

**PILL SPLITTING A RISKY PRACTICE.**

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**ABSTRACT**

The splitting of scored tablets provides a lot of advantages. One advantage is to realize dose flexibility to account for the vast interindividual differences in dose requirements for example in paediatric and geriatric patients, which are often not covered by the existing strengths in the market. Moreover, large-sized tablets can easier be swallowed if broken down before swallowing and tablets costs can often be reduced by splitting brands with higher potency. But not all tablets, mostly unscored tablets, are appropriate for splitting.

Splitting of extended release formulations can effect in an overdose by uncontrolled release of the active constituent and degradation of the compound can arise if an enteric coating is damaged by the splitting process. Whether tablets are appropriate for splitting depends on the properties of the active constituent (e.g. light sensitivity), the galenics, the shape of the tablet, and the profile of the scoreline. Furthermore, not all patients are informed, able, or willing to divide tablets and the majority of the elderly population is not able to break tablets. When split tablets are prescribed it is therefore essential to examine the shape of the tablet, to assess the patients capability and willingness to split tablets, to properly inform the patient about the suitable ways of splitting, and if essential to recommend the use of a tablet splitting device. Patients should be cautioned not to split or break a medicine without checking by means of the health care provider or pharmacist.

**KEYWORDS:** The galenics, the shape of the tablet, and the profile of the scoreline.

**INTRODUCTION**

Tablets are usually split by patients on oral medication treatment, which is a method which may have a few points of interest. It is possible that, it might bolster measurements adaptability, ease gulping, or spare expense. Be that as it may, not all tablets (and basically

not unscored tablets) are appropriate for part. Part of altered discharge tablets may change the impact of a medication and in this way make threat patients wellbeing and breaking point effectiveness. Consequently, unmistakable methods must be taken to maintain a strategic distance from the part of tablets not appropriate for part. A noteworthy point of preference is to accomplish dosage adaptability to represent the impressive interindividual contrasts in measurement prerequisites, for case, in pediatric and geriatric patients, for whom appropriate qualities are frequently not accessible available.<sup>[1,2,3]</sup> It might likewise happen that medications have been distinguished as profitable in signs other than those endorsed by the powers (off mark use) and at lesser measurements than the current qualities, making tablet part an essential assurance venture in such regimens. A significant illustration is the treatment of congestive heart disappointment with spironolactone, which results in unnecessary poisonous quality when in place tablets (whose quality much of the time surpasses the prescribed 25 mg) are taken.<sup>[4]</sup> The part of tablets may prompt unequal breakdown, on the grounds that numerous score lines as of now prompt inadequately reproducible part comes about<sup>[5, 6]</sup> and in light of the fact that numerous patients can't part even scored tablets.<sup>[7]</sup> Essential explanation behind tablet part might be that the accessible dosages fit inadequately to the every day measurements affirmed for a noteworthy sign.<sup>[8]</sup> The division of dynamic medication in an entire tablet and its potential for disintegrating or breaking unequally are identified with medication producing quality certification measures. In one study, utilizing close infrared spectroscopic imaging, vast bunches of dynamic fixing were found in simvastatin tablets fabricated in 4 nations by resultant producers, however not in tablets made by Merck in the US.<sup>[9]</sup> A cutting edge audit found that the utilization of split tablets did not appear to impact the clinical results of patients with hypertension, hyperlipidemia or psychiatric issue.<sup>[10]</sup> The outline of part tablets has fixated on patients utilizing a gadget to split their medication costs. Wellbeing back up plans in the USA are bit by bit additionally asking patients to purchase higher-quality tablets and taking half at once. The American Medical Association and APhA formally contradict obligatory tablet part. Done accurately, part solution tablets can spare cash. Done inaccurately, the practice can make risk quiet wellbeing. The Strategic Directions Committee (SDC) evaluated the displayed writing and contribution from specialists in regards to the effect of the part of tablets on patient consideration.<sup>[11]</sup> Tablet part is likewise utilized as a part of drug store rehearse with a specific end goal to rectify the dosage to be managed. Part is likewise being pushed as a method for lessening doctor prescribed medication costs.<sup>[12]</sup> Scored tablets are regularly part to make conceivable gulping. In the last case, the pieces of the tablet ought to satisfy with the

substance or mass consistency prerequisites of the European Pharmacopeia. For wellbeing experts the data is relied upon to be in the Summary of Product Characteristics (SPCs), the bundle pamphlets (PLs) or Hospital Drug Formularies.<sup>[13]</sup> Cases ought not be part as the base of the highest point of the case. The study delighted that the patient would acknowledge around 75% of the measurement when given the base of the container and around 25% of the dosage when given the highest point of the case.<sup>[14-15]</sup> Tablet part strategies could bring about vacillations in the manage dosage that can be clinically imperative especially for pharmaceuticals with tight helpful files.<sup>[16]</sup> Pill-part happens generally in long haul care offices additionally has suggestion for more seasoned people groups who are as yet living in the group.<sup>[17]</sup> Most of the studies connected with tablet part uncover huge changes in weight/measurement, however few studies assess variability with tight restorative file solutions. In spite of the fact that tablet part can possibly keep patients and medicinal services associations a lot of cash, reasonableness of tablet part ought to be resolved for individual prescriptions and individual patients.<sup>[18]</sup> Part of prescriptions, for example, broadened discharge tablets are unsafe and might be exceptionally risky.<sup>[19]</sup> Measurements variety surpassed an intermediary USP detail for more than 33% of examined half-tablets of warfarin sodium, metoprolol succinate, and lisinopril and seemed, by all accounts, to be more noteworthy for non-scored tablets as contrasted and scored tablets.<sup>[20]</sup>

The division of tablets into two parts additionally gives huge impacts on their medication discharge conduct, and may likewise recommend a significant understanding into the correct utilization of pharmaceutical items.<sup>[21]</sup> Tablet part conveys a danger of mistakes because of misinterpretation of the solution or name guidelines by the drug specialist or patient, separately. By and by, where actualized precisely and with the suitable directing, tablet part does not trade off patient recognition and fulfillment or clinical results contrarily and this was particularly affirmed for statins.<sup>[22]</sup> Because of prudent reasons the specialists are progressively recommending tablets with a similarly high substance of the dynamic fixing, which should then be partitioned by the patient to give singular measurements. Nonetheless, precise dosing must be guaranteed by skilful division. For this, patients need predictable guidelines for part tablets.<sup>[23]</sup> the properties of the dynamic fixing and the galenic type of the arrangement must be considered keeping in mind the end goal to judge whether it is conceivable to separate a tablet without issues, it is obligatory to consider both. Separating of tablets is especially troublesome in postponed activity arrangements and enteric covered plans.<sup>[24]</sup> The part of scored tablets gives numerous preferences. In any case, not all tablets,

for the most part unscored tablets, are fitting for part. Part of expanded discharge details can bring about an overdose by uncontrolled arrival of the dynamic segment and debasement of the compound can happen if an enteric covering is demolished by the part procedure. Whether tablets are appropriate for part taking into account the properties of the dynamic constituent (e.g. light affectability), the galenics, the state of the tablet, and the state of the scoreline. At the point when part tablets are recommended it is in this manner key to see the state of the tablet, to assess the patient's capacity and ability to break tablets, to legitimately illuminate the patient about the fitting method for part, and if important to propose (and teach) the utilization of a tablet part gadget.<sup>[25]</sup> The part of scored tablets gives a ton of points of interest. In pediatric and geriatric patients part may prompt accomplish dosage adaptability to represent the boundless between individual contrasts in measurement necessities, which are regularly not encased by the accessible qualities in the business sector. Extensive estimated tablets can be gulped effortlessly subsequent to part before gulping and cost of pharmaceutical can frequently be diminished by part. However, not all tablets, for the most part unscored tablets, are proper for part. The tablets are reasonable for part relies on upon the properties of the dynamic segment (e.g. light affectability), the galenics, the state of the tablet, and the state of the scoreline. All patients are not educated, competent or willing to part tablets and usually the elderly populace is not capable of breaking tablets. At the point when part tablets are endorsed it is in this manner imperative to see the state of the tablet, to survey the patient's capacity and ability to break tablets, to legitimately educate the patient about the suitable method for part, and if important to inform the utilization concerning a tablet part gadget.<sup>[26]</sup> Digoxin, phenobarbital and prednisolone tablet part delivers exceedingly weight variable half-tablets.<sup>[27]</sup> Unscored tablets couldn't be always separated, however even where scoring was given, it was not associated with more perfect part.<sup>[28]</sup> Extensive dosage deviations or weight misfortunes can happen while part tablets. On the premise of the outcomes in this report, we recommend the utilization of a part gadget when part is required.<sup>[29]</sup> Part unseemly medicines, for example, developed discharge tablets can be unsafe and now and again are exceptionally hazardous. Notwithstanding part prescriptions, more seasoned grown-ups who experience issues gulping pills may likewise squash the pharmaceutical for simplicity of organization. It ought to be encouraged to the patients not to part or pulverize a prescription until and unless in the wake of checking with the medicinal services supplier or drug specialist.<sup>[30]</sup> Pill-part can be utilized to spare cash. Part of 10 mg tablets permit the patient to pay for a large portion of the measure of tablets at a lower cost than the same weight of 5 mg tablets.<sup>[31]</sup> Not all tablets split similarly well. In 2002 study,

Paxil, Zestril and Zolofit was totally part without disposes of. Glyburide displayed extremely poor part with numerous part into a few pieces. Hydrodiuril and Oreticcrumbled. Lipitor did not part neatly and the covering peeled.<sup>[32, 33]</sup> Some tablets break down on endeavoring to part them. Part of tablets likewise gives dosage adaptability, simple to swallow and may likewise diminish the expenses of prescription. Diverse potential outcomes to reduction breaking troubles are breaking guidelines, tablet-splitters and softening up development. Expansive number of components influencing the execution of score lines including shape, size, arch and thickness of the tablet and the structure and gravity of the score line. Execution of score lines can be effortlessly controlled by breaking effortlessness, identicalness of mass of subdivided tablets and loss of mass by the division. European Pharmacopeia gives the cutoff points to the consistency of mass of subdivided tablets. Loss of mass after breaking can be under 1%.<sup>[34]</sup>

## METHODOLOGY

Tablet splitting practice observed for many years as a way of obtaining the prescribed dose of a medication. Patients may be required to split tablets in order to obtain the required dosage form if the required strength is unavailable. Elderly people or children who need reduced doses may not be capable to use liquid formulations. If appropriate low-dose tablet formulations are not available, these patients may need tablets to be split to obtain the appropriate dosage. Patients may possibly save money if there is a cost differential that makes halving tablets economically attractive. However, the procedures of splitting tablets cause numeral problems, some of which are patient-related while others are related to formulations of tablets.

The present research comprises of survey among group of peoples resident in educated areas of Karachi in order to examine awareness of peoples about different hazards arising due to splitting tablets. The survey research was conducted amongst different categories of peoples among the age of 20-50 and examine the awareness of tablet splitting in different population. A survey form based on tablet splitting a risky practice were filled up to approximately 250 peoples and statistical data was conducted in order to achieve that how many peoples are aware about tablet splitting.

## RESULTS

<b>HAVE YOU EVER USED TABLET DOSAGE FORM</b>					
		<b>Frequency</b>	<b>Percent</b>	<b>Valid Percent</b>	<b>Cumulative Percent</b>
Valid	YES	200	100.0	100.0	100.0

<b>WHAT YOU HAVE DONE IF YOU STILL WANT TO SPLIT A TABLET</b>					
		<b>Frequency</b>	<b>Percent</b>	<b>Valid Percent</b>	<b>Cumulative Percent</b>
Valid	BREAK INTO A TWO HALVES IN MIDD	7	3.5	3.5	3.5
	BREAK INTO TWO HALVES IN THE MI	134	67.0	67.0	70.5
	USE A KNIFE OR A CUTTER	6	3.0	3.0	73.5
	USE WATER TO SOFTEN THEM IN ORD	53	26.5	26.5	100.0
	Total	200	100.0	100.0	

<b>DO YOU HAVE ANY IDEA THAT ALL PILL ARE NOT SAFE TO SPLIT</b>					
		<b>Frequency</b>	<b>Percent</b>	<b>Valid Percent</b>	<b>Cumulative Percent</b>
Valid	NO	140	70.0	70.0	70.0
	YES	60	30.0	30.0	100.0
	Total	200	100.0	100.0	

<b>HAVE YOU EVER USED DAILY DOSING CONTAINER?</b>					
		<b>Frequency</b>	<b>Percent</b>	<b>Valid Percent</b>	<b>Cumulative Percent</b>
Valid	NO	107	53.5	53.5	53.5
	YES	93	46.5	46.5	100.0
	Total	200	100.0	100.0	

<b>DO YOU READ MEDICINE LABELS AND FOLLOW DIRECTIONS BEFORE USING TABLETS ?</b>					
		<b>Frequency</b>	<b>Percent</b>	<b>Valid Percent</b>	<b>Cumulative Percent</b>
Valid	NO	74	37.0	37.0	37.0
	YES	126	63.0	63.0	100.0
	Total	200	100.0	100.0	

<b>STUDIES HAVE SHOWN THAT THE ACTUAL DOSE IN EACH HALF OF A SPLIT TABLET OFTEN IS DIFFERENT. DO YOU AGREE ABOUT THIS ?</b>					
		<b>Frequency</b>	<b>Percent</b>	<b>Valid Percent</b>	<b>Cumulative Percent</b>

Valid	AGREE	91	45.5	45.5	45.5
	DISAGREE	53	26.5	26.5	72.0
	STROONGLY AGREE	56	28.0	28.0	100.0
	Total	200	100.0	100.0	

**PILL SPLITTING MAY BE A PERSON'S ONLY OPTION DUE TO FINANACIAL CONSTRAINTS .FOR EXAMPLE, A 90 SUPPLY COULD LAST FOR SIX MONTHS IF THE PILLS ARE SPLIT.DO YOU AGREE ABOUT IT ??**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	AGREE	62	31.0	31.0	31.0
	DISAGREE	78	39.0	39.0	70.0
	STROONGLY AGREE	60	30.0	30.0	100.0
	Total	200	100.0	100.0	

**EXTENDED RELEASE COATED TABLETS CAN'T BE SPLIT. DO YOU HAVE ANY INFORMATION ABOUT IT ?**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NO	118	59.0	59.0	59.0
	YES	82	41.0	41.0	100.0
	Total	200	100.0	100.0	

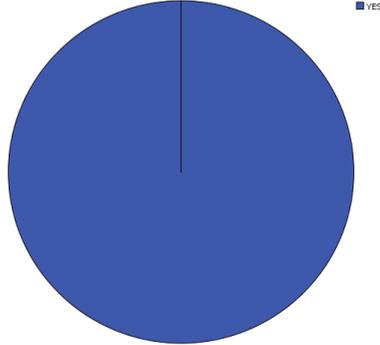
**DO YOU KNOW SOME PILLS MAY DETERIOTE WHEN EXPOSED TO AIR AND MOISTURE FOR LONG PERIODS AFTER BEING SPLIT ?**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	NO	72	36.0	36.0	36.0
	YES	128	64.0	64.0	100.0
	Total	200	100.0	100.0	

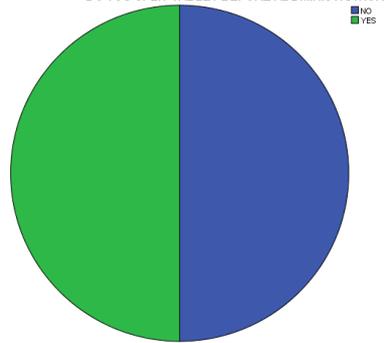
**BY REDUCING THE COST OF PRESCRIPTION MEDICINES, PILL SPLITTING COULD IMPROVE HEALTH OUTCOMES BY HELPING PEOPLE AFFORD THE DRUGS THEY NEED AND COMPLY WITH THE DRUG REGIMENS THEIR DOCTORS RECOMMAND?**

		Frequency	Percent	Valid Percent	Cumulative Percent
Valid	AGREE	84	42.0	42.0	42.0
	DISAGREE	100	50.0	50.0	92.0
	STROONGLY AGREE	16	8.0	8.0	100.0
	Total	200	100.0	100.0	

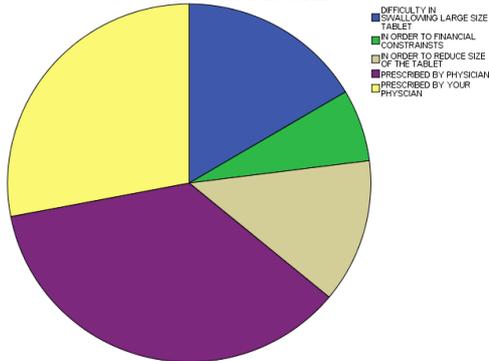
HAVE YOU EVER USED TABLET DOSAGE FORM



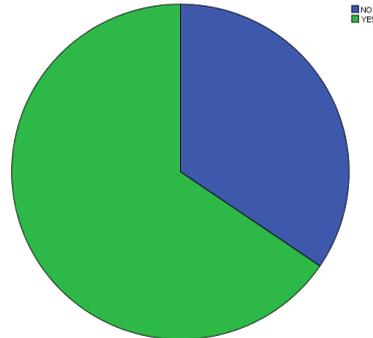
DO YOU SPLIT TABLE BEFORE ADMINISTRATION



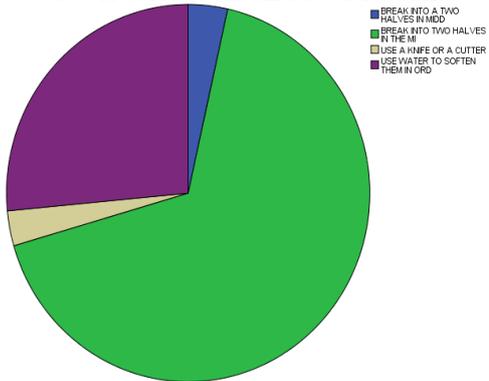
WHY DO YOU SPLIT TABLET



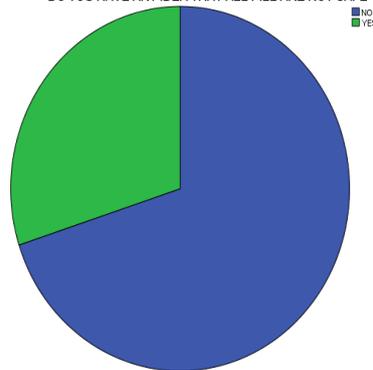
DO YOU THINK THAT SPLITTING TABLETS ARE RISKY



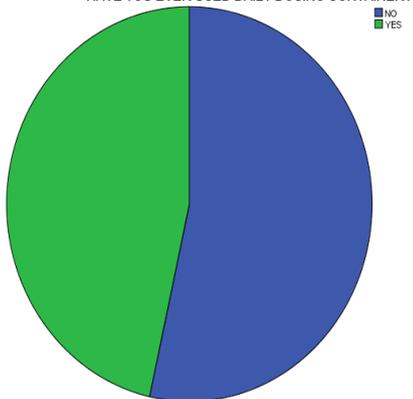
WHAT YOU HAVE DONE IF YOU STILL WANT TO SPLIT A TABLET



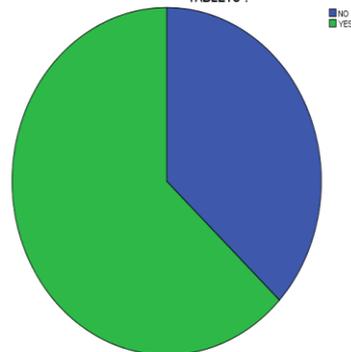
DO YOU HAVE ANY IDEA THAT ALL PILL ARE NOT SAFE TO SPLIT



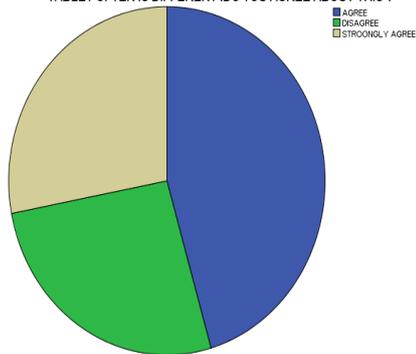
HAVE YOU EVER USED DAILY DOSING CONTAINER?



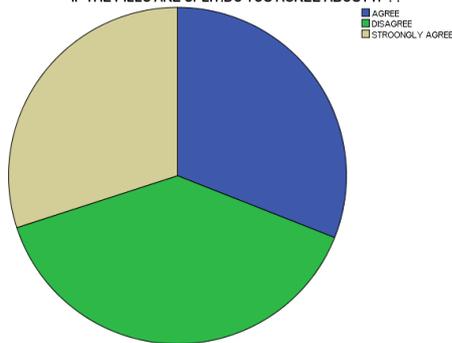
DO YOU READ MEDICINE LABELS AND FOLLOW DIRECTIONS BEFORE USING TABLETS?



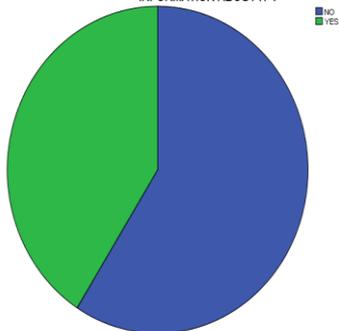
STUDIES HAVE SHOWN THAT THE ACTUAL DOSE IN EACH HALF OF A SPLIT TABLET OFTEN IS DIFFERENT. DO YOU AGREE ABOUT THIS ?



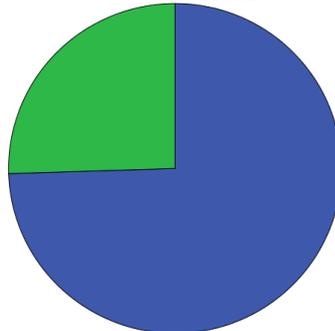
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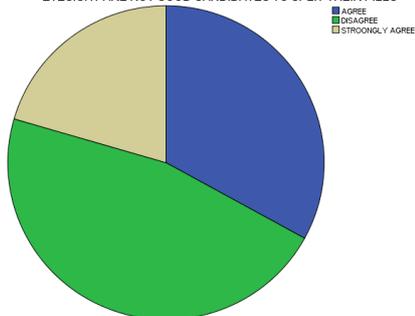
EXTENDED RELEASE COATED TABLETS CAN'T BE SPLIT. DO YOU HAVE ANY INFORMATION ABOUT IT ?



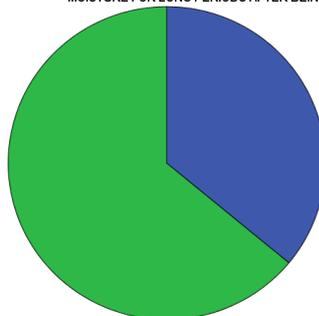
DO YOU USE A PILL SPLITTING DEVICE SO YOU ARE ACCURATELY SPLITTING THE DOSE ?



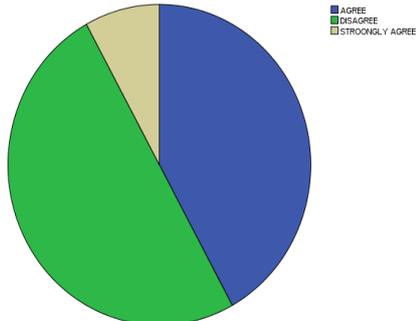
PEOPLES WITH MEMORY PROBLEMS OR IMPAIRED THINKING AND POOR EYESIGHT ARE NOT GOOD CANDIDATES TO SPLIT THEIR PILLS



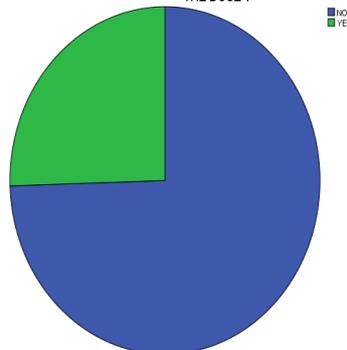
DO YOU KNOW SOME PILLS MAY DETERIOTE WHEN EXPOSED TO AIR AND MOISTURE FOR LONG PERIODS AFTER BEING SPLIT ?

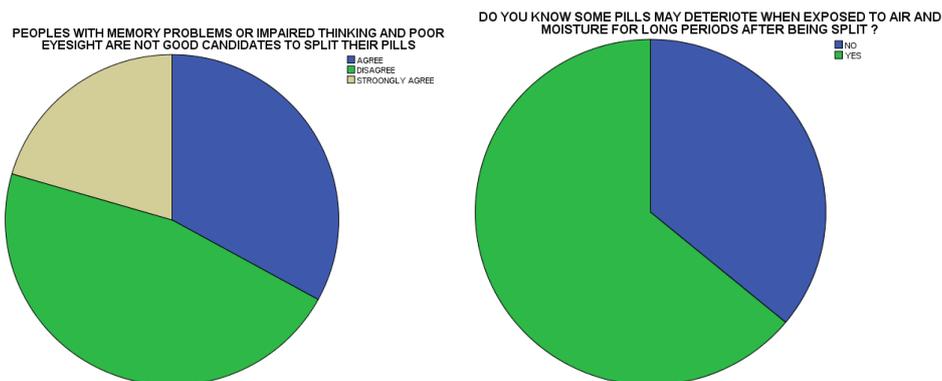


BY REDUCING THE COST OF PRESCRIPTION MEDICINES, PILL SPLITTING COULD IMPROVE HEALTH OUTCOMES BY HELPING PEOPLE AFFORD THE DRUGS THEY NEED AND COMPLY WITH THE DRUG REGIMENS THEIR DOCTORS RECOMMAND?



DO YOU USE A PILL SPLITTING DEVICE SO YOU ARE ACCURATELY SPLITTING THE DOSE ?





## DISCUSSIONS

Majority of the people groups split pills to spare cash and make their drugs last more, as indicated by this study. The study likewise found that more than half of people groups would consider split their pills if their specialist trusted it was safe. Unfortunately, it was found that not each individual asks a specialist or drug specialist before split their pills and numerous are not aware of the danger. Tablets can be part into two by breaking with the fingers nearby a scored line, cutting by method for a blade or utilizing an exceptionally composed tablet cutter. Huge handiness in position and holding the tablet is required. Unequal division of the tablet or a level of exhaustion can appear as a few tablets may crush into more than two sections. Economically available tablet cutters have to to raise the accuracy of tablet part, yet these devices requires a degree of manual handiness in stacking the tablet. Unpredictably molded tablets might not be easy to stack and may not smoothly be partitioning into various parts. Splitting a tablet into quarters is significantly more convoluted and is prone to gain a more prominent rate of tablet wastage and mistake in completing dose. While splitting of tablets may turn out financially savvy, there might be pointless results identifying with the cure of the patient's condition. Tablets that are scored are by and large considered by the organization to be suitable for division and the majority of tablets are made along these lines. Split tablets might be the main choice when a decreased measurement is required. More established individuals or sicknesses, for example, arthritis and Parkinson's illness can bring about diminished grip strength that renders the procedure of split tablets exceptionally difficult. Regardless of the possibility that a tablet cutter device is utilized it may not make good exactness if the patient is practically impeded. Decreasing or expanding dosages, or if more than one tablet is to be partition, complex procedure relating split tablets might be relied upon to reduction understanding consistence. The study have demonstrated that patient consistence is not diminished by utilization of split measurements procedure, in spite of the fact that the outcomes must to be translated with alert as a result of determination tendency.

## CONCLUSION

Splitting pills isn't only potentially money-saving option. Converse with specialist/drug specialist about generics. Regardless of the fact that there wasn't a lower-value choice before, new decisions might be accessible at this point. In the event that our specialist/drug specialist affirms our prescription is protected to part, we'll require a pill cutter. Search for one with an elastic addition to hold the pill so we get parts. Remember that split tablets might be influenced by heat and humidity, so just split each one in turn. Saving money on medicines can be brilliant for our funds, yet just on the possibility that we don't wind up part the distinction with our wellbeing and security. While split tablets may show up financially savvy, there might be difficult outcomes identifying with the treatment of the patient's condition. The choice to split tablets must to be made after appropriate attention. Before split of tablets it have to to be prescribed to check the item data. For the most part just scored tablets ought to be part. Patients ought to be evaluated for their capacity to understand and watch schedule identifying with split tablets. In the event that it requires to partition a tablet, a tablet cutter can be utilized to enhance exactness, yet the patients must think about the best possible utilization of this cutter. Patients must be informed about reasonable stockpiling with respect to split tablets.

## REFERENCES

1. Rodenhuis N, De Smet PAGM, Barends DM (2004) The rationale of scored tablets as dosage form. *Eur J Pharm Sci.*, 21: 305–308
2. Van Santen E, Barends DM, Frijlink HW (2002) Breaking of scored tablets: a review. *Eur J Pharm Biopharm*, 53: 139–145.
3. Cohen JS (1999) Ways to minimize adverse drug reactions. Individualized doses and common sense are key. *Postgrad Med*, 106: 163–172.
4. Wrenger E, Müller R, Moesenthin M, Welte T, Frölich JC, Neumann KH (2003) Interaction of spironolactone with ACE inhibitors or angiotensin receptor blockers: analysis of 44 cases. *BMJ*, 327: 147–149.
5. Cook TJ, Edwards S, Gyemah C, Shah M, Shah I, Fox T (2004) Variability on tablet fragment weights when splitting unscored cyclobenzaprine 10 mg tablets. *J Am Pharm Assoc*, 44: 583–586.
6. Polli JE, Kim S, Martin BR (2003) Weight uniformity of split tablets required by a Veterans Affairs policy. *J Manag Care Pharm*, 9: 401–407.

7. Atkin PA, Finnegan TP, Ogle SJ, Shenfield GM (1994) Functional ability of patients to manage medication packaging: a survey of geriatric inpatients. *Age Ageing*, 23: 113–116.
8. FDA. Best practices for tablet splitting. Available at [www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/ucm184666.htm](http://www.fda.gov/Drugs/ResourcesForYou/Consumers/BuyingUsingMedicineSafely/EnsuringSafeUseofMedicine/ucm184666.htm).
9. MA Veronin and BB Youan. *Medicine*. Magic bullet gone astray: medications and the Internet. *Science*, 2004; 305: 481.
10. MK Freeman et al. Tablet splitting: a review of the clinical and economic outcomes and patient acceptance. Second of a 2-part series. *Consult Pharm*, 2012; 27: 421.
11. Tablet splitting: evaluating appropriateness for patients. Tool for pharmacists from the 2003-2004 APhA Strategic Directions Committee American Pharmacists Association *Journal of the American Pharmacists Association*, 2004; 44(3): 324-325.
12. The practice of splitting tablets: cost and therapeutic aspects Bachynsky, J, Wiens, C, Melnychuk, K *Pharmaco Economics*, 2002; 20(5): 339-346.
13. Misleading score-lines on tablets: facilitated intake or fractional dosing? Arnet, I, Hersberger, KE *Swiss Medical Weekly*, 2010; 140(7-8): 105-110.
14. Dosages involving splitting tablets: common but unnecessary? Berg, C, Ekedahl, A *Journal of Pharmaceutical Health Services Research*, 2010; 1(3): 137-141.
15. Oral medication administration: implications caused by capsule splitting Caldwell, SM, Raitt, JR *Journal of the American Pharmacists Association*, 2010; 50(4): 532-533.
16. Evaluation of split tablets of cardiovascular medicines El-Baseir, M, Bsir, HEL *International Journal of Pharmacy Practice*, 2012; 20(Suppl.2): 46-47.
17. Poster presented at the Royal Pharmaceutical Society (RPS) annual conference, Birmingham, Sep 2012; 9-10.
18. Pill-splitting in a long-term care facility Fischbach, MS, Gold, JL, Lee, M, Dergal, JM, Litner, GM, Rochon, PA *Canadian Medical Association Journal*, 2001; 164(6): 785-786.
19. Tablet splitting: a review of weight and content uniformity: Part 1 of a 2-part.
20. Series Freeman, MK, White, W, Iranikhah, M *Consultant Pharmacist*, 2012; 27(5): 341-352.
21. Crushing or splitting medications: unrecognized hazards Gill, D, Spain, M, Edlund, BJ *Journal of Gerontological Nursing*, 2012; 38(1): 8-12.

22. Analysis of drug content and weight uniformity for half-tablets of 6 commonly split medications Hill, SW, Varker, AS, Karlage, K, Myrdal, PB *Journal of Managed Care Pharmacy*, 2009; 15(3): 253-261.
23. Change in the drug release behavior of theophylline sustained-release tablets after division into two halves Ishitsuka, K, Onuki, Y, Takayama, K *Yakugaku Zasshi*, 2012; 132(2): 225-230.
24. The appropriateness and risks of tablet splitting Mosena, MS, van der Merwe, E *South African Pharmaceutical Journal*, 2009; 76(7): 30-36.
25. Tablet splitting: a little bit risky? (Tablettenteilung: Stückchenweise riskant?) Picksak, G, Stichtenoth, D *Medizinische Monatsschrift für Pharmazeuten*, 2007; 30(9): 340-342.
26. Dividing tablets: why it can be dangerous and what to look out for in practice (Zerkleinern von Tabletten: warum es gefährlich sein kann und was in der Praxis zu beachten ist) Quinzler, R, Haefeli, W *ETMJ (The Medical Journal)*, 2008; (2): 44-47.
27. Tablet splitting (Tabletten teilen) Quinzler, R, Haefeli, W *Therapeutische Umschau*, 2006; 63(6): 441-447.
28. Tablet splitting (Tabletten teilen) Quinzler, R, Haefeli, W *Therapeutische Umschau*, 2006; 63(6): 441-447.
29. Tablet splitting and weight uniformity of half-tablets of four medications in pharmacy practice Tahaineh, LM, Gharaibeh, SF *Journal of Pharmacy Practice*, 2012; 25(4): 471-476.
30. Splitting tablets: the knife is not in fact as bad as it is supposed to be (Tabletten teilen: Messer doch nicht so schlecht wie ihr ruf) Tawab, M, Luhr, G, Bohnet, J, Schubert-Zsilavec, M, Klamb, R *Pharmazeutische Zeitung*, 2011; 43: 156.
31. Tablet-splitting: a common yet not so innocent practice Verrue, C, Mehuys, E, Boussery, K, Remon, J-P, Petrovic, M *Journal of Advanced Nursing*, 2011; 67(1): 26-32.
32. Crushing or splitting medications: unrecognized hazards Gill, D, Spain, M, Edlund, BJ *Journal of Gerontological Nursing*, 2012; 38(1): 8-12.
33. Alexander GC, Casalino LP, Metzler DO. Physician strategies to reduce patients' out-of-pocket prescription costs. *Archives of Internal Medicine*. 2005; 165: 633-636. alexander.uchicago.edu/publications/image/.../OOPC%20mail%20survey.pdf].
34. Cross M (February 2003). "Two for the price of one beauty of pill-splitting catches on". *Manag Care*, 12(2): 36-8. PMID 12658856.

35. Cohen JS (2002). "Tablet splitting: imperfect perhaps, but better than excessive dosing". *J AmPharm Assoc (Wash)*, 42(2): 160. doi:10.1331/108658002763508443. PMID 11926659.
36. Breaking of scored tablets: a review. van Santen E, Barends DM, Frijlink HW National Institute of Public Health and the Environment, Bilthoven, The Netherlands.