BMJ Open

# Development and validation of the INappropriate solid oral dosaGE form modification aSsessmenT (INGEST) Algorithm using data of patients with medication dysphagia from a neurology ward and nursing home in Singapore

Poh Leng Tan ,[1] Wing Lam Chung ,[2] Grant E Sklar,[3] Kai Zhen Yap ,[1] Sui Yung Chan [1]

**To cite:** Tan PL, Chung WL, Sklar GE, *et al*. Development and validation of the INappropriate solid oral dosaGE form modification aSsessmenT (INGEST) Algorithm using data of patients with medication dysphagia from a neurology ward and nursing home in Singapore. *BMJ Open* 2022;**12**:e061774. doi:10.1136/bmjopen-2022-061774

► Prepublication history for this paper is available online. To view these files, please visit the journal online (http://dx.doi.org/10.1136/bmjopen-2022-061774).

Received 23 February 2022
Accepted 12 September 2022



[1]Department of Pharmacy, National University of Singapore, Singapore
[2]Pharmacy Department, Watson's Personal Care Stores Pte Ltd, Singapore
[3]Independent Pharmacist, Vancouver, British Columbia, Canada

**Correspondence to**
Dr Kai Zhen Yap;
phaykz@nus.edu.sg

## ABSTRACT

**Objectives** This study aims to develop and validate a novel implicit tool to assist clinicians in resource-limited settings to promptly assess suitability for modification of solid oral dosage forms (SODFs) during medication prescribing, review and/or administration for patients with dysphagia.

**Design** Literature review and a group discussion were conducted to elicit items for the construction of the INappropriate solid oral dosaGE form modification aSsessmenT (INGEST) algorithm. For its validation, inter-rater reliability among three independent users was evaluated. Accuracy of users' ratings was also evaluated against the screening results using the *Don't Rush to Crush* handbook.

**Setting and participants** Three pharmacists were involved in the development and another three were involved in the validation of the INGEST algorithm using anonymised medication records of 50 patients in a nursing home and a hospital ward; only SODFs that were modified prior to administration were evaluated.

**Results** Following literature review, considerations included by consensus in the INGEST algorithm were the presence of special coating or modified release characteristics of the SODF medications, hazardous nature and taste of the active ingredients, manufacturer's advice and use of tube feeding. Of the 381 SODF medications evaluated, 26 (6.8%) were identified by at least one pharmacist to be inappropriate for modification. Gwet's AC among the three pharmacists in identifying SODF medications inappropriate for modification was 0.75 ($p<0.001$, 95% CI 0.63 to 0.87), and 0.80 ($p<0.001$, 95% CI 0.71 to 0.89) in identifying SODF medications appropriate for modification, suggesting substantial inter-rater agreement. Overall accuracy of each pharmacist's ratings was high, ranging from 93.7% to 95.6%.

**Conclusions** The implicit INGEST algorithm has potential for use by clinicians in nursing home and hospital settings for determining suitability of SODF medications for modification. Further studies should be conducted to assess its external validity and utilisation in daily practice for improving clinical outcomes for patients with SODF dysphagia.

## STRENGTHS AND LIMITATIONS OF THIS STUDY

⇒ This is the first study that aimed to develop a tool to assist clinicians in resource-limited settings in identifying medications that are not suitable for modification, to ensure patient safety.
⇒ During the development of the INappropriate solid oral dosaGE form modification aSsessmenT (INGEST) algorithm, both quantitative and qualitative approaches were employed to bring about deep insights when eliciting items.
⇒ Pharmacists and anonymised records of patients from different care settings were used in this study, to ensure generalisability of the findings.
⇒ Further studies involving different healthcare professionals should be considered for the external validity of the INGEST algorithm.

## INTRODUCTION

Modification of solid oral dosage forms (SODFs) is performed regularly by nurses and caregivers.[1–3] It includes the crushing of tablets or emptying of capsule contents prior to administration.[4] This practice improves swallowability of SODFs in patients with dysphagia; however, it may negate the effectiveness and safety of the drug treatment. The destruction of modified-release characteristics of the SODFs may alter the intended pharmacokinetics of the drugs.[5] Exposure of drugs subsequent to the loss of enteric coating may lead to irritation of the gastrointestinal tract and premature drug degradation.[5] Exposure to light or moisture in the process of modification may also result in the degradation of

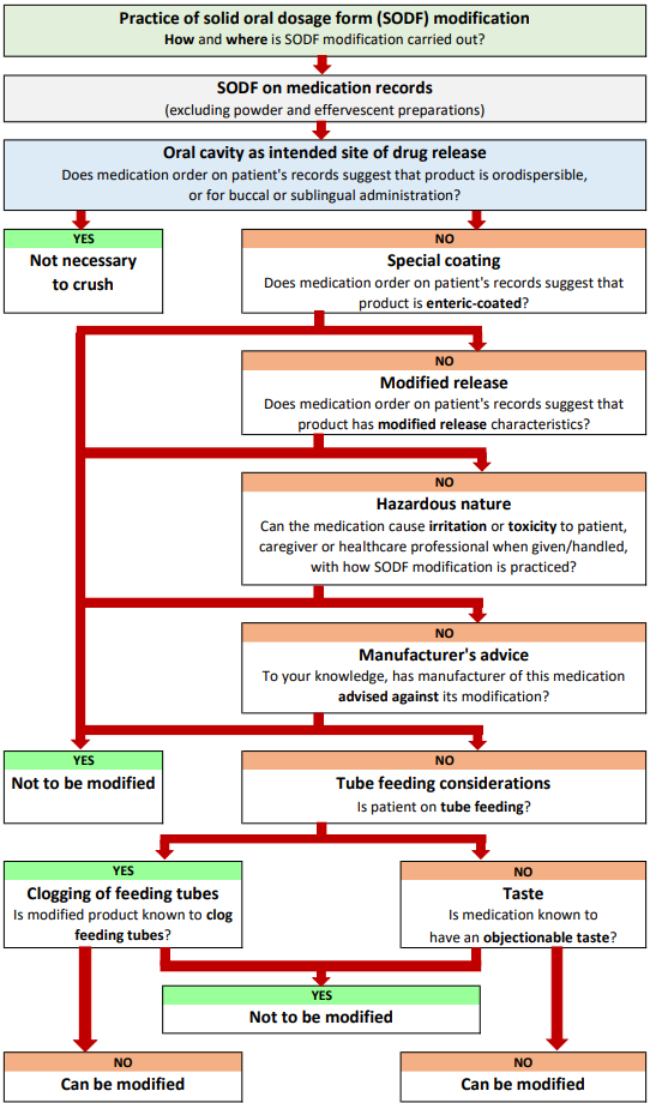


**Figure 1** The INGEST algorithm.

susceptible drugs.[5] Crushing of drugs with narrow therapeutic indices may lead to incomplete drug transfer and subsequent suboptimal doses being administered to patients.[6] Coadministration of crushed medications with enteral feeds or other food may lead to drug–food interactions.[7] Crushing of and/or administering a few SODF medications using the same utensils may lead to drug–drug interactions.[8] In addition, healthcare professionals (HCPs) or caregivers modifying SODFs without adequate protection may be exposed to hazardous drug effects.[5] Furthermore, they may face legal implications when SODFs are modified against manufacturers' recommendations or without prescribers' knowledge.[1]

Information on suitability for crushing or chewing is not a requirement on monographs of SODF medications,[9] and is hence not always available. Numerous explicit resources are available to provide information on drugs that are not suitable to be crushed. However, they present with several limitations. Most of them are not freely available or accessible; they require a paid subscription[10 11] or the purchase of print copies.[12–14] As a result, they are often out of reach of institutions or clinicians with limited budget. Users with access to these resources sometimes find the contents lengthy or not conclusive.[Teh, F. K., Final Year Project Report (2020). PT-5B Modification of Solid Oral Dosage Form: Pharmacists' Perspectives and Improving Care through Development of Guidance. Department of Pharmacy, National University of Singapore] Of the resources that are freely available, the information is not frequently updated or maintained,[15] covers a limited range of medications,[16–18] or is based on products that may not be available locally.[5 18 19]

Inadequate access to drug information during point of care can lead to errors.[20] There is a need to develop a tool to assist clinicians in promptly assessing the suitability of SODF modification during the medication use process encompassing the prescribing, dispensing, administering and monitoring steps.[21] Thus, the aim of this study was to develop and validate the inter-rater reliability and raters' accuracy of a judgment-based (ie, implicit) tool for use by HCPs in assessing the suitability of modifying SODF medications for administration among patients with dysphagia.

## METHOD

### Study design

#### Phase 1

Development of INappropriate solid oral dosaGE form modification aSsessmenT (INGEST) algorithm

Reasons precluding SODF modification ("considerations") were identified through review of common drug information references and resources, namely the British National Formulary (BNF) (79th Edition),[13] the Institute for Safe Medication Practices (ISMP) list of Oral Dosage Forms That Should Not Be Crushed (2020)[18] (ie, ISMP list) and the *Don't Rush to Crush Handbook* (3rd Edition) (ie, DRTC handbook).[19] During a group discussion among three pharmacist authors (TPL, YKZ and CSY), a consensus was reached on the considerations to be included in the algorithm. As patients requiring SODF modification may take medications orally or through enteral tubes, the selected considerations were further categorised based on patients' feeding needs. Finally, the INGEST algorithm was drawn up figure 1.

#### Phase 2

Validation of INGEST algorithm

##### *Sample size calculation and medication data*

To evaluate inter-rater reliability of the INGEST algorithm, cross-sectional de-identified active medication records of patients requiring oral medications to be crushed prior to administration (n=145) were obtained using convenience sampling from a nursing home and a hospital neurology ward. Each patient was assigned a number based on the randomised sequence of integers (1–145) generated on the website random.org.[22] Patients who had been assigned numbers 1–50 were included

in this study. Information on drug names, strengths, dosing frequencies and feeding status were collected for evaluation.

To detect Gwet's agreement coefficient (AC) value of 0.6 with relative error of 0.2, the necessary sample size was 41.[23] The number of patients included in this study met the minimum sample size required for inter-rater reliability analysis.

### *Application of the INGEST algorithm*

Three pharmacists (CWL, GS and TPL) independently applied the INGEST algorithm to the de-identified medication records of 50 patients. CWL and TPL, each had 9 years' experience performing medication reviews at different intermediate-term and long-term care institutions while GS had over 20 years' experience reviewing medications in an acute care hospital. These pharmacists were not employees of the nursing home or hospital where the data were obtained.

Only the SODF medications that had been modified prior to administration were reviewed by the three pharmacists for appropriateness of modification using the INGEST algorithm. Sublingual or orodispersible tablets as well as effervescent or powder formulations had been administered according to manufacturers' instructions without prior modification at both institutions; hence, they were not reviewed by the pharmacists.

When applying the INGEST algorithm, the pharmacists were not allowed to refer to any drug references or resources. Pertinent points related to institution-specific practices of SODF modification were taken into consideration. First, at both institutions, SODF modification had been performed by combining each patient's SODF medications and crushing them at bedside using electronic crushers or manually using the mortar-pestle. Second, contents of omeprazole capsules and esomeprazole tablets were suspended in liquid vehicles before being served to patients. Lastly, nurses did not put on any personal protection equipment (PPE) such as gloves or masks when preparing and administering the medications.

### *Accuracy of pharmacists' findings from the use of INGEST algorithm*

Each pharmacist's accuracy in assessing appropriateness of SODF modification using the INGEST algorithm was evaluated by comparing their ratings against screening based on the DRTC handbook[19] as the gold standard.

## Patient and public involvement

Patients or the public were not involved in the design, or conduct, or reporting, or dissemination plans of our research.

## Statistical analysis

The inter-rater agreement was calculated using Gwet's AC on consultation with a biostatistician. An agreement was considered only if the same medication(s) for a patient had been given the same rating by all three pharmacists in terms of their appropriateness for modification. In addition, pairwise agreements between the three pharmacists were also calculated and reported. The inter-rater agreement was considered substantial if it exceeded 0.61.[24] Microsoft Excel (Microsoft Office 365 ProPlus, Version 16.0.11929.20648) and STATA (StataCorp. 2019. Stata Statistical Software: Release 16. College Station, TX: StataCorp LLC) were used for data analysis.

Accuracy of pharmacists' findings on modified SODF medications was reported as percentage in relation to total number of SODF medications assessed, as well as percentage in relation to the unique SODF medication entries.

# RESULTS

## Inter-rater reliability

Of the 50 patients included in this study, 43 were from the nursing home and 7 were from the hospital neurology ward. These patients were taking a total of 509 SODF medications, of which 128 SODF medications in the forms of powders as well as effervescent, orodispersible or sublingual tablets and were administered as directed by manufacturers' instructions without being crushed, and thus were not reviewed by the pharmacists. The remaining 381 entries of SODF medications were pulverised prior to administration and the INGEST algorithm was applied by each pharmacist to evaluate their appropriateness for modification.

Twenty-six SODF medications (6.8% of 381 modified medications) were identified by at least 1 pharmacist to have been inappropriate for modification. The number of medications identified by each pharmacist to have been inappropriate for modification ranged from 12 to 18. Gwet's AC among the three pharmacists was 0.75 (p<0.001, 95% CI 0.63 to 0.87). Between CWL and TPL, Gwet's AC was 0.72 (p<0.001, 95% CI 0.56 to 0.88), between CWL and GS, Gwet's AC was 0.73 (p<0.001, 95% CI 0.57 to 0.880), and between TPL and GS, Gwet's AC was 0.75 (p<0.001, 95% CI 0.60 to 0.90). This suggests a substantial inter-rater agreement among the three pharmacists, and between each pair of pharmacists.

For medications deemed to be appropriate for modification, Gwet's AC among the three pharmacists was 0.80 (p<0.001, 95% CI 0.71 to 0.89). Between CWL and TPL, Gwet's AC was 0.83 (p<0.001, 95% CI 0.72 to 0.94), between CWL and GS, Gwet's AC was 0.79 (p<0.001, 95% CI 0.66 to 0.91), and between TPL and GS, Gwet's AC was 0.79 (p<0.001, 95% CI 0.66 to 0.91). There was substantial inter-rater agreement among the three pharmacists, and between each pair of pharmacists.

SODF medications deemed inappropriate for modification by all three pharmacists are presented in table 1, which included those with modified-release characteristics as well as those of hazardous nature (potential allergenic, gastrointestinal tract irritant, cytotoxic or teratogenic effects). Table 2 presents the SODF medications determined by one or two of the pharmacists to have

Table 1 Solid oral dosage form medications identified by all three pharmacists to have been inappropriate for modification

| Medications | No. of patients, (%) (n=50) |
|---|---|
| Modified-release products | |
| Gliclazide MR 60 mg tablet | 1 (2) |
| Sodium valproate 300 mg or 500 mg chrono tablets | 2 (4) |
| Products that may cause gastrointestinal tract irritation | |
| Alendronate 70 mg tablet | 1 (2) |
| Dutasteride/ tamsulosin 0.5 mg/0.4 mg capsule | 1 (2) |
| Risedronate 35 mg tablet | 1 (2) |
| Products with potential cytotoxic or teratogenic effect | |
| Letrozole 2.5 mg tablet | 1 (2) |
| Methotrexate 2.5 mg tablet | 1 (2) |
| Total | 8 (16) |

been inappropriate for modification, and the respective reasons. Anti-infectives were assessed by one pharmacist to have potential hazardous effects to patients or caregivers when modified. Another pharmacist had, based on prior knowledge, identified several products deemed by manufacturers to be unsuitable for crushing although the reasons had not been provided in the product leaflets.

Table 2 Solid oral dosage form medications identified by one or two of the three pharmacists to be inappropriate for modification

| Medications | Reasons |
|---|---|
| Identified by any two of three pharmacists | |
| Entecavir 0.5 mg tablet | Hazardous product |
| Isosorbide mononitrate 60 mg CR tablet | Modified-release product |
| Phenytoin 100 mg capsule | Hazardous product<br>Extended-release formulation |
| Identified by any one of three pharmacists | |
| Amoxicillin/ clavulanic acid 625 mg capsule | Hazardous product |
| Doxycycline 100 mg capsule | Hazardous product |
| Fenofibrate 100 mg capsule | Pharmacist's knowledge that crushing is not recommended as per manufacturer's leaflet |
| Iron polymaltose 100 mg tablet | Pharmacist's knowledge that drops are recommended alternatives by manufacturer when crushing is needed |
| Levetiracetam 250 mg tablet | Objectional taste (patient on oral administration) |
| Levodopa/ benserazide 125 mg capsule | Pharmacist's knowledge that crushing is not recommended as per manufacturer's leaflet |
| Omega-3 fish oil capsule | Objectional taste/smell |
| Vitamin $B_1$ 100 mg, $B_6$ 200 mg, $B_{12}$ 200 µg tablet | Pharmacist's knowledge that crushing is not recommended as per manufacturer's leaflet |

### Accuracy of pharmacists' findings against the DRTC Handbook

Of the 381 SODF medications that were modified prior to administration, 15 could not be screened using the DRTC handbook as their monographs were not available in the DRTC handbook. Among the rest of the 366 SODF medications screened using the DRTC handbook, 31 (8.5%) were found to have been inappropriate for modification, while the remaining 335 (91.5%) were appropriate for modification. In contrast, 21 (6.3% of 366) SODF medications were identified by at least 1 pharmacist to have been inappropriate for modification, and 358 (97.8%) as appropriate for modification by applying the INGEST algorithm.

The 366 entries of SODF medications consisted of 94 unique SODF medications. Based on the screening using the DRTC handbook, 18 (19.1%) were found to have been inappropriate for modification and 76 (80.9%) deemed appropriate for modification. On the other hand, 18 (19.1%) unique SODF medication had been identified by at least 1 pharmacist to have been inappropriate for modification and 86 (91.5%) as appropriate for modification.

Overall accuracy of each pharmacist's ratings when compared against the DRTC handbook screening results ranged from 93.7% to 95.6% of the 366 entries of SODF medications, or 87.2%–92.6% of the 94 unique SODF medications. Of the 31 SODF medications identified by the DRTC handbook to be inappropriate for modification, pharmacists accurately detected 35.5%–48.4% of them using the INGEST algorithm. Of the 18 unique SODF medications identified by the DRTC handbook to be inappropriate for modification, 50%–61.1% of them were accurately detected by the pharmacists. In terms of accuracy in detecting SODF medications appropriate for modification, the pharmacists accurately identified 99.1%–100% of the 335 SODF medication according to the DRTC handbook, and 96%–100% of the 76 unique SODF medications. SODF medications found to have been inaccurately rated by at least 1 pharmacist are summarised in table 3.

## DISCUSSION

The INGEST algorithm is the first implicit tool developed to guide pharmacists, nurses and prescribers in assessing the suitability for SODF modification. It takes into consideration the physical attributes of SODFs, as well as feeding status of patients, based on review of current drug references and resources. Substantial inter-rater agreement for the INGEST algorithm was established in this study, regardless of users' backgrounds. This suggests the relevance of the INGEST algorithm to health professionals at different practice settings.

Table 3 Medications found to have been inaccurately rated by pharmacists

| Medications | Pharmacists' ratings (n=3) | Rating from DRTC handbook | Reason(s)[19] |
|---|---|---|---|
| Inaccurately rated by two or more pharmacists | | | |
| Carbamazepine 200 mg tablet | Appropriate (3) | Inappropriate | Hazard (for pregnant handlers) |
| Amoxicillin/ clavulanic acid 625 mg capsule | Appropriate (2)<br>Inappropriate (1) | Inappropriate | Hazard (irritant); mask and gloves should be worn |
| Doxycycline 100 mg capsule | Appropriate (2)<br>Inappropriate (1) | Inappropriate | Hazard (irritant); mask and gloves should be worn |
| Enalapril 10 mg tablet | Appropriate (3) | Inappropriate | Hazard (for pregnant handlers) |
| Olanzapine 5 mg or 10 mg tablet | Appropriate (3) | Inappropriate | Hazard (irritant); mask, gloves and glasses should be worn |
| Paroxetine 20 mg tablet | Appropriate (3) | Inappropriate | Hazard (for pregnant handlers) |
| Spironolactone 25 mg tablet | Appropriate (3) | Inappropriate | Hazard (multiple reasons); mask and gloves should be worn |
| Inaccurately rated by one pharmacist | | | |
| Entecavir 0.5 mg tablet | Appropriate (1)<br>Inappropriate (2) | Inappropriate | Hazard (irritant); mask and gloves should be worn |
| Iron polymaltose 100 mg tab | Inappropriate (1)<br>Appropriate (2) | Appropriate | – |
| Isosorbide mononitrate CR 60 mg tablet | Appropriate (1)<br>Inappropriate (2) | Inappropriate | Modified release preparation |
| Levetiracetam 250 mg tablet | Inappropriate (1)<br>Appropriate (2) | Appropriate | – |
| Levodopa/ benserazide 125 mg capsule | Inappropriate (1)<br>Appropriate (2) | Appropriate | – |

The INGEST algorithm prompts users to seek out necessary information from a range of sources (including patients, caregivers, other HCPs, product packaging and inserts) and carefully assess it before determining suitability for SODF modification. Table 4 summarises possible information sources. For example, it starts by asking users to consider institution-specific practices of SODF modification (figure 1). Such information can be obtained from nursing staff or caregivers directly involved in the preparation of SODF medications for administration to patients. SODFs that undergo modification are then evaluated based on characteristics such as the presence of special coatings and modified-release profiles, which may already be reflected on medication records or labels, or otherwise product packaging or inserts. By asking users about awareness of manufacturers' advice against modification, the INGEST algorithm prompts users to consider other possible reasons precluding SODF modification and confirm against product inserts, if necessary. Finally, in the process of identifying crushed medications that may clog feeding tubes or are bitter when orally administered, users of the INGEST algorithm may approach nurses or caregivers who can add on to users' knowledge of challenges in SODF medication administration.

Table 4 Possible sources of information when applying the INGEST algorithm

| Required information | Possible sources |
|---|---|
| Institution-specific practices of SODF modification | Nurses or caregivers |
| Oral cavity as intended site of drug release | Patient medication records<br>Prescriptions |
| Presence of special coating, modified release characteristics, | Patient medication records<br>Product packaging/label<br>Product inserts |
| Hazardous nature of the drug | Drug references<br>Product inserts |
| Manufacturer's advice | Product inserts |
| Tube feeding status | Patient records<br>Nurses or caregivers |
| Taste | Patients, nurses or caregivers<br>Drug references<br>Product inserts |

INGEST, INappropriate solid oral dosaGE form modification aSsessmenT; SODF, solid oral dosage form.

When asking users about the hazardous nature of SODF medications, the INGEST algorithm allows users to exercise professional judgement with respect to the significance of implications from inappropriate SODF modification in view of institution-specific practices of SODF modification. As such, findings differ among users. For instance, as seen in table 2, one out of the three pharmacists had deemed antibiotics to be inappropriate for modification due to exposure of nurses and other patients to potential hazardous effects during bedside crushing; however, the other two pharmacists did not agree as they opined that such a risk was minimal. According to drug references and resources,[13 18 19] there was no explicit mention about amoxicillin/clavulanic acid capsule or doxycycline tablet being not recommended for modification; however their hazardous nature is highlighted

and the use of PPE during modification is advised.[19] Similarly, one pharmacist had found omega-3 fish oil capsule to be unsuitable for modification due to the unmasking of objectionable taste or smell during administration, which can affect adherence; however, the other two pharmacists disagreed as the patient was on tube feeding and would not be affected by the unmasking of fishy odour. In drug references and resources, information about the suitability of fish-3 fish oil capsule for modification is not available for the triglyceride form,[13 18 19] which the patient in this study was using.

While three drug resources and references[13 18 19] were used to gather reasons precluding SODF modification for the construction of the INGEST algorithm, only the DRTC handbook was used to as the gold standard to evaluate accuracy of pharmacists' findings. This was because the DRTC handbook was the most comprehensive among the three drug resources and references, with monographs dedicated to each drug in SODF; information on their suitability for modification, and recommendations on how to modify was provided.[19] The ISMP list[18] included only SODFs that should not be modified. The list is limited to medications available in North America and it should not be assumed that medications that do not appear on the list are suitable for modification. The BNF[13] provides general reasons against SODF modification, but suitability for modification is not explicitly mentioned for each drug entry.

It was demonstrated that the pharmacists' overall ratings of the modified SODF medications, on application of the INGEST algorithm, was highly accurate in comparison with the screening using DRTC handbook. This was likely contributed by the accurate identification of SODF medications that were appropriate for modification. Pharmacists' accuracy in identifying SODF medications that would be inappropriate for modification was lower. In particular, SODF medications with hazardous nature were inaccurately rated by at least two pharmacists to be appropriate for modification. There are two reasons to explain this finding. First, in the case of carbamazepine, olanzapine, paroxetine and spironolactone, the pharmacists were not cognisant of the potential irritant or teratogenic effects of these SODF medications on modification as such facts are not widely known. Indeed, warnings about modifying these drugs were not reflected in other drug references or resources,[13 15 18] with the exception of the NIOSH list[16] which the DRTC handbook drew reference from. Second, in the case of antibiotics, the pharmacists were aware of the risks of modifying these SODF medications, but two of them did not consider the act to present significant harm to patients and nurses. It should be noted that these SODF medications could in fact be modified, provided that appropriate PPE had been worn to protect nurses and caregivers from their potential hazardous effects.[19] Other safety measures, such as ensuring that pregnant staff and those trying to conceive were not involved in SODF modification, were also not implemented, and could have provided an additional reminder to protect against exposure to occupational hazards.

Entecavir, iron polymaltose, isosorbide mononitrate CR, levetiracetam and levodopa/benserazide tablets were found to have been inaccurately rated by one pharmacist (table 3) to be appropriate for modification when the DRTC handbook was used as the gold standard. Entecavir and isosorbide mononitrate CR tablets were inaccurately rated due to pharmacists' oversight. In the case of iron polymaltose and levodopa/benserazide tablets, locally available product inserts[25 26] recommended swallowing of whole tablets (reasons not provided), although they were deemed by the DRTC handbook to be appropriate for modification. For levetiracetam tablet, the ISMP list[18] advised against its modification on the account of objectional taste; however, it was deemed appropriate for modification by the DRTC handbook.

Evidently, there are incomplete information and conflicting recommendations between different drug references and resources, and HCPs may risk giving inaccurate advice by relying on a single drug reference or resource. Yet, during medication review, it may be time consuming and impractical to consult several drug references and resources to determine suitability of SODF modification. By drawing key reasons precluding SODF modification from a range of drug references and resources, the INGEST algorithm draws users' attention to crucial considerations when deciding suitability of SODF modification, to ensure drug efficacy and safety for patients, nurses and caregivers.

Nonetheless, there are two methodological limitations in this study. First, medication records used for the validation study were purposively obtained from two groups of patients with geriatric preponderance, and who were more likely to have polypharmacy and dysphagia. However, this could have limited the scope of medications reviewed. The validity and usefulness of INGEST algorithm among other patient populations such as infants and young children who would also require SODF modification could be evaluated in future studies. Second, only experienced pharmacists were involved in the validation of the INGEST algorithm. While high accuracy of the pharmacists' ratings using the INGEST algorithm was reported, the same could not be concluded for other HCPs or less experienced pharmacists. Further studies should be undertaken to evaluate INGEST algorithm's external validity and effectiveness in clinical practice in improving health outcomes for patients with dysphagia.

## CONCLUSION

The INGEST algorithm is a validated implicit tool to guide health professionals in assessing suitability for SODF modification. It has been developed through a compilation of common reasons against SODF modification with consensus among authors. When the INGEST algorithm was applied, findings by the three pharmacists were highly consistent, demonstrating a substantial inter-rater

agreement. Overall accuracy of the pharmacists' findings was also high when compared against the DRTC handbook. Further studies on its external validity and utilisation in daily practice for improving clinical outcomes for patients with SODF dysphagia should be considered.

**Acknowledgements** We would like to thank Dr Chan Yiong Huak for the help rendered in the statistical analysis of the findings.

**Contributors** Study concept and design: KZY and SYC. Acquisition of data: PLT. Analysis and interpretation of data: PLT, GES and WLC. Drafting of the manuscript: PLT. Critical revision of the manuscript for important intellectual content: all authors. Final approval and gurantors: PLT, KZY, SYC

**Funding** This research is supported by the "Singapore Ministry of Education Academic Research Fund" Tier 1 (R-148-000-311-114).

**Competing interests** None declared.

**Patient and public involvement** Patients and/or the public were not involved in the design, or conduct, or reporting, or dissemination plans of this research.

**Patient consent for publication** Not applicable.

**Ethics approval** Ethics approval was granted for collection of patient data (N-19-044) by the Institutional Review Board of National University of Singapore. Participants gave informed consent to participate in the study before taking part.

**Provenance and peer review** Not commissioned; externally peer reviewed.

**Data availability statement** Data are available upon reasonable request. Data are available upon reasonable request. Deidentified patient medication records used in this study may be obtained from Tan Poh Leng (ORCID ID 0000-0001-8950-7737) for further studies on the INGEST algorithm.



**ORCID iDs**
Poh Leng Tan http://orcid.org/0000-0001-8950-7737
Wing Lam Chung http://orcid.org/0000-0002-3867-4751
Kai Zhen Yap http://orcid.org/0000-0002-8440-0313
Sui Yung Chan http://orcid.org/0000-0001-5941-6797

## REFERENCES

1 Wright D. Medication administration in nursing homes. *Nurs Stand* 2002;16:33–8.
2 Stubbs J, Haw C, Dickens G. Dose form modification - a common but potentially hazardous practice. A literature review and study of medication administration to older psychiatric inpatients. *Int Psychogeriatr* 2008;20:616–27.
3 Logrippo S, Ricci G, Sestili M, *et al*. Oral drug therapy in elderly with dysphagia: between a rock and a hard place! *Clin Interv Aging* 2017;12:241–51.
4 Richey RH, Shah UU, Peak M, *et al*. Manipulation of drugs to achieve the required dose is intrinsic to paediatric practice but is not supported by guidelines or evidence. *BMC Pediatr* 2013;13:81.
5 SafeRx. Guide for crushing oral medication for residents with swallowing difficulties in residential aged care New Zealand: Waitemata District Health Board, 2018. Available: https://www.saferx.co.nz/assets/Documents/c35d9e078f/RAC_crushing_guide.pdf [Accessed 27 Nov 2021].
6 Shah RB, Collier JS, Sayeed VA, *et al*. Tablet splitting of a narrow therapeutic index drug: a case with levothyroxine sodium. *AAPS PharmSciTech* 2010;11:1359–67.
7 Nunn THS. Report for who on findings of a review of existing guidance/advisory documents on how medicines should be administered to children, including General instructions on compounding preparations and manipulation of adult dosage forms.: World Health Organization,, 2011. Available: https://www.who.int/medicines/areas/quality_safety/quality_assurance/Review-findings-PaediatricMedicnesAdmin_QAS11-400Rev1_22082011.pdf [Accessed 27 Nov 2021].
8 Clauson H, Rull F, Thibault M, *et al*. Crushing oral solid drugs: assessment of nursing practices in health-care facilities in Auvergne, France. *Int J Nurs Pract* 2016;22:384–90.
9 Truong-Le V, Lovalenti PM, Abdul-Fattah AM. Stabilization challenges and formulation strategies associated with oral biologic drug delivery systems. *Adv Drug Deliv Rev* 2015;93:95–108.
10 Do not crush list: IBM Micromedex, 2020. Available: https://www-micromedexsolutions-com.libproxy1.nus.edu.sg/micromedex2/librarian/CS/6A5D57/ND_PR/evidencexpert/ND_P/evidencexpert/DUPLICATIONSHIELDSYNC/DA75BB/ND_PG/evidencexpert/ND_B/evidencexpert/ND_AppProduct/evidencexpert/ND_T/evidencexpert/PFActionId/evidencexpert.IntermediateToDocumentLink?docId=1174&contentSetId=50&title=Do+Not+Crush+List&servicesTitle=Do+Not+Crush+List [Accessed 27 Nov 2021].
11 UpToDate: Wolters Kluwer, 2020. Available: https://www.uptodate.com/contents/search [Accessed 27 Nov 2021].
12 Sansom L. *Australian Pharmaceutical Formulary and Handbook: Pharmaceutical Society of Australia*, 2015.
13 Formulary CJ. *British National Formulary*. 2020. 79th Ed. Pharmaceutical Press, 2020.
14 White RBV. *Handbook of Drug Administration Via Enteral Feeding Tubes*. 3rd Ed. Pharmaceutical Press, 2015.
15 Chan C, Wee A, Leung K. Do not crush list Singapore. Available: https://www.meshlist.net/ [Accessed 27 Nov 2021].
16 NIOSH list of antineoplastic and other hazardous drugs in healthcare settings: Department of Health and Human Services,, 2016. Available: https://www.cdc.gov/niosh/docs/2016-161/pdfs/2016-161.pdf?id=10.26616/NIOSHPUB2016161[Accessed 27 Nov 2021].
17 Meadows T. What injections can be given enterally?: specialist pharmacy service. *United Kingdom Medicines Information* 2020 https://www.sps.nhs.uk/articles/what-injections-can-be-given-enterally/
18 Oral Dosage Forms That Should Not Be Crushed. Institute for Safe Medication Practices, 2018. Available: https://www.ismp.org/recommendations/do-not-crush [Accessed 27 Nov 2021].
19 Australian Don't Rush to Crush Handbook. *3Rd Ed: The Society of Hospital Pharmacists of Australia*, 2019.
20 Lesar TS, Briceland L, Stein DS. Factors related to errors in medication prescribing. *JAMA* 1997;277:312–7.
21 Institute of Medicine. *Preventing medication errors. Washington*. DC: The National Academies Press, 2007: 1–6.
22 Randomness and Integrity Services Ltd. Available: https://www.random.org/sequences/ [Accessed 20 Jan 2021].
23 TEMEL G, Erdogan S. Determining the sample size in agreement studies. *Marmara Medical Journal* 2017;30:101–12.
24 Landis JR, Koch GG. The measurement of observer agreement for categorical data. *Biometrics* 1977;33:159–74.
25 Consumer Medicine Information Maltofer Tablet. Vifor pharma, 2015. Available: https://www.maltofer.com.au/wp-content/uploads/2016/08/maltofer_cmi_document_2015.pdf [Accessed 18 Jun 2022].
26 . Madopar® Levodopa+ benserazide: F. Hoffmann-La Roche LTD; 2019.