

Patient-centered research and practice in the era of genomics: a novel approach

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In recent decades, therapeutic approach has been shifting from "clinician-centered", in which the clinicians assume responsibility as the sole competent person to look after patients' interests and make decisions without the participation of the patients themselves, to "patient-centered". Patient-centered care is defined as respectful and responsive to individual patient preferences, needs and values, and ensures that patient values contribute to shared decision-making.^{1,2}

The simple and reliable way to identify patient preferences, needs and values is to assess the patient's quality of life and other patient-reported outcomes (PRO). The past decade has been characterized by increased attention to PRO assessment from the hematological community. A number of trials focusing on the assessment of quality of life, symptoms and other patient-reported outcomes in patients with hematological malignancies have been performed. Several instruments have been used to evaluate health-related quality of life and symptoms of patients with hematological malignancies, mostly in clinical trials.³

However, it cannot be established that the evaluation of PRO is widely accepted in the clinical practice of hematology. The assessment of the impact of illness on physical, mental and social functioning is an essential element of clinical diagnosis, a major determinant of therapeutic choices and efficacy, and a guide to longer-term care. The traditional approach to medical history taking and physical examination obtained by the clinician may not be sufficient for assessing the full range of health and/or treatment-related problems of patients with hematological malignancies. Clinicians vary widely in their ability to elicit relevant information from their patients, and patients vary in their ability to articulate their problems and concerns.^{4,7} Furthermore, hematologists frequently underestimate the patient's level of psychosocial functioning, depression and the severity of important symptoms, while overestimating other aspects of the disease such as clinical parameters.^{8,9} It is clear that the formal diagnosis describes only the disease, and one cannot get any particular information on the patient's individual characteristics from this formal diagnosis. It is known that the information on PROs received in clinical practice may influence various changes in intervention; the endpoints of individual quality of life measurement are not those associated with the evaluation of the efficacy of a single given treatment in a clinical trial. Thus, the implementation of PRO measures in routine clinical practice in patients with hematological malignancies is greatly needed and there is much demand from hematologists. However, there is no PRO measure that has been developed specially for use in routine hematological practice.

The European Hematology Association Scientific Working Group for "Quality of Life and Symptoms" (EHA

SWG QoL & Symptoms) aims to facilitate patient-clinician communication through the development of a new instrument applicable in routine clinical practice. In this quest, The EHA SWG QoL & Symptoms has adopted a novel approach, placing the concept of "patient-centeredness" at the heart of such an initiative by involving a patient with a hematological malignancy to join the core research team as a "patient research partner". Patient Engagement (PE), or Patient and Public Involvement (PPI), is increasingly viewed as a cornerstone of health-related research activities, practice and policy making. Effective patient engagement can profoundly change how patient-centered research and practice is conceptualised and conducted, resulting in better patient-centered care, management and measurement.¹⁰

With respect to the values that may underpin the process of PE in shared decision-making, the overarching principle is the importance of effective collaborative relationships underpinned by the importance of mutual respect for differing values and skills, greater transparency and the need for clarity in purpose and process (Table 1). "Trust" is something that grows as the patient-clinician relationship develops; trust is more of an outcome – it is important to build an environment where patients can trust. One does not need to agree with the patient, but needs to debate and discuss, and partnership negotiation depends on the nature of involvement. Consequently, the impact of PE will be first on the quality, relevance and credibility of the outcome of the research or shared decision; and second, on the challenges and importance of developing an evidence base for PE practice. Developing

Table 1. Values Underpinning Patient Engagement (PE)/Patient and Public Involvement (PPI).

Improving the quality, relevance and credibility of research.

- Transparency
- Clarity in purpose and process
- New / unique insights: experiential knowledge of patients
- More explicit research
- Asking the 'right' questions
- Enhanced validity: improved relevance and credibility of research to patients' needs

Improve the dissemination and impact of research

- Different approaches to PPI:
- What works for whom, when and in what context
 - What level of representativeness is meaningful and appropriate
 - 'Not just the posh articulate'

Importance of developing the evidence base

- 'How to do effective PPI?'
- Challenges

Developing a genuine relationship between all stakeholders

- A collaborative, respectful, deliberative and transparent relationship based on trust, reciprocity, co-learning and mutual respect

effective relationships between the patient and all other stakeholders is central to both of these sets of values. "Effectiveness" is a shared value that would require knowledge and effort on the part of all participants.

The fundamental right of the patient to have a say and to be empowered in their contribution to the research or therapeutic decision process should be widely valued. However, it is recognised that this requires the establishment of a genuine relationship between the patient and other partners, underpinned by mutual respect, clarity in the roles to be undertaken, and the valuing of different views and perspectives. An awareness of the different approaches to patient-centred practice or patient engagement – and what works, for whom, when and in what context is considered essential to enabling effective involvement, and requires the development of a strong evidence base with which to inform good practice guidance. A patient's job is not to tell the clinician their story, rather it is to bring a reflective voice to the table.

While the voice of patients is gaining power, and effective patient engagement in research and practice has become a reality, in parallel, hematologists are witnessing an evolution in the diagnosis and prognostication of patients through genetic and epigenetic discovery. To stay up-to-date, the WHO has classified tumors of hematopoietic and lymphoid tissues twice - in 2002 and 2008 - and is now in the process of reclassification. Hematologists have several tools to better define (score) prognosis in individual patients. Molecular targeted therapy is following the process with newly approved drugs, which include lenalidomide for myelodysplastic syndrome with deletion 5q chromosomal abnormality; imatinib and other more novel tyrosine kinase inhibitors for chronic myeloid leukemia; ibrutinib, a covalent inhibitor of the enzyme Bruton's tyrosine kinase (BTK), for chronic lymphocytic leukemia; monoclonal antibodies, such as rituximab, which targets CD20 of B cells in non-Hodgkin lymphomas, and elotuzumab, a SLAMF7-directed immunostimulatory antibody for multiple myeloma; and many others.

Modern technology facilitates the determination of diagnosis and prognosis and challenges the role of patients when it comes to the choice of treatment offered, since the latter is becoming ever more "tailored". Certainly, clinicians will tend to emphasize the value of therapeutic approaches, whether marketed or experimental, according to knowledge and experience and the patient will always make the final decision, but, in this fast era of genomics, probably the true modern approach to communication is equality between both patients and clinicians, "bringing different knowledge, needs, concerns, and gravitational

pull but neither claiming a position of centrality".¹¹ This is further supported by the five values which have been defined by the European Patients Forum to underpin meaningful patient involvement: 1) Appropriate representation of patients; 2) Building on diversity and pooling knowledge to achieve more than can be achieved by each partner alone; 3) Equality, providing an empowering environment for patients; 4) Commitment to patient involvement being a positive experience that adds value to the project; and 5) Respect for patients as equal partners.

Thus, the implementation of PRO measures in clinical practice will be of value to help clinicians and patients with hematological conditions to make more informed shared treatment decisions, and might facilitate patient-physician communication and ensure patient-centeredness. Such partnerships require new skills and sustained efforts from all parties: understanding the values that different stakeholders aspire to provide an essential foundation for effective patient engagement. This approach is an ambitious goal of health advocacy. In conclusion, patient-centered research and practice in hematology based on real patient-clinician partnership will help to provide risk adaptive treatment and enhance the quality of care that patients with hematological malignancies receive.

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