EFFECTIVENESS OF PICTOGRAMS IN PATIENTS OR CAREGIVERS IN HEALTHCARE SETTINGS: A SYSTEMATIC REVIEW

A Project Report Submitted to

MANIPAL ACADEMY OF HIGHER EDUCATION

In partial fulfillment for the degree of Doctor of Pharmacy (Pharm D)

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Declaration

We hereby declare that the project titled, **"Effectiveness of Pictograms in Patients or Caregivers in Healthcare Settings: A Systematic Review"** was carried out under the guidance of **Dr. Rajesh V,** Assistant Professor (Selection Grade), Department of Pharmacy Practice, Manipal College of Pharmaceutical Sciences, Manipal Academy of Higher Education, Manipal, Karnataka, India during the academic year 2019-2020.

The extent and source of information derived from the existing literature have been indicated throughout the project work at appropriate places. The work is original and has not been submitted in part or full for any diploma or degree purpose for this or any other university.

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LIST OF ABBREVIATIONS

PRISMA	Preferred Reporting Items for Systematic Reviews and Meta-Analysis
RCT	Randomized control trial
ARVT	Anti-Retroviral Therapy
HIV	Human Immunodeficiency Virus
NICE	National Institute of Clinical Excellence
QOL	Quality of Life
MBL	Menstrual Blood Loss
HBF	Heavy Blood Flow
OTC	Over The Counter
PIL	Patient Information Leaflet
SD	Standard Deviation

ABSTRACT

Background: Pictograms are a graphical symbol that conveys a concept through its pictorial resemblance to a physical object, pictorial representation has shown to have a potential in enhancing patient knowledge.

Methodology: The systematic review was conducted according to PRISMA guidelines. Randomized controlled trials including participants over 18 years older were included in the review. RCTs were included as it reduces certain type of bias by randomly allocating the participants. The risk of bias was assessed using Cochrane risk of bias tool, which assessed 5 different domains and scores were given according to their indication of low, high and unclear risk. The interventions included in these articles were pictograms with text or pictograms with verbal instructions and low literacy plan pictograms.

Result: A total of 965 articles were retrieved through electronic searching, which went through first and second pass screening. Among which articles which did not meet the inclusion criteria were excluded. A total of 15 articles were included for the systematic review. All the included studies showed similar outcomes which said that pictograms had a positive impact on improving patient adherence to their respective medication and helped in decreasing dosing error. Factors such as age, gender, literacy level have a negative impact on adherence. Pictogram intervention improved adherence especially in patients with low health literacy levels than the written/oral interventions.

Conclusion: The current review provided a brief literature on the effectiveness of pictogram in healthcare setting in patients or their caregivers of various age groups. Future studies should be aimed to identify the knowledge gaps and barriers impacting the effectiveness of pictogram for better patient education and safety.

Key Words: Pictograms, health literacy, medication adherence.

INTRODUCTION

1.0 Introduction

In developing countries, the consequences of disease conditions are rapidly increasing due to unhealthy lifestyles, physical inactivity, stress-full mind, and inadequate social and psychological well-being [1]. Drug resistance and unhygienic conditions, both communicable and non-communicable diseases are increasing extensively. These diseases cost an uncountable loss of lives a year and account for about 80% of difference in life expectancy worldwide [2].Prevention is a better way to keep diseases away and remain healthy [3].Education is essential for the development of society; it not only helps in the development of the economy but plays a crucial role in the healthcare sector too. Inadequate understanding of healthcare leads to unsuccessful functioning in a pharmaceutical market designed for informed consumers [4].

Health literacy is the ability to obtain, identify, determine, read, understand and utilize the possibility of health-related information to make relevant decisions and follow up in medical treatments [5].Individuals with adequate health literacy can take appropriate responsibilities on their health condition as well as their family's care [6].Health related information can be provided in many ways which will help in development of health literacy among the population especially in the low health literate population. The different methods such as icons or pictograms can be used to effectively improve the knowledge in these patients [7].

A pictogram is a graphic symbol that conveys a concept through its pictorial resemblance to a physical object. Pictograms can surpass language as they can communicate speakers of many languages equally and effectively, even if language and culture are radically different [8].

Pictograms consist of customized illustrations designed for giving health-related information, which includes indication, dosage form and their respective route of administration. It is not necessary that all the pictograms will be understood throughout every culture and different age groups, and among the people of low literacy level. In the matter of designing, lay participants are given a more active role called a "Pre-Designing Phase" which provides their inputs in the designing of pictograms.

A pharmacist has a crucial role in medication history taking, drug education committees, therapeutic drug committees and integration of technologies. [9]. Usually medication leaflets and instructions for the use of medicines are written in high readability levels, which makes it difficult for the patients in the low health literacy population to adhere to the given medication. Pictogram is the best choice of tool for a better understanding of the drug-related information in patients with low health literacy [3]. Each drug information leaflet containing simple pictograms can be a useful tool in the enhancement of medication adherence and patient knowledge.

Even though the use of pictograms is potential in enhancing patient knowledge, there has been a lesser effort in evaluating the effect of these pictograms in the real-world population [10]. This study aimed to evaluate the effectiveness of the pictogram in improving patient knowledge and adherence to concomitant medication. Additionally, this systematic review will contribute to how positively the pictogram inclusion will affect the results of the intervention in low health literacy patients [11].

AIM

2.0 Aim of Study

- To Study the effectiveness of pictorial health informations on the patients or their caregivers

METHODOLOGY

3.1 Materials and Methods

The following systematic review was carried out conferring to the Preferred Reporting Items of the Systematic Reviews and Meta-Analysis (PRISMA) guidelines.[12] The systematic review aimed at (1) Studying the effectiveness of health information on the patient. (2) To study the effectiveness of pictorial health information in low literacy people. (3) To study the characteristics of pictorial health intervention used in healthcare. (4) It helps us to understand if pictograms affected the increased medication adherence among the low literacy population.

3.2 Inclusion and Exclusion Criteria

Studies such as randomized controlled trial (RCT), blinded or open label were included for in the systematic review. RCT following a cross-over design was excluded from the criteria. The study groups having more than one group were accommodated in the analysis. The reason for inclusion was that RCTs help to reduce a certain source of bias, accomplished by randomly allocated to two or more different groups, treated differently, and compared with a measured response. Articles other than RCTs including systematic reviews, observational studies, case reports, and narrative reviews were excluded. Studies that included with pictogram or pictogram along with text fell under the inclusion criteria whereas studies without the inclusion of pictogram or on the phase of pictogram development were excluded. Participants above 18 years old were included. The population included were of low health literacy.

3.3 Search Methods for Identification of Studies

A systematic conduct of all available articles following randomized controlled trial design was conducted. Studies aimed to find the effectiveness of pictograms on patient adherence and knowledge was screened. Multiple keywords using appropriate Boolean operators were used to build the search. The search was restricted to humans and the English language across the databases.

Electronic Searches:

I. PubMed
II. EMBASE
III. CINAHL
IV. SCOPUS

Searching other Resources

We have hand searched many articles that have been included and relevant comments among the information that can reclaim associated information. For advanced searches, the study database having disputes were identified in ongoing or unpublished trials.

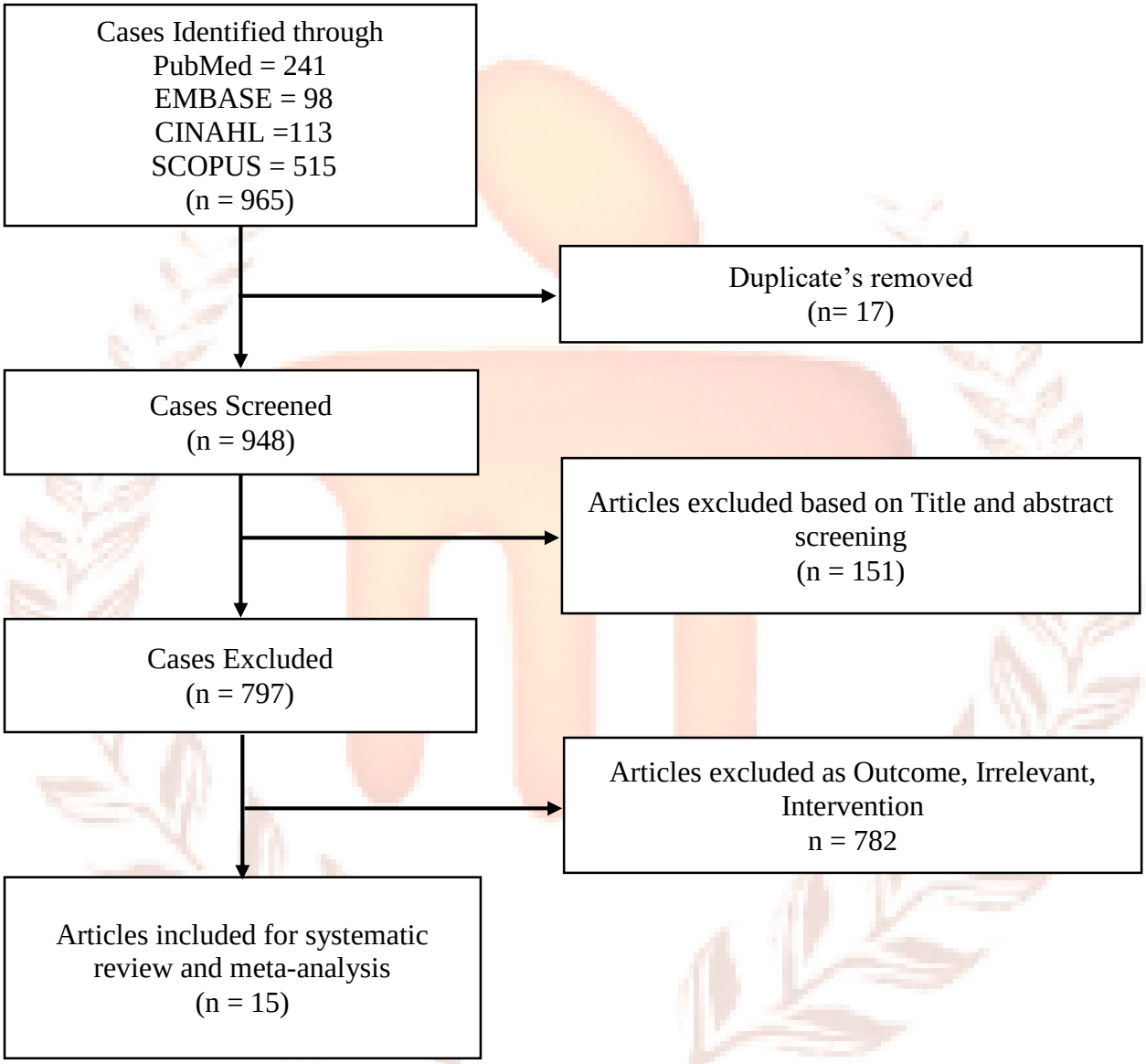

Fig.1 Prisma flow chart

Included Studies

There were 15 RCT with pictograms as a comparator were included.

3.4 Study Design

The 15 RCT (Zerfa 2014) consisted of parallel open label study {Browne 2018, Chan 2014, Dowse 2005, Dowse 2014, Kher 2014, Mansoor 2006, Negrandeh 2012, Phimarn 2018, Yin 2008}, double Blinded parallel group study {Kalichman 2013, Kriplani 2012}, single blinded parallel group study {Braich 2011, Murray 2007}and triple blinded parallel group study {Yin 2017}.

3.5 Interventions

The intervention mostly included pictorial representation in different manner such as Simple PIL, text along with pictograms, low literacy plan with pictogram, verbal instruction along with pictogram, standard and usual care along with pictograms.

3.6 Outcomes

All the included study showed that similar outcome which stated that pictogram had a positive outcome on improving the patient knowledge adhere to their medication and helped in decreasing dosing errors. This study also distinguished other methods with pictogram and suggested that pictogram is indeed a better option for the healthcare management

3.7 Excluded Studies

965 articles were screened out of which 17 were excluded in the first screening, because it was found to be duplicate. In the second screening 151 articles were excluded based on title and abstract. In the third screening 784 articles were excluded they were found to be irrelevant, wrong intervention and negative outcome. In the end 15 articles, be mentioned based on title and abstract.

3.8 Data Extraction and Management

The retrieved articles were screened simultaneously by two authors and in case of any disputes were solved by conversations with the other authors. The articles underwent a first-pass screening in which the title and abstracts were screened across the given inclusion criteria. Furthermore, the articles were analyzed through second pass screening where articles of full text was retrieved for inclusion of articles. Throughout the screening and data extraction process, two authors were involved simultaneously and encase of any accord was solved through consultation.

When multiple intervention groups were assembled, data retrieved from the different databases were combined to analyze for meaningful results. In the presence of multiple groups of participants, data from the group with the efficacy of pictogram better apprehended by the patient to that of a comparator were used in the review. Studies published in various parts, the primary article was used as a reference and secondary papers were necessary for deriving the additional information.

3.9 Assessment of Risk of Bias in Included Studies

Using Cochrane risk of bias assessment tool two review authors independently assessed included articles.[13] The following domains were assessed and scored according to their indication of low (+), high (-) and unclear risk (?) were assigned.

(i) Generation of allocation sequence;

(ii) Allocation concealment;

(iii) Blinding of participants, study personnel and assessors;

(iv) Incomplete outcome data; and

(v) Selective reporting.

Disputes in the studies were resolved by the discussion. The judgments behind each score reported in the table and assessment will be shown for individual study when combined in the figure.

3.10 Measures of Treatment Effect

Number of events in the control and intervention groups of each study to calculate for odds ratio, percentile, variance, etc. were used in case of binary data whereas continuous data, the mean and standard deviations of individual study between the groups were identified. The authors ensured the consistency across the trials to avoid disputes. The 95% confidence interval (CI) was calculated for all outcomes. Considering the legitimate differences, the comparison of significance and guidance of the effect was reported by studies with their presentation.

3.11 Dealing with Missing Data

When data for calculating odds ratio or mean were not accessible, the most advanced scientific data available that facilitated analyses of the included studies (e.g. test statistics, P values, etc.) was utilized. When such data was not possible (e.g. Measure of variation), values were imputed for the missing data by entering the comparable measure used from other pooled studies. Any discrepancies were exposed to sensitivity analysis.

3.12 Assessment of Heterogeneity

To consider clinical and methodological characteristics of the included studies were adequately analogous for meta-analysis to contribute a clinically meaningful summary. The decision for pool studies were made by assessing the statistical heterogeneity by inspection of the Chi square test results and I^2 statistic.

A rough guide to the interpretation of I^2values is as follows:

a) 0% to 40% might not be important;

b) 30% to 60% may represent moderate heterogeneity;

c) 50% to 90% may represent substantial heterogeneity; and

d) 75% to 90% represents considerable heterogeneity.

These overlapping categories were considered, together with outcome uniqueness, in the assessment of heterogeneity.

3.13 Assessment of Reporting Bias

In minimizing potential impact on reporting bias review authors did thorough examination of eligible studies or for any duplicated data present in database. The funnel plot for identifying the publication was not followed for the current review based on the decision by the authors.

3.14 Data Synthesis

Most of the factors were likely to be influenced such as different hospital settings in different countries or difference in participant covariates. The data was combined using random-effects model together to form mixed effect model for population pharmacokinetics. Outcomes with continuous data were assessed for skew. When mean and SD were reported for studies, a rough check was made by determining observed mean minus lowest possible value and divided by standard deviation. If the ratio was >1, it was considered that skew was likely. When skewed was considered likely outcome data were pooled, finding of each of these studies were included in the presentation of overall results for each outcome. (Appendix 1)

Study reference	Country	Study design	N (loss to follow up)	Study Population	Intervention	Control	Adherence Effect Measurement	Result
Braich 2011 [14]	India	Multicentred, Single-blinded, Randomised Control Trial	225 (87)	Low literacy patients on cataract medication of eye drops of post operation	Medication use education: pictograms in clinics; pictograms in home	Verbal instructions on medication use	Bottle amount measurement of eye drops at baseline and 28 days after surgery	Both intervention groups had significantly increased adherence as concluded by measuring percentage of eye drops used
Browne 2018 [15]	South Africa	Randomised Control Trial	116 (33)	Limited literacy HIV patients on ARVs	Medication information: standard care with illustrated information	Standard care	Recognition by question at baseline,1 month, and 3-month post baseline interview	Significantly improved knowledge in intervention group of post baseline
Chan 2014 [16]	Malaysia	Randomised, Parallel, Open- label Study	126 (16)	Patients taking antihypertensive and ant diabetic medications	Medication labels: with enlarged fonts; and incorporating pictograms	Standard regular size text medication labels without pictograms	MMAS-8 at baseline and 4 weeks after intervention	No significant effect on the adherence between the study groups
Dowse 2005[17]	South Africa	Randomised, Parallel, Open- label Study	87 (0)	Patients taking short course antibacterial medication	Medication labels: text along with pictograms	Medication labels: Text only	Pill count/volumetric measurement and self-reporting of adherence after 3-5 days of intervention, combined adherence result	Significantly higher adherence with the intervention group as compared with the control group
Dowse 2014 [18]	South Africa	Randomised, Parallel, Open- label Study	116 (52)	HIV patients on new ARVT	PIL containing text along with pictogram	Standard care	Adherence self-efficacy scale of HIV treatment at baseline and 1,3, and 6 months after intervention	No significant difference on self-efficacy between the study groups

Kalichman 2013 [19]	USA	Randomised, Double-blinded, Parallel Study	446 (45)	Low health literacy HIV patients on ARVT	Adherence counselling: text along with pictograms, tool of choice of adherence; standard adherence of text along with illustrations comic strips and pill box of adherence tool	Counselling on general health improvement	HIV RNA load at baseline and 9 months after intervention, and monthly PIL count from intervention start for 9 months	Patients with marginal health literacy had significantly greater undetectable HIV viral load in both intervention groups compared with the control and patients with low literacy didn't have significant effect on interventions
Kheir 2014 [20]	Qatar	Randomised, Parallel, Open label	123	Limited literacy skills in a culturally diverse multi-ethnic population	Verbal instructions along with text; and pictographic instruction only	Pictogram along with verbal instructions	Systematic approach of group discussions and interviews	Pictorials supported with verbal instructions was comprehended and pictogram only labels are least comprehending
Kripalani 2012 [21]	USA	Randomised, Double blinded, Parallel Study	435	Patients with coronary heart disease	Post card reminders of refill; Illustrated schedule on medication with pictograms; combination of both	Usual care	Reported CMG of electronic pharmacy refill records for 1 year of follow up after intervention	No significant effect on adherence between the study groups
Mansoor 2006 [22]	USA	Randomised, Parallel, Open- label	127 (7)	Low health literacy patients on ARVT	PIL: with pictograms; and without pictograms	Usual care	PIL count and self-reported with questionnaires of approximate of 14 days after intervention	Significantly increased adherence on PIL count and questionnaire of intervention compared with control group
Murray 2007 [23]	USA	Randomised Single-Blinded Study	314 (44)	Heart failure patients ≥0 years of age using cardiovascular medications	Pharmacist intervention: written information and containing pictograms	Usual care	Using prescription records and self- reported of MEMS, MPR and questionnaires	Significant effect on overall adherence between intervention and control group in post

								intervention period. No significant effect on adherence between study groups of self-reporting
Negarandeh 2013 [24]	Kurdistan	Randomised, Open-label, Parallel Study	135 (8)	low health literacy patients with type 2 diabetes	Medication intervention education: teach back method; and with pictograms	Usual care	MMAS-8 at baseline 6 weeks post-intervention	Significantly higher adherence in intervention group compared to control group. But no adherence between intervention groups
Phimarn 2018 [25]	Thailand	Randomised, Parallel, Open- label Study	134	Low literate and poor adherence	Pictogram Instructions	Traditional labels	Brainstorming, interviews and pilot evaluation	Experimental group had significantly higher post intervention understanding score than control group
Yin 2008 [26]	USA	Randomised, Parallel, Open- label Study	245 (18)	Parents or caregivers of children on liquid medications	Medication counselling: with mediation instruction sheets; pictograms; and teach-back	Usual care	Self-reported adherence by interview at baseline 3-5 days after medicine dispensing	Significantly higher adherence in the intervention group with the control group.
Yin 2017 [27]	USA	Randomised, Parallel, Triple-blinded Study	259 (42)	Low literate parents of children with asthma	Asthma action plan: of low literacy plan along with pictogram	Standard care plan	Questionnaire to assess error in knowledge	Intervention group had significantly higher impact than control group
Zerafa 2011 [28]	Malta	Randomised control trial	86 (6)	Cardiac surgery patients on medication	Pharmacist intervention: with written medication information sheets and pictograms	Usual care	Questionnaire of patient compliance after 8 weeks after surgery discharge	Significantly higher patient compliance in intervention group with control group

Table 1. Characteristic of the Included Studies

RESULTS

4.0 Search

Electronic search was conducted in PubMed, EMBASE, CINAHL and SCOPUS that yielded a total number of hits 241, 98, 113 and 515 respectively. A total of 965 articles were identified through this search. Out of 965 articles identified, 17 articles were excluded since they were found to be duplicates. In the second screening, 151 articles were excluded out of 948 articles based on the title and abstract screening. 782 articles were further excluded as outcome, irrelevant and intervention as exclusion criteria. Finally, 15 articles were included in the systematic review.

4.1 Risk of Bias

All the studies included (15) reported adherence to pictogram-based interventions (Appendix 2). The patient groups were mostly who were on antiretroviral medications, cardiac patients, and patients on post-operative cataract medication, patients and care givers with less health knowledge. Quality of the studies were evaluated by two reviewers using Cochrane collaboration Tool. Significant studies were identified as open-label studies (93.3%, High risk). In two studies blinding of participants and key study personnel were ensured (13.3%, low risk). Thirteen trials (86.6%) were reported as high risk of detection bias. Five studies reported an unclear risk of selection bias (33.3%, Allocation concealment). One study reported high risk of attrition bias and 3 studies (20%) reported unclear risk. No study reported high risk or unclear risk of selection bias (random sequence generation). As seen in figure 2, all the studies had at least one dimension with a high risk of bias, but met the acceptable quality.

In this study, we assessed various articles to evaluate the pictograms in patient understanding and medication adherence. From the 15 included studies 3 studies done by Chan [16], Dowse [18], Kripalini [21] did not have a statistically significant pictogram effect on medication adherence. Each study varied with the use of pictograms. In study interventions, pictograms were used alone or in combination with the text-based/written or verbal/oral instructions of medication use. The current review points of the conclusion of improved patient adherence were with the combinational use of pictograms with text-based and/verbal instructions.

A few article reviews resulted in an insignificant effect that were attributed to insufficient data, sample size or required further studies to have a significant conclusion. The adherence was assessed by questionnaire, self-reporting and interviews. Significant evidence was there to conclude that pictogram-based interventions would enhance the medication adherence of patients. The interventional complexity acts as a limitation for the pictogram contrition to medication adherence. Measuring adherence was difficult to evaluate and required standardization methods. In this review, a study by Kalichman et al [19], used pictogram intervention along with adherence counselling of text with a pictogram, and adherence tools of choice of illustration with comic strips and pillbox. So, it was difficult to conclude the adherence effect of pictogram alone from the adherence counselling. The RCT conducted by Negrarandeh et al [24], was done in a diabetic clinic by a nurse among low health literacy patients with type 2 diabetes. The educational medication intervention was through teach back method and pictograms against the usual care as the control group. This resulted with no adherence between the intervention groups and significantly higher adherence in the intervention group as compared with the control group.

Whereas, a study led by Mansoor et al [22], was done on low health literacy patients on antiretroviral therapy (ART) with patient information leaflet (PIL) and without pictograms against the standard care. A significant increase in adherence to patients receiving PIL with pictograms as compared with other groups. Study designs of comparison of interventional groups show only the difference in the use of pictograms. Patient-related factors play a key role in the contribution of medication adherence. Factors such as age, gender, literacy level have a negative impact on adherence. Pictogram intervention improved adherence especially in patients with low health literacy levels than the written/oral interventions. RCT study by Chan [16], Dowse [18], Kripalini [21], Murray [23], Yin [27] and Zerafa [28] doesn't discuss about the role of health literacy for medication adherence. It indicated that the pharmaceutical pictogram is most beneficial for the patients challenged with low health literacy.

Another known factor influencing medication adherence was the nature of the therapy. The RCT study by Browne [15], Mansoor [22], Kalichman [19], and Dowse [18] was on ARVT; Chan [16] was on antihypertensive and anti-diabetic medications; Murray [23] was on cardiovascular medications. But the above-mentioned articles did not specifically describe about prescribed therapies of the included participants. Therapeutic effects are based on dosing and frequency of therapy, patient's attitude, belief, adverse events of the treatment, and effectiveness of the medication. However, the studies performed by Browne [15], Mansoor [22], and Murray [23] stated a significant effect on pictogram-based interventions. The adherence effect was measured by different methods in various studies. Such included the bottle amount measurement, questionnaire self-report interview, pill count, and group discussion, electronic refill records by pharmacy, brainstorming. There was

no single method recommended, and so the studies use a mixed method for measuring the adherence.

The RCT study by Yin et al [26], review the pictogram effects on caregivers in the administration of liquid medication and suggested that it may result in the reduction of dosing error with enhanced comprehension and improved adherence.

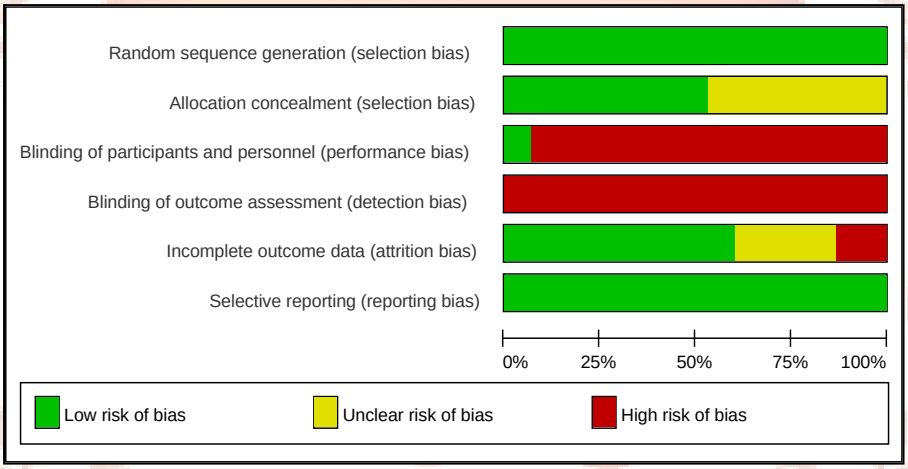

Fig.2 Risk of Bias

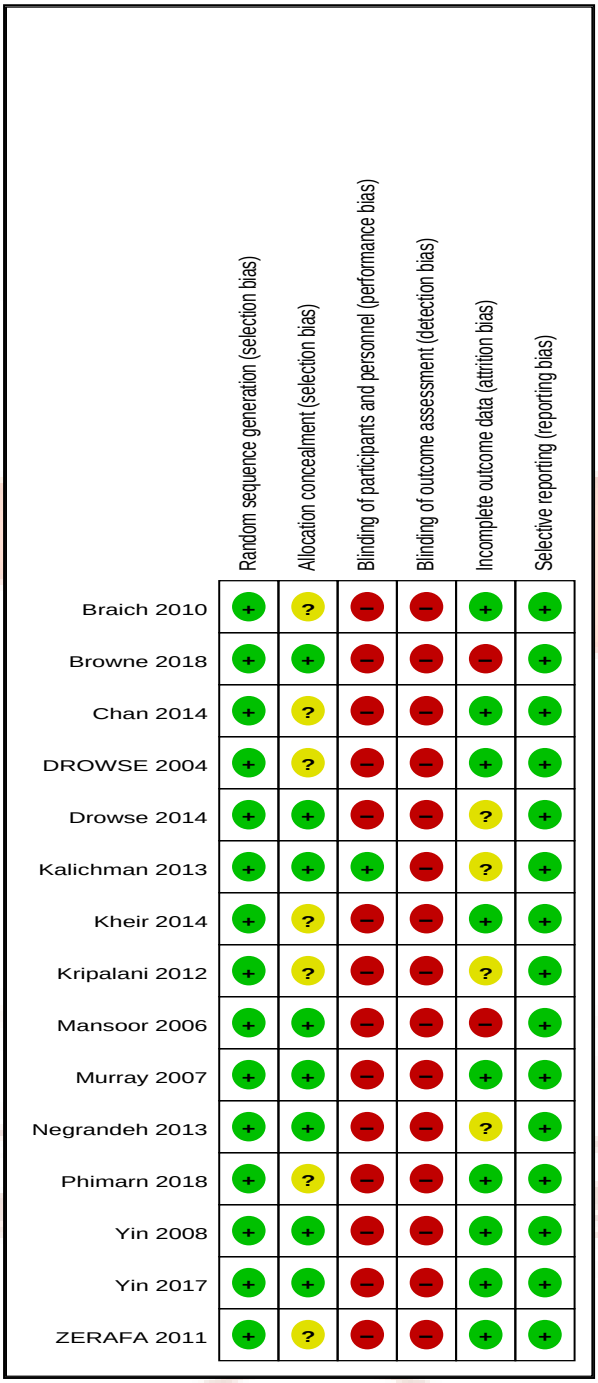

Fig.3 Risk of Bias Graph

DISCUSSION

5.0 Discussion

To understand information about one's own medication is vital for each patient for better medicine use and safety. Various literacy rates across the globe are a potential barrier in the interpretation of written information. The health literacy of patients provides relevance in the development of information tools to provide adequate understanding for such populations [14]. Pharmaceutical Pictograms are a remarkable substitute unless they are not sensitive socially. A various study has tested the effectiveness of pictogram in various settings to identify its usefulness in improving patients' understanding amongst various literacy groups [29]. Pictograms play an evident role in transforming the medical information to improve understanding, adherence and in medication recalling. Even though various forms of pictograms have been developed and tested, the efficacy remains questionable in improving medication related parameters. This can be overcome by providing dedicated patient counselling utilizing the pictograms for better medication use.

A validated model for the design and interpretation of pictograms are the need for the hour for imparting health information and for providing better patient safety [30]. Pictorial aids are also effective in caregivers to assist in the administration of certain dosage forms of medications. Pictograms use will improve the understanding of medication instructions, the dosing accuracy, and also will improve recall information in the caregivers for better patient care. Incorporating pictograms into verbal instructions or counselling on medications or the text instructions was more beneficial than to be used alone. The health literacy level of caregivers will also get contributed by pictorial aid effectiveness [31]. Pictograms will recall, enhance comprehension and adherence with medication information.

The pictograms have the ability in helping the population with low literacy, remains to be a concern, considering the low education level and socioeconomic status of the patient population. Successful establishment of medication safety programs are essential for the development of healthcare setting through the reduction of cost and for delivering better patient care. The increase in rate of right interpretation of pictograms can be of utmost use whenever provided as a replacement to instructions in verbal form. The impact of pictograms in preventing medication administration errors in a health care setting and in improving clinical outcomes needs to be reviewed and studied spontaneously to explore future outcomes of pictograms.

The current systematic review aimed to investigate about the potential effectiveness on patient of medication adherence towards the therapies based on collecting and summarizing the shreds of evidence depending on certain inclusion and exclusion criteria of pictograms. It is usually hard for patients to retain verbally communicated information, for which this short systematic review conducted by Van Beusekom 2018 to evaluate the extent and effects of patient involvement in the design and development of the pictograms for written information of drug. This review included 73 articles which were published between 1993 and 2018, this review focused on two groups, one being the patient party and the other being the non -patient party that helped in the design process of the pharmaceutical pictograms. It showed that the involvement in the design process of lay participants led to pictograms that were preferred in the specific target group. The involvement of lay participants also showed to consistently lead a positive effect on the terms of patient understanding. Overall this review showed involvement of the non-partcipants in the development of pharmaceutical pictograms and provided evidences involving lay end-users in the design process to help to increase the likelihood that resulting pictograms are well-understood, well-

received and aid recalls of the drug information that supports. It is also essential to involve participants that meet the key criteria in the targeted group in the evaluation of pictograms and pictogram based information as it was seen from that different audiences perceive information differently. [32] Similarly, the current review was based on Pictogram alone and pictogram with text as the major intervention. The results of the current study gave a mixed perception of the patients and their care givers in understanding the effectiveness of pictogram

Another review led by Sletvold 2019 and team focused on the impact of pictograms on medication adherence. This study initially included 1283 articles, out of which only 17 articles were included for analysis after excluding the others based on duplication and the inclusion criteria. The study population was diverse in clinical disorders, treatment regimen, terms of age and the level of health literacy. Of the included studies 10 articles reported a statistically significant effect of pictograms used in the studies varied though most of them used pictograms along with text based or verbal instructions. Patient-related factors such as age, long term medication use, and a different type of disease population also affect medication adherence which is why it is necessary to develop pictograms that are focused on the target population. It was concluded that pictograms do serve as a communication tool in combination with verbal or oral instruction to enhance visual attention, comprehension, recall, and adherence to medications. [33] In context to the above study, our study search was conducted till 2019 September and few articles were added which increased the sample population of the present review to give more vivid results. A systematic review based on Magnay 2018 was concerned with the validation process or development of methods for assessing menstrual blood loss which was based on the different strategies used to develop NICE guidelines. 1438 records were retrieved out of which 71 fulfilled the inclusion criteria, which was used to

determine methods to measure the Menstrual Blood Loss (MBL) and to distinguish between the normal and Heavy Blood Flow (HBL), the suitable diagnosing for HMB and routine clinical practice and practical and limitations to research background settings. This review showed that every available method cannot assess MBL. A pictorial representation showed a balance in ease of understanding and validated pictograms in MBL determination in each way using QOL in both clinical and research settings. [34] This study focused on a single population and condition whereas the present study had various intervention and the target population varied among the studies. The interventions were mainly focused on low literacy population and the intervention were keenly designed to improve the adherence and the knowledge in the specific population.

Another review conducted by Chan, 2015 included studies that used pictorial aids with liquid medication and measured its dosing accuracy, comprehension of instruction, recall information and adherence of caregivers. 1363 records were yielded from the search out of which only 5 studies met the search which contained 962 participants, a wide range of liquid formulations were studied including prescription and OTC drugs. Regarding dosing errors, pictograms were given to one half of the population and the other half received text information and it was seen that the group which received pictograms showed fewer mistakes in dosing error. As for the recall of medication, it was also done the same way, one half received pictograms while the other half received the non-pictogram intervention. The group that received pictograms recalled their mediation instructions better as compared to the other group. When all the criteria were combined it was seen that pictorial aids are useful intervention based on the findings. The study had a direct comparison analysis. [35] The study intervention included only pictogram as intervention whereas our study was based on the pictogram alone or with some amount of text with the same. The outcomes measures were

medication adherence more precisely than other outcomes relating to dosing and dosage forms. Only a few studies among the included studies were reviewed for dosage forms where pictograms were efficiently used and served the purpose.

LIMITATIONS

6.0 Limitations

A systematic review included 15 studies. Each of the studies were randomized controlled trials. The trials differed based on the design of blinding where few studies were blinded, and many were open label. This led to high amount of heterogeneity across the studies. The outcomes were reported in various data forms which was a drawback in conducting a meta-analysis. The intervention yielded a mixed response since the pictogram and text were utilized. Future studies focusing on pictograms alone and outcome measured using a uniform tool should be targeted for the design of meta-analysis to determine the effectiveness of pictogram in various healthcare settings.

CONCLUSION

7.0 Conclusion

Pictograms have been an essential tool for educating patients of various literacy groups. The effectiveness of pictograms remains unclear regardless of the group studied. The current review provided a brief literature on the effectiveness of pictogram in healthcare setting in patients or their caregivers of various age groups. Future studies should be aimed to identify the knowledge gaps and barriers impacting the effectiveness of pictogram for better patient education and safety.

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APPENDIX 1

SEARCH STRATEGY

S.No	Database	Keywords	Hits
1	PubMed	"pictograms"[Text Word] OR "pictogram"[Text Word] OR "pictograph"[Text Word] OR "pictographs"[Text Word] AND "medical"[Text Word] OR "medicine"[Text Word] OR "medicines"[Text Word] OR "medication"[Text Word] OR "medications"[Text Word] OR "drug"[Text Word] OR "drugs"[Text Word] AND "Literacy"[Text Word] AND (Clinical Trial[ptyp] AND "humans"[MeSH Terms] AND English[lang])	241
2	SCOPUS	"pictograms" OR "pictogram" OR "pictograph" OR "pictographs" AND "medical" OR "medicine" OR "medicines" OR "medication" OR "medications" OR "drug" OR "drugs" AND "Literacy" AND (LIMIT-TO (DOCTYPE, "ar")) AND (LIMIT-TO (LANGUAGE, "English"))	515
3	EMBASE	'literacy' AND (('pictograms' OR 'pictogram'/exp OR 'pictogram' OR 'pictograph' OR 'pictographs') AND ('medical' OR 'medicine' OR 'medicines' OR 'medication' OR 'medications' OR 'drug' OR 'drugs')) AND [humans]/lim AND [english]/lim	98
4	CINAHL	(TX "literacy") AND (S6 AND S7)	113
	S7	TX "literacy"	42,861
	S6	((TX "medical" OR TX "medicine" OR TX "medicines" OR TX "medication" OR TX "medications" OR TX "drug" OR TX "drugs") AND (S4)) AND (S2 AND S4)	370
	S4	TX "medical" OR TX "medicine" OR TX "medicines" OR TX "medication" OR TX "medications" OR TX "drug" OR TX "drugs"	1,189, 741
	S2	TX "pictograms" OR TX "pictogram" OR TX "pictograph" OR TX "pictographs"	429

Search Strategy September 2019

APPENDIX 2

RISKS OF BIAS

1. AUTHORS NAME: BROWNE 2018

BIAS	AUTHOR'S JUDGEMENT	SUPPORT FOR JUDGEMENT
Random Sequence generation (selection bias)	Low risk	Patients were randomly allocated into control (standard care) or intervention groups (standard care plus additional illustration was provided)
Allocation concealment (selection bias)	Low risk	Patients were randomized via a computerized random number generator to either control (standard care) or intervention (standard care plus a PIL) groups, stratified by education.
Blinding of participants and personnel (performance bias)	High risk	Open-label
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Open-label
Incomplete outcome data (attrition bias)	High risk	The study reported a greater number of dropouts due to lost follow up during the conduct of the study
Selective reporting (Reporting bias)	Low risk	The study protocol was not available for the study, the outcomes reported were according to the objectives

2. AUTHORS NAME: PHIMARN 2018

BIAS	AUTHORS JUDGMENT	SUPPORT FOR JUDGEMENT
Random Sequence generation (selection bias)	Low risk	Patients were randomly allocated into control or experimental groups by draw lots technique
Allocation concealment (selection bias)	Unclear risk	Assigning of participants were based on drawing of label based on their choice from the box of lots.
Blinding of participants and personnel (performance bias)	High risk	Open-label
Blinding of outcome assessment (detection bias) Self-reported outcomes	High risk	Open-label
Incomplete outcome data (attrition bias)	Low risk	There were no dropouts during the conduct of the study
Selective reporting (Reporting bias)	Low risk	Study protocol was not available, the published reports met all the reported outcomes

3. AUTHOR NAME: BRAICH 2010

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random Sequence generation (selection bias)	Low risk	Patients were randomly allocated into two experimental groups and a control group
Allocation concealment	Unclear risk	The method of allocation concealment was not clearly mentioned
Blinding of participants and personnel	High risk	Open-label
Blinding of outcome Assessment	High risk	Open-label
Incomplete outcome data (Attrition bias)	Low risk	There were no dropouts during the study
Selective reporting	Low risk	Study protocol was not available but the published reports met the reported outcomes

4. AUTHOR NAME: DOWSE 2014

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random sequence generation	Low risk	Patients were randomized into either control or intervention group
Allocation concealment	Low risk	The patients were stratified based on their education into either of the groups
Blinding of participants and personnel	High risk	Open-label
Blinding of outcome assessment	High risk	Open-label
Incomplete outcome data	Unclear risk	The dropouts throughout the follow up were large in number, the reason were dropouts were reported accordingly
Selective reporting	Low risk	Study protocol is not available, but the published reports met all the expected outcomes

5. AUTHOR NAME: MANSOOR 2006

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random Sequence generation (selection bias)	Low risk	Patients were randomly allocated into intervention group and a control (usual care) group
Allocation concealment	Low risk	The allocation was based on alternative basis
Blinding of participants and personnel	High risk	Open-label
Blinding of outcome Assessment	High risk	Open-label
Incomplete outcome data (Attrition bias)	High risk	Reasons for dropouts are not clearly specified
Selective reporting	Low risk	study protocol was available, published reports met all the expected outcomes

6. AUTHOR NAME: YIN 2017

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random sequence generation	Low risk	Patients were randomized into intervention group and control group
Allocation concealment	Low risk	Block randomization was done using sealed envelopes arranged in blocks 50 for each site (random order with 25 intervention and 25 control in each block)
Blinding of participants and personnel	High risk	Open-label
Blinding of outcome assessment	High risk	Open-label
Incomplete outcome data	Low risk	No missing outcome data
Selective reporting	Low risk	Study protocol is available, published reports meets all expected outcomes

7. AUTHOR NAME: KALICHMAN 2013

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random sequence generation	Low risk	Patients were randomized using automated randomization generator into marginal and low literacy groups
Allocation concealment	Low risk	The patients were stratified based on their education into either of the groups
Blinding of participants and personnel	Low risk	Blinding of participants and key study personnel ensured and unlikely that the blinding could have been broken
Blinding of outcome assessment	High risk	Open-label
Incomplete outcome data	Low risk	The dropouts throughout the follow up were large in number, the reason were dropouts were reported accordingly (1385 assessed for eligibility ,939 were excluded in which 911 are not meeting inclusion criteria , after baseline interview 28 were lost to follow up
Selective reporting	Low risk	study protocol was not available, but the published reports met all the expected outcomes

8. AUTHOR NAME: NEGRANDEH 2013

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random sequence generation	Low risk	Randomization was done using computer generated randomization
Allocation concealment	Low risk	patients were randomized using center allocation (they contacted patients via telephone) and proper allocation sequence with block size of 5 to assign patients
Blinding of participants and personnel	High risk	Open-label
Blinding of outcome assessment	High risk	Open-label
Incomplete outcome data	Unclear risk	11 patients were excluded from the study due to lost to follow up.
Selective reporting	Low risk	The reported outcomes were as per the methodology presented in the study

9. AUTHOR NAME: YIN 2008

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random sequence generation	Low risk	Randomization was done using the sealed envelopes
Allocation concealment	Low risk	Block randomization was done using sealed envelopes in blocks of 50,25 each for the intervention and control groups
Blinding of participants and personnel	High risk	Open label
Blinding of outcome assessment	High risk	Open label
Incomplete outcome data	Low risk	No missing outcome data
Selective reporting	Low risk	Study protocol is available, published reports meets all expected outcomes

10. AUTHOR NAME: KRIPALINI 2012

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random Sequence generation (selection bias)	Low risk	Patients were randomly allocated into interventional groups (2) and a control group by using computerized random number generator
Allocation concealment	Unclear risk	Treatment assignment was sealed in an opaque envelope for concealment of treatment allocation
Blinding of participants and personnel	High risk	Open-label
Blinding of outcome Assessment	High risk	Outcome assessors were blind
Incomplete outcome data (Attrition bias)	Unclear risk	The dropouts throughout the follow up were large in number, the reason were dropouts were reported accordingly (968 assessed for eligibility ,528 were excluded in which 120 declined screening,358 are not meeting inclusion criteria , 50 declined to participate after baseline interview 5 were withdrew consent
Selective reporting	Low risk	study protocol was not available, but the published reports met all the expected outcomes

11. AUTHOR NAME: KHEIR 2014

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random sequence generation	Low risk	Patients were randomized into 3 study groups
Allocation concealment	Unclear risk	Method of allocation concealment not described, randomly allocated into 3 groups.
Blinding of participants and personnel	High risk	Open label
Blinding of outcome assessment	High risk	Open label
Incomplete outcome data	Low risk	No missing outcome data
Selective reporting	Low risk	Protocol is not available, but the published reports meets all expected outcomes

12. AUTHOR NAME: CHAN 2014

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random sequence generation	Low risk	Randomly allocated into 3 groups of standard, font enlarged, and pictogram incorporated.
Allocation concealment	Unclear risk	Randomly allocated into 3 groups, Method of allocation concealment not described
Blinding of participants and personnel	High risk	Open label
Blinding of outcome assessment	High risk	Open label
Incomplete outcome data	Low risk	No missing outcome data
Selective reporting	Low risk	Study protocol is not available, but the published reports meets all expected outcomes

13. AUTHOR NAME: DROWSE 2004

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random Sequence generation (selection bias)	Low risk	Patients were randomly allocated into experimental group and a control group
Allocation concealment	Unclear risk	The method of allocation concealment was not clearly mentioned
Blinding of participants and personnel	High risk	Open label
Blinding of outcome Assessment	High risk	Open label
Incomplete outcome data (Attrition bias)	Low risk	No missing outcome data
Selective reporting	Low risk	study protocol is not available but published reports meets all the expected outcomes

14. AUTHOR NAME: ZERAFA 2011

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random Sequence generation (selection bias)	Low risk	Patients were randomly allocated into experimental group and a control (usual care) group
Allocation concealment	Unclear risk	The method of allocation concealment was not clearly mentioned
Blinding of participants and personnel	High risk	Open label
Blinding of outcome Assessment	High risk	Open label
Incomplete outcome data (Attrition bias)	Low risk	No missing outcome data, dropouts' number is 9 but the reasons for dropouts are clearly specified
Selective reporting	Low risk	study protocol is not available but published reports meets all the expected outcomes

15. AUTHOR NAME: MURRAY 2007

BIAS	AUTHORS JUDGEMENT	SUPPORT FOR JUDGEMENT
Random Sequence generation (selection bias)	Low risk	Patients were randomly allocated into intervention group and a control (usual care) group
Allocation concealment	Low Risk	The allocation was based on a computerized algorithm
Blinding of participants and personnel	High risk	Open label
Blinding of outcome Assessment	Low Risk	The pharmacist who was blinded to the study group took the medication histories of patients in both the group
Incomplete outcome data (Attrition bias)	Low risk	No missing outcome data, reasons for dropouts are clearly specified
Selective reporting	Low risk	study protocol is available, published reports meets all the expected outcomes

APPENDIX 3

PLAGIARISM REPORT

Pictogram

ORIGINALITY REPORT

12%	7%	11%	8%
SIMILARITY INDEX	INTERNET SOURCES	PUBLICATIONS	STUDENT PAPERS

PRIMARY SOURCES

1	research-repository.st-andrews.ac.uk Internet Source	1%
2	Hege Sletvold, Lise Annie Bjørnli Sagmo, Eirik A. Torheim. "Impact of pictograms on medication adherence: A systematic literature review", Patient Education and Counseling, 2019 Publication	1%
3	Mara M. van Beusekom, Anne H. Kerkhoven, Mark J.W. Bos, Henk-Jan Guchelaar, Jos M. van den Broek. "The extent and effects of patient involvement in pictogram design for written drug information: a short systematic review", Drug Discovery Today, 2018 Publication	1%
4	Chan, H. K., M. A. Hassali, C. J. Lim, F. Saleem, and W. L. Tan. "Using pictograms to assist caregivers in liquid medication administration: a systematic review", Journal of Clinical Pharmacy and Therapeutics, 2015. Publication	1%