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Clustering for Detection of Population Groups at Risk from Anticholinergic Medication

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Abstract—Anticholinergic medication has been associated with events such as falls, delirium, and cognitive impairment in older patients. To further assess this, anticholinergic burden scores have been developed to quantify risk. A risk model based on clustering was deployed in a healthcare management system to cluster patients into multiple risk groups according to anticholinergic burden scores of multiple medicines prescribed to patients to facilitate clinical decision-making. To do so, anticholinergic burden scores of drugs were extracted from the literature which categorizes the risk on a scale of 1 to 3. Given the patients' prescription data on the healthcare database, a weighted anticholinergic risk score was derived per patient based on the prescription of multiple anticholinergic drugs. This study was conducted on 300,000 records of patients currently registered with a major regional UK-based healthcare provider. The weighted risk scores were used as inputs to an unsupervised learning algorithm (mean-shift clustering) that groups patients into clusters that represent different levels of anticholinergic risk. This work evaluates the association between the average risk score and measures of socioeconomic status (index of multiple deprivation) and health (index of health and disability). The clustering identifies a group of 15 patients at the highest risk from multiple anticholinergic medication. Our findings show that this group of patients is located within more deprived areas of London compared to the population of other risk groups. Furthermore, the prescription of anticholinergic medicines is more skewed to female than male patients, suggesting that females are more at risk from this kind of multiple medication. The risk may be monitored and controlled in a healthcare management system that is well-equipped with tools implementing appropriate techniques of artificial intelligence.

Keywords—Anticholinergic medication, socioeconomic status, deprivation, clustering, risk analysis.

I. INTRODUCTION

ANTICHOLINERGIC burden refers to the cumulative effect of medications which contain anticholinergic properties. Anticholinergic medication may lead to cognitive decline among the elderly [1], [6], [9]. Older people are more vulnerable to the anticholinergic adverse drug reaction due to polypharmacy, multi-morbidity, and age related physical dysfunction. Anticholinergic burden has been reported as a significant independent risk factor of events such as delirium, constipation and urinary retention [8], [14]. Recent evidence also shows that the anticholinergic burden risk is associated with social deprivation [16], [4], [7], [12]. For example in a given population people with dementia in the most deprived areas are significantly at higher risk of anticholinergic burden compared to the least deprived areas [11]. In our work socioeconomic impact measured by indices of deprivation is employed to investigate if higher degrees of deprivation is associated with anticholinergic risk burden. Measures of deprivation in the UK include the English Indices of Deprivation, updated in 2019 (IoD2019) based on a set of relative measures of deprivation for small areas identified by different postcodes across England. They are based on seven different domains including income deprivation, employment deprivation, education, skills and training deprivation, health deprivation and disability, crime, barriers to housing and services, and living environment deprivation. The Index of Multiple Deprivation (IMD2019) combines the information from the seven domains according to respective weights to produce an overall relative measure of deprivation. Two other indices of interest (but not used in the current study) are the Income Deprivation Affecting Children Index (IDACI) and the Income Deprivation Affecting Older People Index (IDAOPI). The various IoD2019 metrics measure deprivation on a relative rather than absolute scale so that a neighborhood ranked 2[nd] is more deprived then a neighborhood ranked 4[th], but this does not necessarily mean one is twice as deprived as the other [13], [15].

Ensuring that medicines are prescribed to people from different backgrounds safely based on their needs is fundamental to the role of healthcare professionals. The current study addresses this issue by employing a clustering technique to categorise patients into different risk groups based on their anticholinergic risk scores. The clustering algorithm utilised in the current study is mean-shift clustering, often associated with medical applications [10]. The results of the clustering are used to evaluate how the average risk scores in the clusters are correlated with their corresponding average deprivation scores.

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II. METHODS

The Anticholinergic Cognitive Burden (ACB) Scale measures the absolute risk of any single anticholinergic medicine. It classifies drugs into 3 types with a score of 1 representing a mild risk of cognitive effects and a score of 3 representing where the cognitive effects could be significant [4], [5]. The medication records of 300,000 patients registered with the largest provider of primary care services to the

NHS in England (AT Medics Ltd, London) were utilised for the current study. Only those patients whose prescription records were active were included in the cluster analyses whereas historical records that had ceased at some point in past were excluded. The data are available from the NHS bulk data repository. Restrictions apply to the availability of the data, which were utilised under the license of the current research. Once the medication records are parsed to identify those patients with current prescription records, the individuals are checked against the entries provided in [5] to extract the anticholinergic drugs and their corresponding ACB scores prescribed to each patient. For those receiving anticholinergic prescriptions, the cumulative effect of taking one or more anticholinergic drugs is measured using a Weighted Anticholinergic Risk Score (WARS) calculated for each individual as follows:

$$WARS = n_{c1} * S_{c1} + n_{c2} * S_{c2} + n_{c3} * S_{c3} \quad (1)$$

where n_{c1}, n_{c2}, and n_{c3} refer to the number of anticholinergic drugs prescribed to a patient which belong to classes c1, c2 and c3, respectively. S_{c1}, S_{c2}, and S_{c3} are the related anticholinergic risk scores associated with each class; i.e. S_{c1} = 1, S_{c2} = 2, and S_{c3} = 3. Additionally, the demography of individuals with anticholinegic medication including age, gender and postcodes are extracted from the database. The https://imd-by-postcode.opendatacommunities.org/imd/2019 which maps each postcode to the English IoD2019 is also utilised to identify the deprivation ranks of patients coming from different areas of London. Therefore, WARS scores per patient is calculated according to (1) and those patients with a score of 0 are excluded. The WARS scores form a vector of 18,568 patients (6.2%) prescribed to one or more anticholinergic drugs (mean age 46.93 +/- 22.10). All the medication records were extracted from the database in mid-March of 2020.

III. Mean-Shift Clustering

Clustering is an unsupervised learning method where samples are grouped together based on the similar characteristics of the data (i.e. here, similar risk scores). The clustering algorithms are mainly developed based on two different strategies. They either require the number of clusters to be pre-defined in advance prior to the analysis (e.g. k-mean clustering) or they estimate the number of clusters depending on the characteristics of data. The latter is divided into density-based and hierarchical clustering methods. The hierarchical approach requires a subjective inspection of a dendrogram generated by the method, but mean-shift clustering (a density-based approach) finds the cluster centers (centroids) depending on how data are distributed with no intervention from the user. The mean-shift clustering technique for this work updates the candidates for centroids reflected by a mean of the points within a bandwidth (BW). Whilst this BW can be given prior to processing it can also be estimated using the data, and for this work it is estimated based on a quantile of all the pairwise distances of the data points and which affects the sensitivity of the algorithm in identifying the centroids.

TABLE I
Patients Clustered into Ten Different Risk Groups According to Their WARS Scores

Risk Group (Cluster number)	Average risk per group	Number of patients
1	11.00	15
2	9.00	36
3	8.00	37
4	7.00	167
5	6.00	446
6	5.00	287
7	4.00	1286
8	3.00	5744
9	2.00	1161
10	1.00	9389

All the pre-processing steps including data extraction, cleansing, and manipulation were carried out in Python 3.7.4. The cluster analysis were also undertaken in python using the scikit-learn library and it's default quantile value of 0.3.

IV. Results and Discussion

The results of this work are presented and discussed in three parts. Firstly the results of the mean-shift clustering analysis are reported, secondly the demography of the patients receiving anticholinergic medications is described, and thirdly we evaluate how the population in different risk groups are correlated to the IoD2019 deprivation indices.

Applying mean-shift clustering to the vector of WARS scores returns 10 risk groups presented in Table I. The first risk group of 15 patients with an average WARS risk score of 11.00 are at the highest risk of anticholinergic medication followed by the succeeding clusters. The WARS population distribution is also presented in Fig. 1, indicating that the highest WARS score for the population is 14. The distribution of the highest risk group (group 1) is also shown in the expanded view over WARS values between 10 and 14 and includes 15 patients. This automated process that in this case identifies 15 out of 300,000 patients at risk from anticholinergic medication has significant time and cost saving implications for the health professionals who would traditionally identify such patients through a high dependence on personal knowledge, expertise and manual inspection. Our approach greatly facilitates decision making in clinical processes and medication reviews. It is also worth mentioning that the inspection risk need to be not restricted to the first risk group.

Figs. 2 and 3 represent the demography of patients receiving anticholinergic medication. Fig. 2 shows the Bar and Whisker plot for the average of the age values in different risk groups. The average ages in different risk groups (i.e. different clusters) are marked by the black dots on each bar and are close in value (average ages are between 49 and 56 across the risk groups). Additionally, the average age in all the risk groups is very close to its median (the bold line on each bar) indicating that the age distribution in the groups are not skewed. That is, age is not a variable correlated with average risk in each group. Fig. 3 represents the WARS average risk scores for males versus females across different age groups.

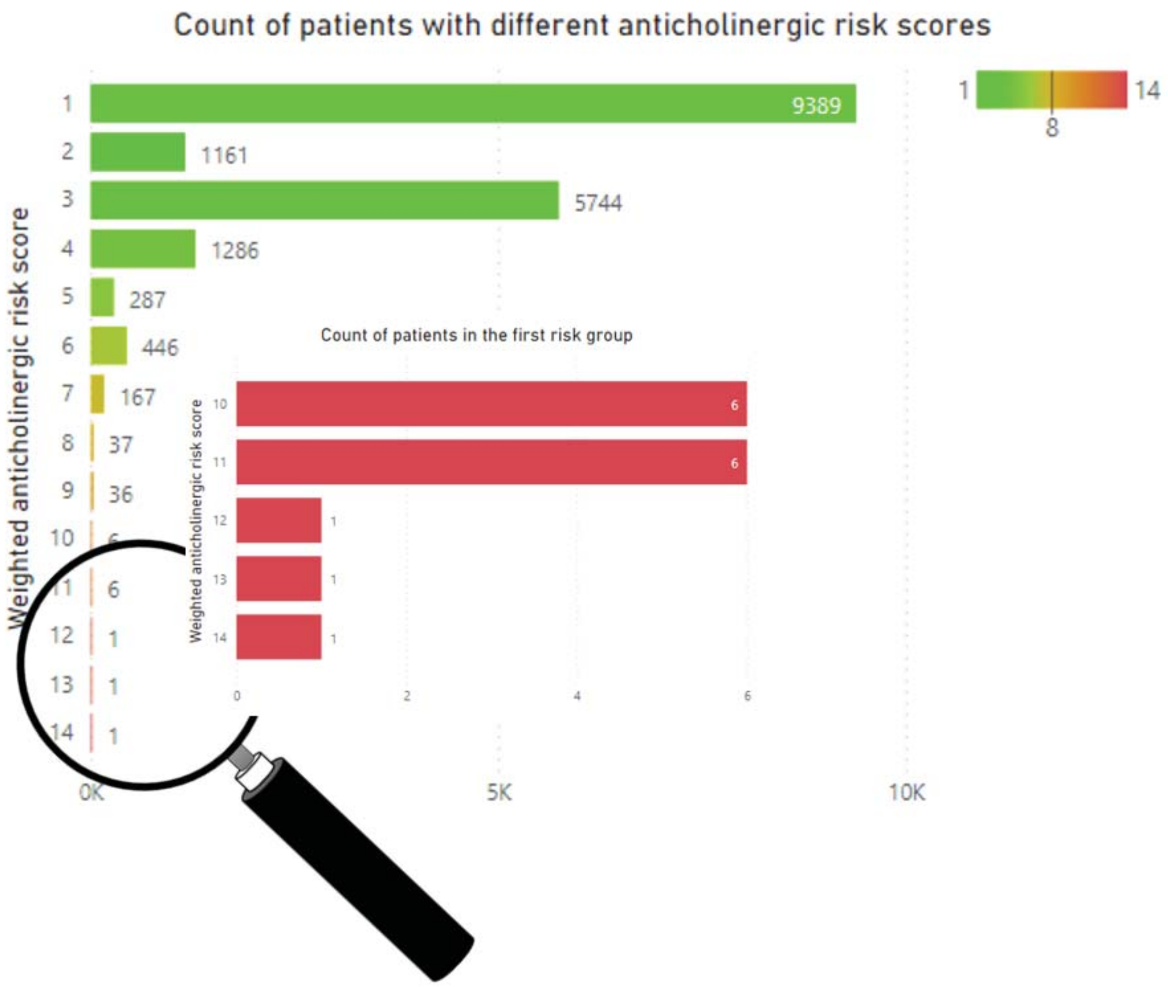

Fig. 1 The green-shaded histogram represents the count of patients with different WARS risk scores with 1 = lowest and 14 = highest score. The expanded red histogram represent the population in risk group 1 at the highest risk of anticholinergic medication distributed over a WARS range of 10 to 14 (the magnifying glass represents the approximate location of the group 1 distribution relative to the whole population)

Whilst the difference is not large it is clear that females on average are at a higher risk of anticholinergic medication compared to males.

Taking into account that past studies suggest that the socioeconomic status of an individual affects their health conditions [2], [3], we have considered how the average risk scores in each group might be correlated with the IoD2019 deprivation scores (which include the important indices of income, employment, and health and disability deprivation ranks). Figs. 4 and 5 show the average income deprivation rank in the 10 clusters derived from the mean-shift clustering algorithm. Fig. 4 presents how on average older people are deprived in different areas of London (different postcodes) whereas Fig. 5 looks at the same index in the same locations with no restriction on age. Both graphs indicate that the first risk group at the highest risk of anticholinergic medications are coming from those areas of London where people are on average more deprived with lower income relative to the population in other risk groups. The lower the average value

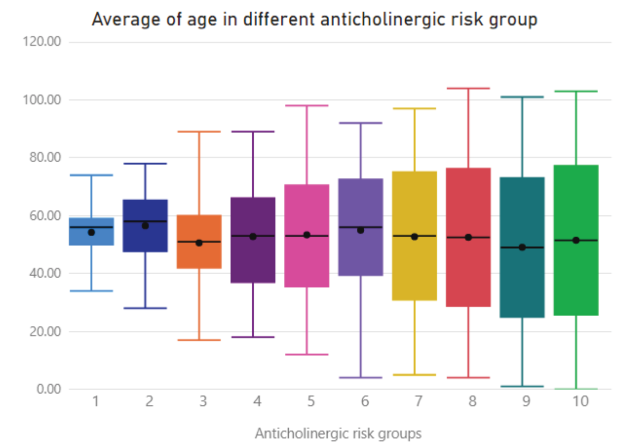

Fig. 2 Bar and Whisker plot for average age in different risk groups. The black dot and bold line on each bar plot represent the population's mean and median respectively. The whiskers (lower and higher ends of each bar plot) are set to the minimum and maximum age values in each risk group

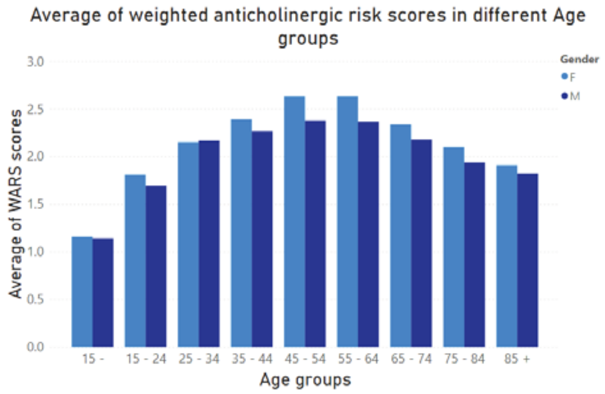

Fig. 3 Average of WARS for patients in different age groups for females versus males

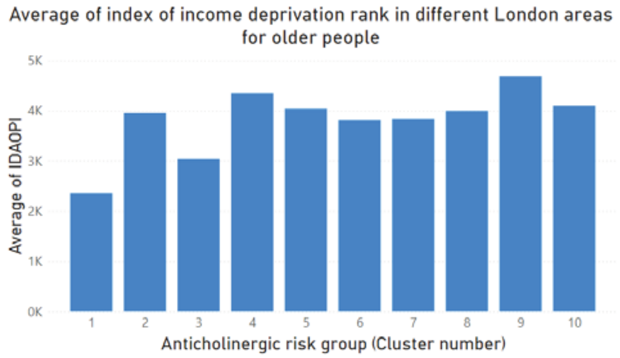

Fig. 4 Average of income deprivation among older people in each risk group based on their London location

on the y axis, the higher the deprivation. There is a weak but clear reduction of deprivation moving from the highest risk group (risk group one) to the lowest risk group (risk group 10).

Fig. 6 represents the average education deprivation rank in the 10 risk groups with the first three groups at a higher deprivation level, whilst Fig. 7 represents the average of the health and disability rank in different areas of London. The population in the first risk group coincides with locations correlated with the highest rank of health and disabilities, followed by the second and third risk groups. Both graphs

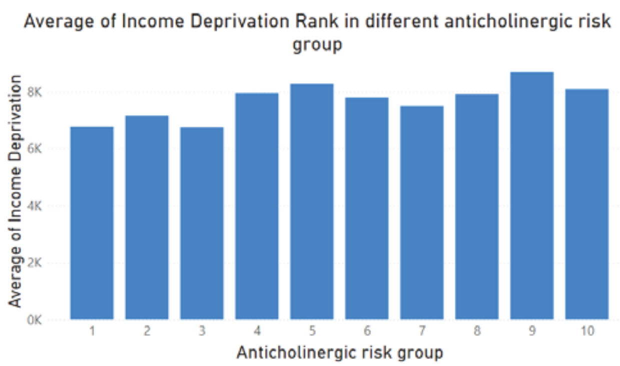

Fig. 5 Average of income deprivation in different locations of London for the population in the 10 different risk groups

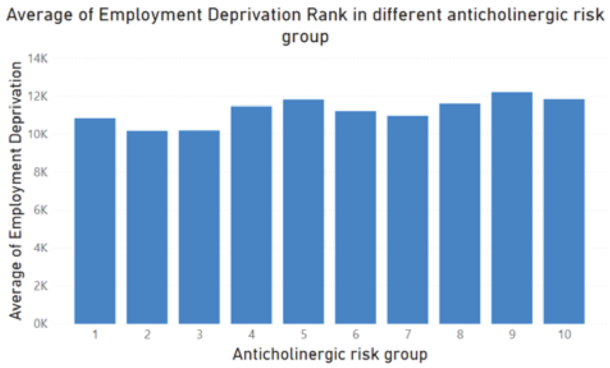

Fig. 6 Average of employment deprivation in different locations of London for the population in the 10 different risk groups

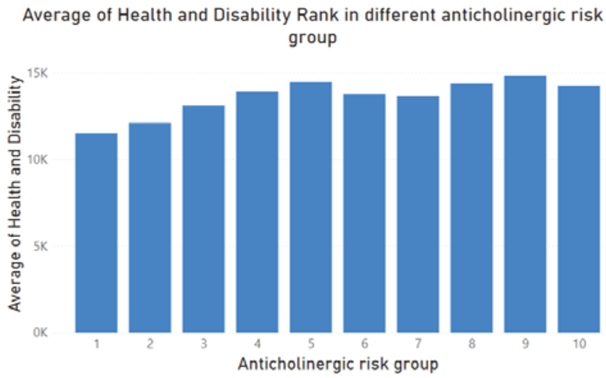

Fig. 7 Average of Health and disability rank in different locations of London for the population in the 10 different risk groups

in Figs. 6 and 7 follow a trend that shows there is an average reduction of education deprivation and health and disability issues while the WARS risk is reduced. Overall the observations of the graphs illustrated in Figs. 4-7 suggest that anticholinergic medication risk is associated with levels of deprivation and socioeconomic status according to different areas of London where the patients live.

V. Conclusion

The current research employed the mean-shift cluttering algorithm to dissociate patients receiving anticholinergic medication into different risk groups. The technique successfully clustered patients in to ten risk groups with the 1st cluster associated with the highest risk group and the 10th associated with the lowest risk group. The first group identifies 15 patients out of 300,000 who are at the highest risk from receiving multiple anticholinergic medication. A current software package implementing this approach has been developed in python has used by a healthcare management provider (AT Medics) and deployed in their system to support the health professional. It has been successfully used to monitor patients at risk from anticholinergic medication. Correlating the results against location-specific measures of deprivation suggests that there is link between socioeconomic status and anticholinergic medication of patients coming from different locations of London.

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