

Trends in Drug Prescriptions in the Outpatient Physician Sector in a German Federal State from 2014 to 2023 Using Morbidity Related Groups, Correlations and Partial Correlations

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Abstract: The pharmaceutical prescription data of all SHI-insured persons in a German federal state are analysed over a period of 10 years. With the help of the International ATC Code, each patient is assigned a Morbidity Related Group (MRG) as the active substance group with the highest costs per year. The leading MRG positions per age are compared between 2019 as the current year before the coronavirus pandemic and 2023 after the coronavirus pandemic. Between the ages of 23 and 31, treatment with antidepressants has come to the fore. Beta-lactam antibacterials and penicillins dominate in early childhood in both years and antithrombotics agents in old age. The correlations between age, polypharmacy and cost percentiles are examined in pairs or as a whole with correlations and partial correlations. All partial correlations of the three variables are greater than the correlations.

1 INTRODUCTION

The costs associated with drugs prescribed by SHI physicians represent a significant financial burden within the context of statutory health insurance (SHI) in Germany, ranking as the second or third largest expenditure category in many regions. In the German state of Schleswig-Holstein, the cost of pharmaceuticals has risen from 1.0 billion euros in 2014 to 1.7 billion euros in 2023. The following analysis is based on all data associated with doctor's prescriptions to SHI patients. It should be noted that over-the-counter medicines are not included in this analysis, as no patient-related data exists for these in general. Additionally, the approximately ten percent of privately insured patients were excluded from the analyses. These calculations fall within the domain of big data, given the number of prescriptions, which range from 7.0 to 8.3 million per year.

In this paper, the focus should be on the patient,

irrespective of which medical practitioner issued the prescription. This is a significant difference to doctor-centred cost-effectiveness analyses. The number of patients included in the analyses varies from year to year, with figures ranging from 1.5 to 1.7 million. The top one percent of expensive patients account for 39-42% of pharmaceutical expenditure, with an annual expenditure of EUR 5,400 in 2014 and rising to EUR 12,100 in 2023. The objective of this paper is not to examine the cost structure and developments in the one per cent of patients with the highest costs; rather, it is to investigate the correlations and developments in the 99 per cent of patients who account for the majority of prescriptions.

We use the five-level international ATC code (Anatomical-Therapeutic-Chemical) introduced by the WHO with specifications relating to the German authorisation law for medicinal products. Germany has the largest number of authorised medicinal products in the European Union and globally. In Germany,

medicinal products are identified by a pharmaceutical central number (PZN). Extensive pharmacological information is available in databases based on this PZN. To illustrate, data regarding the active ingredients, their pharmaceutical forms, and dosages is accessible at a more granular level than that obtained from the ATC code. The prescriptions of multiple active substances for a single patient are represented by the number of ATC codes at the third level (see examples below), which are classified as ATC four-digit codes, cf. (Johnell and Klarin, 2007), (Fricke et al., 2019). The number of active substances is considered as a measure of polypharmacy, although this is not contingent on a specific number. This is connected to the concept of performance auditing as outlined in the MRG (Morbidity Related Groups) framework (refer to (Schuster et al., 2016), (Schuster et al., 2018) and (Schuster et al., 2016)). With regard to the 10-year analysis, the simultaneity considerations relate appropriately to one year at a time. It is not feasible to conduct a longer analysis than 10 years using the original data due to the constraints imposed by data protection regulations. Similarly to the DRG (Diagnosis Related Group) within the hospital sector, the MRG drug group (ATC four-digit) with the highest costs is used as an annualised patient characteristic.

In general, the higher the age, the higher the polypharmacy and the cost percentile. Deviating from this, particularly high costs in the oncological field are found in middle age, for example, but these generally affect the most expensive one per cent of patients and only have a minor impact on the overall view, see (Case and Deaton, 2017), (High, 2004), (Turrentine et al., 2006), (Brennan and Clare, 1980), (Koh et al., 2005), (Delara et al., 2022), (Golchin et al., 2015) and (Weng et al., 2020). The MRG considerations illustrate the circumstances under which particular considerations are beneficial for specific patient groups. However, this is beyond the scope of the present paper. The correlations resulting from the three parameters listed and the partial correlations determined with them show that classical interpretations reach their limits in this respect. Furthermore inverse formulae are provided for calculating the correlations from the partial correlations. These results stem from a relationship to spherical trigonometry, which gives rise to a sine theorem of statistics. The relationship to the corona pandemic is discussed in some places.

2 MATERIALS AND METHODS

The objective of this study is to analyse drug prescription data on all patients with statutory health insur-

ance in the period from 2014 to 2023 for treatments of patients of SHI-doctors from Schleswig-Holstein. The data set includes a patient identifier, the patient's year of birth, and the year in which the prescription was issued. With the exception of minor fluctuations throughout the year, this information serves to determine the patient's age. The pharmacological data is derived from the central pharmaceutical number (PZN) using information from the database.

The flow of data in Germany has historically been characterised by media discontinuities. Following a protracted period of postponement, a comprehensive electronic transmission is presently undergoing development. The biggest media disruption is the scanning of a paper prescription in the pharmacy data centres. Errors pertaining to the patient ID, the doctor ID (which is not directly utilised in our analyses, but is nevertheless pertinent to the allocation to the federal state), the patient's date of birth and the PZN have the potential to impact the evaluations. While these errors can be rectified to a certain extent within the participating institutions, the extent of this rectification is limited.

The ATC classification is an official system for categorising pharmacological agents according to the organ or organ system they affect and according to their chemical, pharmacological and therapeutic properties, cf. (Rübenach et al., 2021). Since 2004, the BfArM institution has published the official version of the ATC classification annually on behalf of the Federal Ministry of Health in accordance with Section 73 (8) of the Fifth Book of the German Social Code (SGB V), see (Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM), 2021). In accordance with Section 73 (8) of the German Social Code (SGB V), the ATC classification is to be adapted to the specific features of the healthcare situation in Germany as required. The official ATC classification is an adaptation of the WHO ATC classification, tailored to the specific requirements of the German pharmaceutical market. The following example in table 1 illustrates the aforementioned concept with reference to the most frequently prescribed active substance in Schleswig in 2023, which bears the ATC code N02BB02:

It should be noted that the ATC system does not adhere to a consistent classification structure, with the levels anatomical, therapeutic and chemical being used in a non-uniform manner.

The Morbidity Related Group (MRG) per patient and analysis period (in this paper across all doctors, in other analyses per doctor) represents the drug group at the Anatomical Therapeutic Chemicals (ATC) level (third level) - in the example N02B - with the high-

Table 1: The five levels of the ATC code with their corresponding ATC classification.

code	different ATC levels	classification
N02BB02	Metamizole sodium	chemical
N02BB	Pyrazolones	chemical
N02B	Other analgetics and antipyretics	therapeutic
N02	Analgetics	therapeutic
N	Nervous system	anatomical

est costs. Consequently, a single 'main medication' is identified for each patient and period, which serves to displace less significant medications in terms of their assigned label, cf. (Schuster et al., 2016) Subsequently, the total costs are allocated to the aforementioned MRG. Furthermore, the analyses calculate the number of these ATC four-digit drugs as a characteristic of polypharmacy, the proportion of costs attributable to the label, and the percentile of the patient's costs in a year-on-year comparison.

From a methodological standpoint, alternative metric scales could be employed in lieu of the cost per PZN.

We define the partial correlations from the correlations ρ_{12} , ρ_{13} and ρ_{23} of the random variables X_1 , X_2 and X_3 with values from the interval $(-1, 1)$ in a general way (see (Kim, 2015) and (Brief et al., 1988)) by:

$$\begin{aligned} \rho_{12,3} &= \frac{\rho_{12} - \rho_{23}\rho_{13}}{\sqrt{1 - \rho_{23}^2}\sqrt{1 - \rho_{13}^2}} \\ \rho_{13,2} &= \frac{\rho_{13} - \rho_{12}\rho_{23}}{\sqrt{1 - \rho_{12}^2}\sqrt{1 - \rho_{23}^2}} \\ \rho_{23,1} &= \frac{\rho_{23} - \rho_{12}\rho_{13}}{\sqrt{1 - \rho_{12}^2}\sqrt{1 - \rho_{13}^2}} \end{aligned} \quad (1)$$

The exclusion of interval limits ± 1 is intended to exclude singularities. Moreover, we define

$$m = \frac{1 - \rho_{12,3}^2}{1 - \rho_{12}^2}.$$

By inserting the definition of the partial correlation, a short transformation yields the following result:

$$m = \frac{1 - \rho_{23}^2 - \rho_{13}^2 - \rho_{12}^2 + 2\rho_{12}\rho_{13}\rho_{23}}{(1 - \rho_{12}^2)(1 - \rho_{13}^2)(1 - \rho_{23}^2)} \quad (2)$$

Due to the symmetry of this expression, the following can be inferred

$$m = \frac{1 - \rho_{12,3}^2}{1 - \rho_{12}^2} = \frac{1 - \rho_{13,2}^2}{1 - \rho_{13}^2} = \frac{1 - \rho_{23,1}^2}{1 - \rho_{23}^2}. \quad (3)$$

In the three-dimensional space of correlations within the specified intervals, we consider the boundary surfaces with partial correlation, with an absolute value

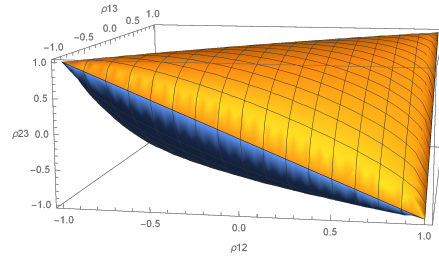


Figure 1: The yellow and blue levels indicate all values of the correlation for which the absolute value of the partial correlation is equal to one.

of 1, using the Mathematica software from Wolfram Research.

The solution of the quadratic equation is derived from the upper and lower boundary surfaces, and once more, the symmetry with regard to the three variables is evident. The boundary surface delineates a partition of the three-dimensional space, wherein the inner area is characterised by partial correlations that are all less than the correlations, while the outer area is distinguished by partial correlations that are all greater than the correlations. In the event that the absolute value of the partial correlations is not equal to 1, the inverse formulae apply:

$$\begin{aligned} \rho_{12} &= \frac{\rho_{12,3} + \rho_{23,1}\rho_{13,2}}{\sqrt{(1 - \rho_{23,1}^2)(1 - \rho_{13,2}^2)}} \\ \rho_{13} &= \frac{\rho_{13,2} + \rho_{23,1}\rho_{12,3}}{\sqrt{(1 - \rho_{23,1}^2)(1 - \rho_{12,3}^2)}} \\ \rho_{23} &= \frac{\rho_{23,1} + \rho_{12,3}\rho_{13,2}}{\sqrt{(1 - \rho_{12,3}^2)(1 - \rho_{13,2}^2)}} \end{aligned} \quad (4)$$

Upon inserting the definition (1) into (4) and employing the symmetry (2), an identity is yielded after a brief calculation. The inverse conclusion then serves to substantiate the proof of (4). Given that the absolute value of the partial correlations is either greater than or less than 1, it can be concluded that the contents of the roots in the denominator in (4) are always positive. The assertion made in the literature that the absolute values of the partial correlations and the correlations are always less than 1 is not correct. One could argue that not all values in the correlation space under consideration can arise from random variables. This is also not true. $m > 1$ is equal to $1 - \rho_{12,3}^2 > 1 - \rho_{12}^2$ and $\rho_{12}^2 > \rho_{12,3}^2$. Analogue for $m < 1$. As a consequence of the aforementioned symmetry, this conclusion also applies to all other correlations and partial correlations. It can be demonstrated that all partial correlations are greater or smaller than the correlation determined by the value of m . This value m can also be determined from the partial correlations. A quick calculation yields

$$\frac{1}{m} = \bar{m} = \frac{1 - \rho_{23,1}^2 - \rho_{13,2}^2 - \rho_{12,3}^2 - \rho_{12,3}\rho_{23,1}\rho_{13,2}}{(1 - \rho_{12,3}^2)(1 - \rho_{23,1}^2)(1 - \rho_{13,2}^2)} \quad (5)$$

The symmetry of the partial correlations and the correlations resulting from (3) is also important here. The geometric background of correlation and partial correlations is discussed in the following sources: (Jackson, 1924), (Bilin Zeng and Wang, 2017), (Thomas and O’quigley, 1993), (Kendall, 1941), (Irwin, 1965), (Maier and Kieseewetter, 1971) and (Good, 1992).

3 RESULTS

For each patient, three values are provided as total numbers per prescription year: age, polypharmacy (number of active ingredients) according to the four digit Anatomical Therapeutic Chemical (ATC) classification system, and cost percentile. Prior to calculating the correlations and partial correlations between these three variables, which can be regarded as random variables, it is necessary to consider the pairwise dependencies per year. In order to provide clarity regarding the figures presented, the years 2014, 2018, 2020 and 2023 have been selected for analysis. This approach allows for the investigation of trends and influences resulting from the coronavirus pandemic. In each instance, the mean value of a second variable is examined as a function of a first variable. As a consequence of this asymmetrical process of averaging, the dependencies in question are typically not reversible. It is pertinent to examine intervals in which the dependencies are approximately linear, as this allows for the imposition of suitable restrictions on the correlations and partial correlations of the three variables. Furthermore, mean values are also obtained for larger deviations from linearity, which are nevertheless relevant. It is important to note that two-dimensional representations do not initially account for the frequency of occurrence of the base variable. This must therefore be considered at the outset. The averaging process yields considerably higher coefficients of determination than the primary data.

The number of patients in figure 2 with drug prescriptions is largely characterised by demographic aspects, with significant variations across different age groups and genders. There has been a notable rise in the number of individuals within the 45 to 65 age bracket between 2014 and subsequent years. The maximum values are determined by the baby boomers and the pre-war generation, with a significant decline occurring in 1945.

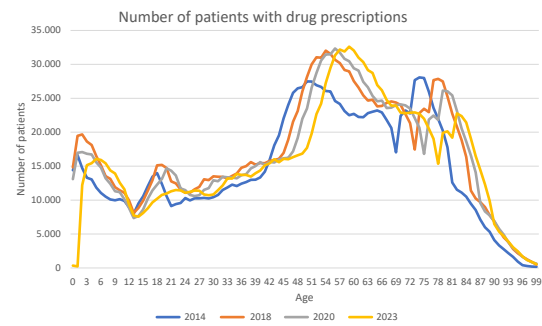


Figure 2: Age progression analysed in 2014, 2018, 2020, 2023 for patients taking medication.

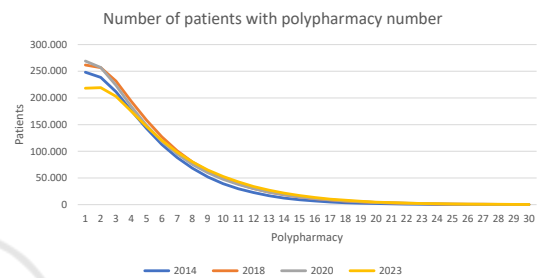


Figure 3: The number of patients exhibiting a polypharmacy value.

In figure 3 there is a slight shift from 2014 to 2023 towards higher case numbers with higher polypharmacy values. The curves can be determined using either Poisson or gamma distributions, the latter of which is a more precise model.

The figure 4 shows a minimum at about 14 years of age and a maximum at about 93 years of age. The polypharmacy value demonstrates a notable increase from 2014 to 2023, rising from approximately 30 years of age. Outside of childhood and old age, the curve displays a monotony and a certain approximation of linearity. The lack of monotony for the whole area of the curve is evident in the inversion of the polypharmacy value with respect to the mean age in Figure 5.

The presence of a single active ingredient is sufficient to result in an average age of over 40 years, and

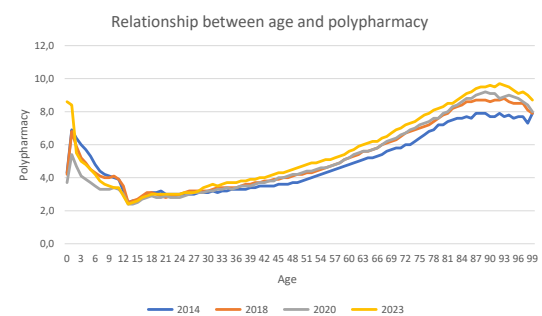


Figure 4: The age-dependent mean polypharmacy score.

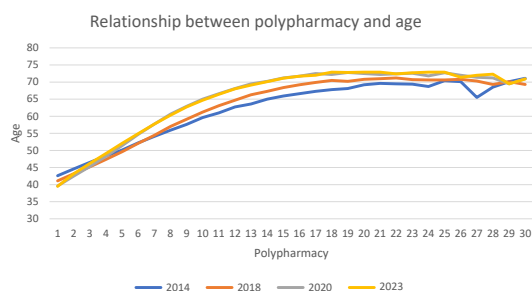


Figure 5: Reversal of the polypharmacy value as a function of the mean age.

thus it is not uncommon for this to occur at an older age. A saturation value of age is reached with the administration of 20 active ingredients. From 2014 to 2023, the median age generally increases to a value indicative of polypharmacy. Conversely, the number of middle-aged patients will decline.

By mapping age to polypharmacy (in this case, rounded to natural numbers) and polypharmacy to age (also rounded to natural numbers), we obtain relevant age groups in relation to polypharmacy through the resulting equal function values in 2023. The age groups are as follows: 1, 2-5, 6-9, 10-29, 30-47, 48-59, 60-67, 68-74, 75-80, 81-87, 88-94 and 95-99. A further iteration of the process results in the formation of larger intervals, namely 1-9, 10-29, 30-74, and 75-99. It is notable that a single additional iteration already yields a constant value of 52.

Conversely, the relevant intervals of polypharmacy in relation to age can be identified by running the figures in sequence. The relevant intervals of polypharmacy can then be identified as follows: 1-3, 4-7, 8-11 and 12-30. A further iteration of the process yields an equal value of 5.

It is of theoretical interest to determine for which initial data cyclic iterations are possible, as they are known for discrete Verhulst equations (cf. (Murray, 2007), (Murray, 2003)).

The figure 6 shown above result from the marginal mean values of the combined case numbers. A comparison of years, as in the two-dimensional figures, is not meaningful in the three-dimensional visualisation. From the 3D maximum, it seems plausible that 52 years is the iterative limit of the marginal projection. In the case of polypharmacy, there is a convergence towards the centre, which in principle could also lead to a cyclical progression.

Figure 7 shows that the age 0 in 2023 will be due to a singularity in data technology. With the exception of the childhood and hunting years, the differences between the years are minimal. It can be observed that significant differences from a linear relationship only exist up to the stages of adolescence and old age.

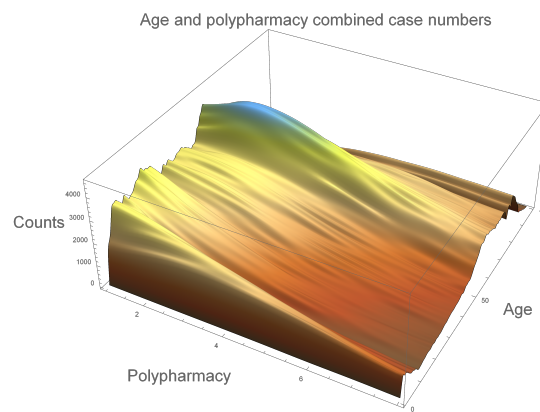


Figure 6: A 3D representation of the combined case numbers between age and polypharmacy.

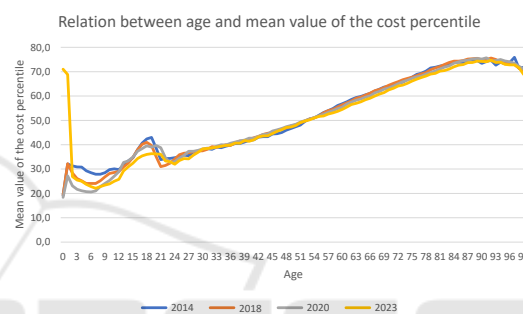


Figure 7: The dependence of age on the mean value of the cost percentile with regard to patients.

The maximum value of the mean in relation to the cost percentile is approximately 75. Conversely, the relationship between the cost percentile and the mean age is illustrated in Figure 8.

The curve is similar to the inverse scenario, exhibiting augmented growth at the outset and a moderately diminished saturation value. Furthermore, an iterative application may prove beneficial in examining the correlation between age and cost percentile, where the conversion from age to cost percentile and

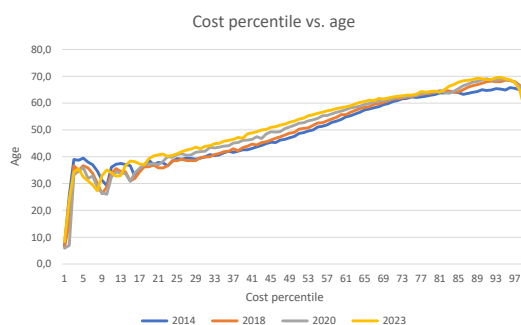


Figure 8: The figure illustrates the mean age for the cost percentiles displayed on the x-axis for the years 2014, 2018, 2020 and 2023.

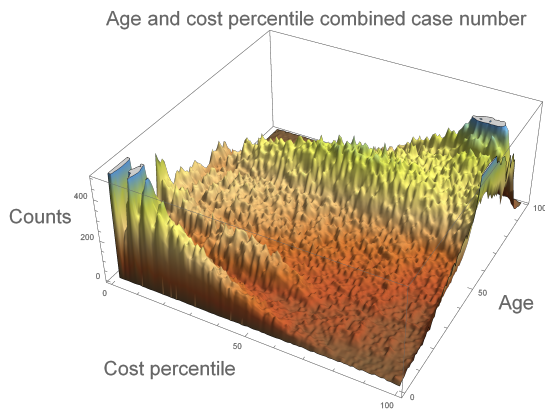


Figure 9: A 3D visualisation for the year 2023.

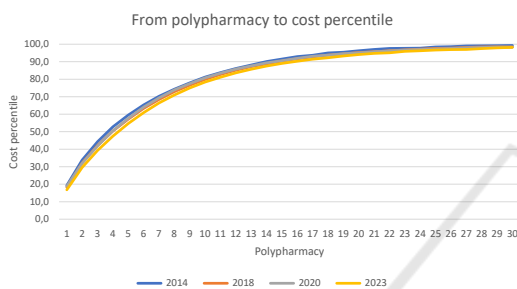


Figure 10: The relationship between the value of polypharmacy and the mean cost percentile.

back converges at a slower rate. Following the third iteration, the resulting age groups are as follows: 1, 2-15, 16-23, 24, 35-53, 54-72 and 73-99 years. Conversely, the cost percentiles are as follows: 1, 2, 3, 4, 5-9, 10, 11-13, 14-50, 51-64, 65-98, and 99-100.

In figure 9 it is important to note the significant local variations and high structural diversity, which is largely obscured in the marginal plots that have been considered thus far due to the smoothing techniques employed. In calculating the correlations and partial correlations, this is taken into account in a comprehensive manner, reflecting the full depth of the data. The larger number of relevant age groups and cost percentiles in the iteration of the two-dimensional transformations is motivated by the greater local variation in Figure 9.

It is notable that the curve demonstrates a consistent monotonic and convex pattern across all years. The cost percentile for the specified polypharmacy value exhibits a slight decline from 2014 to 2023.

The reversal from a cost percentile to a mean value of polypharmacy reveals a departure from monotony in the lower and higher cost segments, as shown in Figure 11.

The differences between the years are greater in this direction. For a given cost percentile, the value of polypharmacy is higher from 2014 to 2023. The

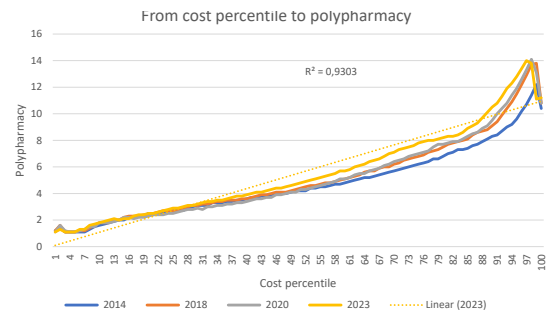


Figure 11: The relationship between the mean cost percentile and the value of polypharmacy.

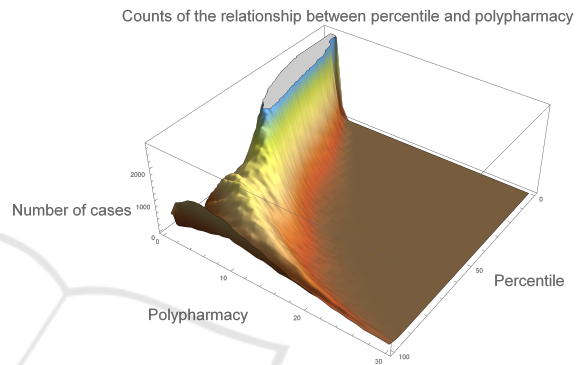


Figure 12: A 3D representation of the combined case numbers between cost percentile and the value of polypharmacy.

year 2020, which was marked by the global spread of the novel coronavirus, resulted in a slight reduction in the observed trend. The regression line for 2023 is illustrated here as an example. Combined with the mean value for the dependent variable, this results in a high correlation coefficient. This is a common phenomenon when analyses are carried out with mean results.

The triple iteration from the cost percentiles to the polypharmacy values and back yields the pertinent cost intervals in relation to polypharmacy, namely 1-7, 8-19, 20-57, 58-65, 66-92, and 99-100.

Conversely, the relevant intervals from the polypharmacy to the cost percentiles and back result after triple iteration of the following values: 1, 2-5, 6, 7-18 and 19-30.

The 3D visualisation of the case numbers is shown in Figure 12.

In the two years compared, 2019 (table 2) and 2023 (table 3), many items are essentially the same. In 2023, antidepressants have moved to the forefront in the 23-30 age group (polypharmacy from 3.2 to 3.5, cost percentile 37.2 to 40.7). This may be indicative of the significant impact the Coronavirus pandemic has had on young adults in particular.

As previously stated, the three variables in ques-

Table 2: The table illustrates the most frequently prescribed MRGs for the year 2019. The age groups that exhibited the same top 1 were summarised.

Age	MRG	2019 Poly-pharmacy	Description
3-9	J01C	[4.0 ; 5.2]	Beta-lactam antibacterials, penicillins
10-12	P03A	[3.1 ; 3.7]	Ectoparasiticides, incl. scabicides
14-22	G03A	[2.2 ; 2.8]	Hormonal contraceptives for systemic use
23-27	R03A	[3.5 ; 3.7]	Adrenergics, inhalants
28-48	H03A	[2.3 ; 2.6]	Thyroid preparations
49-65	R03A	[4.9 ; 7.1]	Adrenergics, inhalants
66-99	B01A	[7.8 ; 10.3]	Antithrombotic agents

Table 3: The table illustrates the most frequently prescribed MRGs for the year 2023. The age groups that exhibited the same top 1 were summarised.

Age	MRG	2023 Poly-pharmacy	Description
2-11	J01C	[3.6 ; 5.4]	Beta-lactam antibacterials, penicillins
12-14	N06B	[3.1 ; 3.5]	Psychostimulants, agents used for ADHD and nootropics
15-22	G03A	[2.3 ; 2.8]	Hormonal contraceptives for systemic use
23-31	N06A	[3.2 ; 3.5]	Antidepressants
33-45	H03A	[2.5 ; 2.7]	Thyroid preparations
46-52	R03A	[5.1 ; 5.8]	Adrenergics, inhalants
53-66	C09C	[4.0 ; 4.5]	Angiotensin II receptor blockers (ARBs), plain
67-99	B01A	[8.3 ; 11]	Antithrombotics agents

tion, namely age, polypharmacy and cost percentile, exhibit a high degree of pairwise dependency. From the preceding observations, it can be determined that there are intervals which exhibit a comparatively high degree of linear dependency. It should be noted that correlations and partial correlations do not require linear dependencies as a prerequisite. Consequently, intervals with large deviations are also of interest, including those relating to low and high age, low and high polypharmacy, as well as small and large cost percentiles in various combinations.

The calculations described in the chapter on materials and methods yield the following results:

The correlations denote:

- ρ_{12} : Age - polypharmacy,
- ρ_{13} : Age - cost percentile of patients,
- ρ_{23} : Polypharmacy - cost percentile

of patients and correspondingly the partial correlations with regard to the other variables.

Table 4: The table describes the correlations between the three variables age, polypharmacy and cost percentile of patients for all years between 2014 and 2023 and 1.5 till 1.7 million patients in each year. Also the modulus m and the partial correlations.

Year	ρ_{12}	ρ_{13}	ρ_{23}	m	$\rho_{12,3}$	$\rho_{13,2}$	$\rho_{23,1}$
2014	0.26	0.68	0.47	1.06	-0.09	0.65	0.41
2015	0.28	0.68	0.48	1.08	-0.07	0.65	0.41
2016	0.29	0.69	0.49	1.08	-0.09	0.66	0.43
2017	0.30	0.69	0.50	1.09	-0.08	0.66	0.43
2018	0.31	0.70	0.51	1.10	-0.07	0.66	0.43
2019	0.32	0.70	0.51	1.11	-0.06	0.65	0.42
2020	0.37	0.71	0.52	1.16	0.01	0.65	0.39
2021	0.37	0.71	0.51	1.16	0.02	0.65	0.37
2022	0.36	0.71	0.51	1.15	0.00	0.65	0.38
2023	0.38	0.72	0.50	1.17	0.04	0.66	0.35

The modulus value m is observed to exceed 1 for all years from 2014 to 2023, exhibiting a monotonic increase with minimal deviation in 2016. This indicates that the absolute partial correlations are less pronounced than the correlations. It is possible for the sign to change, whereby a positive dependency may transform into a negative dependency, or vice versa. This phenomenon occurs from 2019 to 2020, which coincides with the transition from the pre-corona period to the era of the global pandemic.

It is usually argued that an apparent dependence given by the correlation with the partial correlation depends on a third variable, on which 'in truth' the two variables depend. In our analysis, all three variables are interdependent in terms of content, cf. (Runkler and Runkler, 2000) and (Janssen et al., 1994). In this context, it can be posited that one dependency exerts itself as dominant (in this case, the dependency on age and cost percentile) at the expense of another dependency (in this case, the dependency on age to polypharmacy). So far, the literature has lacked compelling exemplars of such interactions. This is despite their potential to occur with great frequency in both medical and economic contexts.

4 CONCLUSIONS

The equations (1) and (4) correspond to the side and angle cosine theorems of spherical trigonometry with various restrictions, but apply more generally here, cf. (Armitage and Eberlein, 2006) and (Good, 1992). First of all, in this context there is no restriction with regard to the triangle inequality in spherical trigonometry. A restriction regarding the value of m can be resolved by swapping the side and angle cosine theorem in the assignment of correlation and partial correlation. The symmetry in the possible values of correla-

tion and partial correlations assumed at the beginning is also not necessary in the formula, since all considerations are retained if one assumes correlation values with magnitudes above 1, but then uses the root extraction as in (4) in (1) over the entire denominator. In this respect, a relationship is then established not only to spherical trigonometry, but also to hyperbolic trigonometry, which provides the description for the addition of velocities in the context of the special theory of relativity.

The MRG offers a distinctive label, which allows for the delineation of a transition between one period (in this case, a year) and the subsequent period. This provides the transition coefficients that are employed as the constituent elements of a matrix. The eigenvector corresponding to the largest eigenvalue of the matrix determines the limit distribution that would result as the limit value if this transition were to be frequently applied as a Markov process. This permits an examination of the discrepancy between the current distribution and the limit distribution.

Since this long-term analysis in the Big Date context determined the dominant Morbidity Related Drug Group drug group with the changes, the results can be used in health policy decisions. In Schleswig-Holstein, this is included in the negotiations between the statutory health insurance funds and the Association of Statutory Health Insurance Physicians. Of particular importance are changes caused by the coronavirus pandemic, which must be distinguished from long-term trends that existed before it. Another important point is the treatment of patients with a high level of polypharmacy, as guidelines from specialist associations are geared towards specific disease patterns and comparatively little consideration is given to interaction effects.

In future, it should be investigated more closely what proportion of patients in the highest cost percentile are affected by very high-priced drugs for rare diseases. For patient-centred evaluations, cross-doctor considerations are important, which are rarely available for data protection reasons.

REFERENCES

- Armitage, J. V. and Eberlein, W. F. (2006). *Elliptic functions*, volume 67. Cambridge University Press.
- Bilin Zeng, K. C. and Wang, C. (2017). Geometric views of partial correlation coefficient in regression analysis. *AL JOUR*, 6(3):51.
- Brennan, M. E. and Clare, P. H. (1980). The relationship between mortality and two indicators of morbidity. *Journal of Epidemiology & Community Health*, 34(2):134–138.
- Brief, A. P., Burke, M. J., George, J. M., Robinson, B. S., and Webster, J. (1988). Should negative affectivity remain an unmeasured variable in the study of job stress? *Journal of applied psychology*, 73(2):193.
- Bundesinstitut für Arzneimittel und Medizinprodukte (BfArM) (2021). ATC-Klassifikation mit definierten Tagesdosen DDD. <https://www.dimdi.de/dynamic/de/arzneimittel/atc-klassifikation>. Accessed: 18.12.2024.
- Case, A. and Deaton, A. (2017). Mortality and morbidity in the 21st century. *Brookings papers on economic activity*, 2017:397.
- Delara, M., Murray, L., Jafari, B., Bahji, A., Goodarzi, Z., Kirkham, J., Chowdhury, M., and Seitz, D. P. (2022). Prevalence and factors associated with polypharmacy: a systematic review and meta-analysis. *BMC geriatrics*, 22(1):601.
- Fricke, U., Günther, J., Niepraschk-von Dollen, K., and Zawinel, A. (2019). Anatomisch-therapeutisch-chemische Klassifikation mit Tagesdosen für den deutschen Arzneimittelmarkt. https://www.wido.de/fileadmin/Dateien/Dokumente/Publikationen/Produkte/Arzneimittel-Klassifikation/wido_arz_atc_gkv_ai_2019.pdf. Accessed: 18.12.2024.
- Golchin, N., Frank, S. H., Vince, A., Isham, L., and Meropol, S. B. (2015). Polypharmacy in the elderly. *Journal of Research in Pharmacy Practice*, 4(2):85–88.
- Good, I. (1992). C389. partial correlation and spherical trigonometry, ii.
- High, K. P. (2004). Infection as a cause of age-related morbidity and mortality. *Ageing Research Reviews*, 3(1):1–14.
- Irwin, J. (1965). Note on the addition formula for the jacobian elliptic functions and their connexion with the theory of correlation, in statistics. *The Mathematical Gazette*, pages 425–427.
- Jackson, D. (1924). The trigonometry of correlation. *The American Mathematical Monthly*, 31(6):275–280.
- Janssen, J., Laatz, W., Janssen, J., and Laatz, W. (1994). Korrelation. *Statistische Datenanalyse mit SPSS für Windows: Eine anwendungsorientierte Einführung in das Basissystem*, pages 347–357.
- Johnell, K. and Klarin, I. (2007). The relationship between number of drugs and potential drug-drug interactions in the elderly: a study of over 600 000 elderly patients from the swedish prescribed drug register. *Drug safety*, 30:911–918.
- Kendall, M. (1941). The relationship between correlation formulae and elliptic functions. *Journal of the Royal Statistical Society*, 104(3):281–283.
- Kim, S. (2015). ppcor: an r package for a fast calculation to semi-partial correlation coefficients. *Communications for statistical applications and methods*, 22(6):665.
- Koh, Y., Kutty, F. B. M., and Li, S. C. (2005). Drug-related problems in hospitalized patients on polypharmacy: the influence of age and gender. *Therapeutics and clinical risk management*, 1(1):39–48.

- Maier, W. and Kiesewetter, H. (1971). Funktionalgleichungen mit analytischen Lösungen. (*No Title*).
- Murray, J. (2003). Mathematical biology ii. spatial models and biological applications. *Springer-Verlag, New York*.
- Murray, J. D. (2007). *Mathematical biology: I. An introduction*, volume 17. Springer Science & Business Media.
- Rübenach, S. P., Stahl, T., Zawinell, A., Niepraschk-von Dollen, K., Knecht, B., Schüssel, K., Telschow, C., and Schröder, H. (2021). Nutzung von Arzneimittelverordnungsdaten der gesetzlichen Krankenversicherung für die Krankheitskostenrechnung. *WISTA-Wirtschaft und Statistik*, 73(2):97–110.
- Runkler, T. A. and Runkler, T. A. (2000). Datenanalyse und Modellierung. *Information Mining: Methoden, Algorithmen und Anwendungen intelligenter Datenanalyse*, pages 53–109.
- Schuster, R., Emcke, T., von Arnstedt, E., and Heidbreder, M. (2016). Morbidity Related Groups (MRG) for epidemiological analysis in outpatient treatment. In *Exploring complexity in health: An interdisciplinary systems approach*, pages 783–787. IOS Press.
- Schuster, R., Ostermann, T., Heidbreder, M., and Emcke, T. (2018). Relations of Morbidity Related Groups (MRG), ICD-10 Codes and Age and Gender Structure in Outpatient Treatment. In *HEALTHINF*, pages 322–328.
- Thomas, G. and O’quigley, J. (1993). A geometric interpretation of partial correlation using spherical triangles. *The American Statistician*, 47(1):30–32.
- Turrentine, F. E., Wang, H., Simpson, V. B., and Jones, R. S. (2006). Surgical risk factors, morbidity, and mortality in elderly patients. *Journal of the American College of Surgeons*, 203(6):865–877.
- Weng, Y.-A., Deng, C.-Y., and Pu, C. (2020). Targeting continuity of care and polypharmacy to reduce drug–drug interaction. *Scientific reports*, 10(1):21279.