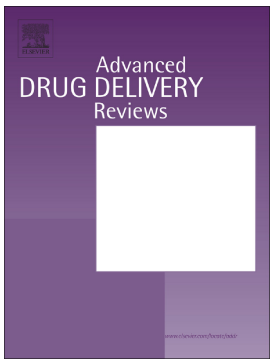

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Dosage form modification and oral drug delivery in older people

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Abstract

Many people cannot swallow whole tablets and capsules. The cause ranges from difficulties overriding the natural instinct to chew solids / foodstuff before swallowing, to a complex disorder of swallowing function affecting the ability to manage all food and fluid intake. Older people can experience swallowing difficulties because of co-morbidities, age-related physiological changes, and polypharmacy. To make medicines easier to swallow, many people will modify the medication dosage form e.g. split or crush tablets, and open capsules. Some of the challenges associated with administering medicines to older people, and issues with dosage form modification will be reviewed. Novel dosage forms in development are promising and may help overcome some of the issues. However, until these are more readily available, effective interdisciplinary teams, and improving patient health literacy will help reduce the risk of medication misadventures in older people.

Graphical abstract

Keywords: solid oral dosage forms, crushing tablets, opening capsules, dosage-form modification, polypharmacy, swallowing difficulties, health literacy, dysphagia

1 Why is swallowing pills so difficult for some people?

Solid oral dosage forms e.g. pills, tablets, capsules are excellent drug delivery systems as they are often cheap to manufacture, and conveniently deliver medicines into the body – but only if people can swallow them. There is an enormous array of solid oral dosage forms in use, or undergoing research and development. However, many people, regardless of age, have trouble with swallowing solid oral medication dosage forms whole [1].

Swallowing solid oral medications whole, without chewing, is a learned skill [1]. Children are taught to chew food properly before they swallow it. Chewing reduces the particle size of foodstuff, mixes food particles with salivary enzymes to begin chemical digestion, and forms a bolus that can be safely swallowed without being aspirated. The gag reflex is a protective mechanism to eject anything too big to be safely swallowed. Therefore, people are both hardwired and trained to chew even the smallest of foods e.g. a raisin, and swallowing hard substances without chewing involves overriding this natural reflex [2, 3]. For instance, people expect to chew a cashew nut before swallowing it. Therefore, asking patients to swallow, without chewing a whole tablet or capsule, which in many cases may be bigger than a cashew nut, can be challenging (Figure 1).

A previous bad experience with swallowing a solid dosage form can lead some people to modify some or all of their medication dosage forms [4]. This practice may also have been behaviour learnt from parents or relatives as a child, or children may never have been explicitly taught, or learned how to swallow solid dosage forms [1]. Solid oral dosage forms vary in sizes, shapes and colours, and there is a preference for those that are small, coated, arched, oblong/oval in shape and white in colour [5]. Nevertheless, solid oral dosage forms of various sizes and shapes can be swallowed. Not unexpectedly, perception is important, as in a recent study, 23% of 152 adults who reported no difficulty swallowing foods or drinks, visually assessed a size 00 capsule as being “too large to swallow whole”. Yet only 3% were physically unable to accomplish the task when asked to swallow a 00 capsule with water [6].

As many as 50-60% of older people in hospitals and aged care facilities experience impaired swallowing function (dysphagia). Swallowing food and fluids is difficult for these people, and there is an increased risk of choking or aspiration [7-9]. Carers for

people living with dysphagia may primarily be concerned about maintaining adequate nutrition and hydration. However, people's ability to take oral medications is an important problem that needs to be considered at the point of dosage form design, prescribing and dispensing. Unfortunately, this consideration is often overlooked, and the person administering the medication is usually left to find a way to help the patient swallow their medications [10, 11].

2 Prevalence of pill swallowing difficulties

It is challenging to estimate the proportion of people that find it difficult to swallow solid oral dosage forms because the methodology and the population being investigated varies between research studies. Reports indicate between 10% and 40% of adults have difficulties swallowing solid oral medications (Table 1). There is more data available regarding the prevalence of dysphagia (Table 2), particularly among older people.

Table 1. Studies reporting the prevalence of people having experienced problems swallowing whole solid medications at some time. Age range and mean ± SD of respondents is provided in parentheses, and details specific to the older population are provided where it was described or could be extracted from the article.

Country and setting	Total number of respondents	Problems swallowing whole solid dose forms	
		Proportion of total respondents	Proportion of older respondents
Germany [4]; general practice patients taking at least one solid oral dose form, questionnaire	1051 adults (18 – 80+; 61.8 ± 15.6 years)	37.4%	27% (≥ 70 years)
US [12]; adults, online survey	679 adults (18 – 65+ years)	40%	26% (≥ 65 years)
Australia [13]; customers of community pharmacies, interview	369 adults (18 – 60+ years)	16.5%	14.7% (≥ 60 years)
Switzerland [14]; customers of community pharmacies taking 3 or more solid oral dose forms, interview	410 adults (19 – 96; 66.5 ± 14.8 years)	22.4%	-
Norway [15]; general practice patients; questionnaire	6158 adults (1 – 70+ years)	26%	-
Jordan [16]; outpatients taking at least one oral solid dose form, interviews	1250 adults (18 – 90 years)	10.4%	-
UK [17]; community pharmacy customers taking	156 adults (≥ 65; 74 ± 5.7	n/a	7.8% (≥ 65 years)

at least one oral medicine, interview	years)		
New Zealand [18]; community-dwelling, taking at least one prescription medicine, telephone interview	316 adults (75 – 98 years)	n/a	14% (≥ 75 years)
Belgium [19]; community pharmacy customers using at least one chronic medicine, cross-sectional observational study	338 adults (70 – 90+ years)	n/a	14.8% (≥ 70 years)

Table 2. Examples of studies reporting the prevalence of dysphagia amongst people living at home in the community, in aged care facilities, or admitted to geriatric units in hospital. Age range and mean ± SD of respondents is provided in parentheses, and details specific to the older population (and age criteria) are provided where it was described or could be extracted from the article.

Country and setting	Total number of respondents	Dysphagia	
		Proportion of total respondents	Proportion of older respondents
In the community			
UK [17]; community pharmacy customers taking at least one oral medicine, interview	156 adults (≥ 65; 74 ± 5.7 years)	n/a	11%
UK [20]; otherwise healthy, living in the community, questionnaire	634 adults (69 – 98 years)	n/a	11.4%
Japan [21]; living at home in the community, questionnaire	1313 adults (≥ 65 years)	n/a	13.8%
Netherlands [22]; living in the community, interview	130 adults (87 – 95; 89.6 ± 2.3 years)	n/a	16%
Netherlands [23]; general population in the community, telephone survey	2600 adults (18 – 97 years)	12.1%	16.3% (> 60 years)
USA [24]; general practice patients, questionnaire	947 adults (46.2 ± 16.2 years)	22.6%	-
USA [25]; independent-living community residents, questionnaire	107 adults (≥ 65; 75 ± 6 years)	n/a	15.9%

In aged care facilities			
South Korea [26]; residents of aged care facilities, observation	395 adults (65 – 103; 80.8 ± 8.0 years)	n/a	52.7%
Canada [27]; residents of aged care facilities, observation	349 adults (71 – 108 years)	n/a	68%
UK [28]; residents of aged care facilities, prior clinical diagnosis	166 adults (> 70 years)	n/a	22.9%
Admissions to hospital geriatric units			
Spain [8]; admissions with pneumonia, clinical assessment	134 adults (84.5 ± 6.8 years)	n/a	55%
Belgium [29]; admissions to geriatric units, clinical assessment	1262 adults	n/a	43%

Dysphagia becomes more common with increasing age [23, 24], so it is tempting to expect that medication swallowing problems also become more common. However, where a wide age range has been surveyed, a lower proportion of older people report difficulty swallowing tablets compared with younger people [4, 12, 13, 15]. This has been suggested to be associated with differences in physiological and anatomical differences in the size and function of the oral and oesophageal regions [4]. Additionally, medicine use tends to increase with age, so it is possible that people become more adept at swallowing these dosage forms with practice. However, older people with dysphagia are likely to be under-represented in studies focussed on community-based individuals that survey the healthier, ambulatory members of the population who attend their GP rooms, collect their own medicines from the pharmacy or are willing and capable of completing surveys [4, 13]. Indeed, up to 68% of residents of aged care facilities have been reported to exhibit symptoms of dysphagia, which is considerably higher than amongst older people living in the community (Table 2).

3 Age related changes to physiological processes of swallowing

The act of swallowing requires coordination between sensorimotor and neuromuscular processes to ensure foods and liquids follow the intended gastrointestinal route to the oesophagus, and do not ‘go down the wrong way’ into the airways. Older people, as a natural part of the ageing process, take longer to swallow because more time is required for chewing and bolus manipulation. A generalised decrease in all muscle mass and muscle strength, including those in the mouth and throat potentially reduces swallowing effectiveness. This can be compounded by reduced sensations of residue collecting in the throat, along with ageing-related postural changes affecting head position, which increase the risk of aspiration. Further changes to the oesophagus may ensue, reducing the efficiency of bolus movement into the stomach. This is known as presbyphagia, the natural changes in healthy swallowing that put older people at risk of developing dysphagia [9, 30]. For the most part, healthy older adults can compensate to maintain coordination and effective swallowing, albeit more slowly than in their youth. The maintenance of disease-free presbyphagia is important for safeguarding good health in older people.

Decline into medically-recognised dysphagia is commonly associated with the development of co-morbidities, or stresses such as changes in dentition [9, 31]. Swallowing is a very complex process, and conditions that disrupt the central coordination of swallowing, such as stroke, Parkinson’s disease, or head injury, often lead to dysphagia. Changes at a structural level, through malignancies and other diseases of the throat, affect swallowing function, as can radiation therapy to the head and neck region, and inflammatory disorders such as Crohn’s disease [9, 31]. The development of xerostomia (dry mouth), for example through an autoimmune disease such as Sjogren’s syndrome affecting salivary output, can play a key role in the decline into dysphagia. Saliva lubricates solid oral dosage forms, preventing them from sticking to the throat or oesophagus, so xerostomia can contribute to problems with swallowing medicines.

Medications are themselves a major contribution to the development of dysphagia, through their role in causing dry mouth, and other adverse drug reactions that can impact upon ability to swallow. Examples of adverse drug reactions are the reduced

muscle coordination of the mouth, throat and oesophagus (e.g. phenothiazines and haloperidol, and heavily sedated patients), and direct injury such as ulceration or irritation of the mucous membranes and oesophagus (e.g. cytotoxics, non-steroidal anti-inflammatory drugs, tetracyclines, bisphosphonates). Xerostomia is a particularly important side effect, since an estimated 80% of the most commonly prescribed medicines cause xerostomia [32]. As saliva production is largely regulated by the parasympathetic nervous system, medicines with strong anticholinergic properties, i.e. antipsychotics, antidepressants, antihistamines, are widely recognised as having xerostomia as a side effect. For older people, anticholinergic burden or load needs to be considered. That is, the cumulative effects of taking a number of medicines with weak anticholinergic effects, e.g. anticonvulsants, analgesics, blood pressure agents, diuretics, can be as significant as a single highly anticholinergic agent [33]. Older adults are commonly prescribed multiple concurrent medications to manage multiple comorbidities. Polypharmacy (being prescribed five or more medicines) is itself associated with negative clinical outcomes for patients e.g. increased burden of disease, medication misadventures and adverse drug events, hospitalisation and increased mortality [34].

The problems associated with being unable to safely or effectively swallow solid oral dosage forms is compounded if the medicines require multiple doses each day. As such, a vicious cycle is propagated in which co-morbidities may not be adequately or appropriately managed because the patient cannot swallow the solid oral dosage forms, and in turn, more medicines may be prescribed to help manage the deteriorating patient.

4 Options for people who cannot swallow solid oral dosage forms

When people experience difficulty swallowing their solid oral dosage forms whole without chewing, they may choose to avoid taking the medication, or implement strategies to make the medicine easier to swallow [4, 12-14, 16]. While these strategies are not unique to older people, they are very relevant in discussions around administering medicines to this patient cohort. Clinical guidelines can provide recommendations for administering medicines to people unable to swallow solid oral medicines. However, strategies that patients or carers use may be in direct contrast to clinical expert recommendations, e.g. the modification of medication dosage forms, which will be discussed in Section 5.

Patients clinically diagnosed with dysphagia are generally expected to have difficulties swallowing both solids and liquids. Therefore swallowing solid oral dosage forms, and potentially liquid dosage forms, becomes challenging and may need to be avoided due to the risk of aspiration [35, 36]. It has been estimated that up to 7% of foreign bodies aspirated into the airways are medications [37], e.g. iron pills, tetracycline tablets, sucralfate, and sometimes with fatal results [37-40]. Aspiration of tablets or capsules is challenging to diagnose as the foreign body may not have been recognised as an aspiration event at the time, may not be identified as a foreign body on x-ray as the medication is not radiolucent, or may have dissolved. Extra care should be taken when administering medication to people where swallowing coordination, or protective cough and gag reflexes are affected [41], and these patients should be observed for signs of potential aspiration [42].

4.1 Alternative commercially manufactured dosage forms

An option to bypass the use of a solid oral dosage form is to seek an alternate commercially available dosage form of the medicine, such as a dispersible or effervescent tablet, change to a different route of administration or consider a different medicine within the same therapeutic class that is commercially available as an appropriate dosage form. Clearly this has cost implications, and the majority of the medicines are only available in limited delivery formats. Interestingly, even when more clinically appropriate alternatives are available, apparently patients, carers, and healthcare professionals continue to modify medication dosage forms [43-46], based on the perception that non-coated, non-modified-release tablets are safe to cut and crush.

Some commercially available dosage forms that can be alternatives to traditional solid oral dosage forms include [47]:-

- Non-solid oral dosage forms e.g. concentrates, elixirs, emulsions, films (extended release), solutions, suspension (delayed and extended release), granules (delayed release), chewing gum, liquids, oils and drops, pellets, powder (extended release), solutions, suspensions (extended release), syrups.
- Non-traditional solid oral dosage forms that do not need to be swallowed whole e.g. tablets that are chewable, effervescent, dispersible, oral

disintegrating, oral disintegrating extended release; oral disintegrating delayed release; troches and lozenges.

- Parenteral dosage forms e.g. metered aerosols, enemas, implants, injections (lipid complex, liposomal, extended release), patches, dry powder inhalers, metered solutions, metered sprays, suppositories.

However, many of the non-solid oral dosage forms are only available as paediatric formulations. Similarly, there is a very limited number of medicines that are formulated as non-traditional solid oral dosage forms because of complexities and cost to manufacture. Furthermore, oral liquids, or solid oral dosage forms are an aspiration risk for people with dysphagia. Parenteral dosage forms are also limited in their usefulness because many medicines are available via the oral route only. Additionally, trained personnel are required to administer some of the dosage forms e.g. injections, implants, and there are challenges with drug absorption and formulation because of the characteristics of the medicine e.g. hydrophilic drugs cannot easily be absorbed transdermally via a patch; or pulmonary delivery via inhalers. Inhalers also have the added concern around incorrect inhaler techniques, and whether older people have the manual dexterity to use the devices. Finally, some of the parenteral dosage forms would be restrictive and inconvenient for the patient to self-administer particularly if they need a large number of medicines concurrently, or with repeated dosing e.g. suppositories, enemas.

4.2 Extemporaneously compound medicines into an appropriate dosage form.

Extemporaneous compounding is the preparation of a therapeutic product for an individual patient in response to an identified need, e.g. inability to swallow commercially available dosage forms. Compounded preparations have generally not been assessed for safety and efficacy. Their use is off label and is based on extrapolation from the component ingredients [48]. In clinical practice, patients do not seek extemporaneous compounding as an option for overcoming difficulties with swallowing solid oral medicines. This is possibly because of lack of awareness of compounding as an option, or logistics and cost of sourcing these products may be prohibitive for many patients. For example, in Australia, many of the compounded medicines are not government subsidised, meaning patients need to cover the entire cost of the medicine out of their own pocket.

The raw material of the active pharmaceutical should ideally be sourced for extemporaneous compounding but sometimes this is not realistic or achievable. As such, crushed tablets or the contents of capsules are often used as the source of the active ingredient for extemporaneous compounding of oral liquid formulations by a pharmacist [49]. The presence of insoluble excipients in the commercial solid dosage form usually means the formulation must be a suspension. The formulation for these suspensions can be complex to design, requiring consideration of powder wetting, vehicle viscosity, preservation and flavouring [50]. Additionally, the length of time a compounded version retains its chemical and physical characteristics is usually unknown, and interactions between the active ingredient and excipients from the original solid dosage form can be more important than degradation by standard routes such as oxidation and hydrolysis [51]. Thus, extemporaneous preparations invariably have short expiry dates, though this is usually through lack of information on the preparation than a reflection of true stability [48].

4.3 Removing unnecessary medicines.

Older people may be taking medicines for years on end for no particular reason, because no-one told them to stop the medication. Optimising medication therapy, and ceasing medicines that are no longer necessary can reduce the pill burden on patients [34]. Reducing polypharmacy can also reduce the risk of side effects that may contribute to a patient's ability to swallow (section 3).

5 Modifying solid oral dosage forms

Many patients and carers will modify solid oral dosage forms to make medicines easier to swallow [43-46]. Dosage form modification can be as simple as chewing a tablet before it is swallowed. Capsules can be opened, and tablets may be split by hand or a sharp kitchen knife, or crushed between two spoons, or with a pestle and mortar. An array of splitting and crushing devices are also commercially available.

5.1 Dangers of modifying solid oral dosage forms

Regardless of the motivation and intention behind these practices, there are inherent risks and dangers associated with modifying solid oral dosage forms (Table 3). A recognition of the potential problems associated with modifying, then administering a dosage form, have led to development of resources that provide guidance on these practices [42, 52]. Although these resources are commonly prepared with the

regulatory situation of a specific country in mind, the clinical information is generally widely applicable across different jurisdictions. The importance of not altering dosage forms that are designed to have modified release properties is fairly well recognised amongst health professionals, as the consequences can be severe [42, 53, 54]. Reduced dose delivery through loss during crushing and transfer is less commonly a consideration, as spills and residual powder along with sharing of crushing vessels are often seen during observational research [44, 45, 55-57]. In fact, at least 5-10% of every dose, and probably more than that, is not delivered to the patient [58-60]. Rinsing the crushing vessel with water, and consuming that water can significantly reduce drug loss [58, 61] but this is not an approach commonly observed in practice. Additionally, as water may pose safety challenges for patients with dysphagia, standard clinical practice is to pour the powder out of the crushing device into another receptacle containing the food or thickened fluid (Section 6.1). Unless the food or fluid is completely consumed and the vessel is licked clean, it is unlikely the entire dose will be ingested. Therefore, drug loss and variability in dose delivery across the whole administration process needs further exploration.

Table 3. Potential problems associated with modifying solid dosage forms

Problem		Outcome
Altered efficacy and adverse effects		
	Destruction of modified-release characteristics.	• Rate and extent of drug dissolution and absorption increases. • Increased risk of fluctuations to supra-optimal and sub-therapeutic blood levels. • Patients have died as a result of taking crushed modified-release dosage forms [42, 53, 54].
	Destruction of coatings designed to protect the medication from the patient, or protect the patient from the medication (e.g. enteric coatings and the stomach).	• Reduced efficacy through sub-therapeutic blood levels when drug is degraded in the stomach. • Adverse events due to medication irritating the stomach.
Inaccurate dosing		
	Powder loss during crushing and transfer e.g. spilled or left behind in vessel [44, 45, 55, 57]. Estimates: from 3-13% loss using a mortar & pestle [58, 59], to 30% loss with an electric grinder [60].	• Incomplete dosing and/or inconsistent dosing of medicines. • Can be clinically significant e.g. thyroxine delivered by a feeding tube led to a hypothyroid state due to loss during crushing and transfer [57]. • Particular concern for vulnerable patients, or medicines with a narrow therapeutic window.
Incorrect administration		

	Sharing of crushing devices without cleaning [44, 45, 55-57].	• Risk of cross-contamination.
	Mixing with meals or drinks.	• Risk of administration to wrong person. • Concerns also arise if people do not finish consuming the entire meal or drink.
	Incorrect route of administration.	• Risk of nursing staff mistaking oral syringes/dispensers for IV syringes. • Fatalities have occurred because oral medicines have been injected intravenously [42, 62].
	Delivery of crushed powder directly into enteral feeding tubes.	• Clogged feeding tubes. • Needs to be reduced to a fine powder and dispersed in water, and then flushed through the tube with plenty of rinsing [42, 63].
Occupational exposure		
	Contact with drug particles by direct handling or aerosolisation during dose form modification.	• Risk of exposure to toxic medications by staff. • Reports of infertility, abortion, and stillbirth in females handling chemotherapeutics [64, 65], hypersensitivities to antibiotics, contact dermatitis to chlorpromazine [49].
Legal implications		
	Modification of original dosage form leads to 'off-label' use unless explicitly identified by manufacturer directions.	• Prescriber and/or person administering the medication is responsible for adverse events [42, 66].

6 Administering modified solid oral dosage forms

After the solid oral dosage form is modified, the powdered tablets, or capsule contents may be mixed with food or fluid to help make the medicine easier to administer and swallow. A spoonful of food such as yoghurt, jam, custard, honey, apple sauce, pudding, and drinks such as fruit juices, are often used as vehicles for medicine delivery. Powdered medication may also be sprinkled across an entire meal [47-50], problems of which have already been introduced in Table 3. Regular use of sticky, highly sugared products that adhere to the mouth (e.g. honey or jam) should be avoided, especially for those with dysphagia for whom strict oral care is particularly important. Strict oral care reduces development of caries and proliferation of pathogenic oral bacteria that is a contributing factor to the development of aspiration pneumonia [41].

Generally, crushing conventional immediate release tablets or opening capsules and mixing the contents with a small quantity e.g. one or two tablespoons of food seems

to have a comparatively small and insignificant effect on drug dissolution or absorption from crushed tablets [67-71]. However, the potential for impairment and variation in bioavailability should not be discounted. For instance, mixing crushed phenytoin tablets with pudding impaired absorption compared to apple sauce [72], and mixing enteric-coated beads of didanosine with yoghurt or apple sauce delayed absorption [73]. Food-drug interactions also need to be considered e.g. acidic foods such as pureed fruit can interfere with medication stability, and grapefruit, apples and oranges can affect the pharmacokinetic profile, and therefore pharmacodynamic outcomes of some drugs. Similarly, yoghurt and pudding containing milk products should not be used to administer medicines interacting with dairy products or calcium [49].

6.1 Mixing with thickened fluids

Patients with dysphagia have the texture of their food and liquids modified to reduce choking risk. The viscosity of liquids is increased using thickeners to slow liquid flow, allowing better control of the swallowing process to reduce aspiration risk [43, 74-76]. The liquids are thickened to varying degrees according to dysphagia severity [77], and may be used as the vehicle for powdered medication delivery.

In vitro testing in simulated gastric environments showed thickening agents could significantly impair the release of conventional tablets that were crushed. For example, crushed tablets of warfarin and carbamazepine showed only 14% dissolution after 30 minutes when mixed with a spoonful of thickened water [71]. Similar restrictions on drug dissolution were observed when elixirs or suspensions were mixed with thickeners [59]. The microstructure of the thickening agents appeared to trap the crushed medicine impeding their release; and the thicker the liquid the more impaired the release [78]. In addition, the ionic charge on a commonly used thickening agent (xanthan gum) theoretically may further complicate drug release [79].

Preliminary *in vivo* testing with crushed paracetamol and water thickened with xanthan gum, suggested that changes with drug absorption was unlikely to be clinically significant [6]. Shear forces exerted during swallowing may be expected to break up the thickened fluid globules, reducing droplet size and increasing drug release [78], and this is likely to be an important reason for differences between *in*

vitro and *in vivo* testing. However, the potential for a clinically significant effect of a polysaccharide gum-based thickener on a medication with a narrow therapeutic index should not be understated, particularly considering absorption of whole digoxin, penicillin and metformin tablets may be reduced when consumed with guar gum as a source of dietary fibre [80, 81].

6.2 Inconsistent practices

Unidentified, or inconsistent approaches to dosage form modification may make it more difficult for clinicians to stabilise patients on medication regimens. This is particularly relevant if more than one person is likely to be responsible for drug preparation and administration e.g. hospitals, aged care facilities and group homes [82]. Additionally, older people are particularly vulnerable during transition between care settings, and are at an increased risk of experiencing adverse outcomes or medication misadventure due to miscommunication between healthcare providers [83].

6.3 The healthcare team and work environment

Gathering information about a patient's ability to swallow solid oral dosage forms, and dosage form modification practices is not always a priority for healthcare professionals [84]. It has become an 'orphan task' as the issue does not clearly fall within the defined roles and responsibilities of any one healthcare professional *per se*. Patients are unlikely to offer information about their ability to swallow, or difficulties managing solid oral dosage forms, unless they are specifically asked [84-86]. On the occasions where information is gathered about a patient's swallowing ability, and dosage form modification practices, this information tends not to be easily located, non-standardised terminology is used, and there is no single consistent place to source this information.

Workplace culture and governance structures will also influence how healthcare professionals manage patients who experience difficulty swallowing solid oral dosage forms e.g. availability and accessibility of relevant resources, and communication and continuity of care in transfer of information between healthcare professionals [82, 84]. For instance, validated bedside screening tools and referral pathways specific for swallowing difficulties of solid oral medicines do not currently

exist for healthcare professionals. Similarly, nurses self-report regularly discussing medication dosage form modification with other healthcare professionals, which may be related to their roles being at the forefront of administering medicines to patients [84], However, there are also reports of nurses performing dosage form modifications without checking with the prescriber, leading to situations where modification was unnecessary, or where more suitable alternate forms of the medications were available [10, 45, 87].

Healthcare professionals will most likely advise a patient reporting difficulty with swallowing a non-modified-release, non-coated tablet, to modify their medication dosage form [84]. Worryingly, a small number of healthcare professionals would advise patients to modify or split a modified-release or coated solid oral dosage form [84], and some nurses or carers modify these types of medications before administration to their patients [43]. For the most part, healthcare professionals are concerned with modifying dosage forms with modified release properties or coatings, but only where there was a suffix attached to the product name to indicate this characteristic. However, since the suffix of medications can be omitted from prescriptions [88], this can inadvertently lead to dosage forms being inappropriately modified [53].

6.4 Patient understanding of dosage form modification and health literacy

Patients are reluctant to ask healthcare professionals for advice about difficulties with swallowing their medications and whether to modify solid medication dosage forms [4, 13, 22, 84, 89]. There are misconceptions that swallowing difficulties is an inevitable part of aging [22], others find it embarrassing, or do not think healthcare professionals can help [4]. Instead, many people take advice from friends and family or decide on their own to modify their medications [13], and where there is low individual health literacy, then incorrect or misleading information gets shared. Patients recognise there are “issues with modifying medication dosage forms” [4, 13], i.e. that the medication would be ‘affected’, but could not provide reasoning or further details. They were most concerned about the taste of the medication, and issues around inconvenience and cleanliness, but were less informed about other effects [13].

Low levels of individual health literacy is associated with poor management of chronic conditions such as persistent pain, cardiovascular disease, respiratory disease; and poor participation in healthcare processes [90]. For example, medication labels affixed to medication boxes or bottles provide patients with instructions about how to take the medicines as prescribed. This often includes ancillary cautionary and advisory labels which are intended as an adjunct to the information pharmacists provide when dispensing medicines [49]. These labels can include warnings about special handling instructions as unintended exposure e.g. dosage form modifications, can cause harm to the patient and/or their carer. There may also be additional instructions alerting patients about appropriate use of medicines, which may include swallowing the dosage form whole, without crushing or chewing [49]. Unfortunately, many patients misunderstand and misinterpret these instructions [91, 92], or they may not even notice the affixed ancillary cautionary and advisory labels [93].

7 Avoiding inappropriate dosage form modification practices, and improving medication administration to older people

Issues associated with dosage form modification, and administering solid oral dosage forms to people who cannot swallow them is multifaceted. Where dosage form modification is unavoidable and necessary, reducing the risk of harm is the focus. An integrated and collaborative approach will help overcome some of these issues. This needs to start at dosage form design, to practices around preparation and administration of modified dosage forms and effective communication amongst interdisciplinary teams, and increasing patient awareness of issues with dosage form modification and swallowing difficulties.

7.1 Dosage form design

Manufacturers are advised to consider patient acceptability with regards to the size of oral medicines when designing and producing commercial solid oral dosage forms [94]. The United States Food and Drug Administration provide guidance on tablet size, shape and texture/coatings, weight, surface area, disintegration time and propensity for swelling, for generic oral solid dosage forms to help improve swallowability, which would be relevant for all drug manufacturers [95]. A solid oral dosage form which is the size of a cashew nut or almond should be re-considered for its appropriateness to be swallowed whole (Figure 1). Formulations that allow

dispersion of the medication in food or liquid prior to swallowing e.g. capsules containing enteric coated beads or pellets for proton pump inhibitors are a good solution for many people with swallowing difficulties, but can be comparatively more costly to manufacture. Orally disintegrating/dispersing tablets and mini-tablets are two approaches with potential for large scale use. For example, mini-tablets (tablets that have a maximum 3 mm diameter) can be produced on conventional tablet presses [96]. Orally dispersing tablets or films can use relatively simple equipment, and as printing technologies develop at a fast pace the cost of production will come down [97].

Alternatively, targeting alternative routes of administration would relieve the burden of oral delivery, e.g. nasal, pulmonary, and transdermal routes, though age-related differences in physiology must be considered during the design and testing phases [98]. However, development and widespread application of alternative, more patient-friendly dosage forms are a longer term solution to a problem that needs to be addressed now. Therefore the focus also needs to be on immediate changes that can be made to help older people to take their oral solid dosage forms, and reduce the risks associated with dosage form modifications.

7.2 The interdisciplinary team and practices around dosage form modification

It is imperative that healthcare professionals are more assertive in deliberately considering a patient's ability to swallow when prescribing, dispensing, or administering medicines. Initiating these conversations is as simple as asking 'Do you ever have trouble swallowing tablets?' together with 'Do you ever cut or crush your medicine?'. Clinicians can take the answer into consideration when making clinical decisions with the patient, who are then more likely to receive appropriate advice on how to swallow or modify their medication dosage forms.

Unfortunately, the answer to "who" of the healthcare professionals should assume this orphan task is still unclear, and will largely depend on the structure and functioning of the interdisciplinary team, and the care setting. A recent multidisciplinary study in geriatric hospital units reported a positive impact on the number of medicines crushed, and the number of patients receiving crushed medicines, when patient swallowing ability and dosage form modification practices were collected as part of routine admission and medication history information

gathering [99]. This collected information must then be documented using standardised terminology in an accessible location that all healthcare professionals will and can consistently access. In another study, a study of two Canadian care facilities found records of dysphagia were inconsistently included in multiple locations e.g. at the pharmacy, medication administration records and nursing care plan. However, nurses only responded consistently to the medication administration record, so work processes in the facility were changed so the speech pathologists used consistent terminology, and documented recommendations into the medication administration record for nurses and doctor's orders, and 'dysphagia alerts' were introduced to pharmacy software [82]. This change positively impacted upon reducing inappropriate prescribing, dispensing and administration of medicines to people with dysphagia [82].

Encouraging information flow, and having ready access to relevant expertise knowledge and resources will reduce the risk of inappropriate dosage form modification practices. Workflow processes will need to be changed in order to deliberately and consistently discourage inappropriate dosage form modifications. For example, medicines that must not be crushed should be packaged separately from those that can be crushed. Creation of standard operating procedures and provision of staff training may help to facilitate consistency in relation to practices such as dosage form modification, and administration of medicines to people with swallowing difficulties. Development of validated and convenient bedside screening tools and referral pathways specific for swallowing difficulties of solid oral medicines would help healthcare professionals to quickly, easily, and reliably determine if a patient is truly experiencing dysphagia. These can be helpful for determining if patients simply have difficulty swallowing solid-oral dosage forms, or if they require further referrals to another member of the interdisciplinary team e.g. speech pathologist for investigations.

Effective interdisciplinary teams with shared-understanding of the roles, responsibilities and expertise of the other members of the team improve patient health outcomes [100, 101]. Best practice also looks for continuity of care, and including patient and/or carers as active participants in the clinical decision-making process to tailor care to patient needs e.g. considerations around ability to swallow

solid dosage forms. Speech pathologists (sometimes known as speech and language therapists) are skilled in the education of swallowing, particularly those who specialise in working with children or older people. However, given prescribers, pharmacists and nurses are directly involved in medication provision, they are ideally positioned to provide information on improving medication swallowing techniques for people who dislike or have an aversion to swallowing solid oral dosage forms. As such, targeting education towards these healthcare professionals regarding swallowing techniques for solid oral dosage forms may be most efficient.

7.3 Strategies for helping people to swallow solid oral dosage forms whole, without chewing

For people *without* dysphagia, it is possible to learn to swallow solid oral medications whole. Most of the resources focus on teaching pill-swallowing to children and adolescents, including those with autism or developmental delays [102], because by this age it is too expensive, inconvenient or impractical to give large volumes of paediatric liquid formulations. It is also possible for older adults to change their habits and learn to swallow medications whole.

Given the oral cavity can detect something as fine as a human hair (0.075 mm or 75 microns), strategies need to facilitate solid oral dosage forms to be swallowed without being detected and ejected. The essential element of learning to swallow medications involves 'hiding' the solid dosage form from the highly sensitive oral sensory receptors, and three broad strategies can be used (Table 4).

Table 4. Strategies used by speech pathologists to teach people how to swallow solid dose forms whole without chewing.

Strategy	Action	Outcome	Comment
Disguise as smooth bolus	Place inside typical food item e.g. yoghurt, pudding, wrapped in small piece of bread	Brain recognises it as 'food' as the oral receptors feel the smooth moist bolus and allow it to pass through the oral cavity for swallowing without chewing	Food-drug interaction possible, so this is not the preferred option
Disguise as water bolus	Place on tongue towards the front of the mouth. Take a mouthful of liquid, and swallow just as the solid dose form begins to float. Follow quickly with 2-3 swallows of	Oral receptors detect the water bolus, and cannot recognise the solid dosage form being swallowed. The water moves through the mouth at sufficient velocity, like a surfer being caught in a wave, so the solid dosage	Requires practise

	water.	form is submerged in the water and hidden from the sensory receptors.	
Systematic desensitisation	Start with swallowing whole something very small and gradually increase the size. E.g. start with a small piece of a jelly candy, for example one-third of a Jelly Baby. When this is managed without difficulty, gradually increase until the size of a medication is reached.	Desensitise the oral receptors to the urge to chew	Use in combination with water bolus

When swallowing solid dosage forms, postural adjustments can also facilitate a safe swallow. The head should be kept in either a neutral position or with the chin tipped down towards the chest [103]. Flicking the head back opens the airway in much the same way that a 'head back' position (Figure 2) opens the airway for pulmonary resuscitation, and provides the solid dose with a direct trajectory to the lungs. Thus, although some people may think a head back position helps to swallow whole tablets [103], it should be avoided. People who tip or flick their heads back are attempting to 'hide' the solid dose from the oral sensory receptors by making it 'fly' through the oral cavity, avoiding the sensory receptors to take the dose directly to the back of the mouth where the swallow reflex is initiated.

Products marketed for helping people swallow medications whole are easily accessible, especially via the internet. Lubricating the passage of the medication through the oropharyngeal tract can improve the medication swallowing experience. Examples of commercial products include those that apply a coating (e.g. Medcoat [104, 105]) or gel (e.g. Gloup) to the medication, or a spray applied to the tongue and oral mucosal membranes (e.g. Pill Glide [106, 107]). There are also cups and straws that suspend the medication above the drink so it is carried into the mouth together with the liquid in much the same way as disguising the solid dosage form in a water bolus (Table 4). However, the effectiveness of most of these devices have not been independently established, and comparisons have not been made between them.

7.4 Increasing awareness of issues and patient health literacy

Assertive information gathering by healthcare professionals will help begin to increase patient awareness of the risks associated with dosage form modification and challenges administering medicines to older people. A simultaneous approach to improving patient health literacy, from both an individual patient, and a health environment perspective is required [90]. Health literacy is more than just language literacy, and includes considerations around patient skills, knowledge, and motivation to make effective decisions about their health. Similarly, the health literacy environment includes infrastructure, policies, processes etc. which make up the health system, and how that impacts upon the way patients engage or navigate with the health services. Therefore, healthcare professionals must also consider a patient's health literacy when prescribing, dispensing, administering, and providing information about medicines to older patients and/or their carers.

8 Conclusion

Swallowing a solid dosage form is a learned skill, requiring people to override their natural instincts to chew solid objects. Older people commonly experience swallowing difficulties because of aged-related physiological changes, co-morbidities, and polypharmacy. The strategy healthcare professionals and patients often use to make medicines easier to swallow, is to modify the dosage form. An integrated and collaborative approach is needed to reduce inappropriate dosage form modifications, and improve medication administration to older people. This needs to start from the point of dosage form design, to what medication is prescribed and dispensed, and how it is administered to/by the patient. Promising opportunities exist with novel dosage form designs that can bypass the need for solid oral dosage forms. However, until these delivery devices become more readily available, affordable and accessible, integrated approaches to improve healthcare professional awareness, work processes, and patient health literacy would contribute significantly to reducing the practice of inappropriate dosage form modification.

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11 Figure captions

Figure 1. The relative size of a coin (US dime), cashew, a modified-release tablet, cashew nut, soft gelatine capsule, and almond. Each square is 5 mm x 5 mm.

Figure 2. The head should be in a neutral position (A) or tipped forward (B) for safe swallowing of solid doses. Flicking the head back (C) opens the airway, providing a direct trajectory for the solid dose to the lungs.

Graphics Abstract

Figure 1

Figure 2