Brief Report

Exploring translational gaps between basic scientists, clinical researchers, clinicians, and consumers: Proceedings and recommendations arising from the 2020 mine the gap online workshop

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ABSTRACT

Objective: To provide a summary of the translational gaps in musculoskeletal research as identified in the Mine the Gap workshop and propose possible solutions.

Methods: The Mine the Gap online workshop was hosted on October 14th and 15th, 2020. Five international panels, each comprised of a clinician, clinical researcher and basic scientist, presented gaps and proposed solutions for the themes of biomechanics, pain, biological measurements, phenotypes and imaging. This was followed by an interactive panel discussion with consumer insights.

Results: A number of translational gaps and proposed solutions across each of the five themes were identified. A consumer panel provided constructive feedback highlighting the need for improved resources, communication and shared decision making, and treatment individualisation.

Conclusion: This brief report provides a greater understanding of the diverse work and gaps relevant to fundamental/discovery scientists, clinical researchers and clinicians working across the musculoskeletal field. The numerous translational gaps highlight the need to improve communication and collaboration across the musculoskeletal field.

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1. Introduction

Musculoskeletal disease remains a major cause of disability worldwide [1]. As researchers in this space, we are encouraged to shift our activities to be more translational, fostering the interdisciplinary integration of basic research, clinical research and population-based research with the long-term aim of improving public health [2]. However, many translational gaps exist between research scientists, healthcare professionals and patients. This results in clinical assessment and management approaches that are not recommended, evidence-based [3] or acceptable to individuals with the condition [4]. These gaps may be due to ineffective communication between basic scientists, clinical researchers, and clinicians, but may also be due to system or process matters, worldwide [5].

An online workshop entitled ‘Mine the Gap’ was hosted on October 14th and 15th, 2020 to bring together an international panel of speakers comprised of a clinician, clinical researcher and fundamental/discovery scientist across five themes (biomechanics, pain, biological measurements, phenotypes and imaging). These themes were selected by the organising committee of senior scientists and early career researchers to represent a diversity of topics that would have application across a broad range of musculoskeletal conditions without the intention to address all possible topics of relevance for specific conditions or treatments. The international panel comprised experts with diverse backgrounds, including physiotherapy, rheumatology, orthopaedic surgery, radiology, veterinary medicine and surgery, and fundamental/discovery science. The workshop was intended for individuals involved and/or working in broad areas concerning musculoskeletal conditions, including researchers and clinicians. For each theme, a fundamental/discovery scientist, clinical researcher and clinician presented their perspectives on the theme topic and identified translational gaps. Following each thematic presentation section, a consumer perspective was presented, followed by an interactive panel discussion. The workshop concluded with a panel discussion summarising the gaps identified and discussed potential strategies to mine these gaps moving forward. The major aim of this online workshop was to identify translational gaps in musculoskeletal research and potential solutions across the five themes. This report provides a summary of the discussions and conclusions from the workshop.

2. Themes

Each theme is described below. The translational gaps and possible solutions are presented in Table 1.

2.1. Theme I: laboratory biomechanics to clinical application of biomechanics

Osteoarthritis (OA) is considered, at least in part, a mechanical disease and biomechanical factors play a critical role in the onset and progression of osteoarthritis. However, the mechanisms by which biomechanics influence joint health and pathology are not fully understood and involve a complex interplay between physical factors and cellular responses in various tissues of the joint. Often, gait analysis is used as a research tool in lower limb OA to determine joint loading. However, compared to other conditions such as cerebral palsy (CP), gait analysis is not often used as a clinical tool in OA management. In CP, three-dimensional gait analysis, along with a comprehensive physical examination is used to determine impairments causing gait deviations in children, which then informs which treatment options or surgical procedures might be appropriate. Tools such as three-dimensional gait analysis can assist in tailoring surgical interventions to individual needs and can provide a quantifiable measurement of outcome following surgery. Research using three-dimensional gait analysis has helped to translate research findings from biomechanical studies into clinical practice but a critical step in OA will be to ensure that measures make a meaningful contribution to decision making. To date, many measures have been proposed, but few have been shown to provide relevant information.

2.2. Theme II: measurement of pain in pre-clinical models vs. patient-reported outcomes

The complex nature of pain as both a symptom and disease, and the heterogeneous nature of OA, makes OA pain assessment challenging. The measurement of pain in pre-clinical animal studies greatly differs from how pain is assessed in patients with OA. In a clinical research setting, there have been various methodologies utilised in an attempt to identify underlying pain mechanisms. Currently, pain questionnaires and quantitative sensory testing are the most clinically relevant measures, but there remains considerable debate regarding their interpretation. Pain is the main reason for patients to seek care from a physician and patient-reported outcome measures (PROMs) are recommended to be used in a clinical setting to help assess the efficacy of interventions. However, current guidelines for clinical use of these PROMs are lacking despite their recommendations.

2.3. Theme III: biological measurements (animal or human) to clinical application

The basic science of biomarkers has progressed significantly from examining candidate articular cartilage matrix degradation products with the development of a range of new technologies. However, a biomarker to monitor OA disease onset, progression and/or effectiveness of OA therapies is still lacking. Evidence-based laboratory medicine should aim to only perform tests with high diagnostic accuracy that improve patient outcomes, while being cost-effective. Clinically, identifying those at risk of disease progression by using a biomarker such as a blood test would represent an important breakthrough in OA management.

2.4. Theme IV: phenotypes

OA is a pathological syndrome with multiple aetiologies with subtype-specific mechanisms that drive joint-tissue damage and the development of symptoms. Pre-clinical animal models allow detailed investigation of observations and pathologies identified in patients. They are central to an improved understanding of the pathobiology of OA and the development of disease/symptom-modifying OA drugs. Currently, with animal models, there is no consensus on how closely they model human disease, and disparity between those used to study structural pathobiology versus pain. In clinical practice, there is wide variability in the long-term disease trajectory and responses to treatment. Pain radiographs typically used for knee OA may conceal the range of potential pathways leading to OA and does not allow for risk stratification and targeted treatment. There has been an increasing focus on the identification of OA phenotypes such as symptomatic or structural progression, using a combination of pre-clinical and clinical data with sophisticated statistical approaches. An improved interpretation of findings from pre-clinical models may help to stratify OA patients by their pathophysiology (“endotypes”). Predicting patient response in a clinical setting is a challenge due to the mix of biopsychosocial factors which may confound response to management. In addition to the first-line management of OA (advice/education, exercise, weight loss/management), some patients may require additional pharmacological or surgical intervention. Identifying patients who will respond to a given intervention in the early stages of seeking care would be clinically and economically advantageous.

2.5. Theme V: neuromusculoskeletal imaging

Neuromuscular conditions are painful and disabling. The
## Table 1
Major gaps and proposed solutions across the five themes.

| I. LABORATORY BIOMECHANICS TO CLINICAL APPLICATION OF BIOMECHANICS | CLINICIAN | CLINICAL RESEARCHER | FUNDAMENTAL-DISCOVERY SCIENTIST |
| --- | --- | --- | --- |
| **Gap(s):** Many children with cerebral palsy (CP) will undergo orthopaedic surgery to improve gait and preserve function. 3D gait analysis provides detailed information about complex gait patterns, allowing orthopaedic surgeons to tailor surgery to an individual’s needs. Software based on the conventional gait model is used in most clinical gait laboratories. However, known limitations in the model can affect data output and influence surgical decision-making. For example, difficulties determining the transepicondylar axis of the knee can result in inaccurate measurement of hip joint rotation during walking. **Solution(s):** Solutions to address these limitations have been presented, but many have not been widely adopted in clinical practice. For example, methods to improve repeatability of hip rotation measurement have proved challenging for children with physical impairments to perform or deemed difficult to establish due to additional time and training required. Any solutions to enhance repeatability of gait lab output need to be applicable to those of all abilities and limitations referred for gait analysis. Minimising additional demands on the patient is important to translate a new tool into clinical practice. | | |
| **Gap(s):** Successful clinical trial outcome measures do not reach widespread use in the clinical context. This is in part due to differing values, goals and assumptions between efficacy and effectiveness research, and the application of outcome measures in a real-world context and its feasibility. **Solution(s):** Formulation of a translational culture in clinical practice, improve consistency of “measurement language” between researchers and clinicians. Use advances in technology and statistics to develop novel chronic pain measurement tools Identification of truly meaningful outcomes measures that clinicians can prioritise and act upon. Pilot and phased implementation of outcome measures to ensure feasibility and uptake. | | | |
| **Gap(s):** Lack of gold standard measurement to assess a new test against, unacceptable assay variation, over-estimation of diagnostic accuracy through inappropriate study design, lack of clinical outcome studies, lack of cost constraint that allows testing with low clinical utility. Clinicians should beware of relying on laboratory measurements without incorporating prior clinical probabilities. **Solution(s):** Methodological standards for designing and reporting studies of diagnostic accuracy, including standardised expression of association between biomarker and disease outcome (e.g., hazard ratio/standard deviation) and assessing dependence of biomarker associations on other clinical factors. | | | |
| **Gap(s):** Majority of OA research has investigated the influence of gait parameters in isolation; however, it is likely that multiple biomechanical variables interplay with each other to characterise movement strategies. **Solution(s):** Hypothesis-generating analyses of existing OA biomechanical datasets to explore complex movement strategies in people with OA and subsequently examine the relevance of distinct movement strategies with clinical outcomes. Robust longitudinal studies to evaluate the association between biomechanical outputs from gait models informed with patient-specific parameters and clinical outcomes. Machine learning techniques may provide a novel way to capture information of equivalent quality as can be generated from laboratory data through wearable sensors in a real-world setting | | |
| **Gap(s):** Pain is what the person says it is. The construct is difficult to measure. Bedside clinical assessment (e.g., Quantitative Sensory Testing) of pain mechanisms is blunt and confounded by many factors – psychological, general health, time of measurement, etc. There is poor translation from animal to clinical models. **Solution(s):** Standardised language about pain and pain mechanisms. | | | |
| **Gap(s):** Osteoarthritis biomarker field has seen much activity and an extensive clinical literature in the last decades, however, basic scientific discovery, validation, qualification and reporting standards have lagged behind. The most promising molecular targets and assays still rest largely on face validity and lack both proof of origin and clinical relevance. **Solution(s):** Improve systematic evaluation of the evidence which requires a coordination of the entire biomarker research agenda – which requires international multi-team collaborations. Such collaborations will enable the use of case definitions with standardised and transparent criteria, gold standard clinical end points, standardised and transparent | | |
| **Gap(s):** The magnitudes and modes of joint loading which result in pathological changes and disease progression are poorly understood. The mechanisms by which cellular-level signals influence tissue homeostasis, and their interaction with systemic factors (including genetics) needs to be determined. **Solution(s):** A fundamental understanding of biomechanics in normal and pathological conditions from the whole body to subcellular levels is required. With this knowledge, identification of the cellular mechanotransduction pathways may provide new therapeutic targets to enhance tissue regeneration or alter the course of OA. Such information will hopefully lead to the development of new physical or pharmacologic therapies. | | | |

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IV. PHENOTYPES

Gap(s):
Predicting response to management based on patient characteristics alone is challenging and often influenced by many patient characteristics (e.g., presence of persistent pain and/or psychosocial factors).

Clinical decision making regarding different management approaches (e.g., non-surgical, surgical) can be especially difficult for those with a higher severity of disease.

Solution(s):
A clinical decision tree incorporating measures of progressively increasing sophistication (and expense) as required may assist stratified care, matching appropriate care to patients.

V. NEUROMUSCULOSKELETAL IMAGING

Gap(s):
Significant discordance between the use of imaging in clinical practice and the findings of studies looking at the utility of imaging in various musculoskeletal conditions.

Imaging techniques in basic science and clinical research in MSK pain require technology and data processing which are not always available in routine clinical imaging.

Solution(s):
Diagnostic imaging should be reserved for specific or serious pathology. Imaging should be clinically relevant and have the potential to influence management. Be mindful of the high prevalence of asymptomatic pathology in the musculoskeletal system with increasing age.

Gap(s):
The prediction of recovery following trauma involves a complex interplay between biological, psychological and environmental processes. Biopsychosocial data and imaging (CT and MRI) data can be compared.

Solution(s):
Imaging based methods to quantify alterations in brain, spinal cord anatomy and whole-body skeletal muscles as potential markers of poor recovery. Normative datasets are required across the lifespan and considering sex-as-a-biological variable

pathophysiology of chronic neuropathic pain remains poorly understood and the current management remains at symptomatic rather than mechanistic levels. Changes in the brain have been shown to be responsible for the generation and maintenance of chronic neuropathic and/or nociceptive pain, without any peripheral input. There is growing evidence to suggest that neuronal-glial interactions may underlie the development of chronic pain of numerous types (including neuropathic) in pre-clinical studies, however, it remains unknown how such interactions transition from an acute to chronic pain state. Advances in magnetic resonance imaging (MRI) technologies and analysis methods allow for improved visualisation and quantification of morphology of the skeletal muscles, the spinal cord and brain. The growing field of radiomics, the field of study which aims to mine large amounts of quantitative features from medical images using data characterisation algorithms have contributed to large datasets and combined with the patient’s pain experience may add to the biopsychosocial model in understanding pain. Clinically, there is widespread use of imaging which has highlighted the prevalence of pathology in both symptomatic and asymptomatic participants, raising the tenuous relationship between imaging abnormalities and the clinical course. Despite the limited predictive value of imaging findings identifying the modifiable pain generator, Patients are often focused on the need for imaging investigations to inform management.

3. Consumer impressions

Each session was well received by the consumers and impressions provided were generally constructive. General themes which arose were related to: i) the need for patient-friendly resources which explain different conditions and treatment options; ii) effective communication and shared decision-making between patients and healthcare professionals, using patient-appropriate language and understanding potential health literacy barriers; iii) better allocation of resources to evidence-based osteoarthritis management programs, instead of imaging which does not change clinical management of OA; iv) individualisation of treatment– OA is multi-faceted and patients have their own treatment preferences.

This brief report provides a greater understanding of the diverse work and gaps relevant to fundamental/discovery scientists, clinical researchers and clinicians working across the musculoskeletal field. Numerous gaps and proposed solutions across each of the five themes were identified, many of which solutions are focused on the design of research studies in the fundamental/clinical research field (e.g., higher methodological quality, longitudinal studies, standardisation of methods/language) all concluding the need for a multidisciplinary approach. The results of the workshop will be widely disseminated in an
aim to enhance communication and foster collaborations between groups, ultimately leading to improved translation of research.

Credit author statement

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