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# Accepted Manuscript

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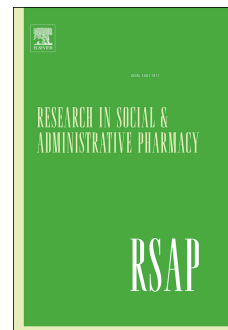
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## The knowledge, attitudes and beliefs of patients and their carers around oral dosage form modification: a systematic review of the qualitative literature

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## Article Synopsis

Research has shown that modification of oral medicines is common in both primary care and long-term care settings. However, this practice can alter drug safety and efficacy *in vivo*. This article describes a qualitative systematic review conducted to synthesise the available qualitative research on the knowledge, attitudes and beliefs of patients, healthcare professionals and patients about oral dosage form modification. Key factors influencing modification were elucidated. The synthesis highlights the need for increased engagement with and assessment of individual patient's formulation requirements, which needs to be supplemented with evidence-based recommendation and multidisciplinary input into decision making.

**The knowledge, attitudes and beliefs of patients and their carers around oral dosage form modification: A systematic review of the qualitative literature**

ACCEPTED MANUSCRIPT

## Introduction

Medication represents one of the most common and most important therapeutic interventions of modern medicine. However, key to optimising drug therapy is ensuring that the right patient receives the right drug at the right dose by the right route at the right time.<sup>1</sup> Although oral dosage forms (ODF), such as tablets and capsules, are preferred by both healthcare professionals (HCPs) and patients, modifications may be necessary to facilitate administration of the right dose or to allow administration via the oral route. ODF modification can be defined as, “any alteration of an oral dosage form that can be performed at the point of administration”.<sup>2</sup> These modifications are undertaken to facilitate medicine administration to patients with difficulty swallowing the intact dosage form (e.g. crushing tablets or opening capsules) or to facilitate fractional dosing (administration of part of an ODF to allow administration of a lower dose e.g. splitting tablets). Studies have shown that between 24.1% and 31.0% of all tablets prescribed for adult patients in primary care are split prior to administration,<sup>3,4</sup> with data from long term care indicating that 35.4% of older adults receive at least one split medication.<sup>5</sup> ODF modifications to overcome swallowing difficulties are also prevalent, with up to one third of all occasions of medicine administration to older patients in long term care facilities involving ODF modification.<sup>6</sup> Data from primary care suggest that between 9.0% and 37.4% of adult patients experience difficulty swallowing tablets and capsules, with the majority of those affected modifying the dosage form to overcome these difficulties.<sup>7,8</sup>

There are a number of safety and efficacy concerns around modified medicines such as reduced dose accuracy, reduced drug stability and the potential to affect the pharmacokinetic and pharmacodynamic profile of the drug *in vivo*.<sup>9-14</sup> Guidelines advise that modifications should only be undertaken as a “*last resort*”<sup>15</sup> when “*other methods have been considered*”.<sup>16</sup> Additionally, there is growing concern amongst regulatory agencies about fractional dosing.<sup>17, 18</sup> However, despite this,

evidence shows that ODF modifications are a routine part of clinical practice.<sup>3, 19, 20</sup> While modifications may be necessary due to a lack of appropriate licensed formulations,<sup>4, 5, 19</sup> it is clear from the literature that modifications occur even in situations where alternative formulations are available<sup>3, 4, 21</sup> and / or in situations where the modification is expressly prohibited by the manufacturers guidelines.<sup>3, 4, 20, 21</sup>

Whilst quantitative studies have provided useful evidence on the prevalence of ODF modifications and highlighted concerns, they have not elucidated the factors that influence the decision to modify. HCPs prescribe, dispense and administer modified ODF,<sup>4, 22</sup> and patients modify medicines without the knowledge of their healthcare providers.<sup>4, 22, 23</sup> These studies have shown that both HCPs and patients: have concerns about the appropriateness of modifications; experience difficulty when modifying medicines and; display significant knowledge deficits about ODF modification.<sup>4, 20, 22, 24</sup> Qualitative research methods can provide an insight into the knowledge, attitudes and beliefs of those who modify to gain a deeper understanding of the factors that influence behaviour and practice. Qualitative studies have been undertaken to investigate ODF modification, but to date, no systematic review of this literature has been conducted.

## **Study Purpose**

The aim of this systematic review is to synthesize the available qualitative research on the knowledge, attitudes and beliefs of adult patients, healthcare professionals and carers about ODF modification.

## Methods

Details of the protocol for this systematic review were registered on PROSPERO and can be accessed at [http://www.crd.york.ac.uk/PROSPERO/display\\_record.asp?ID=CRD42015023494](http://www.crd.york.ac.uk/PROSPERO/display_record.asp?ID=CRD42015023494).

### Search strategy

A systematic literature search of the following databases, from inception to September 2015, was undertaken: PubMed, Medline (EBSCO), EMBASE, CINAHL, PsycINFO, Web of Science, ProQuest Databases, Scopus, Turning Research Into Practice (TRIP), Cochrane Central Register of Controlled Trials (CENTRAL) and Cochrane Database of Systematic Reviews (CDSR). No language or time restrictions were placed on the initial search. A comprehensive search strategy was devised, using index and free-text terms, related to (i) patients, healthcare professionals or carers, (ii) medicine modification, (iii) knowledge and (iv) qualitative research. The search strategy was initially developed by the primary author (AMG) and subsequently approved by a qualified medical librarian prior to undertaking the searches. The reference lists of included studies were hand-searched to identify additional relevant studies. Citation tracking of included studies was also undertaken. A search for grey literature was completed; by searching the OpenGrey database, internet searching and using personal knowledge to identify further potentially relevant sources. The initial search was undertaken in September 2015 and an updated search was undertaken in June 2016.

### Study selection

Titles were screened by one reviewer (AMG) to remove studies that did not meet the eligibility criteria. Each abstract was independently screened by two reviewers (AMG-full set and LJS or AMC). The full-text of articles identified as potentially eligible based on the abstract were obtained and assessed independently by two reviewers for inclusion (AMG and LJS or AMC) according to *a priori*



inclusion and exclusion criteria. In the case of any discrepancies between reviewers at any stage, a third reviewer independently examined the study and following discussion, a consensus on inclusion was reached by all three reviewers.

### **Eligibility criteria**

Studies were eligible for inclusion if they met the following criteria: (i) used qualitative data collection and analysis methods; (ii) the full-text was available in English; (iii) included adult patients (18 years or more) who required ODF to be modified to meet their individual needs; (iv) included carers or HCPs (doctors, nurses, pharmacists, speech and language therapists) of patients who require ODF to be modified. For studies undertaken using mixed methods, only the qualitative component was included. Debate exists as to whether survey data is considered qualitative or quantitative, which has posed an issue in previous qualitative systematic reviews.<sup>25</sup> It was decided *a priori* that surveys would be excluded if the results were purely quantitative in nature, as this data lacks the necessary “*conceptual depth and richness*”,<sup>26</sup> which is an approach that has been utilised previously.<sup>27</sup> Quantitative studies, systematic reviews, meta-analyses, meta-syntheses, editorials, commentaries, letters and conference abstracts were excluded. The primary outcomes of interest were patient, HCP and carer knowledge, attitudes and beliefs about the modification of ODF.

### **Data extraction**

The data extraction form developed by the National Institute for Health and Care Excellence<sup>28</sup> was modified by one reviewer (AMG) to meet the requirements of the systematic review. Data from the included studies were extracted by one reviewer (AMG). A second reviewer (AMC) independently verified the extracted data. Any disagreements were resolved by discussion and a consensus was reached by both reviewers.

## Quality appraisal

The quality of the included papers was independently assessed by two reviewers (LJS and AMG) using the Critical Appraisal Skills Programme (CASP) tool for Qualitative research.<sup>29</sup> The CASP tool was chosen as it allows for assessment of the rigour, credibility and relevance of qualitative research.<sup>30</sup> In the case of disagreements between reviewers regarding study quality, a third reviewer (AMC) independently assessed study quality and following discussion a consensus was reached by all three reviewers. There is debate about the value of undertaking a formal quality assessment for qualitative studies.<sup>31</sup> Therefore, for this review, assessment of study quality was not used to guide inclusion or exclusion of studies but rather to moderate the findings of the review based on the quality of the studies contributing to the final analytical themes.

## Data Synthesis

The thematic synthesis approach, as discussed by Thomas and Harden (2008),<sup>32</sup> was used to synthesise the findings of the eligible studies. The thematic synthesis approach was chosen as it offers the advantage of *“staying ‘close’ to the results of the primary studies, synthesising them in a transparent way, and facilitating the explicit production of new concepts and hypotheses”*.<sup>32</sup> Through this process, analytical themes are generated that offer new interpretations that “go beyond” the results of the primary studies.<sup>33</sup> The thematic synthesis approach involves three stages: (i) free line-by-line coding of the findings of the primary studies; (ii) organisation of “free codes” into descriptive themes; (iii) development of analytical themes.<sup>32</sup> QSR International’s NVivo 10 Qualitative Data Analysis Software was used as an aid to the synthesis process. Initial line-by-line coding of all text labelled “Results” or “Findings” in eligible studies was performed independently by two reviewers (LJS and AMG). The coded text was compared to check that coding was assigned correctly and consistently. The generation of the descriptive themes was undertaken by two reviewers (LJS and

AMG) during a group discussion. A third reviewer (AMC) independently examined and verified the descriptive themes generated and consensus was reached by all three reviewers. Finally, the descriptive themes were used to generate analytical themes. Analytical themes were initially generated by two reviewers (AMG and LJS) independently, following this a number of group discussions were undertaken to consolidate the analytical themes identified.

This systematic review is reported in accordance with the Enhanced Transparency in Reporting the Synthesis of Qualitative Research (ENTREQ) guidelines.<sup>33</sup>

## **Results**

### **Study Selection**

In total, 6911 articles were identified from the database search. Following the removal of 1456 duplicates, 5455 remained. Following the title screen, 5290 records were excluded. Of the 165 articles that were examined for eligibility based on the abstract, 129 were excluded. The remaining 36 full-text articles were reviewed to identify those that met the inclusion criteria for the review. During this stage, 31 articles were excluded. Two additional studies were identified through citation tracking of the included articles, no additional records were identified from hand-searching the reference lists. Therefore, seven articles were included in the systematic review. No additional eligible studies were identified in the updated search in June 2016. Figure 1 outlines the process of study selection.

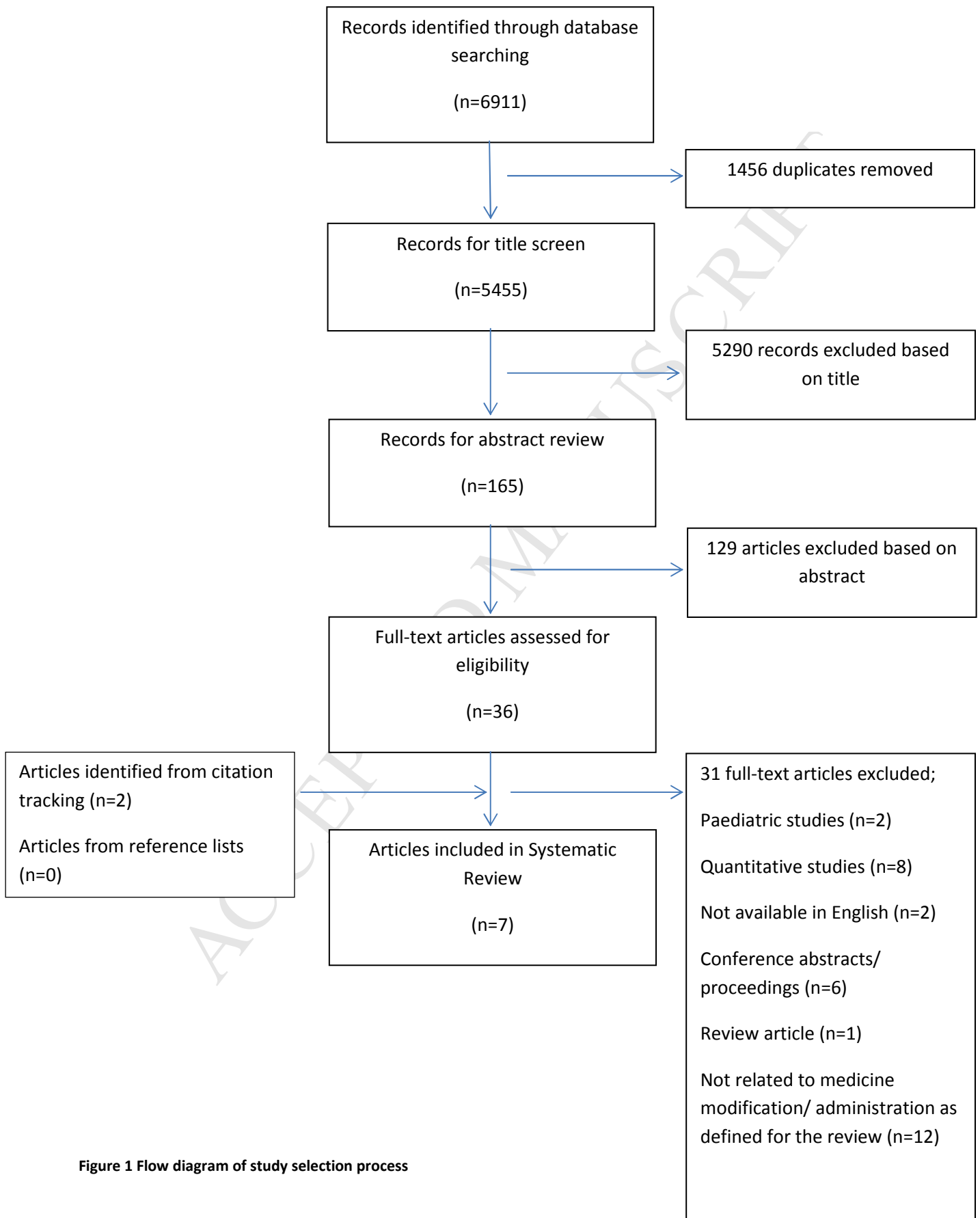


Figure 1 Flow diagram of study selection process

## Study Characteristics

The characteristics of the included studies are summarised in Table 1. The views of HCPs were examined in three of the studies: one study included nurses,<sup>34</sup> one included physicians<sup>35</sup> and one included a mixed sample of HCPs.<sup>36</sup> The remaining four studies investigated the views of patients.<sup>37-40</sup> All of the studies involving HCPs were directly related to the topic of this review.<sup>34-36</sup> For the studies involving patients, one study directly addressed the topic of interest.<sup>38</sup> Of the remaining three studies undertaken in patient cohorts, two investigated the problems experienced by patients in managing their medication<sup>39, 40</sup> while one examined factors related to adherence.<sup>37</sup> For these three articles, a number of the findings addressed the topic of interest and these findings were included in the synthesis for the review. Modifications to facilitate fractional dosing were discussed in three of the studies,<sup>37, 39, 40</sup> while modifications for swallowing difficulties were the topic of consideration for four of the studies.<sup>34-36, 38</sup>

**Table 1 Characteristics of included studies (listed alphabetically according to first author)**

Reference (Year)	Location	Participants (n)	Method	Analysis	Aim	Analytical Themes
Barnes <i>et al.</i> (2006) <sup>34</sup>	South Australia	Registered Nurses (n=11)	Semi-structured interviews	Thematic analysis broadly following Ekman and Segesten	To explore issues concerning the nursing practice of altering medication dose forms prior to administration of medicines to residents in homes for older people	Patient-centred individuality and variability Communication Knowledge and uncertainty Complexity
Borgsteede <i>et al.</i> (2011) <sup>37</sup>	The Netherlands	Patients with type 2 diabetes mellitus (T2DM) (n=20)	Semi-structured interviews	Content analysis and constant comparison	To explore both factors related to high and lower levels of adherence that patients experienced in their medication use and to reflect upon the findings in the context of patient education and shared decision making.	Patient-centred individuality and variability Knowledge and uncertainty Complexity
Kelly <i>et al.</i> (2009) <sup>36</sup>	United Kingdom	HCPs including consultant physicians, nurses, pharmacists, dietitian, speech and language therapist and a senior lecturer in pharmacy practice (n=10)	Focus group	Content analysis using Colaizzi's method	To identify the problems experienced by a range of healthcare professionals related to administering medicines to patients with dysphagia and the solutions they use to overcome them	Patient-centred individuality and variability Communication Knowledge and uncertainty Complexity
Kelly <i>et al.</i> (2010) <sup>38</sup>	United Kingdom	Patients (n=11)	Semi-structured interviews	Content analysis using Colaizzi's method	To understand the experiences of taking medication for older people with dysphagia	Patient-centred individuality and variability Communication Knowledge and uncertainty Complexity
Notenboom <i>et al.</i>	The	Patients aged	Semi-	Coded according	To identify the practical problems that	Patient-centred individuality and

(2014) <sup>39</sup>	Netherlands	≥70 years (n=59)	structured interviews	to a coding scheme; Framework type analysis	older people experience with the daily use of their medicines and their management strategies to address these problems and to determine the potential clinical relevance of thereof	variability Knowledge and uncertainty Complexity
Pergolizzi Jr <i>et al.</i> (2014) <sup>35</sup>	United States of America	Physicians of (n=34)	Semi-structured phone interviews	Content analysis	To understand the knowledge, attitudes, and practices of physicians and the beliefs/perceptions of patients regarding the treatment of chronic pain in the presence of dysphagia	Patient-centred individuality and variability Communication
Tordoff <i>et al.</i> (2010) <sup>40</sup>	New Zealand	Patients ≥65 years (n=20)	Semi-structured interviews	Grounded theory and constant comparison	To explore how people 65 years and older in New Zealand manage their medicines in their own homes and the problems and concerns they might have with taking them	Patient-centred individuality and variability Communication Knowledge and uncertainty Complexity

## Quality Appraisal

A summary of the results of the quality appraisal for the included studies is shown in Table 2. All of the studies provided a clear statement of the aims of the research, used qualitative methodology appropriately, and employed an appropriate research design and recruitment strategy. Three of the studies did not provide sufficient detail about data collection<sup>35, 36, 39</sup>, with two of the studies not discussing data saturation<sup>35, 36</sup> and one not providing detail about the use of a topic guide.<sup>39</sup> Four of the studies did not address reflexivity which relates to the researcher considering their role and potential bias.<sup>34-36, 39</sup> Two of the studies did not provide sufficient detail about the data analysis process, particularly in relation to the number of researchers who performed the analysis.<sup>35, 36</sup> Finally, one study did not state whether ethical approval had been obtained, did not provide participant quotes to substantiate findings or discuss in detail the findings in light of existing evidence or the implications for practice.<sup>35</sup>



Table 2 Quality appraisal of included studies using the Critical Appraisal Skills Programme (CASP) Qualitative Research Checklist<sup>29</sup>

	Barnes <i>et al.</i> (2006) <sup>34</sup>	Borgsteede <i>et al.</i> (2011) <sup>37</sup>	Kelly <i>et al.</i> (2009) <sup>36</sup>	Kelly <i>et al.</i> (2010) <sup>38</sup>	Notenboom <i>et al.</i> (2014) <sup>39</sup>	Pergolizzi Jr <i>et al.</i> (2014) <sup>35</sup>	Tordoff <i>et al.</i> (2010) <sup>40</sup>
Clearly stated aim(s)?	√	√	√	√	√	√	√
Qualitative methodology appropriate?	√	√	√	√	√	√	√
Appropriate research design?	√	√	√	√	√	√	√
Appropriate recruitment strategy?	√	√	√	√	√	√	√
Data collection?	√	√	U	√	U	X	√
Reflexivity?	U	√	U	√	U	X	√
Ethical issues considered?	√	√	√	√	√	X	√
Rigorous data analysis?	√	√	U	√	√	X	√
Clear statement of findings?	√	√	√	√	√	U	√
Value?	√	√	√	√	√	√	√

Legend: √= Yes, X= No, U= Unclear

## Analytical Themes

Four themes emerged from the synthesis: (i) patient-centred individuality and variability; (ii) communication; (iii) knowledge and uncertainty and (iv) complexity.

### Patient-Centred Individuality and Variability

The central role of the patient and the importance of recognising the inherent inter- and intra-patient variability emerged as a strong theme in all studies.<sup>34-40</sup> Individuality is key, and variability of individual patient's needs and requirements has an important role in ODF modification. Although Tordoff *et al.* (2010)<sup>40</sup> reported that, "Most people had no difficulty swallowing tablets", it was clear from all the studies that many patients experience difficulty with medication administration and modification. A number of factors contribute to this variability including: medical conditions,<sup>34-36, 38</sup> patient-related factors<sup>34, 36-40</sup> and medication-related factors<sup>34-40</sup> which can be further complicated by family and institutional influences on decision making.<sup>34, 36</sup>

Many medical conditions can lead to dysphagia/ difficulty swallowing medicines thereby complicating medicine administration,<sup>34-36, 38</sup> including; stroke,<sup>34, 38</sup> cognitive impairment/dementia,<sup>34, 36</sup> cancer,<sup>35</sup> Parkinson's Disease<sup>34, 36</sup> and epilepsy.<sup>36</sup> However, the variable nature of these medical conditions further complicates ODF administration<sup>36, 38</sup> as individual patients, despite having similar diagnoses, may have very different medication formulation requirements, "The first major theme is the broad spectrum of dysphagia... *'There are three different categories of patient we've got here which give us problems with dysphagia'.....* each variation of dysphagia brings its own problems in relation to medicine administration".<sup>36</sup> In addition, the natural progression of these medical conditions means that a progressive decline in function is observed<sup>35, 36, 38</sup> or conversely, an improvement in swallowing capability can occur, "In the case of participants who were stroke survivors, swallowing could gradually improve".<sup>38</sup> Therefore, continuity of medication can be problematic with disease progression.<sup>35, 36, 38</sup> It is clear that formulation choice and decisions

regarding modification for individual patients are complicated by inherent variability; due to disease stage and severity.

Individual patient-related factors were reported in all studies as being important regulators of how medicines are administered. These included; patient decision making for example choosing not to take medicines due to difficulty swallowing<sup>34, 36-38</sup> or chewing medicines,<sup>39, 40</sup> patient medication preferences such as wanting to continue previous administration practices<sup>34, 38, 40</sup> or preferring to modify medicines despite intact swallow.<sup>34, 38</sup> In addition, administration practices varied, not only from patient to patient, but also for an individual patient from administration-to-administration and from day-to-day<sup>34, 38</sup> depending on additional factors including their mood at the time of administration, time of day and the number of medicines being administered.

Medication related factors including the size,<sup>34, 37-40</sup> texture,<sup>38</sup> shape,<sup>38</sup> taste,<sup>34, 36, 38, 39</sup> number of medicines<sup>34, 35, 37, 38</sup> and viscosity of oral liquids<sup>36</sup> were reported by patients and HCPs as impacting on medication suitability and patient acceptability. However, the importance of medication characteristics varied from person to person,<sup>34, 36, 38, 40</sup> "Small tablets were generally easier to swallow than large ones although one participant found small round ones the hardest to swallow. Three participants found large tablets difficult and two said that size and shape were irrelevant".<sup>38</sup> Therefore, the preferred formulation characteristics vary from patient to patient, which is a crucial factor complicating medicine administration.

The reasons that patients receive modified medicines may not be solely related to the individual patient's needs, requirements or preferences. Family members influence on HCPs decision making was discussed in two studies.<sup>34, 36</sup> This influence may result in HCPs making decisions based on family member's priorities rather than patients' preferences, "*... [some] families tend to pill count and cost monitor and many of them prefer us to press on with the tablets and crush them rather than the [liquid] alternative which they prefer not to pay for ... [t]here have been occasions where we've disregarded the resident's request and favoured the family's insistence in relation to the crushing of*

medication.”.<sup>34</sup> Institutional and professional issues were also discussed as important factors influencing medicine administration practices. Barnes *et al.* (2006)<sup>34</sup> highlighted the pressure placed upon nurses to ensure prescribed medicines are administered, “All but one nurse presented the need to ensure that prescribed medications were administered as the dominant imperative”, along with the pressure to complete medicine administration in a timely manner, “Thus, the overall organizational requirements, including completion of the medication round, often took precedence over attending to individual needs of particular residents”.<sup>34</sup>

Numerous options were discussed to overcome difficulties with formulations including changing the formulation for example to oral liquids,<sup>34-36, 38</sup> discontinuing unnecessary medications,<sup>36, 40</sup> using various coping strategies e.g. the chin-tuck position or using food or various liquids to facilitate intake<sup>38-40</sup> or modifications.<sup>34-40</sup> It was noted that alternative formulations were often not available<sup>34, 35</sup> or there was a lack of knowledge about the availability of alternatives.<sup>34, 38</sup> However, even in situations where alternative formulations were available other problems arose including; cost<sup>34-36</sup>; unsatisfactory formulation characteristics<sup>36</sup>; and poor patient acceptability.<sup>36, 38</sup> Therefore, these issues can result in alternatives not being fit for purpose and modifications of ODF are preferable or necessary.

## Communication

The importance of communication was a recurring theme in the majority of included papers.<sup>34-36, 38, 40</sup> While communication plays an important role in the optimisation of medicine administration and modification practices, poor communication and lack of communication presents a significant barrier that may negatively influence medicine administration. Two distinct lines of communication were seen; communication between patients and their HCP and communication between HCPs.

### Communication between patients and their healthcare professionals

Communication between patients and their HCPs also influenced modification practices and the selection of appropriate alternatives that avoided the need for modification. In general, patients had a positive view of their HCPs.<sup>36, 38</sup> However, there were examples of poor communication between patients and HCPs, which negatively impacted upon medication adherence; “One man, finding it hard to break his aspirin tablets into quarters as prescribed, asked his GP to change them to the type he’d had in hospital. *‘I’ve told him but he don’t take any notice.’*”<sup>40</sup> Good communication and continuity of care was important to patients, with locums unpopular as they are unfamiliar with the patient and their needs and preferences, “Key points were the need for GP continuity and the recognition that locums...are a drawback...So I thought, ‘Don’t call the locum!’”,<sup>38</sup> “Variability of pharmacist was also identified as a problem, even when the patient went to the same pharmacy: ‘Also, where we go it always seems to be a different pharmacist. You never see the same ones. There doesn’t seem to be a consistent one there’.”<sup>38</sup>

One of the barriers to effective communication seems to focus on the HCPs reactive, rather than proactive, approach to patient’s difficulties or preferences.<sup>35, 36, 38</sup> This is compounded by the observation by Barnes *et al.* (2006),<sup>34</sup> that individual patient’s medication formulation requirements are not routinely or systematically assessed. As a result, HCPs are unaware of patient’s requirements and make decisions about medicines for their patients without fully appreciating their needs. This was particularly true in the case of pharmacists with patients reporting that different formulations were dispensed without the patient’s views being sought, “Participant 3’s pharmacist had changed the formulation of one of his medicines from a smooth-coated, torpedo-shaped tablet to a chalky form that he found difficult to take, and he put the change down to the tablets being cheaper”.<sup>38</sup> However, communication should ideally be a two-way process and patients admitted that they often neglect to inform their HCPs about the difficulties they experience with medications.<sup>36, 38</sup> This may be due to many reasons; (i) aphasia,<sup>36</sup> (ii) carers collecting medicines,<sup>38</sup> (iii) patient’s lack of knowledge

that alternative formulations may be available<sup>38</sup> or (iv) patients unwilling to question HCP decisions.<sup>36,38</sup>

### **Communication between healthcare professionals**

Extensive inter-professional communication, to discuss individual patient's needs was reported in two studies,<sup>34,36</sup> *"We speak to the pharmacist for him to have a look at what medications they're on to see if those can actually be crushed before we actually give them crushed ... [h]e (pharmacist) will... give us a suggestion as to what tablet, what alternatives we can use...and then we discuss it with the medical officer..."*<sup>34</sup> However, this inter-professional communication often takes place on an informal basis rather than being a routine and systematic process, "Nurses were concerned that they were working in an information vacuum, due to limited information resources and informal communication with other healthcare professionals".<sup>34</sup> While on the whole communication and information sharing between healthcare professionals was noted as an aid to decision making, a key issue, highlighted by Kelly *et al.* (2009)<sup>36</sup> centred on 'data flow', with necessary information not being available to the appropriate individual in a timely fashion. Data flow problems arise due to deficits in communication practices for example; prescriptions tend not to specify the necessary formulation or that a patient has dysphagia,<sup>36</sup> and communication between specialists and primary care is problematic.<sup>38</sup> The varying expertise of the different members of the multidisciplinary team further compound these communication deficits, "Even if medicine charts do contain information on dysphagia there are problems identifying a common language...Thus, as identified by the speech and language therapist: *"We are not always sure what we should say.."*".<sup>36</sup> Therefore, the input of many different HCPs is often necessary to make the most appropriate decision, but the lack of a formal communication process hinders this. A formal, systematic process of communication between HCPs would ensure that all the necessary information is available for decision-making and would facilitate information and expertise sharing on a routine basis.

## Knowledge and Uncertainty

Knowledge about medicine modification and administration was an important theme that emerged from the synthesis. Although confidence in one's knowledge and abilities was reported by one nurse, *"...I rely on my own knowledge of medication, which has always been quite comprehensive because I've always dispensed medication and I'm quite experienced"*,<sup>34</sup> it was clear that overall there was a significant knowledge deficit and uncertainty about medicine modification and administration amongst both HCPs,<sup>34, 36</sup> *"... you're participating in a practice that you're really not totally au fait with"*<sup>34</sup> and patients,<sup>37, 38</sup> *"One of the issues that participants identified was their own lack of knowledge"*.<sup>38</sup> This knowledge deficit arose due to a lack of information and guidance related to medicine modification, particularly for HCPs.<sup>34, 36</sup> It was noted by Kelly *et al.* (2009)<sup>36</sup> that there is little formal guidance or information provided by the manufacturers and industry as modifications are generally unlicensed, *"...absence of information because medicine formulations are frequently altered in order to administer them to dysphagic patients and so are given outside licence"*.<sup>36</sup> This was reiterated by Barnes *et al.* (2006)<sup>34</sup> who highlighted the deficits of commonly used resources, *"We have a series of medication resources, but not necessarily associated with the crushing of tablets, more associated with what the tablets are for"*.<sup>34</sup>

Consequently, the lack of explicit information resources results in a reliance on informal information provided by HCPs or continuation of previous medication modification and administration practices. For HCPs, seeking the advice and recommendations of other members of the multidisciplinary team was commonly undertaken,<sup>34, 36</sup> *".. the nurses reported discussing individual resident's medication needs with pharmacists and doctors"*.<sup>34</sup> However, although generally helpful, it was noted that different HCPs have different priorities with the result that nurses reported receiving conflicting advice which complicated decision making, *"When the nurses sought advice about how to decide between the various options with which they were faced, they were sometimes given varying and contradictory advice. Different professional disciplines (nursing, medicine and pharmacy) that are*

involved in the provision of residential care had conflicting views about what should be done”.<sup>34</sup> However, it is acknowledged that no one HCP has all the knowledge and expertise necessary to make an informed decision for individual patients, “... *the knowledge related to dysphagia and medication that falls within each professional’s sphere of expertise*”.<sup>36</sup> Therefore, multidisciplinary team involvement is vital to ensure that all necessary expertise is available. HCPs also relied on their previous experience and practice to guide decision making, “*Nurses tend to put their own interpretation on how things are done – governed by perhaps their social background in nursing, by their experience in nursing, by their academic experience in nursing*”.<sup>34</sup> The lack of a standard knowledge base, reliance on previous practice and varying interpretation of guidance, leads to varying and inconsistent practices.

Patients were very reliant on information provided by HCPs,<sup>37, 38</sup> “...*you follow his [the doctor’s] advice.. The pharmacy provides those big information sheets, with everything written clearly. Well you read everything*”.<sup>37</sup> Therefore, HCPs have an important role in providing information, knowledge and skills to patients, formally through the provision of verbal and written instructions but also informally, through observation of HCP practice.<sup>36, 38</sup> However, both HCPs<sup>36</sup> and patients<sup>38</sup> acknowledged that inconsistent practice by HCPs led to patient confusion regarding best practice, “... *each time a different nurse gave it [the medicine] they gave it in a different form... so how the patient was meant to learn which form they should do when they go home ... it would very confusing I would imagine*”.<sup>36</sup> Similarly to HCPs, patients also relied on their previous experience and reported the use of various coping mechanisms to overcome difficulties with their medications including using food or warm fluids, the chin tuck position to facilitate swallowing and using tablet devices or learned techniques to facilitate fractional dosing.<sup>37-40</sup>

Due to this knowledge deficit, patients and HCPs expressed concerns, fears and worries about modifying medicines, including concerns about the accuracy of fractional dosing,<sup>37, 39</sup> the effect of the modification on the pharmacological action of the drug including absorption, the



pharmacokinetic profile and adverse effects.<sup>34, 36, 38</sup> There were also concerns about the methods used to modify medicines including the potential for cross-contamination.<sup>36</sup> Conversely, some HCPs expressed apprehension about not modifying medicines as this may lead to medicine discontinuation or choking.<sup>34, 36</sup>

## Complexity

Complexity was a key theme that emerged from the synthesis. Although complexity was a factor associated with the themes discussed previously, the overall complexity associated with nearly every aspect of decision making for ODF modification ensured its importance as an analytical theme. This complexity was particularly related to the need to balance the advantages and disadvantages associated with modification and the complexity of the healthcare structure. Medicine modification was seen to be both necessary and advantageous as it (i) facilitated administration of vital medicines,<sup>34, 38</sup> (ii) promoted adherence<sup>36, 38</sup> and (iii) overcame some of the concerns regarding choking<sup>34</sup> or medicine discontinuation due to difficulty swallowing.<sup>36</sup> It also facilitated the administration of the correct dose for individual patients.<sup>39</sup> However, there was a conflict between these advantages and the accepted disadvantages of modification (including the lack of information,<sup>34, 36</sup> difficulty modifying medicines,<sup>37, 39, 40</sup> the unlicensed nature of administration,<sup>36</sup> the impact on nursing workload and time management,<sup>34</sup> the taste of modified medicines<sup>34, 36, 38</sup> and concerns around the efficacy and safety of modified medicines.<sup>34, 36, 38, 39</sup> This conflict must be negotiated by HCPs and patients. Decision making is complicated by the observation by Kelly *et al.* (2009), "Although both problems and solutions were discussed by the group, they were not separate issues because a solution in one area could be a problem in another"<sup>36</sup>, which highlights the dilemma faced when trying to balance the conflicting aspects of medicine administration and modification. This leads to professional, therapeutic and ethical dilemmas.

This “complex” environment contributes significantly to the challenge of optimising ODF administration practices. Barnes *et al.* (2006)<sup>34</sup> summed up the situation, “This complex and ‘messy’ environment meant that the implementation and evaluation of the process of alteration of medications, rather than being systematic and orderly, was often *ad hoc*”. This complexity arises due to a number of inter-related factors; the lack of a systematic, proactive assessment of patient’s needs, the absence of clear, explicit evidence based guidance for staff and patients, the informal communication structures and the hierarchical structure of the healthcare system.

## Discussion

This systematic review synthesised the available qualitative research evidence on the knowledge, attitudes and beliefs of patients and HCPs about the modification of oral dosage forms. Key challenges include; the variability of individual patient’s requirements, poor communication practices and lack of knowledge which when combined with the multi-faceted healthcare environment complicate decision making regarding ODF modification and administration. Although there were a limited number of eligible studies, particularly involving patients, the strength of this review lies in the fact that the synthesis included studies investigating the perspectives of both HCPs and patients. This provides a deeper understanding of the challenges encountered from prescribing right through to medication-taking behaviour. In addition, the diverse nature of patients in the included studies is a strength of the systematic review as it highlights the range of experiences encountered. The similarity of findings between studies adds to the validity of the findings and highlights key areas that need to be addressed. However, it also served to elucidate differences in the knowledge, beliefs and priorities of patients and HCPs which may give rise to misunderstandings and conflict in practice.

This review highlights that ODF selection for patients is complicated by the variable nature of patient's needs and preferences, which is influenced by the interplay between patient's medical conditions, patient's preferences, formulation characteristics as well as external influences including family input. Whilst it is widely accepted and recommended that healthcare providers treat the patient as an individual and "*for services to be tailored to respond to the needs, preferences and values of the patient*",<sup>41</sup> the continual move towards clinical guidelines, protocols and treatment algorithms has raised concerns about the standardization of medical care at the expense of individualised patient-centred care.<sup>42</sup> While there are on-going efforts to ensure that patient's preferences are considered in the implementation of evidence based guidelines, it is clear from this synthesis that variability of patient disease state and preference is a major factor that must be considered when choosing appropriate formulations. Therefore, communication, between patients and healthcare professionals and between different HCPs, is vital. This review has also illustrated however that poor communication between patients and their HCPs is widespread and results in poor awareness of patient's needs. This finding is consistent with previous studies which report that patients do not discuss their difficulties with medication with their HCP and HCPs do not routinely enquire about these difficulties.<sup>8, 23</sup> There is a clear need for the routine evaluation of patient's ODF requirements prior to the prescribing, dispensing and administration of medication. A previous quantitative systematic review called for the development and routine use of a validated screening tool to identify patients with difficulty swallowing medication.<sup>6</sup> Use of such a tool may help to overcome the current communication deficit and informal, *ad-hoc* assessment process. Communication between members of the multidisciplinary team, particularly at transitions of care was also shown to be suboptimal which is in-line with previous literature.<sup>43</sup> Continuity of healthcare at transitions of care is a major challenge facing the healthcare system.<sup>44</sup> Again, a formal, systematic process of communication may help to address this, as structured communication has been shown to improve the effectiveness of information transfer and communication between HCPs.<sup>45</sup>

In order to make appropriate decisions for individual patients, HCPs require timely access to evidence based information. A clear issue that emerged from the synthesis is the lack of information about the appropriateness of ODF modifications which created a knowledge deficit and subsequent concern amongst HCPs. Given that patients rely on their HCPs to provide advice about medication use, this invariably results in a lack of knowledge amongst patients about ODF modification. Previous research has shown an absence of explicit information to support clinician decision-making regarding modifications.<sup>3, 19</sup> The absence of accurate, evidence-based information contributes to the concerns of patients and HCPs and the complexity of decision making. Improved education regarding ODF modification may be one method of improving knowledge, however, this needs to be supplemented by increased availability of information about the potential consequences of modification of medicines.

This review has highlighted the complexity associated with ODF modification and the challenges of optimising ODF administration. Interventions to reduce inappropriate tablet splitting, have focused on the prescriber and utilised a computerised decision support and warning system.<sup>46, 47</sup> Both studies reported that the computerised system reduced the frequency of inappropriate splitting, with Hsu *et al.* (2014)<sup>47</sup> reporting a substantial effect on prescribing behaviour. However, Quinzler *et al.* (2009)<sup>46</sup> reported that half of all alerts were not acted on by the physician despite a more suitable formulation being available in 82% of cases. Bourdenet *et al.* (2015)<sup>48</sup> investigated if practice recommendations on crushing tablets could lead to an improvement in crushing practices. Following the implementation of these recommendations, significant reductions in medicine crushing and inappropriate crushing were seen. A study by Hanssens *et al.* (2006)<sup>49</sup> found that a two day training program improved nurses knowledge about medicine administration for patients with swallowing problems and feeding tubes, however, the impact of this improvement in knowledge on practice was not assessed. The results of this synthesis suggest that a complex, multi-faceted intervention will be required to optimise ODF modification practices and future interventions should be cognisant of the findings of this review. Any intervention or quality improvement initiative must consider all the

factors and challenges encountered by patients and HCPs in daily practice. This review has served to highlight some of the prominent influencing factors. A gap in the literature is the absence of qualitative research investigating carer's perceptions of ODF modification. Further research investigating the views of HCPs and patients is also necessary given the limited evidence available. In particular, given the observation that many patients without any clinical evidence of dysphagia are modifying ODF without the knowledge of their healthcare professional, further research directly focusing on ODF modification from the perspective of patients is required. Only one such study has been reported to date.

The results of the synthesis suggest that to optimise ODF modification and administration practices, input is needed from patients and all members of the multidisciplinary team. The needs of patients should be routinely and systematically assessed when medications are prescribed and dispensed. Decision-making should take into consideration the individual needs of the patient but reliable and pertinent information from drug manufacturers, guidelines and recommendations from healthcare colleagues are needed to support this.

There were a number of limitations associated with this review. For three of the studies involving patients the review topic was not the sole focus of the studies, therefore, not all the findings were relevant for inclusion in the synthesis. The inclusion of English language articles only, may hinder the generalizability of the findings.

## **Conclusion**

Through synthesis of the existing qualitative literature, the findings of this systematic review have highlighted that key factors influencing the knowledge, attitudes and beliefs of patients and their healthcare professionals about oral dosage form modifications are patient-centred individuality and variability, communication, knowledge and uncertainty, and complexity. These factors can act as

both barriers and facilitators to medicine administration and modification. It is evident from the synthesis that the individual needs of patients should be routinely and systematically assessed and that decision-making should be based on evidence based recommendations with multidisciplinary input. Further research is needed to optimise ODF modification practices and the findings of this synthesis should inform the development of future interventions.

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## **Contributions of authors**

AMG was responsible for protocol design, study selection, data extraction, quality assessment, synthesis of findings, drafting and critical revision of the manuscript and approval of the final manuscript.

LJS was responsible for protocol design, study selection, quality assessment, synthesis of findings, critical revision of the manuscript and final approval of the manuscript.

AMC was responsible for protocol design, study selection, data extraction, review of synthesis findings, critical revision of the manuscript and final approval of the manuscript.

MK was involved in discussion and review of the thematic synthesis findings, critical revision of the manuscript and final approval of the manuscript.

### **Conflicts of interest**

None.

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