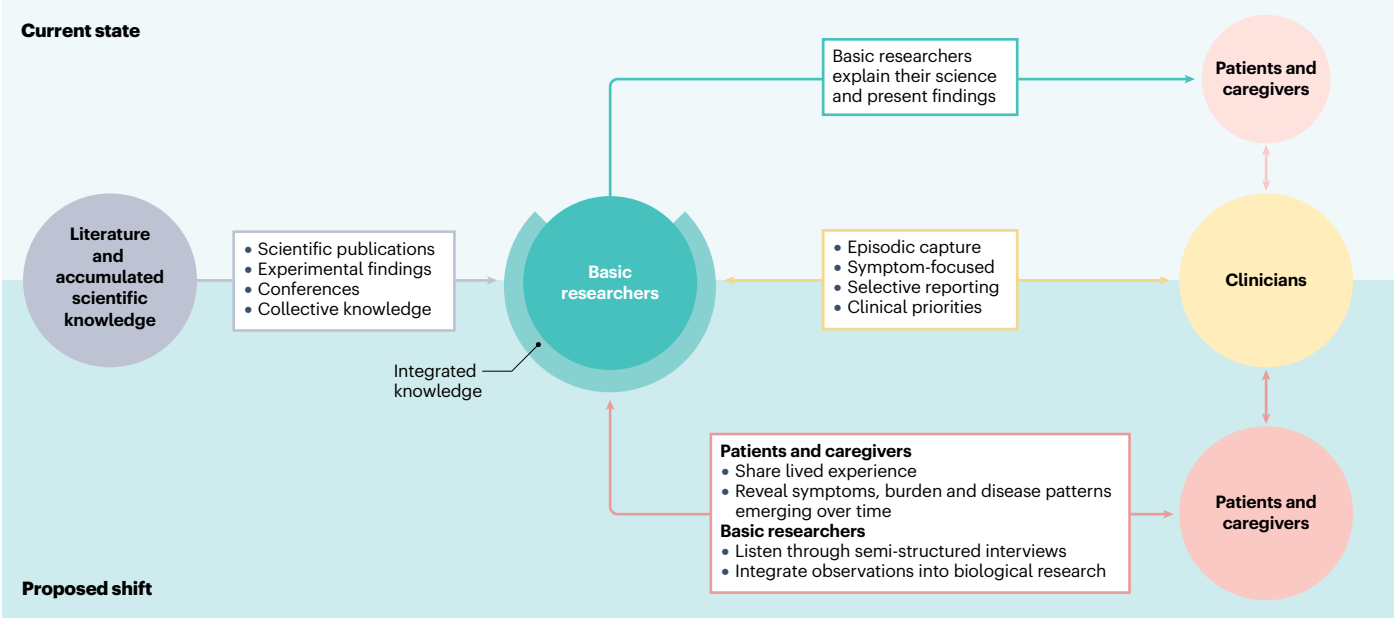

Fig. 1 | Integrating the patient and caregiver voice into basic research knowledge. Currently, basic researchers draw knowledge primarily from scientific literature and clinicians. Patients and caregivers interact with basic researchers only indirectly through clinicians, and knowledge transfer generally flows from basic researchers towards patients. In a proposed shift, the flow of information should flip, so that patients and caregivers become a direct and prominent source of knowledge for basic researchers. Semi-structured interviews serve as the tool to capture rich, experiential knowledge that is systematically inaccessible through conventional channels. The combination of all three knowledge sources provides a broader, more representative integrated knowledge base.

work connects to real lives can sustain scientists' patience and creativity for breakthrough research. In addition, patients and caregivers report that researchers' willingness to listen to their experiences, rather than just their symptoms, represents a profound form of respect that strengthens trust in the research enterprise itself[8].

Listening to patients and caregivers has always been important, but several converging changes now make integrating their perspectives into basic research both urgent and achievable. First, technological advances have removed longstanding barriers. Artificial intelligence enables transcription across languages, pattern recognition in qualitative data and large-scale analysis. In addition, social networks connect patient communities across continents, making global engagement feasible rather than aspirational. Second, funding providers and research bodies increasingly prioritize patient-centred approaches as evaluation criteria[9]. Some nations have embedded these principles in governmental research policy, signalling institutional commitment beyond individual investigator choice[10]. Third, science itself has become less insular. Methodological boundaries that once seemed inviolable now permit expanded cross-disciplinary exchange[11]. Young investigators in particular are increasingly open to inspiration beyond traditional disciplinary silos. This intellectual flexibility creates receptivity to methods that would previously have been dismissed. Finally, as research becomes increasingly computational, abstract and removed from tangible impact, direct engagement with lived experience has become essential to maintaining relevance and purpose. The question is no longer whether to integrate patient voices into basic research, but how quickly this becomes standard practice.

A call to action

The transformation begins with recognizing patients and caregivers as reliable sources of knowledge for basic science. This does not mean turning basic researchers into qualitative researchers. Rather, it means adopting qualitative approaches as methodological tools to enrich and redirect laboratory work towards questions that matter. Listening to lived experience should be fundamental practice, not confined to clinical settings. It represents intellectual humility, as it creates space for expertise that we may not have been trained to recognize. However, a change of mindset alone is not sufficient. Training programmes should integrate patient engagement as core competency, funding should support research that defines patient-centred questions before the launch of large studies, and academic advancement should reward meaningful engagement with patient communities. These changes require institutional courage: recognizing patient knowledge as legitimate evidence and measuring research impact by the relevance of research directions and their potential clinical impact.

The methodologies exist and the need is clear. What remains is to make patient engagement an expectation, not an aspiration. Researchers should include patient experiences in shaping their fundamental questions. This will help to ensure that biomedical research not only advances molecular understanding of disease but also addresses patient-relevant aspects of disease and burden.

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Competing interests

The authors declare no competing interests.