A Methodology Based on Subgroup Discovery to Generate Reduced Subgroup Sets for Patient Phenotyping

Antonio Lopez-Martinez-Carrasco[1][a], Jose M. Juarez[1][b], Manuel Campos[1,2][c] and Bernardo Canovas-Segura[1][d]
[1]*Med AI Lab, University of Murcia, Spain*
[2]*Murcian Bio-Health Institute (IMIB-Arrixaca), Spain*

Keywords: Methodology, Patient Phenotyping, Subgroup Discovery, Reduced Subgroup Set.

Abstract: Subgroup Discovery (SD) is a supervised machine learning technique that mines a set of easily readable features of patients with a medical condition in the form of a subgroup set (called patient phenotype). However, using only the output obtained by a single execution of an SD algorithm hinders the discovery of the best phenotypes since it is difficult for clinicians to choose the most suitable algorithm, its best hyperparameters and the quality measure. Therefore, we propose a new phenotyping approach based on SD that evaluates the outcomes of different SD algorithms to obtain a final patient phenotype with a reduced dependency on the initial conditions of these executions and to ensure diversity in terms of coverage of the subgroups from this phenotype. For that, we first define the problem of mining a patient phenotype in the form of a reduced subgroup set and, after that, we propose a new 6-step methodology to tackle this problem. Moreover, we carry out experiments driven by this methodology and focused on the antibiotic resistance problem by using the MIMIC-III public database and the patients infected by an Enteroccous Sp. bacterium resistant to Vancomycin as a target. Finally, we obtain a phenotype formed of 7 subgroups.

1 INTRODUCTION

Finding a set of observable features of patients with a medical condition has become a core issue in the clinical research field. This task is denominated as patient phenotyping and these patient features are denominated as patient phenotypes (Wojczynski and Tiwari, 2008). Patient phenotyping is useful for discovering novel and possibly unexpected relations between patient attributes, generating clinical hypotheses, or supporting medical experts decision-making, among others. Therefore, the development of new machine learning (ML) methods to find patient phenotypes is a key area in the health informatics research field.

A relevant application of the patient phenotyping is the antibiotic resistance problem, which, according to main healthcare organizations, is one of the growing and most alarming problems in the clinical field. This problem takes place when microorganisms become resistant to antimicrobials, causing antimicrobials to lose their effectiveness in combating microorganism infections. In this context, ML-guided patient phenotyping can be applied to automatically discover patient phenotypes related to the antibiotic resistance problem.

Subgroup Discovery (SD) (Atzmueller, 2015) is a suitable approach by which to tackle patient phenotyping. SD is a supervised machine learning technique whose main objective is to extract a simple and legible set of relations among attributes from a dataset regarding a target attribute of interest. These individual relations are denominated as subgroups. This technique is used to model a subgroup set for descriptive and exploratory data analysis, generating hypotheses, or extracting patterns, among others. An essential aspect of this technique is to compute the quality of the individual subgroups obtained. For that, a quality measure is used, which is a function that assigns a numerical value to a subgroup according to different properties from the dataset.

Although the SD technique is useful and generates easily readable phenotypes in the form of subgroup sets, using only the output obtained by a sin-

[a] https://orcid.org/0000-0002-2990-886X
[b] https://orcid.org/0000-0003-1776-1992
[c] https://orcid.org/0000-0002-5233-3769
[d] https://orcid.org/0000-0002-0777-0441

Lopez-Martinez-Carrasco, A., Juarez, J., Campos, M. and Canovas-Segura, B.
A Methodology Based on Subgroup Discovery to Generate Reduced Subgroup Sets for Patient Phenotyping.
DOI: 10.5220/0012321200003657

In *Proceedings of the 17th International Joint Conference on Biomedical Engineering Systems and Technologies (BIOSTEC 2024) - Volume 2*, pages 346-353
ISBN: 978-989-758-688-0; ISSN: 2184-4305

gle execution of a specific SD algorithm could involve certain disadvantages. One of them concerns the SD algorithm itself and its initial hyperparameters. In this sense, an SD algorithm could implement either an exhaustive or heuristic exploration strategy, return either all subgroups explored or the top-k subgroups explored, implement different pruning, and accept the use of different quality measures. Besides, different implementations of the same algorithm could incorporate other hyperparameters further than the originally defined ones (e.g., exploration depth). All the aforementioned characteristics make the subgroup set obtained by an SD algorithm highly variable and dependent on the initial conditions of the algorithm, thus causing the subgroups mined by different SD algorithms or by different hyperparameters can be notably different. Another disadvantage is the large number of subgroups that could be mined by a certain SD algorithm execution (pattern explosion problem), increasing the subgroup set size and making the result hardly readable and interpretable by experts in these cases.

Taking all this into account, we propose and develop a new approach based on the evaluation of the overlap between the subgroup sets mined by different SD algorithm executions to obtain a reduced subgroup set. More precisely, the main contributions of this research are (1) the definition of the problem of mining a patient phenotype in the form of a reduced subgroup set and (2) a new 6-step methodology that tackles this problem and allows the involvement of clinical experts in the process. The idea behind this methodology supported by the SD technique is based on a previously developed work (Lopez-Martinez-Carrasco et al., 2021), which consisted of finding patient cohorts by evaluating the overlap between different executions of a certain clustering algorithm.

The experiments carried out in this research are driven by the 6-step methodology proposed and the results obtained are compared with another descriptive SD method.

2 PROBLEM STATEMENT

This section provides the formal definitions related to the problem of mining a patient phenotype in the form of a reduced subgroup set.

An attribute a is a unique characteristic of an object, which has an associated value. An example of an attribute is $a = headache : yes$. Moreover, the domain of a, denoted as $dom(a)$, is the set of all unique values that a can take. Note that an attribute can be nominal or numeric depending on its domain. An instance i is a tuple of attributes of the form $i = (a_1, \ldots, a_m)$. Given the attributes $a_1 = fever : no$ and $a_2 = headache : yes$, an example of an instance is $i = (fever : no, headache : yes)$. A dataset d is a tuple of instances of the form $d = (i_1, \ldots, i_n)$. Given the instances $i_1 = (headache : yes, fever : no)$ and $i_2 = (headache : yes, fever : yes)$, an example of a dataset is $d = ((headache : yes, fever : no), (headache : yes, fever : yes))$. Moreover, the notation $v_{x,y}$ is used to indicate the value of the x-th instance i_x and its y-th attribute a_y from a dataset d.

Given an attribute a_y from a dataset d, a binary $operator \in \{=, \neq, <, >, \leq, \geq\}$ and a value $w \in dom(a_y)$, then a selector e is defined as a 3-tuple of the form $(a_y.characteristic, operator, w)$. Informally, a selector is a binary relation between an attribute from a dataset and a possible value of its domain. An example of a selector is $e = (headache, =, yes)$.

Given an instance i and a selector e, then i is covered by e if the binary expression "$v_{x,y}\ operator\ w$" holds *true*. Otherwise, i is not covered by e.

Given a dataset d, a pattern p is a list of selectors of the form $< e_1, \ldots, e_j >$ in which all attributes of the selectors are different. It is interpreted as a conjunction of selectors that represents a list of properties of a subset from d. Additionally, the pattern size is defined as the number of selectors that it contains.

Given an instance i and a pattern p, then i is covered by p if i is covered by all selectors $e \in p$. Otherwise, i is not covered by p.

Given a pattern p and a selector e, a subgroup s is a pair (p, e) in which the pattern is denominated as 'description' and the selector is denominated as 'target'. Additionally, the subgroup size is defined as the number of selectors that its description contains. An example of subgroup is $s = (< (headache, =, yes), (fever, =, no) >, (flu, =, no))$.

Given two subgroups s and s', s' is a refinement of s (denoted as $s \prec s'$) if s' has the same target as s, i.e., $s'.target = s.target$, and has an extended description, i.e., $s'.description = concat(s.description, < e_1, \ldots, e_j >)$.

Given a subgroup s and a dataset d, a quality measure q is a function that computes one numeric value according to s and certain metrics from d (Atzmueller, 2015).

Focusing on a specific subgroup s and a specific dataset d, different metrics with which to compute quality measures can be defined: (1) true positives (tp), defined as the number of instances i from the dataset d that are covered by the subgroup description $s.description$ and by the subgroup target $s.target$; (2) false positives (fp), defined as the number of instances i from d that are covered by $s.description$, but not by $s.target$; (3) true population (TP), defined as

$$
\begin{array}{llll}
subgroup_1\text{:} & \text{IF} & description_1 & \text{THEN} \quad distribution_1(target) \\
subgroup_2\text{:} & \text{IF} & description_2 & \text{THEN} \quad distribution_2(target) \\
 & & \vdots & \\
subgroup_k\text{:} & \text{IF} & description_k & \text{THEN} \quad distribution_k(target)
\end{array}
$$

Figure 1: Example of a subgroup set with k subgroups in the form of a decision set.

the number of instances i from d that are covered by $s.target$, and (4) false population (FP), defined as the number of instances i from d that are not covered by $s.target$.

Some examples of quality measures are Piatetsky Shapiro ($PS = (tp + fp) \cdot (\frac{tp}{tp+fp} - \frac{TP}{TP+FP})$), Weighted Relative Accuracy ($WRAcc = \frac{tp+fp}{TP+FP} \cdot (\frac{tp}{tp+fp} - \frac{TP}{TP+FP})$) or Incremental Response Rate ($IRR = \frac{tp}{tp+fp} - 1 + \frac{FP-fp}{FP}$).

A subgroup set ss is an unordered collection of subgroups of the form $ss = \{s_1, s_2, \ldots, s_k\}$. It can be interpreted as a decision set of the form "if", meaning that all subgroups from the set apply independently from the rest (Lakkaraju et al., 2016). An example is depicted in Figure 1.

The SD problem consists of exploring the search space of a dataset d to mine a subgroup set ss in which the quality value, computed with a quality measure q, for each individual subgroup $s \in ss$ is greater or equal to a given $threshold$. Some examples of SD algorithms are SD-Map (Atzmueller and Puppe, 2006), VLSD (Lopez-Martinez-Carrasco et al., 2023a) or BSD (Lemmerich et al., 2010), among others.

Two different subgroups generated by any SD algorithm are redundant when both cover the same portion of instances from a specific dataset. In this context and according to their coverage, one of them is called the dominant subgroup and the other is called the dominated subgroup, allowing the latter to be deleted. Therefore, two types of dominance relations can be stated: (1) close (Garriga et al., 2006), and (2) closed-on-the-positives (Lemmerich et al., 2010). Considering both dominance relations, other examples of SD algorithms are CBSD (BSD with the close dominance relation) and CPBSD (BSD with the closed-on-the-positives dominance relation).

Given a collection of subgroup sets $\{ss_1, ss_2, \ldots, ss_n\}$, the overlap function of is a function that evaluates the overlap between these subgroup sets by computing their intersections and returns another subgroup set. Formally: $of(\{ss_1, ss_2, \ldots, ss_n\}) = \bigcap_{i=1}^{n} ss_i$.

Finally, the subgroup set returned by an overlap function of is denominated as a reduced subgroup set and is denoted as rss. In this context, we use a reduced subgroup set rss to represent a phenotype.

3 METHODOLOGY

This section describes the proposed 6-step methodology with which to tackle the problem defined in Section 2, allowing the involvement of clinical experts in the process. This methodology is shown in Figure 2 and consists of the following steps:

Step 1 consists of extracting the data from the clinical source(s) to later preprocess it. This preprocessing comprises different tasks such as data cleaning or data transformation, among others, which are necessary to obtain the final dataset (denominates as the mining view). Note that different SD algorithms accept different data formats (e.g., only nominal attributes, only numerical attributes, both nominal and numerical attributes, etc.). Therefore, it is necessary to ensure that the mining view has the correct format according to the SD techniques that will be used in the following steps. Step 1 also includes the selection of the pair attribute-value that will be used as a target in all SD algorithm executions.

Step 2 is formed of two phases: (1) splitting the mining view as many times as different algorithms and hyperparameters will be applied, and (2) for each split, selecting the specific SD algorithm and its hyperparameters that will be applied over this split. In this step, the greater the number of splits and different algorithms and hyperparameters, the lower the dependency between the algorithms, the hyperparameters and the final subgroup set mined and, therefore, the more reduced the final subgroup set will be. However, using an excessive number of splits, algorithms, and hyperparameters may imply that the intermediate subgroup sets obtained do not overlap each other and, therefore, that the rss is either of poor quality or even empty. In Step 2, it is also possible to duplicate a certain split to apply different algorithms and/or hyperparameters to the same data. Concerning this step, remember that the target established in the first step must be used in all the SD algorithm executions.

Step 3 consists of executing all SD algorithms with their hyperparameters over the corresponding splits to obtain the subgroup sets, one per algorithm. These intermediate subgroup sets are denoted as $ss_1, ss_2, ss_3, \ldots, ss_n$. Note that these subgroup sets are intermediate phenotypes that are highly dependent on the specific SD algorithms and hyperparameters

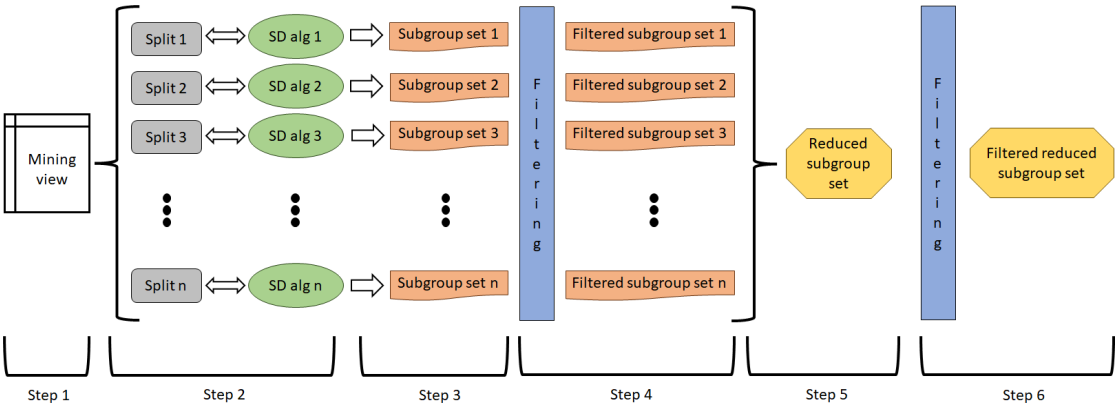

Figure 2: 6-Step methodology proposed.

used to generate them. Therefore, they will be combined later to generate the *rss*, i.e., the final phenotype with a reduced dependency concerning each of the multiple SD algorithms executed.

Step 4 consists of filtering each subgroup set generated by the SD algorithms in the previous step, obtaining a new collection of subgroup sets denoted as $fss_1, fss_2, fss_3, \ldots, fss_n$. The applied filters can be of two types: (1) automatic filters, based on certain computable criteria, for example, the quality measure of the subgroups contained in the subgroup set or rules designed by experts, among others, and (2) manual filters, applied directly by experts and based on their knowledge and experience.

Step 5 is based on the execution of the overlap function to combine all filtered subgroup sets obtained previously to generate the *rss*. This means that, given the collection of subgroup sets $\{fss_1, fss_2, fss_3, \ldots, fss_n\}$, then the function $of(\{fss_1, fss_2, fss_3, \ldots, fss_n\})$ is executed. Once the *rss* is generated, it is also possible to reorder its subgroups by using another different quality measure.

Finally, Step 6 consists of filtering the *rss* from the previous step to obtain the phenotype $frss$. In both Steps 4 and 6, either automatic or manual filters can be applied and domain experts actively participate in the confection of the phenotypes. These filtering processes could be supported by visualization tools for clinicians' decision-making.

4 EXPERIMENTS AND RESULTS

The objective of the experiments carried out in this work was to test our methodology regarding the defined problem as well as its suitability to identify patient phenotypes in the context of antibiotic resistance. For that purpose, we used real clinical data obtained from MIMIC-III, which is a public dataset that contains health data related to more than 45,000 patients treated in ICUs (intensive care units) and around 60,000 admissions between the years 2001 and 2012. This database contains data related to demography, laboratory tests, vital sign measurements or administered medications, among others. In addition, the experiments presented and described in this section are driven by our 6-step methodology.

4.1 Step 1

First, we extracted data from the MIMIC-III public database to compose a mining view in which each instance was a strain of a population of a microorganism obtained in a culture (laboratory test) of a patient during one of their admissions. During this process, we applied a preprocessing phase to delete duplicate instances and attributes, delete empty attributes or those with only one value, and discretize numerical attributes since SD algorithms used only accept this type of attributes. The mining view had 9,240 instances and 12 attributes, which are described in Table 1. Finally, we used as a target the patients infected by an Enteroccous Sp. bacterium resistant to Vancomycin, i.e. Class = Yes, having therefore 2,126 positive instances and 7,114 negative instances.

4.2 Step 2

The next step was to split this mining view. In this case, we generated 5 different stratified splits (with no duplicates). For each split, we assigned the following algorithms and hyperparameters: for the split 1 (1,849 rows), the SD-Map algorithm with the Piatetsky Shapiro quality measure and with no minimum quality thresholds; for the split 2 (1,848 rows), the VLSD algorithm with the WRAcc quality measure (defined between -1 and 1, both included) and a minimum quality threshold of 0; for the split 3 (1,848

Table 1: Mining view details.

Attribute name	Attribute description
Patient gender	Male or Female
Patient age	Child, Adult or Elderly
Admission location	Patient's location before arriving
Dischage location	Patient's location after discharging
Culture specimen type	Specimen which was tested in the culture for bacterial growth
Service when culture	Service where the patient resided when the culture was done
ICU when culture	ICU where the patient resided when the culture was done
Readmission	If the patient was in the hospital in the past
Days between admission and first ICU	Zero, or One or more
Previous Vancomycin treatments	If the patient was treated with vancomycon before
Culture month	Month when the culture was done
Class	Enteroccous Sp. bacterium resistant to Vancomycin (Yes / No)

rows), the BSD algorithm with Piatetsky Shapiro quality measure, with no minimum quality thresholds and with a maximum of 1,000 subgroups (i.e., the best 1,000 subgroups); for the split 4 (1,848 rows), the CBSD algorithm with WRAcc quality measure, with no minimum quality thresholds and with a maximum of 1,000 subgroups (i.e., the best 1,000 subgroups), and for the split 5 (1,847 rows), the CPBSD algorithm with Piatetsky Shapiro quality measure, with no minimum quality thresholds and with a maximum of 1,000 subgroups (i.e., the best 1,000 subgroups). All these algorithms and quality measures are implemented in the *subgroups* python library, which is available on PyPI or [1].

4.3 Step 3

The next step was to actually run the algorithms. After executing the SD-Map algorithm over split 1, we obtained a subgroup set ss_1 with 1,315,110 subgroups. After running the VLSD algorithm over split 2, we generated a subgroup set ss_2 with 374,817 subgroups. After executing the BSD algorithm over split 3, we mined a subgroup set ss_3 with 1,000 subgroups. After running the CBSD algorithm over split 4, we obtained a subgroup set ss_4 with 1,000 subgroups. Finally, after executing the CPBSD algorithm over split 5, we mined a subgroup set ss_5 with 1,000 subgroups.

In this point, remember that we used different algorithms with different quality measures and hyperparameters over different datasets (obtained after splitting the initial mining view). The five subgroup sets obtained are intermediate phenotypes that are highly dependent on the five SD algorithms and hyperparameters used to generate them.

4.4 Step 4

After executing all the SD algorithms, we mined a total number of 1,692,927 subgroups, which would be relatively high for direct human intervention in case these were the final phenotypes to analyse. Therefore, we applied an automatic filtering process based on the quality measure of the subgroups from each subgroup set obtained. For that, for each subgroup set, we only selected those subgroups whose quality measure value was greater than or equal to a certain threshold. Figures 3, 4, 5, 6, and 7 shows the number of subgroups that we finally obtain in each SD model when varying the quality measure threshold. Note that these figures serve as visual support for the clinical experts' decision-making.

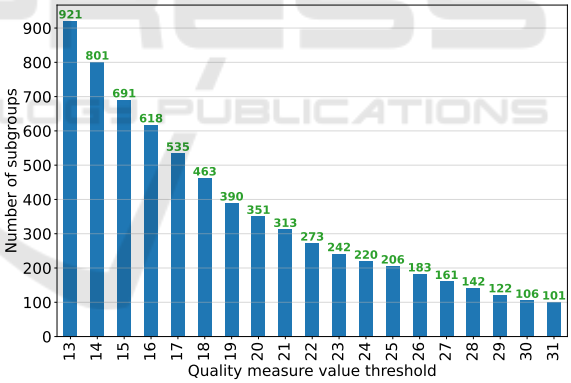

Figure 3: Step 4 - Subgroup set 1 (ss_1).

For the subgroup set 1 (i.e., ss_1), we established a threshold value of 23, obtaining therefore a filtered subgroup set fss_1 with 242 subgroups. For the subgroup set 2 (i.e., ss_2), we set a threshold value of 0.02, obtaining therefore a filtered subgroup set fss_2 with 104 subgroups. For the subgroup set 3 (i.e., ss_3), we established a threshold value of 23, obtaining therefore a filtered subgroup set fss_3 with 247 subgroups. For the subgroup set 4 (i.e., ss_4), we set a threshold value of 0.01, obtaining therefore a filtered subgroup set fss_4 with 234 subgroups. Note that, in this case, there is a higher concentration of subgroups at values close to 0. Finally, for the subgroup set 5 (i.e.,

[1] https://github.com/antoniolopezmc/subgroups

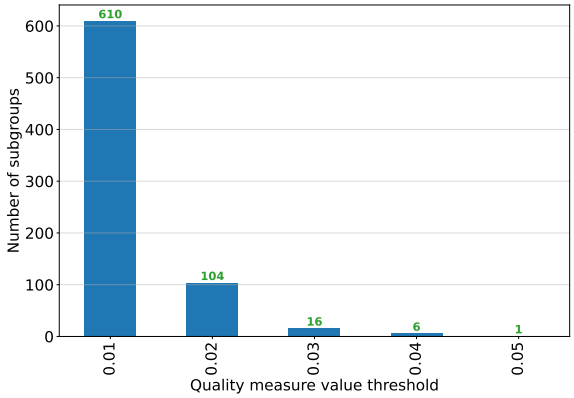

Figure 4: Step 4 - Subgroup set 2 (ss_2).

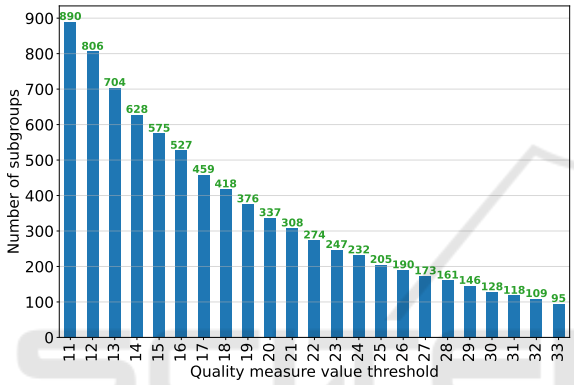

Figure 5: Step 4 - Subgroup set 3 (ss_3).

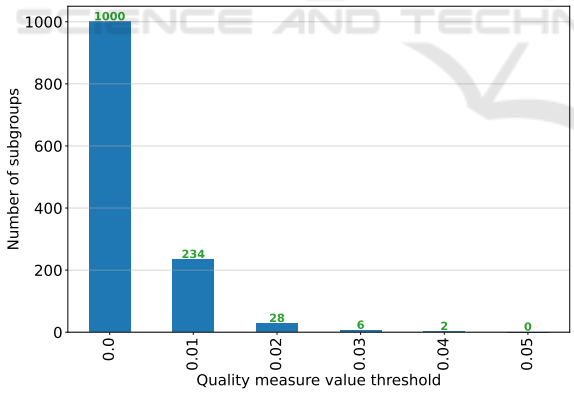

Figure 6: Step 4 - Subgroup set 4 (ss_4).

ss_5), we established a threshold value of 20, obtaining therefore a filtered subgroup set fss_5 with 255 subgroups.

After applying this filtering process, we had a total number of 1,082 subgroups, which would also be relatively high for direct human intervention in case these were the final phenotypes to analyse. For this reason, these filtered phenotypes were combined in Step 5.

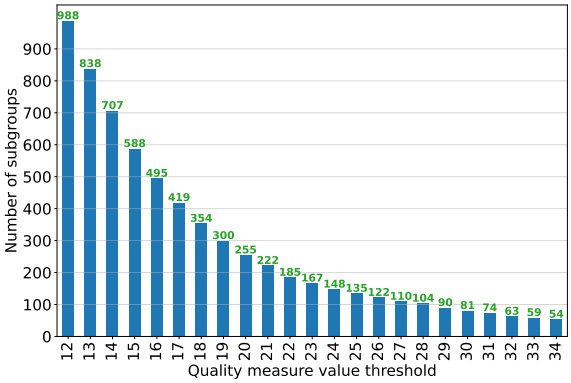

Figure 7: Step 4 - Subgroup set 5 (ss_5).

4.5 Step 5

This step consisted of applying the overlap function in order to combine fss_1, fss_2, fss_3, fss_4 and fss_5 to obtain *rss*. In these experiments, we used the overlap function of defined in Section 2. Once applying the overlap function over all previous filtered subgroup sets, i.e. $of(\{fss_1, fss_2, fss_3, fss_4, fss_5\})$, we obtained a *rss* with 14 subgroups. After that, we reordered the subgroups contained in the *rss* by using the IRR quality measure, considering the mining view completely.

4.6 Step 6

Finally, the last step of our methodology consisted of filtering the *rss* to obtain the $frss$, which was the final phenotype generated by our methodology. In this case, we applied an automatic filtering process based on the deletion of subgroup refinements. For that purpose, for each pair of distinct subgroups s_1 and s_2 from *rss*, we deleted the subgroup with lower quality if s_2 is a refinement of s_1 or s_1 is a refinement of s_2. An advantage of this filter is that it allows for a reduction of the number of instances simultaneously covered by different subgroups from $frss$. After applying this filtering process, we finally obtained a $frss$ with 7 subgroups, which are shown in Table 2.

At this point, it is necessary to remember that both *rss* and $frss$ are two phenotypes with a reduced dependency on the previous SD algorithms and hyperparameters used.

The obtained phenotype (Table 2) describes adult male patients admitted to the surgical service (SURG) and in the surgical ICU (SICU) who were readmitted in the hospital and spent one day or more between the hospital admission and the admission in the first ICU, and in which the cultures were swab. Additionally, the subgroup descriptions from $frss$ have either two or three selectors. With respect to the phenotype

Table 2: Step 6 - Filtered reduced subgroup set $frss$.

Subgroup description	Positive instances (tp)	Negative instances (fp)	IRR
icu_when_culture = 'SICU', patient_age = 'ADULT', service_when_culture = 'SURG'	250 (12%)	178 (3%)	0.559
readmission = 'yes', service_when_culture = 'SURG'	370 (17%)	384 (5%)	0.437
culture_specimen_type_ description = 'SWAB', readmission = 'yes'	322 (15%)	372 (5%)	0.412
culture_specimen_type_ description = 'SWAB', patient_age = 'ADULT'	416 (20%)	481 (7%)	0.396
days_between_admission_ and_first_ICU = 'OneDayOrMore', service_when_culture = 'SURG'	354 (17%)	460 (6%)	0.370
culture_specimen_type_ description = 'SWAB', patient_gender = 'M'	454 (21%)	600 (8%)	0.346
days_between_admission_ and_first_ICU = 'OneDayOrMore', patient_age = 'ADULT'	487 (23%)	673 (9%)	0.325

coverage, Table 2 also shows that the subgroups individually considered always cover less than 25% of the positive instances and less than 10% of the negative instances.

4.7 Comparison of the Results

This section compares the $frss$ obtained by our methodology with the model obtained by another descriptive SD method in terms of coverage by analysing the overlap between the dataset instances covered by both models. More precisely, we focus on previous research (Lopez-Martinez-Carrasco et al., 2023b) in which the DSLM algorithm along with the mining view presented in Section 4.1 were used to mine two patient phenotypes in the form of diverse top-2 subgroup lists. This comparison process showed, according to the Dice coefficient, an overlap of 50% between $frss$ and the first subgroup list and 62% between $frss$ and the second subgroup list. This means that our methodology was able to mine a patient phenotype in which, at least, half of the instances were the same as the ones generated by a phenotyping SD method based on the Minimum Description Length (MDL) principle (Grünwald, 2007) and a compression gain metric.

5 DISCUSSION

In this section, we discuss our proposed 6-step methodology and its application to the MIMIC-III database in the context of patient phenotyping applied to the antibiotic resistance problem.

With respect to Step 1, it is highly dependent on the data that we have, the specific problem that we are handling and the concrete clinical target to study. In this work, we present a clinical database with real data and, after a preprocessing, we obtain a mining view with 9,240 instances and 12 attributes.

Concerning Step 2, there are two aspects to consider. The first one is the number of splits, which determines the quality of the final output of the methodology. If we have a lower number of splits, algorithms and hyperparameters, then the *rss* will remain highly dependent on those few splits, algorithms and hyperparameters used. However, if we have a higher number of splits, algorithms and hyperparameters, then the reduced phenotype may be of poor quality since there is no overlapping between the intermediate subgroup sets. The second one is the quality measure used in each SD algorithm. Each quality measure is designed to focus on different dataset characteristics and, therefore, obtain subgroups with these characteristics (e.g., more general subgroups, more specific subgroups, etc.). For this reason, the utilization of different quality measures allows us to mine a reduced phenotype containing subgroups that share all these characteristics at the same time. Additionally, this methodology offers the possibility of duplicating the same split to apply different algorithms and/or hyperparameters to the same data. However, it is advisable not to abuse this duplication in certain cases since we can produce that some instances and/or subgroups have a greater weight than others.

Regarding Step 3, SD is a highly parallelisable technique since, in general, all subgroups obtained by a certain SD algorithm can be represented as a tree or as a lattice. For this reason, each algorithm could be executed in parallel to improve the methodology performance. Focusing on the WRAcc quality measure, it prioritises those subgroups that cover more positive instances than negative ones. This means that all subgroups obtained with the mining view or the splits and this quality measure had values close to 0 because the number of negative instances is always higher than the number of positive instances.

Concerning Step 4, this is a step in which the domain experts can participate. For this reason, different visualization methods, apart from those used in this work, can be defined and provided to help experts' decision-making.

Regarding Step 5, this work defines and uses a specific overlap function (see Section 2), although other functions to obtain reduced subgroup sets could be also explored and defined.

With respect to Step 6, it is especially useful in case the *rss* has such a large number of subgroups that it is hardly readable and interpretable by experts. In this work, we applied a filter based on the deletion of subgroup refinements, obtaining therefore a $frss$ with 7 subgroups in which the shared instances between different subgroups have been reduced. This is useful to increase the diversity in terms of coverage, i.e., to have subgroups that explain as different dataset regions as possible.

Finally, not only the third step can be executed in parallel. It is also possible to parallelize steps 2 and 4 to enhance the methodology performance.

6 CONCLUSIONS

This research was developed to provide clinicians with a new approach for obtaining patient phenotypes with a reduced dependency on the specific SD algorithm(s) and hyperparameters used. For that, we first defined the problem of mining a patient phenotype in the form of a reduced subgroup set and, after that, we proposed a new 6-step methodology based on the evaluation of the overlap between the output of different SD algorithm executions.

The experiments carried out in this work were focused on the antibiotic resistance problem and were driven by our methodology. Besides, we used the MIMIC-III public database as a data source and we established the patients infected by an Enteroccous Sp. bacterium resistant to Vancomycin as a target. We obtained a phenotype $frss$ with 7 subgroups which described adult male patients admitted to the surgical service (SURG) and in the surgical ICU (SICU) who were readmitted in the hospital and spent one day or more between the hospital admission and the admission in the first ICU, and in which the cultures were swab. Moreover, each subgroup from the final phenotype covered 25% of the positive instances and 10% of the negative instances as maximum. Additionally, this phenotype was compared in terms of coverage with the diverse top-2 subgroup lists obtained by the DSLM algorithm. We used the Dice coefficient for this comparison, obtaining an overlap of 50% between $frss$ and the first subgroup list and 62% between $frss$ and the second subgroup list.

Finally, future work can focus, for example, on using other visual support techniques in the methodology (apart from the already used in this work), explore other overlap functions, or integrate other techniques such as the MDL principle in the phenotype generation process.

ACKNOWLEDGEMENTS

This work was partially funded by the CONFAINCE project (Ref: PID2021-122194OB-I00) by MCIN/AEI/10.13039/501100011033 and by "ERDF A way of making Europe", by the "European Union", and by the GRALENIA project (Ref: 2021/C005/00150055) supported by the Spanish Ministry of Economic Affairs and Digital Transformation, the Spanish Secretariat of State for Digitization and Artificial Intelligence, Red.es and by the NextGenerationEU funding. This research was also partially funded by a national grant (Ref: FPU18/02220), of the Spanish Ministry of Science, Innovation and Universities (MCIU).

REFERENCES

Atzmueller, M. (2015). Subgroup Discovery - Advanced Review. *WIREs: Data Mining and Knowledge Discovery*, 5(1):35–49.

Atzmueller, M. and Puppe, F. (2006). SD-Map - A Fast Algorithm for Exhaustive Subgroup Discovery. In *Knowledge Discovery in Databases (PKDD 2006)*, pages 6–17.

Garriga, G., Kralj Novak, P., and Lavrac, N. (2006). Closed Sets for Labeled Data. volume 9, pages 163–174.

Grünwald, P. D. (2007). *The Minimum Description Length Principle*, volume 1. The MIT Press.

Lakkaraju, H., Bach, S. H., and Leskovec, J. (2016). Interpretable Decision Sets: A Joint Framework for Description and Prediction. In *Proceedings of the 22nd ACM SIGKDD International Conference on Knowledge Discovery and Data Mining*, page 1675–1684.

Lemmerich, F., Rohlfs, M., and Atzmüller, M. (2010). Fast Discovery of Relevant Subgroup Patterns. In *The Florida AI Research Society*.

Lopez-Martinez-Carrasco, A., Juarez, J. M., Campos, M., and Canovas-Segura, B. (2021). A methodology based on Trace-based clustering for patient phenotyping. *Knowledge-Based Systems*, 232:107469.

Lopez-Martinez-Carrasco, A., Juarez, J. M., Campos, M., and Canovas-Segura, B. (2023a). VLSD - An Efficient Subgroup Discovery Algorithm Based on Equivalence Classes and Optimistic Estimate. *Algorithms*, 16(6).

Lopez-Martinez-Carrasco, A., Proença, H. M., Juarez, J. M., Leeuwen, M. v., and Campos, M. (2023b). Novel approach for phenotyping based on diverse top-k subgroup lists. In *Artificial Intelligence in Medicine*, pages 45–50.

Wojczynski, M. K. and Tiwari, H. K. (2008). Definition of Phenotype. In *Genetic Dissection of Complex Traits*, volume 60, pages 75–105.