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The Difficulties of Managing Pain in People Living with Frailty: The Potential for Digital Phenotyping

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Abstract

Pain and frailty are closely linked. Chronic pain is a risk factor for frailty, and frailty is a risk factor for pain. People living with frailty also commonly have cognitive impairment, which can make assessment of pain and monitoring of pain management even more difficult. Pain may be sub-optimally treated in people living with frailty, people living with cognitive impairment and those with both these factors. Reasons for sub-optimal treatment in these groups are pharmacological (increased drug side effects, drug–drug interactions, polypharmacy), non-pharmacological (erroneous beliefs about pain, ageism, bidirectional communication challenges), logistical (difficulty in accessing primary care practitioners and unaffordable cost of drugs), and, particularly in cognitive impairment, related to communication difficulties. Thorough assessment and characterisation of pain, related sensations, and their functional, emotional, and behavioural consequences (“phenotyping”) may help to enhance the assessment of pain, particularly in people with frailty and cognitive impairment, as this may help to identify who is most likely to respond to certain types of treatment. This paper discusses the potential role of “digital phenotyping” in the assessment and management of pain in people with frailty. Digital phenotyping is concerned with observable characteristics in digital form, such as those obtained from sensing-capable devices, and may provide novel and more informative data than existing clinical approaches regarding how pain manifests and how treatment strategies affect it. The processing of extensive digital and usual data may require powerful algorithms, but processing these data could lead to a better understanding of who is most likely to benefit from specific and targeted treatments.

Key Points

- Pain can be challenging to assess and treat in older people living with frailty.
- Pain assessment can be improved by collecting more information about features associated with pain that can be observed (phenotyping).
- Digital methods may add value to the phenotyping of pain and may improve care for older people living with frailty and pain.

1 What Makes Pain in Frail Older Adults Special?

Pain is a problem regardless of age [1]. For a young, fit, and healthy person, chronic pain is often a considerable challenge that both diminishes and draws upon the individual’s mental and physical reserves. With increasing age, mental and physical reserves are further diminished due to the accumulation of comorbidities and age-related decline; this is called frailty [2]. Frailty is closely linked to cognitive impairment; the presence of frailty significantly increases the risk of developing cognitive impairment and dementia [3–5]. Cognitive impairment itself, whether associated with frailty or not, also diminishes an individual’s reserves, such as the ability to apply self-management strategies to reduce pain.

Chronic pain and frailty are linked [6]. Pain is more prevalent in people living with frailty compared to robust older people [7]. The relationship between chronic pain and frailty is bidirectional; pain predicts the development of frailty, and

frailty predicts the development or worsening of pain [8–11]. Multiple different processes, behaviours, and exposures are likely to drive both these relationships, including the immune-inflammatory response to stress, dysregulation of endocrine and immune processes, and reduced physical activity [12–16]. Due to the overlap between pain and frailty, we have argued that chronic pain itself may be an under-appreciated indicator of the frailty state; tools to identify frailty tend to focus upon muscular functioning and rarely include pain [17].

Older people living with frailty may have pain from multiple sources and sites, occasionally without a formal clinical diagnosis or clear evidence of a causative pathology. This can challenge clinicians aiming to provide targeted, tailored interventions for pain. A thorough assessment and characterisation of pain, related sensations, and their functional, emotional, and behavioural consequences (“phenotyping”) may help to enhance the assessment of pain, particularly in the complex states seen in people with frailty and cognitive impairment. Phenotyping includes assessing the type, severity, and sites of pain, aggravating and relieving factors, and associated factors and behaviours, alongside imaging, laboratory, and sensory function testing. Phenotyping is distinguished from an approach that considers pain more simplistically and tends to result in people with different pain phenotypes being offered the same treatment [18, 19].

Digital phenotyping is concerned with observable characteristics in digital form, more specifically those that are obtained from sensing-capable devices and other sensors, and may present deeper and novel information, adding to existing clinical approaches [20, 21]. Digital phenotyping is defined as the use of moment-to-moment quantitative and descriptive data that are automatically generated (for example, heart rate, blood pressure, skin conductance, and movement) and collected by technological devices such as wearables, mobile devices, or video cameras [22, 23]. The outcomes of digital phenotyping we designate as “digital biomarkers”, which are meant to complement traditional biomarkers (for example, non-specific autonomic, behavioural, and reflex responses) and can shed light on individualised descriptions of the complex, nonlinear, and heterogeneous processes specific to the human body.

In this paper, we elaborate the challenges of the management of chronic pain in people with frailty and, hence, the additional complexity of pain phenotyping in these people. We also introduce the concept of digital phenotyping and its potential additional value.

2 Challenges of Pain Management in Older People Living with Frailty

Reasons for undertreatment of pain in frail older people are summarised in Figure 1.

2.1 Pharmacological Challenges

Pain is more than a nociceptive stimulus, and the way the pain is experienced, expressed, and understood is related to several biological, psychological, and social factors [24]. In most chronic pain management contexts, the first recommended line of treatment is with non-pharmacological interventions. These could include—but are not limited to—self-management strategies, maintenance of physical activity, and psychological therapies [25]. Pharmacological interventions can then follow if required. Non-pharmacological approaches should not be overlooked in acute pain contexts, such as the stabilisation of a fractured bone. In urgent and extreme cases, analgesic medication can be introduced alongside non-pharmacological interventions as first line.

Whilst older people living with frailty are most likely to receive medication because they often have multimorbidity, they are also the very people in whom drugs should be used with caution. This is primarily due to the fact that older people living with frailty are more vulnerable to drug side effects and more likely to suffer effects of polypharmacy [26]. Polypharmacy is the consumption of multiple medications, and is more common among older people, and especially those who live with frailty. This can potentiate the effect of undesirable side effects. In older people living with

Reasons for undertreatment of pain in frail older persons

- ageism and self-ageism
- Fear and reality of side effects
- Fear of addiction and tolerance
- Risk of drug interactions
- Low prioritization of pain over other conditions (e.g. when reducing polypharmacy)
- Unclear clinical story
- Communication (bidirectional) problems
- Cognitive problems
- Monitoring difficulties
- Cost of prescription medication
- Difficulty in accessing general practitioners (GPs) for prescriptions or difficulty in accessing the local pharmacy

Fig. 1 Reasons for undertreatment of pain in frail older people

frailty, drug–drug interactions and cumulative effects such as anticholinergic burden are commonly encountered. An example of a drug–drug interaction is when buprenorphine is used concomitantly with antidepressants in people living with dementia, and can be poorly tolerated due to increased psychiatric and neurological side effects [27]. Moreover, many frequently prescribed drugs have weak anticholinergic properties that on their own are clinically not noticeable, but in polypharmacy, people may be taking several such drugs and the cumulative effect of them—the anticholinergic burden—can often be equivalent to the effect of a powerful anticholinergic drug. These concerns, in addition to concerns about age-related renal impairment, make clinicians wary of prescribing analgesics [28, 29].

Ageing-related changes in hepatic and renal function, muscle to fat ratios, and volumes of distribution will affect drug pharmacokinetics; the dose and interval of certain drugs may need to be adjusted accordingly. For example, after accounting for physiological changes, adjusted plasma concentrations of morphine in older people were similar to that of younger people [30]. However, adjusting doses and intervals to match each individual's physiology is difficult to do because of the absence of sufficiently precise information about their physiological state, and dose adjustment can have an impact on drug effectiveness. Further, pharmacokinetic changes such as those a result of altered blood–brain permeability and pharmacodynamic changes such as altered target receptor density make the overall effectiveness of many drugs less predictable in older people than in younger people [31, 32].

A further challenge is a concern over the safety of long-term analgesic drug use, particularly where there is cognitive impairment [32]. A systematic review of trials in older people with dementia found sparse evidence for the tolerability of transdermal opioids, and also concluded that, although relatively safe, the risk of liver damage with long-term use of paracetamol was undetermined [33]. Both paracetamol and opioids are the most commonly used analgesic drugs used in older people, particularly in people living with dementia [34]. When considering whether to start or stop any of these drugs, these factors should be borne in mind.

2.2 Non-pharmacological Challenges

Non-pharmacological interventions for pain vary widely in type. This term refers to interventions to inform and educate patients or staff (typically about analgesic drug use), psychological interventions such as cognitive behavioural therapy, exercise, and sensory stimulation such as acupuncture [35–37]. The evidence for the efficacy of these interventions and in whom they are most effective is limited and unclear. One reason is that there is less research funding

for such interventions compared to that for drugs. Further, people with frailty and those with cognitive impairment are often excluded from studies [38]. The lack of robust research makes it difficult for clinicians to advise such interventions, and their provision may be limited.

People living with frailty are also less likely to participate in active non-pharmacological pain management strategies that maintain normal function. They may see the onset of chronic pain as an inducement to become less active, believing that pain is an inevitable aspect of ageing. Older people often choose to adapt their daily living activities and stop doing previously valued activities altogether, findings that are explained in fear-avoidance models in chronic pain [39–41]. Clinicians may also encourage or impose this perspective on their patients. Older people living with frailty may also be less proactive and confident in trying new strategies and be reluctant to seek formal help [40, 42]. In addition, older people with cognitive impairment may experience apathy and a decreased ability to problem-solve, and the use of self-management strategies may be more difficult to carry out.

2.3 Ageism

Another important issue to account for in managing pain in older people is ageism and self-ageism. Although not all older people experience chronic pain, many people and older people themselves often believe that pain is a natural part of ageing [24]. This belief may lead the person to not complain or consult their clinician about pain, and is another important reason why pain in older people is not adequately assessed. There is evidence that this negative age stereotype and discrimination amongst older people is associated with lower intensity of analgesic management and increased development of chronic pain [43, 44]. Ageism is also present in many healthcare professionals, and may be overt or subconscious. Some healthcare professionals might stereotype older people as stoic, or be cognitively and perceptively impaired, with communication difficulties. They may conclude that these older people are unable to participate in pain management decisions [45, 46], thus impacting the care patients receive. Ageism is also endemic in drug licensing and medical research. Historically, eligibility for participation in clinical trials or for a drug often included arbitrary chronological age cut-offs. The evidence base for much of drug treatment may thus not apply well to current populations who are both older and have more comorbidities. These factors may affect how older people are offered, and make choices, about treatment options for pain.

2.4 Communication

A further challenging aspect of managing pain in the older person living with frailty can be communication. Communication challenges lead to suboptimal assessment of pain. When pain is not well assessed, its management will invariably be suboptimal [47]. Pain can be difficult to describe even in the absence of a communication deficit. Deafness, a common impairment in people living with frailty, makes history-taking more difficult, and yet a thorough assessment of pain is heavily dependent upon the history. This can often be largely overcome with training, time, and communication aids, but frequently, these are lacking [48]. Language or cultural differences between the patient and the clinician can make communication even more challenging. Multimorbidity may mean that patients have multiple different pains, in different sites, with different histories, aetiologies, and consequences. This adds to the challenge for patients when explaining their pain to a clinician.

Not only can it be difficult for the person with pain to express themselves, it is also difficult for the clinician to interpret and record what they hear. For example, a commonly used approach is to ask patients to provide a numerical value to their pain experience, but the validity of doing so has been challenged [49]. Multiple words can be substituted for pain (for example, soreness, hurt, stiffness), and a person may sometimes deny they are in pain but agree that they are sore. A narrative approach in which the patient is asked to tell their pain stories, with use of similes and metaphors, rather than posing direct questions, is likely to yield a better understanding of what pain is like for that older person, as well as how it impacts on their wellbeing [50]. However, this takes training, time, and patience to perform well.

People living with both frailty and cognitive impairment deserve special consideration. The presence of language and memory impairments makes it even more challenging to effectively communicate a complex pain experience or the effects of interventions. People living with cognitive impairment often have difficulty recalling the course of their pain or its relation to activities. They have trouble understanding and responding to self-report pain instruments, such as the numeric rating scale, visual analogue scale, or the verbal rating scale [51]. Where such deficits are marked, observational instruments that rely on non-verbal pain indicators such as vocalisations, body movements, and facial expressions are often used [52–54]. However, not all non-verbal pain indicators are specific for pain and may be expressions of distress due to unmet needs such as companionship or continence care. Further, implementation of these approaches into practice is inconsistent across hospital, community, and

long-term care. There are also potential ethical issues. A person with cognitive impairment may not have the ability to understand the risks and benefits of treatment and weigh up these issues to come to an informed decision. There might also be a regular caregiver or advocate for the older person with cognitive impairment who can help in making decisions in the best interests of the patient, but they will have their own perspectives and potential biases, for example, about analgesic drugs, and these may influence how management decisions are made.

3 Phenotyping in Order to Enrich the Comprehensive Assessment of Pain

In reality, no matter how diligent the clinician is in history taking and how well pain is described, the mechanisms underlying an individual's pain may be difficult to classify. Thus, the management of pain should not be focused solely on the direct aspects of pain (such as severity or site), but should also attend to understanding the complex psychosocial factors that are frequently associated with pain. These factors may sometimes be identified and measured (for example, depressive states or low mood), but the frequency, circumstances, and disease-specific states in which they occur in the context of pain are unclear. Pain management should include both sensory and emotional components, addressing problems experienced by the patient and also their caregivers and loved ones. Characterisation of observable, identifiable factors may provide discrete targets for intervention and improve overall pain management in older people living with frailty.

Phenotyping is defined as identifying observable characteristics of an organism, usually by means of biomarkers or other assessment outcomes, where specific aspects that make an individual more likely to respond to a certain treatment need to be identified in order for treatment to be most beneficial [55]. Phenotyping of pain can be done through clinical means: detailed analysis of pain quality and severity, associated symptoms, and identifiable features of non-verbal expressions or observable clinical signs that are specific for pain. In addition to clinical assessment, deep phenotyping of pain may be obtained using objective measures such as quantitative sensory testing and sensory profiling [19]. Psychosocial and sleep factors associated with pain are also core elements of pain phenotyping [56].

3.1 Digital Phenotyping in Frailty and Cognitive Impairment

Currently, digital phenotyping is a fertile front line of transdisciplinary research. New digital biomarkers are being designed through collaborative design and knowledge between engineering fields (computer or data science, systems engineering, applied mathematics) and clinical partners. Digital phenotyping may present new and valuable insight in older people living with frailty and cognitive impairment, which would overcome to some extent the recall and language required to express pain or functional impairment.

In practice, digital phenotyping implementation requires devices equipped with sensors to collect real-time data from the monitored person. The caregiver accessing these data would be able to estimate a longitudinal trajectory based on the digital biomarkers combined with other information, such as medication times, and then decide whether or not to change or continue with current treatment. Trajectories can then be measured that account for other factors such as diagnosis and context. This entire process allows for highly individualised longitudinal estimations to be made for the person receiving care in a timely manner.

For example, in Parkinson's disease, research has been focused on designing wearable technology that documents gait and movement analysis in real time, to enable correlation with medication times and therefore a better understanding of treatment efficacy. This enables a more dynamic, temporal phenotyping of the movement disorder and identification of digital biomarkers to improve tracking of disease trajectories for clinical care and research [57]. Technology such as wearables and perhaps machine vision could give information from outside the clinical encounter. This could be helpful, for example, in revealing patterns and possible consequences in areas where the history is notoriously unrevealing, for example, sleep. This could augment the information available to clinicians in those with cognitive and memory impairment.

3.2 Digital Phenotyping in Pain

There remain few off-the-shelf solutions to estimate pain or precursors of pain using sensing devices specifically for groups marginalised by mainstream industry (for example, older people living with frailty) at the time of writing this article. However, international research efforts are dedicated to continuing to develop and validate these techniques for such groups [58–60].

Specific to pain, digital phenotyping might usefully supplement the limited information available in those with communication, language, or memory deficits. For instance,

facial expressions and vocalisations could be picked up by facial expressions scanners and artificial intelligence utilising natural language processing algorithms. Abnormal or reduced movement and other physiological cues such as change in heart rate and respiratory rate may be sensed by wearable technology and flag up early physiological changes in the person with cognitive impairment [61]. Some examples of technology that could be used in the digital phenotyping of pain that might help are listed in Table 1.

Digital pain phenotyping may also help with dissecting different components of pain in people with multiple pathologies, for example, whether an older person living with frailty has arthritis of multiple joints or multiple painful pathologies at once. Advanced data analysis (based on signal processing and/or artificial intelligence) could provide more sensitive and accurate information regarding the most prominent sources of pain in the body and the type and character of pain, thereby enabling more targeted biological treatment. Digital phenotyping may also help with providing feedback during therapy. For instance, if pain is associated with a specific gait deficit, improving the deficit might precede improvement in pain. This would encourage continuing therapy engagement if accompanied by early, sensitive digital information, which is not always clinically perceptible. Furthermore, people might exercise more effectively if digital technology can inform them that they are doing it as they should.

Personalisation of monitoring of the response to treatment is another potential benefit. For example, some people may become restless when in pain, others may develop a tachycardia or raise their blood pressure or breathing rate, whilst others might become less active. None of these biomarkers are specific for pain, as opposed to other forms of distress. With the help of digital phenotyping, clinicians might identify an individual's particular (digital) pain signal, and then use a digital monitor to assess change over time. In people who can self-report pain, change in digital biomarkers may be used to evaluate correlation with self-reported pain. While some work has been done in assessing the utility of digital phenotyping in cognitive impairment [61], future research questions should consider how the information gained might be more specific for pain rather than underlying distress from other causes, and also discriminate pain from other emotions. If pain can be assessed digitally, then the effects of pain treatments should also be able to be monitored in the same way. The challenge for the clinician would be to assimilate this knowledge into their clinical judgment to provide more holistic pain assessment and management.

Table 1: Examples of monitoring technologies that could be used in digital phenotyping of pain

Types of digital technology modalities	Examples of digital technology modalities and data types	Observable features	Potential uses for pain assessment and management
Actigraphy	Wearable devices (often wrist-worn), from commercial brands, e.g. Garmin, Polar, Apple, that calculate e.g. step counts, MET scores	Movement, GPS tracking, MET tracking, step count	Data relating to assessment of consequences of pain, pain patterns, guided training
Personal sensing	Wearable devices, mobile phones, sensors embedded in clothing or beds (e.g. pressure mats, socks, gloves, jewellery); these are often equipped with sensors for EDA, temperature, heart rate and heart rate variability; text, voice and video sensing for mobile phones and tablets	Physiological parameters such as heart rate, respiratory rate, sleep/awake patterns	Differentiation between acute and chronic pain based on change in physiology, pain estimation based on behaviour. Accentuation of clinical assessment, for example, pressure mats inbuilt with sensors for people with pressure ulcers
Brain activity monitors	BIS, traditional EEGs and other technologies that use EEG electrodes, ECG, sEMG	Change in sleep patterns, brain wave activity	May be more suited to people who have very little speech (e.g. learning disability) or with low consciousness levels, e.g. ITU settings
Multi-modal systems	PSG and environmental sensors, wearable devices	Change in sleep patterns, change in activity and/or agitation levels, pacing patterns, activities of daily living estimation, reactions to medication	Assessment of pain during the night, assessment of sleep problems in relation to pain, assessment of motor and activity-related parameters in relation to pain, assessment of agitation
Non-contact monitoring systems	Video/facial expression analysis, infrared, radar	Sensing of subtle changes in facial expressions, sensing of pressure to skin or other bodily strain that might cause discomfort from people who are unable to communicate	Video and facial recognition algorithm-based apps already in use to supplement clinical assessment
Natural language processing	Language analysis: grammar, wording, word frequency; ontology-based analysis	Ability to extract significant and relevant terms from text	Summarising detailed accounts of pain experience where clinical time is short
Other technologies based on artificial intelligence (knowledge-based systems, neural network, Bayesian modelling, decision support systems, etc.) and based on formal methods (signal processing, system dynamics, nonlinear modelling, linear and nonlinear statistics, etc.)	Estimates of clinically relevant outcomes, which require clinical knowledge to design	All or most of the above	All or most of the above

BIS bispectral index, *ECG* electrocardiography, *EDA* electrodermal activity, *EEG* electroencephalogram, *GPS* global positioning system, *MET* metabolic equivalent, *PSG* polysomnography, *sEMG* surface electromyogram, *ITU* intensive therapy unit

3.3 Digital Phenotyping: Some Pitfalls

Although the use of digital technology and artificial intelligence in particular may have many potential benefits, there are some pitfalls to consider. There is currently reduced uptake of technology usage among older people compared to younger people, particularly if proactive use is required (for example, wearable devices). Reasons for this are multifactorial, and amongst other things, being of lower socioeconomic status, being older in age, and having no access to laptops or tablets is associated with reduced engagement [62, 63]. Older people living with frailty in particular have reduced uptake of digital technologies compared to older people who are more robust [64]. However, particularly since the coronavirus disease 2019 (COVID-19) pandemic, the percentage of older people engaging with digital technology has increased, and the narrowing digital divide between old and young should be seen as an opportunity [65, 66].

The ethics of obtaining information without informed consent, for example, with machine vision, needs to be deliberated prior to use. The privacy and data security of vulnerable older people living with frailty must be protected. In addition, a wealth of information does not mean that all information is useful or that positive signals pertain to the clinical question (i.e. non-specificity). Increased information may be overwhelming for older people and their loved ones, and may lead to the person and the clinician being over-anxious. In addition, some older people may also not accept or be fully compliant with the technology, which influences accuracy of the measurements, and while this issue is mitigated by swapping wearable sensors with environment-based, unobtrusive devices, the latter cannot follow patients outside their residence. Moreover, some techniques pertaining to artificial intelligence carry over substantial bias from the dataset used during training. The information used in creating the algorithm might not represent the true underlying population of older adults with frailty and calls into question the generalisability of data being collected. Furthermore, obtaining collateral information through digital technology to accentuate the pain phenotype is desirable, but future research should set out to determine whether they improve outcomes compared to standard care.

In addition, the clinician will need to maintain clinical skills in assessment and clinical reasoning, whilst harnessing the potential of digital technology as a tool and not regard it as a substitute diagnostician. Over-reliance on digital technology can de-skill clinicians, change the clinician–patient relationship, and reduce trust in clinical judgment. The clinician may also be less likely to treat a person on a symptomatic basis, simply because a machine does not give the expected signals. All these issues should

be borne in mind when embracing the benefits that digital technology has to offer.

4 Future Directions

Digital solutions for tasks and problems are becoming more and more ingrained into daily life, and are likely to be a significant part of the future of healthcare. Compared to robust individuals, older people with frailty and cognitive impairment may benefit more from technological advances that enable early recognition and characterisation of pain and monitoring of treatment efficacy. The pain phenotype of the individual will then be analysed alongside evidence of organ dysfunction, multimorbidity, and the patient's psychosocial and functional status in order to have a fuller and richer picture of pain in individual contexts. More comprehensive data collection through digital phenotyping might enable powerful algorithms and tailoring of treatment options and a better understanding of who benefits from specific and targeted treatments.

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