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1 **Acceptability of oral solid medicines in older adults with and without**
2 **dysphagia: a nested pilot validation questionnaire based observational**
3 **study**

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Abstract

Older patients (aged 65 years and over) are the major consumers of medicines and many barriers affect their ability in taking medicines orally, especially swallowing difficulties. Moreover, the characteristics of differing medicine formulations might have an impact on their acceptability in older patients. The aims of this study were to validate a Medicines Acceptability Questionnaire (MAQ) and to assess acceptability of oral solid medicines in older ambulatory patients with and without dysphagia. One hundred and fifty six older patients attending community pharmacies were recruited and attended face to face interviews. Two questionnaires were administered during the interviews, the validated Sydney Swallow Questionnaire (SSQ) assessing oral and pharyngeal swallowing function and the newly developed Medicines Acceptability Questionnaire (MAQ) evaluating patient acceptability of oral solid medicines. Seventeen (11%) participants displayed symptoms compatible with swallowing difficulties identified by the SSQ. Participants with swallowing difficulties were considered themselves more likely to have problems in swallowing tablets and capsules of large sizes (11 mm and 13 mm tablets and size #00 capsules) compared to participants without dysphagia. Dispersible/effervescent tablets and orally disintegrating tablets were considered to be the most acceptable in this cohort, followed by mini-tablets. Chewable tablets and granules were the least favoured. Consistently higher acceptability scores were seen in the dysphagic population than in the non-dysphagic population for all of the dosage forms that were easier to swallow than tablets and capsules. The development of these formulations will assist in medication taking in older patients with dysphagia and potentially their adherence to drug treatments.

Keywords: geriatric, elderly, swallow, medication, acceptance, preference

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47 **1. Introduction**

48 Patient acceptability to a pharmaceutical dosage form is critical to ensure adherence and
49 therapeutic outcomes, especially in children and older people (F. Liu et al., 2014).

50 Acceptability has previously been defined as “an overall ability of the patient and caregiver
51 (defined as ‘user’) to use a medicinal product as intended (or authorised)” (P. Kozarewicz,

52 2014). The European Medicines Agency has required the assessment of patient acceptability

53 to be an integrated part of paediatric medicinal product development (E. M. A. (EMA), 2013;

54 P. Kozarewicz, 2014). However, acceptability of medicines in older adults has been largely

55 overlooked. Older patients (aged 65 years and over) account for 50% of the medicine

56 prescriptions in the UK (Z. Rajaei-Dehkordi and G. McPherson, 1997). The oral route remains

57 the most preferred mode for medicine administration; however, there are barriers for older

58 patients to take medications orally (F. Liu et al., 2014). Swallowing difficulties (dysphagia) are

59 common in older people which affect their ability to take oral medicines, especially tablets

60 and capsules (C. M. Steele et al., 1997; I. Strachan and M. Greener, 2005). Consequently,

61 medicines are often modified such as crushing tablets or capsules opened to assist

62 administration to older patients (J. Kelly and D. Wright, 2009; D. Wright, 2002). This leads to

63 unlicensed use of medicines and can potentially cause ineffective use or toxicity of the

64 medicine (S. Stegemann et al., 2012).

65

66 Characteristics of a pharmaceutical dosage form, such as the size, shape, and surface texture

67 of a tablet, have an impact on how easily a solid oral medicine can be swallowed and pass

68 through the pharynx and oesophagus (K. S. Channer and J. P. Virjee, 1985; K. T. Evans and G.

69 M. Roberts, 1981; H. Hey et al., 1982; A. B. Overgaard et al., 2001). Previous knowledge on
70 these effects has been demonstrated in healthy young subjects; however, this remains
71 unclear in older people especially those with existing swallowing difficulties. The type of
72 formulation might be another factor affecting the ability and willingness of older patients to
73 take their medicines. A number of solid oral dosage forms that are “easier to swallow” than
74 tablets and capsules have been made available in recent years including orally disintegrating
75 tablets (ODTs), dispersible tablets, mini-tablets and multi-particulates (granules). As most of
76 these formulations are designed and developed for paediatric use, acceptability of some of
77 these dosage forms in children has been reported (I. T. Cohen et al., 2005; J. Motte et al.,
78 2005; D. Nasrin et al., 2005). For older patients who cannot swallow tablets, the availability
79 of these formulations could be beneficial. The use of dispersible/effervescent tablets and
80 ODTs has been demonstrated in older patients (A. J. Bayer et al., 1988; J. C. Nelson et al.,
81 2006). Especially, ODTs have been proven to be easier to swallow than conventional tablets
82 for patients with dysphagia (G. Carnaby-Mann and M. Crary, 2005). However, evidence in the
83 acceptability of these solid dosage forms in older patients is still sparse. This research is a pilot
84 study where a Medicines Acceptability Questionnaire (MAQ) was initially developed and
85 validated before assessing the acceptability of a range of solid oral medicine dosage forms in
86 older ambulatory patients attending community pharmacies and investigating the association
87 between patient acceptability and the presence of swallowing difficulties.

88

89 **2. Materials and Methods**

90

91 **2.1 Study population and setting**

92 The study was approved by the Ethics Committee of University of Hertfordshire
93 (LMS/SF/UH/00081) and was conducted at community pharmacies in the South East England
94 area in the UK during October to November 2014. A convenient sample of pharmacies was
95 recruited to participate in the study. The pharmacist in charge in each pharmacy was
96 informed the purpose of the study and approached consecutive patients attending the
97 pharmacy during week-day (Monday to Friday) opening hours who were eligible for the study.
98 The eligibility criteria include patients aged 65 years or over and prescribed at least one oral
99 medicine. No financial incentive was received by the pharmacies for participating in the study.

100

101 Given the stated aims, the primary endpoint of the study was the proportion of primary care
102 older patients having swallowing difficulties. Based on the literature, prevalence of
103 swallowing difficulties in community dwelling older adults was estimated as 11% (G. Holland
104 et al., 2011). Approximately 150 participants would need to be enrolled to ensure a desired
105 precision of at least 5%.

106

107 2.2 Administration of the Sydney Swallow Questionnaire (SSQ)

108 The SSQ is a validated questionnaire and composed of 17 questions assessing oral and
109 pharyngeal swallowing function with responses entered onto a 101 mm visual analog scale
110 except for question 12 (R. C. Dwivedi et al., 2010; K. L. Wallace et al., 2000). The SSQ was
111 administered to the participants during an interview which took place in the private
112 consultation room in the pharmacy. The participant placed a mark on the horizontal line of
113 the visual analog scale. The first millimeter of the line was disregarded and a score of 0-100
114 was calculated by measuring the distance from the center of the mark to the first millimeter
115 of the line for each question. A mark placed within the first millimeter of the line was scored

116 as zero. Question 12 contains 6 categorical responses each representing a score of 0, 20, 40,
117 60, 80 or 100. The maximum possible total score for the SSQ was 1700, with higher score
118 indicating greater severity of swallowing dysfunction. Analogous to the description of Holland
119 et al. (G. Holland et al., 2011), a score greater than 200 was considered indicating
120 symptomatic dysphagia.

121

122 2.3 Pilot of the Medicines Acceptability Questionnaire (MAQ)

123 The MAQ comprised 15 questions evaluating patient acceptability of oral solid medicines. The
124 questions were developed around three major topics. The first topic (3 items) covers general
125 health status of the participant, number of oral medicines currently taking and any difficulties
126 in taking solid oral medicines. The health status of the participant was measured using a 5-
127 point Likert scale. Excellence in general health was ranked as a score of 1 and a score of 5
128 represented the health perception being poor. The second topic (5 items) evaluates
129 participants' perception on the size and shape of tablets and capsules in relation to difficulties
130 in swallowing. The participants were shown a printed diagram of tablets of varying sizes and
131 shapes (Appendix). Samples of 9 mm tablets (the middle size of all sizes presented) of each
132 shape were taped onto the diagram to provide visual representatives of the size and shape.
133 Participants were also shown samples of hard gelatin capsules (HGC) of different sizes (4#, 3#,
134 2#, 1#, 0# and 00#). They were then asked from what size they will start to have difficulty to
135 swallow the tablets and capsules.

136

137 The third topic (7 items) assesses participants' acceptability of other alternative solid
138 medicine dosage forms to tablets and capsules, including mini-tablets, granules in a sachet,
139 dispersible/effervescent tablets, orally disintegrating tablets (ODTs) and chewable tablets.

140 These dosage forms are referred to as “alternative solid oral dosage forms” throughout this
141 article. The participants were shown samples of all formulation types and were given an
142 explanation of how the formulation should be administered. Mini-tablets were shown to
143 participants as mini-tablets filled in HGCs. Granules were presented as sprinkles onto food.
144 Dispersible tablets were presented as a drink with a minimum amount of 60 ml (or half a glass)
145 water required to dissolve the tablet. ODTs were described as melting/dissolving on the
146 tongue and chewable tablets were explained as needing to be chewed before swallowing.
147 They then provided their opinion on the formulation including past experience in using the
148 formulation, giving a score of 0-10 indicating their acceptance with 10 being the most
149 acceptable. Open-ended questions were also used to obtain opinions of the participants on
150 good and bad points of each formulation. The open-ended questions were analysed by
151 reporting the percentages of participants stating the same comments on a formulation.

152

153 The content/face validity of the MAQ was assessed by two experts in the field acting as
154 respondents. Cronbach’s alpha test was conducted to evaluate the level of reliability and
155 internal consistency using the Statistical Package of the Social Sciences (SPSS) version 22.0
156 (IBM Corp., Armonk, NY, USA). Cronbach’s alpha scores of 0.7 or above were deemed as
157 acceptable according to Nunnally and Bernstein (J. Nunnally and L. Bernstein, 1994). The MAQ
158 was administered to the participants during the interview together with the SSQ. The
159 interviews were conducted by two of the authors (AG and JB). Three pilot interviews were
160 conducted in the presence of both interviewers to reach a consensus on how to conduct the
161 interview and the subsequent interviews were conducted by one interviewer per participant.

162

163 2.4 Data analysis

164 Data analysis was performed using the Statistical Package of the Social Sciences (SPSS) version
165 22.0 (IBM Corp., Armonk, NY, USA). The results are reported as mean \pm standard deviation
166 (SD). Spearman's nonparametric correlation was used to identify the presence of significant
167 correlations between total SSQ score and age of participants or number of solid oral
168 medicines taken daily. The Mann-Whitney U test was conducted to assess links between
169 gender of participants and total SSQ score, and comparing the means of participants' self-
170 perceived health status between the dysphagia and non-dysphagia group. Chi-Square test
171 was conducted to evaluate the relationship between dysphagic status of the participant and
172 difficulty in swallowing tablets and capsules. The Kruskal Wallis test was used to assess
173 significant relationship between total SSQ score and participants' self-perceived health status.

174

175 2.5 Materials used to conduct the interviews

176 Samples of tablets, capsules and other solid dosage forms that were presented to the
177 participants during interviews are listed in Tables 1 and 2. Samples of formulations were
178 purchased as commercial products where possible to represent medicines used in real life.
179 When a suitable commercial product was not identified to represent a formulation, placebo
180 samples were used (9 mm arched round tablets).

181

182

183 **3. Results**

184 3.1 Validation of the Medicines Acceptability Questionnaire (MAQ)

185 The content/face validity of MAQ was established by experts. Any items where questions
186 were raised were modified and the revised versions were tested again until there were no
187 further questions. The total Cronbach's alpha score was calculated as 0.940 and scores after

188 eliminating any items from the questionnaire were in the range of 0.928 – 0.945, indicating
189 good reliability and internal consistency of the questions.

190

191 3.2 Participant demographics and the Sydney Swallow Questionnaire (SSQ) scores

192 Fifteen pharmacies were approached and of these 10 (including both chain-pharmacies and
193 independent pharmacies) agreed to participate in the study. The main reason given by the
194 pharmacies for refusing to participate was that the pharmacist had limited time available to
195 help recruiting participants. A total of 165 patients were approached by the pharmacists and
196 156 (94.5%) were recruited to participate in the study. The average age of the participants is
197 74.0 ± 5.7 (mean \pm SD) years and 80 (51.3%) participants were females. All participants
198 completed both the SSQ and the MAQ successfully.

199

200 Seventeen (11%) participants had SSQ scores ≥ 200 , indicating symptomatic dysphagia or
201 swallowing difficulty. The mean total SSQ score across all participants was 92.2 ± 168.7 (mean
202 \pm SD, range 0.0-1026.0) and for participants with significant symptoms of dysphagia it was
203 497.2 ± 246.6 (mean \pm SD, range 211.4-1026.0). There was no significant correlation between
204 age and SSQ dysphagia score ($r=0.050$, $p=0.537$) and no statistically significant relationship
205 between gender and SSQ dysphagia score ($r=-0.040$, $p=0.624$).

206

207 The mean score for the self-perceived health status of all participants was 3.2 ± 1.1 (mean \pm
208 SD, 1=excellent and 5=poor). There was a significant correlation between general health
209 status score and SSQ dysphagia score ($r=0.250$, $p=0.002$). The mean health status scores were
210 3.9 ± 1.0 (mean \pm SD) and 3.1 ± 1.1 (mean \pm SD) for participants with and without dysphagia
211 respectively. On average, the participants were prescribed 5.1 ± 3.8 (mean \pm SD) oral solid

212 medicines on a daily basis. Sixty five (42%) participants took 5 or more solid oral medicines
213 daily. A significant relationship was present between number of oral solid formulations taken
214 daily by the participants and SSQ dysphagia score ($r=0.171, p=0.033$).

215

216 3.3 Ability to swallow tablets and capsules in patients with and without dysphagia by the MAQ

217 A total of 12 (7.8%) participants experienced ongoing difficulties in swallowing tablets and

218 capsules according to the results from the MAQ. Figure 1 shows percentage of participants

219 who has chosen the size and shape of tablets that were perceived as starting to cause

220 difficulty in swallowing. Between 46% and 64% of the participants without swallowing

221 difficulties (SSQ score lower than 200) reported no problem of swallowing any of the tablets

222 sizes for the different shapes presented compared to 6%-12% of the participants with

223 swallowing difficulties (SSQ score higher than 200; Figure 1). The majority of participants with

224 dysphagia found that tablets of sizes 11 mm and 13 mm might started to cause difficulties in

225 swallowing; the percentages of participants selecting 11 mm or 13 mm were 52.9%, 52.9%,

226 58.8% and 64.7% for flat round, arched round, oblong and oval tablets respectively.

227

228 Similar results were observed regarding difficulties in swallowing capsules of different sizes in

229 participants with and without dysphagia (Figure 2). Around 40% participants with no

230 dysphagia deemed themselves having no problem of swallowing any of the capsule sizes

231 presented, compared to only 6% in participants with dysphagia. In participants with

232 dysphagia, over a third (35%) selected size #00 as that which started to cause problems in

233 swallowing; however, around 30% of these participants also considered size #2 to be difficult

234 to swallow.

235

236 3.4 Acceptability of alternative solid oral dosage forms

237 A low proportion of participants had had experience of using the alternative solid oral dosage
238 forms, except for dispersible/effervescent tablets which were referenced mainly to soluble
239 paracetamol and dispersible aspirin tablets as examples (Table 3). The acceptability scores of
240 different oral solid dosage forms are shown in Figure 3. Participants described the good/bad
241 points they considered for each formulation as listed in Table 4.

242

4. Discussion

A range of medicine formulations have been made available for patients who find it difficult to swallow tablets and capsules. However, the acceptability of these formulations in targeted patient groups is often unclear. This pilot study is the first attempt to evaluate the acceptability of a range of solid oral dosage forms in older patients with and without dysphagia, using the newly developed Medicines Acceptability Questionnaire (MAQ). The content validity and reliability of the MAQ was established and the results of this study can be compared to future investigations. In our study, the prevalence of (symptoms compatible with) dysphagia in this older population attending community pharmacies was found to be 11%. This is in agreement with a study by Holland et al. in which 11.4% of participants of a community dwelling older population in England was found to have scores on the SSQ compatible with dysphagia (G. Holland et al., 2011). This also broadly agrees with or is slightly lower than other published data on prevalence of dysphagia in older primary care patients (B. R. Bloem et al., 1990; P. H. Chen et al., 2009; K. Kawashima et al., 2004). In this study, age and gender of the participant did not significantly affect dysphagia score. Studies have reported that increasing age is associated with increased severity and prevalence of dysphagia in elderly populations (G. Holland et al., 2011; K. Kawashima et al., 2004). However, Szczaesniak et al. studied SSQ score in a non-dysphagic population and found that there was no significant correlation between age and SSQ score (M. M. Szczesniak et al., 2014). The majority of the participants in the current study were non-dysphagic, which might have contributed to the non-significant relationship between age and dysphagia score. It is also possible that the size of the cohort (n=156) was not large enough to see such an effect.

Almost half of participants took 5 or more solid oral medicines daily, which qualifies as polypharmacy by definition of some published studies (D. Gnjjidic et al., 2012; U. Junius-Walker et al., 2007; D. Koper et al., 2013). In addition, there was a significant relationship between dysphagia (SSQ) score and number of oral medicines taken on a daily basis. Marquis et al. did not find a significant relationship between difficulties in swallowing solid medicines and number of prescribed tablets among primary care adult patients who have at least 3 daily solid oral medications prescribed (J. Marquis et al., 2013). Marquis et al. (2013) used patients' self-reported difficulties in swallowing solid medications instead of the validated questionnaire (SSQ) and this difference in methodology might have contributed to the deferring outcomes from the current study.

It has been documented that size and shape of tablets and capsules affect the "swallowability" and oesophageal transit in adults. Generally, difficulty in swallowing tablets increases with size (H. Hey et al., 1982; A. B. Overgaard et al., 2001). However, most of the published studies are conducted in healthy young subjects and limited information is available on the ability of older adults especially those with swallowing difficulties to swallow tablets and capsules. In the current study, participants with dysphagia (SSQ scores > 200) were more likely to have difficulties in swallowing tablets and capsules of the given sizes and shapes compared to non-dysphagic participants. Oblong and oval tablets were considered slightly easier to swallow than flat round and arched round tablets, which is in agreement with previous reports that large tablets of oblong and oval shapes are easier to swallow and pass esophagus faster than round tablets (K. S. Channer and J. P. Virjee, 1985; H. Hey et al., 1982; A. B. Overgaard et al., 2001). Schiele et al. (2013) reported that round tablets of 8 mm in diameter started to cause swallowing difficulties in patients and for oval and oblong tablets

the length of tablets reached 15 mm and 16 mm respectively to causing problem in swallowing (J. T. Schiele et al., 2013).

Amongst the alternative solid oral dosage forms, dispersible/effervescent tablets ranked highest in acceptability score. Previous use of dispersible/effervescent tablets has the highest proportion of participants giving a positive response. A national survey across the UK showed that 90% of what was prescribed or sold over the counter to older people for long-term use which were regarded as being “easy to swallow” were effervescent tablets (W. Baqir and A. Maguire, 2000). This familiarity with the type of the formulation and mode of administration might contribute to the high acceptance to these formulations.

ODTs and mini-tablets were also deemed acceptable in both the dysphagia and non-dysphagia populations, following dispersible tablets. The main advantages of ODTs reported by the participants were convenient to use and easier to swallow. Indeed, previous work has indicated that ODTs require less effort to swallow than conventional tablets in patients with dysphagia (G. Carnaby-Mann and M. Crary, 2005). The use of ODTs in older patients has been documented, especially in patients with Parkinson’s and Alzheimer’s diseases, and patients under antipsychotic treatments who might be purposely non-adherent (V. Danileviciute et al., 2009; B. J. Kinon et al., 2003; P. A. Nausieda, 2005). The mini-tablets (4 mm in diameter) were considered easier to swallow than normal tablets due to small size by the participants. Mini-tablets (3 mm) were deemed appropriate for use in patients with Parkinson’s disease, due to the potential of providing individualized dosage (S. Bredenberg et al., 2003). However, concerns were raised in respect of difficulties in handling and seeing these smaller formulations by participants in our study and the study contacted by S. Bredenberg et al.

(2003). Future research is needed in investigating acceptability of mini-tablets of smaller sizes, multiple dosages and the potential of using dispensing devices in older patients.

Chewable tablets and granules were considered as the least acceptable amongst the alternative dosage forms. Chewable tablets were useful in paediatric medicines for children over 2 years old (T. M. Michele et al., 2002). However, they might not be appropriate for use in older patients, as there has been a reported decline in chewing ability in older age primarily due to tooth loss (I. A. Kida et al., 2007; P. Peltola and M. M. Vehkalahti, 2005). Granules were not favored amongst the participants mostly due to reluctance in mixing medicines with food and concerns on incomplete dosing.

For all of the alternative solid dosage forms, consistently higher acceptability scores were seen in the dysphagia population than in the non-dysphagia population. Participants with dysphagia (SSQ scores > 200) are more likely to experience problems in taking their medicines in the form of tablets and capsules. The current study shows that formulation characteristics play a role in medicine acceptability in older patients. It is therefore important to make available a variety of formulation choices for older patients who find swallowing tablets and capsule difficult. The European Union legislation in paediatric medicines has prompted the development of formulations suitable for children (P. Kozarewicz, 2014). The increasing availability of paediatric formulations could benefit older patients; however, there are distinct differences between the two populations (F. Liu et al., 2014). Consequently, explicit considerations should be given to the older population to address their unique and specific needs in drug therapy and medicine use.

The study has its limitations. The study recruited a convenient sample of community pharmacies which might introduce selection bias. The patients' self-reported difficulties in swallowing solid medicines were not compared with the current medications prescribed to the patients which might have correlated better with the types and characteristics of formulations that the patients can or cannot take. Diagrams of tablets of different sizes and shapes (except for 9 mm tablets) were presented instead of real samples which might affect participants' judgement in ability to swallow. The study focused on oral solid dosage forms and liquid medicines were not included. The need for liquid formulations might be higher in nursing homes and hospitals and these settings would be ideal to assess the acceptability to liquid medicines in future studies. The acceptance scores of the alternative dosage forms were not directly compared with that of tablets and capsules, which would be useful information for further investigation.

5. Conclusions

A significant proportion of older patients attending community pharmacies have symptoms compatible with dysphagia. These patients are more likely to have difficulties in swallowing tablets and capsules compared to those with no dysphagia. Healthcare professionals should identify patients with high risk of having problems swallowing their medicines and assist in selecting most appropriate medicine dosage forms. The development and availability of alternative oral formulations other than conventional tablets and capsules will likely to assist in medication administration and management in patient with dysphagia and might lead to better adherence.

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Appendix: Images of tablets of different sizes and shapes

References

- (EMA), E. M. A., 2013. Guideline on pharmaceutical development of medicines for paediatric use.
- Baqir, W., Maguire, A., 2000. Consumption of prescribed and over-the-counter medicines with prolonged oral clearance used by the elderly in the Northern Region of England, with special regard to generic prescribing, dose form and sugars content. *Public Health* 114, 367-373.
- Bayer, A. J., Day, J. J., Finucane, P., Pathy, M. S., 1988. Bioavailability and acceptability of a dispersible formulation of levodopa-benserazide in parkinsonian patients with and without dysphagia. *J Clin Pharm Ther* 13, 191-194.
- Bloem, B. R., Lagaay, A. M., van Beek, W., Haan, J., Roos, R. A., Wintzen, A. R., 1990. Prevalence of subjective dysphagia in community residents aged over 87. *Bmj* 300, 721-722.
- Bredenberg, S., Nyholm, D., Aquilonius, S. M., Nystrom, C., 2003. An automatic dose dispenser for microtablets-a new concept for individual dosage of drugs in tablet form. *Int. J. Pharm.* 261, 137-146.
- Carnaby-Mann, G., Cray, M., 2005. Pill swallowing by adults with dysphagia. *Archives of Otolaryngology-Head & Neck Surgery* 131, 970-975.
- Channer, K. S., Virjee, J. P., 1985. The effect of formulation on oesophageal transit. *J Pharm Pharmacol* 37, 126-129.
- Chen, P. H., Golub, J. S., Hapner, E. R., Johns, M. M., 3rd, 2009. Prevalence of perceived dysphagia and quality-of-life impairment in a geriatric population. *Dysphagia* 24, 1-6.
- Cohen, I. T., Joffe, D., Hummer, K., Soluri, A., 2005. Ondansetron oral disintegrating tablets: acceptability and efficacy in children undergoing adenotonsillectomy. *Anesth. Analg.* 101, 59-63.
- Danileviciute, V., Sveikata, A., Adomaitiene, V., Gumbrevicius, G., Fokas, V., Sveikatiene, R., 2009. Efficacy, tolerability, and preference of mirtazapine orally disintegrating tablets in depressed patients: a 17-week naturalistic study in Lithuania. *Medicina (Kaunas)* 45, 778-784.
- Dwivedi, R. C., St Rose, S., Roe, J. W., Khan, A. S., Pepper, C., Nutting, C. M., Clarke, P. M., Kerawala, C. J., Rhys-Evans, P. H., Harrington, K. J., Kazi, R., 2010. Validation of the Sydney Swallow Questionnaire (SSQ) in a cohort of head and neck cancer patients. *Oral Oncol.* 46, e10-14.
- Evans, K. T., Roberts, G. M., 1981. The ability of patients to swallow capsules. *J Clin Hosp Pharm* 6, 207-208.
- Gnjidic, D., Hilmer, S. N., Blyth, F. M., Naganathan, V., Waite, L., Seibel, M. J., McLachlan, A. J., Cumming, R. G., Handelsman, D. J., Le Couteur, D. G., 2012. Polypharmacy cutoff and outcomes: five or more medicines were used to identify community-dwelling older men at risk of different adverse outcomes. *Journal of clinical epidemiology* 65, 989-995.
- Hey, H., Jorgensen, F., Sorensen, K., Hasselbalch, H., Wamberg, T., 1982. Oesophageal transit of six commonly used tablets and capsules. *Br Med J (Clin Res Ed)* 285, 1717-1719.
- Holland, G., Jayasekaran, V., Pendleton, N., Horan, M., Jones, M., Hamdy, S., 2011. Prevalence and symptom profiling of oropharyngeal dysphagia in a community dwelling of an elderly population: a self-reporting questionnaire survey. *Dis Esophagus* 24, 476-480.
- Junius-Walker, U., Theile, G., Hummers-Pradier, E., 2007. Prevalence and predictors of polypharmacy among older primary care patients in Germany. *Family practice* 24, 14-19.
- Kawashima, K., Motohashi, Y., Fujishima, I., 2004. Prevalence of dysphagia among community-dwelling elderly individuals as estimated using a questionnaire for dysphagia screening. *Dysphagia* 19, 266-271.
- Kelly, J., Wright, D., 2009. Administering medication to adult patients with dysphagia. *Nursing standard* 23, 62-68.
- Kida, I. A., Astrom, A. N., Strand, G. V., Masalu, J. R., 2007. Chewing problems and dissatisfaction with chewing ability: a survey of older Tanzanians. *Eur J Oral Sci* 115, 265-274.
- Kinon, B. J., Hill, A. L., Liu, H., Kollack-Walker, S., 2003. Olanzapine orally disintegrating tablets in the treatment of acutely ill non-compliant patients with schizophrenia. *Int J Neuropsychopharmacol* 6, 97-102.

- Koper, D., Kamenski, G., Flamm, M., Bohmdorfer, B., Sonnichsen, A., 2013. Frequency of medication errors in primary care patients with polypharmacy. *Family practice* 30, 313-319.
- Kozarewicz, P., 2014. Regulatory perspectives on acceptability testing of dosage forms in children. *International journal of pharmaceutics* 469, 245-248.
- Liu, F., Ranmal, S., Batchelor, H. K., Orlu-Gul, M., Ernest, T. B., Thomas, I. W., Flanagan, T., Tuleu, C., 2014. Patient-centred pharmaceutical design to improve acceptability of medicines: similarities and differences in paediatric and geriatric populations. *Drugs* 74, 1871-1889.
- Marquis, J., Schneider, M. P., Payot, V., Cordonier, A. C., Bugnon, O., Hersberger, K. E., Arnet, I., 2013. Swallowing difficulties with oral drugs among polypharmacy patients attending community pharmacies. *Int J Clin Pharm* 35, 1130-1136.
- Michele, T. M., Knorr, B., Vadas, E. B., Reiss, T. F., 2002. Safety of chewable tablets for children. *The Journal of asthma : official journal of the Association for the Care of Asthma* 39, 391-403.
- Motte, J., Pedespan, J. M., Sevestre, M., Chiron, C., Groupe, A. M. E., 2005. [Acceptability and tolerance of sodium valproate, a new sustained-action granule formulation, in monotherapy for epileptic children from 3 years old]. *Arch. Pediatr.* 12, 1533-1539.
- Nasrin, D., Larson, C. P., Sultana, S., Khan, T. U., 2005. Acceptability of and adherence to dispersible zinc tablet in the treatment of acute childhood diarrhoea. *Journal of Health, Population and Nutrition*, 215-221.
- Nausieda, P. A., 2005. A multicenter, open-label, sequential study comparing preferences for Carbidopa-Levodopa orally disintegrating tablets and conventional tablets in subjects with Parkinson's disease (vol 27, pg 58, 2005). *Clinical Therapeutics* 27, 360-360.
- Nelson, J. C., Hollander, S. B., Betzel, J., Smolen, P., 2006. Mirtazapine orally disintegrating tablets in depressed nursing home residents 85 years of age and older. *Int J Geriatr Psychiatry* 21, 898-901.
- Nunnally, J., Bernstein, L., 1994. *Psychometric theory*. McGraw-Hill Higher, INC, New York.
- Overgaard, A. B., Hojsted, J., Hansen, R., Moller-Sonnergaard, J., Christrup, L. L., 2001. Patients' evaluation of shape, size and colour of solid dosage forms. *Pharmacy world & science : PWS* 23, 185-188.
- Peltola, P., Vehkalahti, M. M., 2005. Chewing ability of the long-term hospitalized elderly. *Spec Care Dentist* 25, 260-264.
- Rajaei-Dehkordi, Z., McPherson, G., 1997. The effects of multiple medication in the elderly. *Nurs. Times* 93, 56-58.
- Schiele, J. T., Quinzler, R., Klimm, H. D., Pruszydlo, M. G., Haefeli, W. E., 2013. Difficulties swallowing solid oral dosage forms in a general practice population: prevalence, causes, and relationship to dosage forms. *Eur J Clin Pharmacol* 69, 937-948.
- Steele, C. M., Greenwood, C., Ens, I., Robertson, C., Seidman-Carlson, R., 1997. Mealtime Difficulties in a Home for the Aged: Not Just Dysphagia. *Dysphagia* 12, 45-50.
- Stegemann, S., Gosch, M., Breitzkreutz, J., 2012. Swallowing dysfunction and dysphagia is an unrecognized challenge for oral drug therapy. *International journal of pharmaceutics* 430, 197-206.
- Strachan, I., Greener, M., 2005. Medication-related swallowing difficulties may be more common than we realise. *Pharmacy in Practice*.
- Szczesniak, M. M., Maclean, J., Zhang, T., Liu, R., Cook, I. J., 2014. The normative range for and age and gender effects on the Sydney Swallow Questionnaire (SSQ). *Dysphagia* 29, 535-538.
- Wallace, K. L., Middleton, S., Cook, I. J., 2000. Development and validation of a self-report symptom inventory to assess the severity of oral-pharyngeal dysphagia. *Gastroenterology* 118, 678-687.
- Wright, D., 2002. Medication administration in nursing homes. *Nurs. Stand.* 16, 33-38.

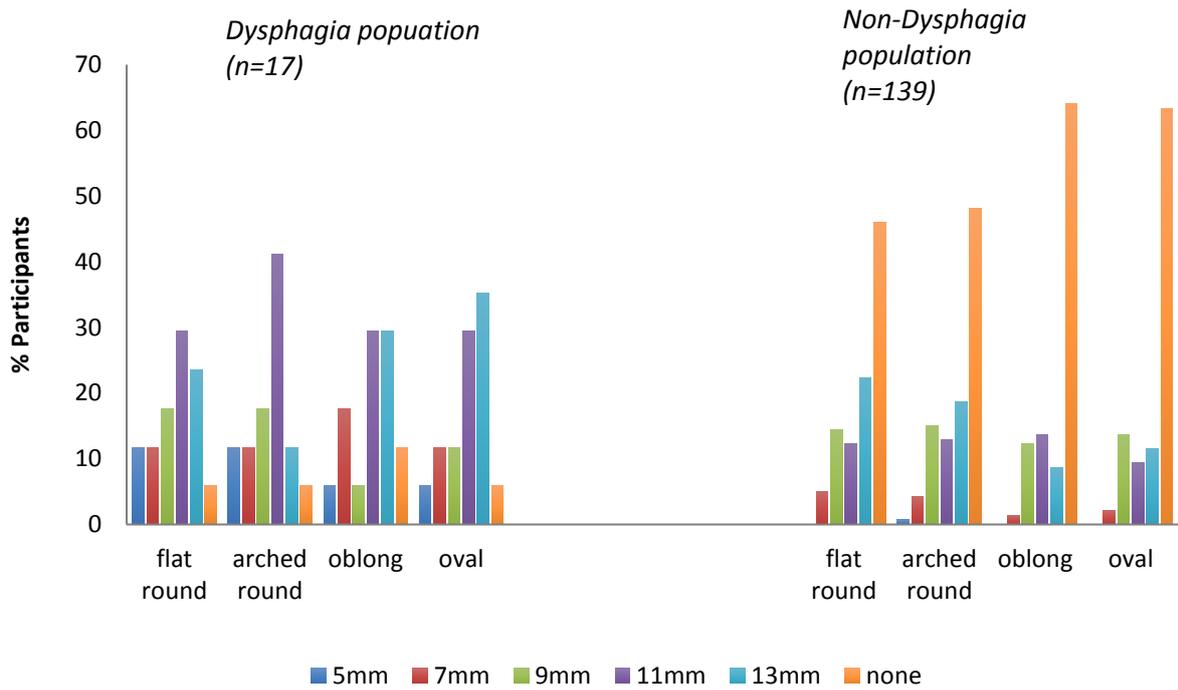


Figure 1. Percentage of participants selecting the tablet size and shape that started to cause difficulty in swallowing.

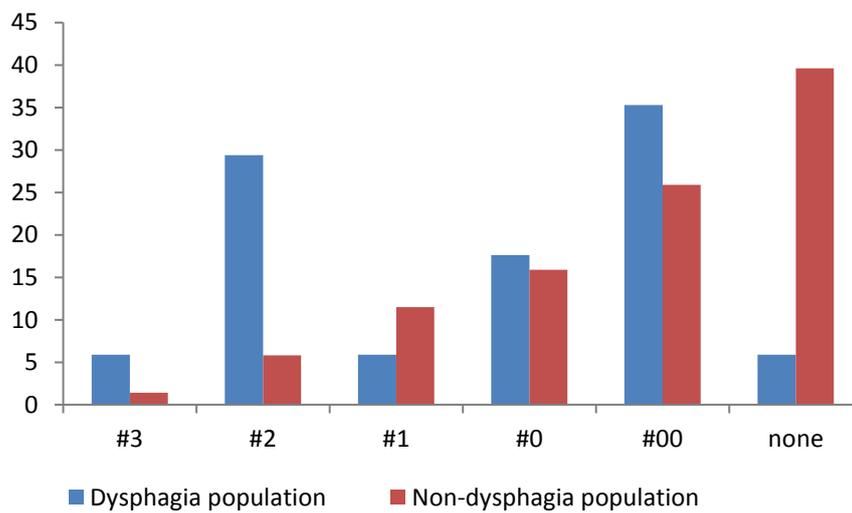


Fig 2. Percentage of participants selecting the capsule size that might start to cause difficulty in swallowing

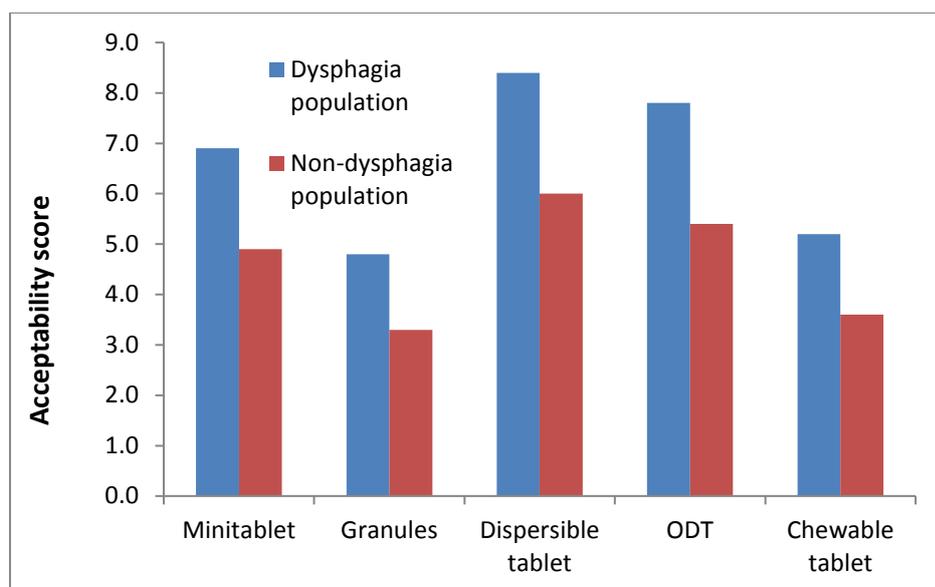


Fig 3. Acceptability scores of different oral solid dosage forms (ODT: orally disintegrating tablet).

Table 1. Products used to represent 9 mm tablets in different shapes

Tablet shape	Product used
Flat round	Imodium Instants tablets (McNeil Products Ltd)
Arched round	Placebo tablets produced at University of Hertfordshire laboratories (Ingredients: 99% lactose monohydrate, 1% magnesium stearate, compressed using a CPR-6 single punch tablet press, Isopak Limited)
Oblong	Zirtek 10 mg tablets (UCB Pharma Limited)
Oval	Finasteride 5 mg tablets (Dr Reddy's Laboratories (UK) Ltd)

Table 2. Products used to represent various oral formulations

Type of formulation	Products used
Capsule	Hard gelatin capsule shells of sizes #00, #0, #1, #2, and #3 (supplied by Capsugel, Morristown, New Jersey, USA) filled with lactose monohydrate

Mini-tablet	Round shaped mini-tablets (4 mm) was obtained as the content of Inconex XL 4 mg Prolonged-release Capsules (Sandoz Ltd)
Granules	Fybogel sachet (Reckitt Benckiser Healthcare (UK) Ltd)
Dispersible tablet	Boots soluble paracetamol tablets (The Boots Company PCL)
Orally disintegrating tablet (ODT)	Imodium Instants melt (McNeil Products Ltd)
Chewable tablet	Gaviscon double action chewable tablets (Reckitt Benckiser Healthcare (UK) Ltd)

Table 3. Number of participants who had previously used the flexible solid oral formulations.

Formulation	Number (%) of participants who have previously used the formulation
Mini-tablets	8 (5%)
Granules	17 (11%)
Dispersible/effervescent tablets	107 (68%)
Orally disintegrating tablets	34 (22%)
Chewable tablets	47 (30%)

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2 Table 4. Participants' impression on the flexible solid oral dosage forms.

Formulation	Advantages	Participants (%)	Disadvantages	Participants (%)
Dispersible/effervescent tablets	• Easy to swallow; less harsh than swallowing tablets	19	• Require water; takes long to dissolve	5
	• Good for those with swallowing difficulties	8	• Cannot use on the move – takes long to dissolve	17
	• Nice to drink	40	• Concerns on taste	38
Mini-tablets	• Small, easy to swallow	24	• Difficult to see for visually impaired	9
	• Good for those with swallowing difficulties	23	• Do not want to mix food with medicine	23
	• Can take more than one at once	8	• If food is not completed consumed, patient does not receive full dose	6
	• Can be sprinkled onto food	6	• Concerns on taste	28

Granules	• Good for those with swallowing difficulties	26	• Do not want to mix food with medicine: Presentation and flavour of food can be ruined	28
	• Can be sprinkled onto food	9	• Opening sachet can be difficult for those with poor manual dexterity	12
	• Come in various flavours	11	• Need to finish meal to get whole dose	9
			• Concerns on appearance	8
			• Concerns on taste	15
Orally disintegrating tablets	• Melts itself, minimal effort and thought required	12	• Patients can be tempted to swallow early	7
	• Good for those with swallowing difficulties	10	• Patients may remove formulation from the mouth before it is fully dispersed leading to sub-therapeutic outcomes	6
	• No water required: easy to take	63	• Can leave residual and after-taste in the mouth	5
	• Convenient/quick when on the go	10	• Concerns on taste	54

Chewable tablets	• No water required: Easy to use	18	• Patients who wear dentures	5
	• Good for tablets which are too large and cannot be swallowed	5	cannot use.	
	• Good for those with swallowing difficulties	9	• Can get stuck in teeth – hard for those with dentures	6
	• It is sweet-like so does not appear as if you are taking a medicine	15	• Chewing time is long	36
			• Concerns on taste	12

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