**Utilisation and expenditure of anti-cancer medicines in Kosovo; findings and implications**

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# **Abstract**

**Introduction:** The Ministry of Health (MoH) leads and organizes health policy in Kosovo, which includes procurement and provision of medicines. Cancer medicines are part of this. There are concerns with their affordability in view of growing costs and high profile. This is similar in Kosovo where anti-cancer medicines compose a special group of medicines, with most available medicines part of the Ministry of Health’s Essential List of Medicines. National drug utilization is available to guide future activities. However, there has been limited analysis of anti-cancer medicines to date. Such analyses are important to guide future care within limited resources. Consequently, the objective of this study is to undertake such research in Kosovo to provide future guidance. **Method**: Document utilisation and expenditure on anti-cancer medicines (ATC L) initially from 2011 to 2013, especially for anti-cancer medicines on the essential medicines list. In addition, document current systems for procuring and managing anti-cancer medicines in Kosovo. **Results**: There was appreciable variability in the utilization of anti-cancer medicines over the years, with low or limited use of some anti-cancer medicines on the essential medicine list. This is a concern in view of their documented effectiveness. From 2011 to 2013, € 16.49 million, or 13.5% of total expenditure, was spent on anti-cancer medicines (ATC L). The process of selection of new medicines begins with suggestions from doctors at the University Clinical Centre in Kosovo. **Conclusion**: The analysis has shown concerns with current utilization patterns for anti-cancer medicines in Kosovo. This needs to be addressed as part of improving the drug management process to optimize patient care within available resources. Future years and reforms will be assessed to improve current utilization and expenditure patterns.

Key words: Drug utilization, cancer medicines, reimbursement, Kosovo, VEN analysis

**1. Introduction**

Health authorities across countries have for many years published annual medicine consumption data, which have been widely used among key stakeholder groups. This includes monitoring the influence of ongoing reforms and initiatives, and using the outputs to plan future initiatives and budgets (1-4). This is particularly the case in a number of European countries where health authorities and health insurance agencies strive towards universal access within finite budgets.

Currently in Kosovo, the Ministry of Health (MoH) leads and organizes health policy processes, achieving many of its objectives through subordinate institutions such as the Kosovo Medicines Agency (KMA). KMA is responsible for the public health of the population through ensuring drug safety, quality, and efficacy, as well as overseeing the importation of medicines into Kosovo and conducting analyses of overall drug consumption.

However, little is known about medicine consumption in Kosovo, although data for 2011-2013 was published by the KMA in 2014; similarly, for anti-cancer medicines. New anti-cancer medicines are typically seen as a special group of medicines as this is an emotive area, leading generally to greater leeway for pricing considerations and funding than patients with other disease such as cardiovascular diseases or mental health (5, 6). There are growing concerns worldwide with prices of cancer medicines rising up to ten fold during the past ten years in some countries despite often limited health gain (7, 8). This causes concerns especially in countries with fixed budgets with resultant opportunity cost implications for patients with cancer and other diseases (9, 10) leading to prescribing restrictions and other measures to limit the use and reduce the prices of new cancer medicines (11, 12). Consequently in European countries with appreciable pressure on resources such as Kosovo, there is an imperative need to review current utilization and expenditure patterns for cancer medicines, as well as the selection process for new anti-cancer medicines, to make sure available resources are being optimally used. In recent years the prevalence of cancers in Kosovo is increasing (13). In 2015, the greatest incidence was for melanomas and other malignant neoplasms of the skin with 411 new cases in 2015, breast neoplasms were 274 new cases, malignant tumors of digestive system with 262 new cases, malignant tumors of the genital organs with 257 new cases. These were out of a total of 1751 new cases of cancer in Kosovo 2015 (14).

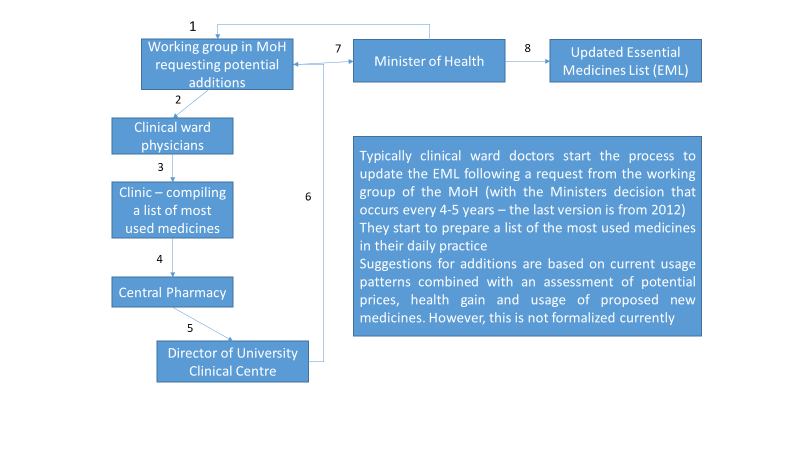
In addition, there are reports following MoH workshops that in 2017 there is an increasing trend in the total number of cancers in Kosovo, and that some of these cases are due to better diagnostics and awareness campaigns leading to more patients being diagnosed earlier (AJ personal communication).

In Kosovo, the Kosovo University Clinical Center Service (KUCCS) is a key institution in Kosovo’s health system since all of the hospitals that offer secondary and tertiary level care such as the University Clinical Centre of Kosovo (UCCK) function within its framework. The Oncology Institute operates within the UCCK framework. This institute, among others, also deals with the overall management of cancer patients in Kosovo, including chemotherapy and radiotherapy. The supply of medicines in UCCK is undertaken through the central pharmacy which supplies all clinics.

However, little is known generally about medicine consumption in Kosovo although drug consumption data for 2011-2013 was published by the KMA in 2014. In addition, the procurement process of the MoH is now centralized as recommended by the World Health Organization and the World Bank (15). In contrast, the other processes are now decentralized since every hospital since 2015, through its own structures, is responsible for the planning, selection, and ordering of medicines and equipment,

The current selection process to update the oncology medicine list begins with physicians, in this case those in the Institute of Oncology. The list and suggestions are subsequently reviewed by the head of the clinic, the central pharmacy director and the general director of the hospital. After this process, the suggested updated list is submitted to the professional working group of the Ministry of Health for the final review and approval by the Minister of Health. Figure 1 illustrates this process.

Figure 1 – Selection process for updating the Essential Medicines List for new anti-cancer medicines (building on Quick et al (16))



Once the list is signed by the Minister, the second part of the drug management process proceeds, i.e. the procurement of the medicines from the agreed essential medicines list intended for hospital use. This process is carried in a centralized way from MoH for all the hospitals in Kosovo, with the system transparent to help reduce possible corruption (17). After this, the process is continued with the distribution to the central pharmacies (of each hospital) from where available medicines are supplied to all the clinics. This process is under the supervision of the chief pharmacists of the hospitals ready for clinicians to use the oncology medicines in their clinics.

Consequently, the aim of this paper is to critically review utilization and expenditure of anti-cancer medicines in Kosovo including the selection processes for listing medicines in Kosovo. The findings will be used to suggest future strategies in Kosovo to improve the use of cancer medicines within available resources, building on the expertise of the co-authors working with health authorities across Europe including Kosovo and wider, and their networks.

**2. Methodology**

The drug utilization and expenditure data was obtained from the MoH and the wholesale drug suppliers, similar to other disease areas (18). Due to the lack of electronic reporting systems currently in Kosovo, unlike the Nordic countries and Scotland as well as other central and eastern European countries (19-25), these data have to be manually recorded. Kosovo’s pharmaceutical sector has 2 main sectors: the private sector where drug dispensing for ambulatory care patients is achieved through the 621 pharmacies in the country (26) and the public sector that includes hospitals supplied with medicines from the Essential List of Medicines, previously procured through the central procurement of the Ministry of Health. These medicines are provided only to hospitalized patients.

The utilization of anti-cancer drugs in Kosovo is based on 58 molecules currently available in the Essential Medicine List (EML) according to their generic name or International Nonproprietary Name (INN) (27) each calendar year For this initial study, data were collected from wholesalers for the 2011-2013 period (28), as all of the licensed wholesalers in Kosovo are obliged to make an application to the Kosovo Medicines Agency for all the medicines they import including their INN name, brand (originator) name, dosage form, strength, serial number, and quantity. The reason for the three year period was that this was the first official publication by the KMA on drug consumption in Kosovo, providing a basis for the future (29). The methodology is based on the ATC drug classification methodology, which is internationally recognized as the standard for undertaking drug utilization research (30-34). Data sets recorded including the dose, strength, unit quantity, price per unit and overall expenditure for each anti-cancer medicine. Expenditure was recorded in Euros as this is the official currency in Kosovo.

Other sources of drug consumption data include the hospital selection and planning of the medicines process with data collected from the working group in the MoH (Ministers decision 60/13 – 16/04/2013 and 74/13 -05/06/2013). This group has the duty of categorizing the various medicines including cancer medicines into VEN (Vital, Essential, Necessary) categories as per WHO recommendations (35), with the role of one of the authors (AJ) as a consultant to MoH. The data were further analyzed and interpreted for this publication. The data were collected in Microsoft Excel and subsequently converted into informative figures and tables.

The analysis of oncology medicines is based on the essential list of cancer medicines approved by the Ministry of Health (which is also public). The list of medicines will be broken down by their overall expenditure during the study period, then by overall class and year before concentrating on the anti-cancer medicines with the highest expenditures. Anti-cancer medicines are classified by VEN (Vital, Essential and Necessary) from the working group of the MoH. This is similar to the VEN analysis (Vital, Essential and Necessary) and ABC analysis (typically Class A medicines include 10% to 20% of the items under consideration but constitute 75% to 80% of total expenditure, Class B constitute 10% to 20% of the items under consideration but 15% to 20% of total expenditure, with Class C the remaining ones but only 5% to 10% of total expenditure) methodology of the WHO  (16, 35, 36). The analysis of the 15 anti-cancer medicines with the highest expenditures will use different time periods in view of the appreciable variation that can occur across the years.

According to the WHO Anatomical Therapeutic Chemical (ATC) classification system, the active substances were divided into different groups according to the organ or system on which they act and their therapeutic, pharmacological and chemical properties (30, 37). Medicines are classified in groups at five different levels including fourteen main groups (1st level), and further divided into different pharmacological/therapeutic subgroups (2nd level).  The 3rd and 4th levels are the chemical/pharmacological/therapeutic subgroups and the 5th level is the chemical substance. The analysis of medicines according to their ATC classification is used for comparative purposes (38) and to provide an overview and trend in medicine utilisation related to the different therapeutic areas.

**3. Results**

In this analysis, according to the ATC Level 3, the L01X subgroup of cancer medicines have the greatest expenditure and are also more utilized than other anti-cancer medicine groups, followed by the L03A group — the immunostimulants (Figures 2 and 3).

Figure 2 – Expenditure of anti-cancer medicines in Kosovo 2011 to 2013 (Adapted from Drug Consumption in Kosovo (38))

NB: L01A = [ALKYLATING AGENTS](https://www.whocc.no/atc_ddd_index/?code=L01A)**,** L01B **=** Antimetabolites, L01C = Plant Alkaloids and other natural products, L01D = Cytotoxic antibiotics and other related substances, L01X = Other neoplastic agents, L02A = Hormones and related substances, L02B = Hormone antagonists and other related substances, L03A = Immunostimulants, L04A = Immunosuppressants

Figure 3 - Breakdown of individual anti-cancer medicines by expenditure each year (Adapted from Drug Consumption in Kosovo (38))

From Figure 3, it can be seen that only a few anti-cancer medicines currently have high expenditures in Kosovo, with expenditure on bevacizumab, rituximab and the interferons increasing but variable expenditure on trastuzumab. These anti-cancer medicines were chosen for illustrative purposes to demonstrate the appreciable variation in expenditure that can occur between the years, as well as limited expenditure on certain proven anti-cancer medicines out of the list of 58 essential medicines currently available. Analysis of the 15 highest expenditure items (Figure 4) gives us further details of key anti-cancer medicines to concentrate on for future analysis. Figure 5 depicts the anti-cancer medicines with the lowest expenditures in recent years, again providing baseline data for future policies and guidelines.

Figure 4. Analysis of the 15 anti-cancer ordered with the highest monetary value including VEN analysis

NB: Different time periods are used for this analysis versus yearly utilization analysis

Figure 5. Analysis of the 20 anti-cancer ordered with the lowest expenditure (including those available but not ordered) including VEN analysis

NB: Different time periods are used for the ABC analysis versus yearly utilization analysis

Overall, Figures 4 and 5 represent the total expenditure, and the VEN categorization, for the various anti-cancer medicines being utilised in Kosovo. They show that medicines that have a low value per unit (ampoule), such as € 2 or € 3 per ampoule or similar, did not appear to be ordered by the Oncology Institute whilst there was a tendency to procure higher cost medicines. This may be due to the availability of biological medicines targeting specific oncology categories commanding higher prices. From Table 1, it can be seen that the last 15 anti-cancer medicines of the Kosovo essential medicine list (Appendix 1) sorted by their expenditure within a year have zero orders, whilst the other five products towards the end of the list amounted to € 2,572, which is less than the expenditure on two ampoules of the first anti-cancer medicine in the list (Table 1).

Table 1 - Expenditure and VEN analyses of anti-cancer medicines in Kosovo

|  |  |  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- | --- | --- |
| Nr | Generic Name | Pharmaceutical form | Dose & Volume | V | E | N | 12 month quantity | Price/Unit | Expenditure |
| 1 | TRASTUZUMAB | conc. per sol per inf | 440mg | V |  |  | 1320 | € 1,550.00 | € 2,046,000.0 |
| 2 | BEVACIZUMAB | conc. per sol per inf | 400mg/16ml |  | E |  | 6400 | € 309.00 | € 1,977,600.00 |
| 3 | IMATINIB MESYLATE | tbl | 400mg |  | E |  | 12600 | € 98.30 | € 1,238,580.00 |
| 4 | RITUXIMAB | conc. per sol per inf | 500mg |  | E |  | 600 | € 1,145.00 | € 687,000.00 |
| 5 | CAPECITABINE | tbl | 500mg | V |  |  | 210000 | € 2.33 | € 489,300.00 |
| 6 | SORAFEMIB | tbl | 200mg |  | E |  | 10800 | € 36.50 | € 394,200.00 |
| 7 | ERYTHROPOETIN BETA | prefilled syringe | 30000 IU | V |  |  | 1800 | € 165.00 | € 297,000.00 |
| 8 | IBANDRONATE | conc. per sol per inf | 6mg | V |  |  | 2160 | € 125.00 | € 270,000.00 |
| 9 | PEMETREXED | plv per conc. per sol | 500 mg |  |  | N | 240 | € 990.00 | € 237,600.00 |
| 10 | GOSERELIN | prefilled syringe | 10.8 mg | V |  |  | 480 | € 302.00 | € 144,960.00 |
| 11 | DOCETAXEL | conc. and dil per sol per inf | 40mg/ml, 2ml | V |  |  | 4800 | € 23.73 | € 113,904.00 |
| 12 | FILGRASTIM | sol per inf | 48 MIU | V |  |  | 3000 | € 36.00 | € 108,000.00 |
| 13 | RITUXIMAB | conc. per sol per inf | 100mg |  | E |  | 400 | € 230.00 | € 92,000.00 |
| 14 | TEMOZOLAMIDE | caps | 250 mg | V |  |  | 1680 | € 50.86 | € 85,444.80 |
| 15 | PEMETREXED | plv per conc. per sol | 100 mg |  |  | N | 240 | € 220.00 | € 52,800.00 |
| 16 | CISPLATIN | plv per sol per inj | 50mg | V |  |  | 3960 | € 13.00 | € 51,480.00 |
| 17 | ANASTRAZOL | tbl | 1mg | V |  |  | 60000 | € 0.82 | € 49,200.00 |
| 18 | IBANDRONATE | tbl | 50mg | V |  |  | 7392 | € 6.00 | € 44,352.00 |
| 19 | GEMCITABIN | plv per sol | 1000mg | V |  |  | 1800 | € 19.90 | € 35,820.00 |
| 20 | CARBOPLATINE | sol per inf | 10mg/ml, 45ml | V |  |  | 1400 | € 24.50 | € 34,300.00 |
| 21 | CIPROTERONE ACETAT | tbl | 50mg | V |  |  | 39600 | € 0.77 | € 30,492.00 |
| 22 | DOXORUBICIN | plv per inj | 50mg | V |  |  | 3480 | € 8.20 | € 28,536.00 |
| 23 | OXALIPLATIN | conc. per sol per inf | 100mg | V |  |  | 1800 | € 15.00 | € 27,000.00 |
| 24 | GEMCITABIN | plv per sol | 200 mg | V |  |  | 3600 | € 6.00 | € 21,600.00 |
| 25 | INTERFERON ALFA 2a | prefilled syringe | 3 MIU/5ml |  |  | N | 1560 | € 13.50 | € 21,060.00 |
| 26 | DACARBAZIN | plv per sol per inf | 200mg | V |  |  | 900 | € 22.66 | € 20,394.00 |
| 27 | FLUDARABIN | tbl | 10mg |  | E |  | 600 | € 29.00 | € 17,400.00 |
| 28 | BCG | plv per sol | 81-100mg |  |  | N | 200 | € 70.00 | € 14,000.00 |
| 29 | DOXORUBICIN | plv per inj | 10mg | V |  |  | 2880 | € 3.00 | € 8,640.00 |
| 30 | IFOSFAMIDE | plv per inj | 1g | V |  |  | 420 | € 18.90 | € 7,938.00 |
| 31 | ETOPOSIDE | sol per inf | 100mg | V |  |  | 1800 | € 3.73 | € 6,714.00 |
| 32 | CHLORAMBUCIL | tbl | 2mg |  |  | N | 600 | € 10.00 | € 6,000.00 |
| 33 | 5 FLUOURACIL | sol per inj | 50mg/ml, 10ml | V |  |  | 2000 | € 2.56 | € 5,120.00 |
| 34 | TAMOXIFEN | tbl | 20mg | V |  |  | 48000 | € 0.10 | € 4,656.00 |
| 35 | FLUDARABIN | plv per sol per inj | 50 mg |  | E |  | 120 | € 30.00 | € 3,600.00 |
| 36 | MESNA | tbl | 400mg | V |  |  | 840 | € 3.90 | € 3,275.16 |
| 37 | VINBLASTIN | sol per inj | 1mg/ml, 10ml | V |  |  | 340 | € 5.88 | € 1,999.20 |
| 38 | HYDROXICARBAMIDE | caps | 500mg |  |  | N | 10000 | € 0.15 | € 1,500.00 |
| 39 | TIOGUANINE | tbl | 40mg |  |  | N | 200 | € 2.50 | € 500.00 |
| 40 | CALCIUM FOLINAT | sol per inj | 10mg/ml, 5ml | V |  |  | 80 | € 4.20 | € 336.00 |
| 41 | METHOTREXAT | tbl | 2.5mg | V |  |  | 1500 | € 0.13 | € 195.00 |
| 42 | METHOTREXAT | sol per inj | 50mg/ml,1ml | V |  |  | 60 | € 3.19 | € 191.40 |
| 43 | ASPARAGINASE | sol per inj | 10MIU, 10ml |  |  |  | 36 | € 2.00 | € 72.00 |
| 44 | BLEOMICIN | plv per sol per inf | 15IU | V |  |  | 0 | € 26.60 | € - |
| 45 | CITARABIN | sol per inj | 100mg/ml, 1ml |  |  | N | 0 | € 3.50 | € - |
| 46 | CYCLOPHOSPHAMID | plv per sol | 200mg | V |  |  | 0 | € 2.59 | € - |
| 47 | CYCLOPHOSPHAMID | plv per sol | 1000mg | V |  |  | 0 | € 5.69 | € - |
| 48 | DAUNORUBICIN | plv per inj | 20mg |  |  | N | 0 | € 12.23 | € - |
| 49 | 5 FLUOURACIL | sol per inj | 50 mg/ml, 5ml | V |  |  | 0 | € 1.68 | € - |
| 50 | IRINOTECAN | conc. per sol per inf | 20mg/ml, 5ml | V |  |  | 0 | € 18.00 | € - |
| 51 | 6 MERCAPTOPURIN | tbl | 50mg |  |  | N | 0 | € 1.50 | € - |
| 52 | MELFALAN | tbl | 2mg |  |  | N | 600 |  | € - |
| 53 | PACLITAXEL | conc. per sol per inf | 100mg | V |  |  | 0 | € 16.00 | € - |
| 54 | PACLITAXEL | conc. per sol per inf | 30mg | V |  |  | 0 | € 6.30 | € - |
| 55 | PROCARBAZINE | tbl | 50mg |  |  | N | 0 |  | € - |
| 56 | SODIUM CLODRONAT | caps | 800 mg |  |  | N | 0 | € 3.94 | € - |
| 57 | SODIUM CLODRONAT | conc. per sol per inf | 60mg/ml, 5ml |  |  | N | 0 | € 15.86 | € - |
| 58 | VINCRISTIN | sol per inj | 1mg/ml, 1ml | V |  |  | 0 | € 8.50 | € - |

Table 1 shows that 8 medicines, which are categorized as vital, comprise 13.7% of the essential list of cytostatics. These products have not been ordered at all by the competent authority. In addition, there are 15 molecules that have not been ordered at all (from the three categories V, E and N) which comprise 25.86% of the oncology list.

**4. Discussion**

We believe there are interesting findings from this study to provide future direction to the authorities in Kosovo. When comparing our findings (Figures 2 to 5) with Norway, a European country with one of the highest GDP per capita versus Kosovo with one of the lowest, dissimilarities can be seen. This is especially evident when comparing the L01X subgroup in 2013, which makes up 61.8% of the ATC L group in Kosovo, while the same subgroup only constitutes 22% of the ATCL group in Norway (39). The L04A group (Immunosuppressant’s) comprised 55% of the total expenditure in Norway compared to Kosovo where this same subgroup constituted only 2% of the ATC L group in 2013 (Figures 2 and 3).

The appreciable differences in the relative consumption of anticancer medicines between countries may be regarded as a lack of available resources in Kosovo, alternatively, resources are being wasted in one country versus another. On the other hand, differences in percentage utilization among specific medicines in an ATC group across similar time periods, such as immunosuppressant’s, can be considered as an indication to further evaluate current treatment patterns to optimize care within finite resources. According to Figure 5 and Table 1, paclitaxel in the essential list, which is included in two dosage forms (30 mg and 100 mg), is shown to have zero orders; a medicine which now has quite a low acquisition cost and significantly lower prices than other anti-cancer medicines currently being used for similiar indications. In the taxenes group, docataxel and paclitaxel have been key components in chemotherapy regimens since the 1990s’, and they are usually prescribed after anthracycline-based chemotherapy (40). In the paper by Webber-Foster *et al*, it is not specified which taxane is preferred since they are considered similar in effectiveness albeit with differences in side effects and costs (40). More lives could potentially be saved with pacilatexel but with higher costs than docataxel (40), although this is not universal. The WHO expert committee for instance concludes that both taxanes should be available for breast cancer treatment. This is because at the present, their use, based on available evidence, is different according to specific subgroups of patients and concomitant treatments. In addition, there are no cost effectiveness data currently available for different settings, or for different outcomes, leading to both taxanes currently being included in the latest WHO essential list of medicines (41, 42). A representative of the anthracycline group (ATC - L01DB) — daunorubicin also has zero orders (Table 1). This is also a cause for concern. Such changes can also be noticed with other medicines in Table 1.

The inclusion of cancer medicines in the essential medicine list, and their free availability in hospitals, has benefited a great number of patients with cancer with currently 100% co-payment for medicines in ambulatory care. However, this will only continue if there is good use of existing resources to treat patients with cancer through robust processes for pricing, reimbursing, and funding of medicines, along with robust process for regularly monitoring their use against agreed guidance.

Table 1 and Figures 3 to 5 show that only a few anticancer medicines have very high expenditure in Kosovo, but there are variations in their use across the years causing concern as to the most effective use of limited resources. The significant differences in the ordering of cancer medicines such as bevacizumab, trastuzumab, and capecitabine, suggest current processes are not coordinated. In addition, in different indications in Kosovo, there currently appears different protocols for treatment causing confusion (AJ personal communication). This has implications for any treatment approach in hospitals in Kosovo. In addition, 13.7% of cancer medicines were categorized as vital (Table 1) had zero orders, which is a concern as these medicines are regarded as very necessary. Similarly, 15 products from the essential list of cytostatics (from the three categories V, E or N), or 25.86% of these medicines, had zero orders (Figure 5, Table 1). From closer scrutiny (Table 1), it can be seen that the prices for these products do not surpass € 26.00 per ampoule, whilst medicines costing over € 1,000.00 per ampoule have orders that in total make up the largest expenditures (Figures 3 and 4).

As a result, we believe competent authorities nationally and in hospitals, coupled with the new procurement process, should review and update their processes to make the selection and planning process of anti-cancer medicines a continuous and robust process that adheres to the regulations for essential medicines and pharmacoeconomic analyses. This is currently not the case. In addition, there should be regular monitoring of their use and expenditure in practice against agreed single rather than multiple guidance to improve future care efficiently as seen in other countries such as Sweden (11, 43). There are serious concerns if there are different guidance from different national and international groups giving conflicting advice (44) as this is not in the best interest of any key stakeholder group

Pharmacoeconomic analysis according to Pallis *et al* (45) should help improve decision-making in Kosovo in such a way that would optimize the use of already limited resources dedicated to the treatment of cancer patients. This is essential within limited resources according to the concept of opportunity cost (9).

We accept there are a number of limitations with this study. This includes the fact that there is currently no information on the extent people are travelling from neighboring countries to Kosovo for treatment. There is also no doubt that available data bases contain incomplete information as there is currently considerable reliance on manually recorded information. However, we believe our findings are robust providing future direction to all key stakeholder groups in Kosovo in this important disease area.

**5. Recommendations**

In view of our findings, we believe the Ministry of Health in Kosovo should take a leading role updating current regulations by which the process of selection for new and existing medicines, and including/excluding medicines from the essential list, including active disinvestment where appropriate, is more clearly defined. In addition, the MoH should clearly define the use and need of pharmacoeconomic analyses to aid reimbursement and funding decisions, encourage the use of drug utilization studies to monitor the use of anti-cancer medicines in routine care as well as update and consolidate treatment protocols into a single source replacing current confusion. Regularly monitoring utilization and expenditure on anti-cancer medicines will highlight if any agreed essential medicines are currently not being used. Key clinicians should be part of any guideline development and monitoring processes to enhance their adherence to jointly agreed medicines and their use, which has worked well in other countries. Separately, the MoH should also look at its procurement process, including prices for similar medicines in neighboring countries, to again optimize the use of available resources. Pharmacoeconomics, including value based pricing, should be part of this.

Furthermore, the MoH could also explore the potential of delegating some of its responsibility to a working group, which could include Drug and Therapy Committees, to regularly monitor the prescription and consumption of medicines in high priority areas such as cancer. In this way, the drug management cycle would be improved as all the parts of the chain would be more precisely monitored and performed. The inclusion of electronic systems in the future will further help with such processes. This will form part of future research projects in Kosovo.

**6. Conclusion**

We have shown concerns with current procedures, utilization and expenditure of anti-cancer medicines in Kosovo, including limited or no utilization of currently deemed essential anti-cancer medicines. The findings have been used to make suggestions to improve processes to better manage patients with cancer within Kosovo given limited resources. These will be followed up in the future to help improve the care of these patients in Kosovo with likely continued limited resources.

**Acknowledgements and conflicts of interest**

The authors declare they have no conflicts of interest

**Key messages**

* There are concerns with current utilization patterns of anti-cancer medicines in Kosovo as there was no utilization of some anti-cancer medicines considered vital, essential or necessary
* Only a few anticancer medicines have very high expenditure; however, there are variations in their use across the years causing concern as to the most effective use of available resources
* The MoH should review its drug procurement processes to ensure prices procured help optimize the management of patients with cancer within available resources
* The MoH should also carefully consider introducing updated selection processes and the pricing for new medicines, including updating DTCs, as well as potentially introducing the external reference pricing, pharmacoeconomic analyses and other approaches, to help optimize the use of available resources.

**References**

1. Godman B, Wettermark B, van Woerkom M, Fraeyman J, Alvarez-Madrazo S, Berg C, et al. Multiple policies to enhance prescribing efficiency for established medicines in Europe with a particular focus on demand-side measures: findings and future implications. Frontiers in pharmacology. 2014;5:106.

2. Wettermark B, Godman B, Neovius M, Hedberg N, Mellgren TO, Kahan T. Initial effects of a reimbursement restriction to improve the cost-effectiveness of antihypertensive treatment. Health policy. 2010;94(3):221-9.

3. Wettermark B, Zoega H, Furu K, Korhonen M, Hallas J, Norgaard M, et al. The Nordic prescription databases as a resource for pharmacoepidemiological research--a literature review. Pharmacoepidemiology and drug safety. 2013;22(7):691-9.

4. Sakshaug S, Furu K, Karlstad O, Ronning M, Skurtveit S. Switching statins in Norway after new reimbursement policy: a nationwide prescription study. Br J Clin Pharmacol. 2007;64(4):476-81.

5. Haycox A. Why Cancer? PharmacoEconomics. 2016;34(7):625-7.

6. New 50 million pound cancer fund already intellectually bankrupt. Lancet. 2010;376(9739):389.

7. Kelly RJ, Smith TJ. Delivering maximum clinical benefit at an affordable price: engaging stakeholders in cancer care. The Lancet Oncology. 2014;15(3):e112-8.

8. WHO. Access to new medicines in Europe: technical review of policy initiatives and opportunities for collaboration and research. Available at URL: <http://www.euro.who.int/__data/assets/pdf_file/0008/306179/Access-new-medicines-TR-PIO-collaboration-research.pdf?ua=1>

9. Barrett A, Roques T, Small M, Smith RD. How much will Herceptin really cost? BMJ. 2006;333(7578):1118-20.

10. Ghinea H, Kerridge I, Lipworth W. If we don’t talk about value, cancer drugs will become terminal for health systems. Available at URL: <http://theconversation.com/if-we-dont-talk-about-value-cancer-drugs-will-become-terminal-for-health-systems-44072>

11. Matusewicz W, Godman B, Pedersen HB, Furst J, Gulbinovic J, Mack A, et al. Improving the managed introduction of new medicines: sharing experiences to aid authorities across Europe. Expert review of pharmacoeconomics & outcomes research. 2015;15(5):755-8.

12. Ferrario A, Kanavos P. Managed entry agreements for pharmaceuticals: the European experience. EMiNet, Brussels, Belgium. Available at URL: <http://eprints.lse.ac.uk/50513/> 2013

13. Ministry of Health of Kosovo (2017). Health Sectorial Strategy 2017-2021. Available at URL: <http://www.kryeministri-ks.net/repository/docs/Strategjia-sektoriale-e-shendetesise-final-nentor-2016-ALB.pdf>.

14. Statistical Agency of Kosovo (2016) Health Statistics in 2015. Available at URL: <http://ask.rks-gov.net/sq/agjencia-e-statistikave-te-kosoves/sociale/shendetesia-dhe-mireqenia-sociale>.

15. Lopert R. World Bank (2015) Republic of Kosovo - Review of Oncology Formulary. World Bank Report. August 2014.

16. Quick JD, Hogerzeil H Hogerzeil, Rankin, JR, Dukes MNG, Laing R, Garnett A, O'Connor RW. Economics, pharmaceuticals in Managing drug supply : the selection, procurement, distribution, and use of pharmaceuticals. Management Sciences for Health in collaboration with the World Health Organization. Edited by Quick et al. West Hartford, Connecticut : Kumarian Press Available at URL: <http://appswhoint/iris/handle/10665/41908>. 1997.

17. PUBLIC PROCUREMENT MONITORING AT THE MINISTRY OF HEALTH - TRANSPARENTITIS VIRUS. March 2016. Available at URL: <http://www.kdi-kosova.org/publikime/74-2016-03-31-virusi-transparentitis_eng_final_isbn.pdf>.

18. WHO. Antimicrobial Medicines Consumption (AMC) Network. 2017. Available at URL: <http://www.euro.who.int/en/publications/abstracts/antimicrobial-medicines-consumption-amc-network.-amc-data-20112014-2017>

19. Alvarez-Madrazo S, McTaggart S, Nangle C, Nicholson E, Bennie M. Data Resource Profile: The Scottish National Prescribing Information System (PIS). International journal of epidemiology. 2016;45(3):714-5f.

20. Wallerstedt SM, Wettermark B, Hoffmann M. The First Decade with the Swedish Prescribed Drug Register - A Systematic Review of the Output in the Scientific Literature. Basic & clinical pharmacology & toxicology. 2016;119(5):464-9.

21. Wettermark B, Zoega H, Furu K, Korhonen M, Hallas J, Nørgaard M. The Nordic prescription databases as a resource for pharmacoepidemiological research—a literature review. Pharmacoepidemiol Drug Saf. 2013;22.

22. Godman B, Shrank W, Andersen M, Berg C, Bishop I, Burkhardt T, et al. Policies to enhance prescribing efficiency in europe: findings and future implications. Frontiers in pharmacology. 2010;1:141.

23. Markovic-Pekovic V, Skrbic R, Godman B, Gustafsson LL. Ongoing initiatives in the Republic of Srpska to enhance prescribing efficiency: influence and future directions. Expert review of pharmacoeconomics & outcomes research. 2012;12(5):661-71.

24. Kalaba M, Godman B, Vuksanovic A, Bennie M, Malmstrom RE. Possible ways to enhance renin-angiotensin prescribing efficiency: Republic of Serbia as a case history? Journal of comparative effectiveness research. 2012;1(6):539-49.

25. Voncina L, Strizrep T, Godman B, Bennie M, Bishop I, Campbell S, et al. Influence of demand-side measures to enhance renin-angiotensin prescribing efficiency in Europe: implications for the future. Expert review of pharmacoeconomics & outcomes research. 2011;11(4):469-79.

26. Pharmacies in Kosovo (2017). Kosovo Medicines Agency. Available at URL: <https://cloud.akppm.com/public.php?service=files&t=e13af25d11ae958885f3c201a595b6af>

27. SH Krasniqi ea. Drug Register 4. Kosovo Medicines Agency. Prishtinë Kosovë. 2015.

28. Ministry of Health of Kosovo (2015), Analysis of the Essential List for 2013 including VEN and ABC indicators. Prishtina, Kosovo.

29. Jakupi A. Drug Consumption in Kosovo 2011-2013, Kosovo Medicines Agency. Prishtinë Kosovë. Available at URL: <http://akppm.com/>

30. WHO. WHO Collaborating Centre for Drug Statistics Methodology. ATC/ DDD Index. Available at URL: <https://www.whocc.no/>

31. Bachhav SS, Kshirsagar NA. Systematic review of drug utilization studies & the use of the drug classification system in the WHO-SEARO Region. The Indian Journal of Medical Research. 2015;142(2):120-9.

32. Chlabicz M, Chlabicz S, Marcinowicz L, Rogowska-Szadkowska D, Pytel-Krolczuk B, Leszczynska K. Outpatient use of systemic antibiotics in Poland: 2004-2008. Przeglad epidemiologiczny. 2014;68(3):435-41, 543-7.

33. Versporten A, Bolokhovets G, Ghazaryan L, Abilova V, Pyshnik G, Spasojevic T, et al. Antibiotic use in eastern Europe: a cross-national database study in coordination with the WHO Regional Office for Europe. The Lancet Infectious diseases. 2014;14(5):381-7.

34. Dumartin C, L'Heriteau F, Pefau M, Bertrand X, Jarno P, Boussat S, et al. Antibiotic use in 530 French hospitals: results from a surveillance network at hospital and ward levels in 2007. The Journal of antimicrobial chemotherapy. 2010;65(9):2028-36.

35. WHO. Analysing and controlling pharmaceutical expenditures. Available at URL: <http://apps.who.int/medicinedocs/documents/s19617en/s19617en.pdf>.

36. Holloway K, Green T. Drug and therapeutics committees. A practical guide on behalf of the WHO in collaboration with MSH. Available at URL: <http://apps.who.int/medicinedocs/pdf/s4882e/s4882e.pdf>

37. WHO. WHO Collaborating Centre for Drug Statistics Methodology. Guidelines for ATC Classification and DDD Assignment. 2017. Available at URL: <https://www.whocc.no/filearchive/publications/2017_guidelines_web.pdf>

38. WHO. Introduction to Drug Utilization Research. Available at URL: <http://apps.who.int/medicinedocs/pdf/s4876e/s4876e.pdf>

39. Sakshaug S SH, Berg Ch, Blix H, Litleskare I, Granum T. Legemiddelforbruket i Norge 2012-2016/Drug Consumption in Norway 2012-2016. Folkehelseinstituttet/Norwegian Institute of Public Health. 2016.

40. Webber-Foster R, Kvizhinadze G, Rivalland G, Blakely T. Cost-effectiveness analysis of docetaxel versus weekly paclitaxel in adjuvant treatment of regional breast cancer in New Zealand. PharmacoEconomics. 2014;32(7):707-24.

41. NHS CeVEAS. Review of the available evidence on Taxanes (Paclitaxel and Docetaxel) for Breast Cancer FOR THE INCLUSION IN THE WHO MODEL LIST OF ESSENTIAL MEDICINES. Available online from: <http://www.who.int/selection_medicines/committees/expert/18/applications/8_submission_taxanes.pdf>.

42. WHO. WHO Model List of Essential Medicines - March 2017; Amended August 2017. Available online from: <http://www.who.int/medicines/publications/essentialmedicines/20th_EML2017_FINAL_amendedAug2017.pdf?ua=1>.

43. Godman B, Oortwijn W, de Waure C, Mosca I, Puggina A, Specchia ML et al. Links between Pharmaceutical R&D Models and Access to Affordable Medicines. A Study for the ENVI COMMITTEE. Available at URL: <http://www.europarl.europa.eu/RegData/etudes/STUD/2016/587321/IPOL_STU(2016)587321_EN.pdf>.

44. Kibuule D, Mubita M, Naikaku E, Kalemeera F, Godman BB, Sagwa E. An analysis of policies for cotrimoxazole, amoxicillin and azithromycin use in Namibia's public sector: Findings and therapeutic implications. International journal of clinical practice. 2017;71(2).

45. Pallis A, Tsiantou V, Simou E, Maniadakis N. Pharmacoeconomic considerations in the treatment of breast cancer. ClinicoEconomics and outcomes research. 2010;2:47-61.