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Analysis of the Consumption of Non-Oncological Medicines: A Methodological Study on Patients of the Ada Cohort

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Citation: Barigelletti, G.; Tagliabue, G.; Fabiano, S.; Trama, A.; Bernasconi, A.; Tresoldi, C.; Perotti, V.; Tittarelli, A.; Ada Working Group. Analysis of the Consumption of Non-Oncological Medicines: A Methodological Study on Patients of the Ada Cohort. *Healthcare* **2021**, *9*, 1121. <https://doi.org/10.3390/healthcare9091121>

Academic Editor: Pedram Sendi

Received: 28 June 2021

Accepted: 25 August 2021

Published: 30 August 2021

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Abstract: Cancer patients are identified as fragile patients who are often immunodepressed and subject to secondary diseases. The Ada cohort comprises cancer survivors aged 15–39 years at diagnosis included in 34 Italian cancer registries. This study aimed to analyze the possible excess of non-cancer medicines use on the basis of the medicine database of the Ada cohort. Records of medicines present in the pharmaceutical flows collected by eight Lombardy cancer registries and used by patients with any type of cancer were extracted for the year 2012. Medicine consumption data were processed to assign a defined daily dose value and to evaluate the consumption of medicines belonging to different groups of the ATC (Anatomical Therapeutic Chemical) classification. The values were compared with values in the Lombardy population. Medicine consumption related to 8150 patients was analyzed, for a total of 632,675 records. ATC groups A and C for females and group N for both sexes showed significant increases. Group J for males and group M for females showed intermediate increases, and group H for both sexes showed smaller increases. This method allowed the identification of excess medicine use to reduce cancer therapy side effects and primary disease sequelae in this group of patients.

Keywords: medicine consumption; defined daily dose; adolescents and young adults; cancer patients; fragility; pain

1. Introduction

The Ada project (Adolescent and Young Adult Cancer Survivors in Italy) [1], includes a database of patients who received a cancer diagnosis when aged between 15 and 39 years. In addition to information on the patients and their cancer types, the database lists the sources of the information, which are commonly collected by cancer registries (CRs). Among the most important sources are hospital discharge records, pathology laboratory data, outpatient data, and pharmaceutical prescription records.

The Ada database includes a total of 112,392 records of incident cancer cases between 1976 and 2015 related to 108,777 patients. The records were collected and sent to the database by 31 Italian population CRs and 3 Italian specialist CRs.

In recent years, there has been a significant decrease in the number of hospital discharge records (Figure 1), formerly the main source of epidemiological information. It is therefore useful to evaluate the potential of other sources of information, such as the source considered in the present study: medicine prescriptions.

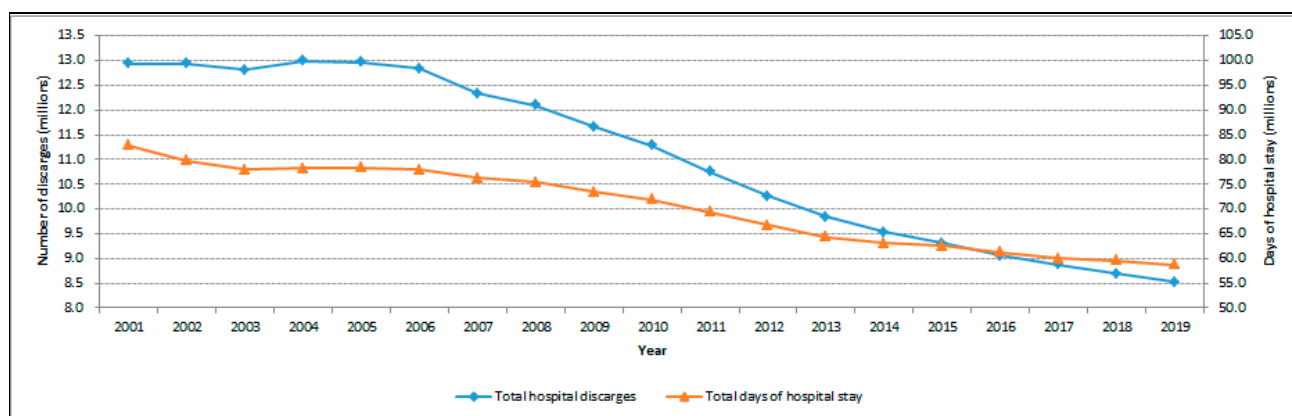


Figure 1. Italian trend of the overall volume of hospital discharges and days of hospital stay. Source: Italian Ministry of Health [2].

The pharmaceutical prescription records in the Ada database represent prescriptions issued according to the standards of the Italian National Health System (SSN). They may be subject to full or partial reimbursement according to the following prescription classes: A (life-saving medicines), C (non-essential medicines), and H (medicines for hospital use). Over-the-counter medicines and those prescribed without reimbursement by the SSN are not considered here since their prescription does not follow well-defined protocols, and they are not always reported.

The pharmaceutical prescription records are mainly composed of two data flows:

- (1) The T flow is dispensed by community pharmacies, i.e., local pharmacies open to the public. This flow includes all medicines [3] distributed by the SSN upon payment of a co-payment or free of charge.
- (2) The F flow is dispensed by hospital pharmacies or by the local services of the Public Health Agency (ATS, USL or AUSL in Italy). This flow comprises various types of medicines, which may vary from region to region and which in the Lombardy region include:
 - a. Innovative hospital medicines;
 - b. Outpatient medicines;
 - c. Off-label medicines;
 - d. Hyposensitizing therapies;
 - e. Medicines issuable by specialist prescription only;
 - f. Medicines administered to foreigners with an individual Temporarily Present Foreigner (STP) code;
 - g. Medicines for rare diseases;
 - h. Medicines delivered at hospital discharge for the first cycle of care;
 - i. Medicines distributed by penitentiary institutions;
 - j. Medicines distributed by Local Public Health Agencies;
 - k. Medicines administered in hospital to patients with hemophilia;
 - l. Medicines under risk-sharing agreements;
 - m. Some blood components;
 - n. New antiviral medicines for HCV treatment;
 - o. Others.

Objectives

The hypothesis underlying the study was that there might be an excess consumption of non-cancer medicines in adolescent and young adult cancer patients. A consequent objective was to analyze and possibly justify the reasons for this consumption. As far as we know, there have been no previous studies analyzing the non-cancer medicine consumption in this specific group of fragile patients [4].

2. Materials and Methods

2.1. Data Selection

Of the 34 CRs contributing data to the Ada database, 14 provided pharmaceutical dispensation data. A total of 2,328,057 records for the years 1980–2012 were available. Since the highest coverage in the database was for the years 2010 to 2012, we decided to evaluate medicine consumption in 2012, the more recent year. The database included 280,812 registrations for 2012, relative to 12 CRs. To obtain correct and complete terms of comparison despite the absence of an internal standard, we chose 8 CRs in the Lombardy region among these 12 CRs, as their data could be compared with data available on the web (Lombardy Open Data [5]). The data of eight Lombardy population CRs were used for comparison, covering a total of 8,370,359 inhabitants, 4,307,101 females, and 4,063,258 males.

Since the goal was to evaluate and compare the consumption of medicines by adolescent and young adult cancer patients and since Lombardy Open Data allows to select data for the age group between 18 and 39 years, all patients of this age group with previous or recurrent cancer, incident according to the IARC (International Agency for Research on Cancer)-ENCR (European Network on Cancer Registries) criteria for all available years, who had taken medicines in 2012, were selected. For this group of patients, we extracted the medicine dispensation records in the pharmaceutical Ada database for flows T and F and prescription classes A (life-saving), C (non-essential), and H (hospital use).

2.2. Data Elaboration

All pharmaceutical records selected were subsequently processed in order to:

- a. Calculate the punctual prescription units of medicines for 2012;
- b. Group the records by pairing the patients with the marketing authorization numbers (AIC codes) of the medicines they had taken;
- c. Add the NDP (number of defined daily doses (DDDs) in the package) to each patient + AIC pair;
- d. Calculate the total number of DDDs for each patient + AIC pair.

The analysis involved the assignment for each type of dispensing (package with AIC) of an NDP, which is the result of multiplying the product of the DDDs by the total quantity of active ingredient present in the package.

Some problems were encountered at this point: some AICs lacked an NDP because the regulatory body had not assigned it due to technical impossibility, and several pharmaceutical records had wrong AICs or had been assigned an AIC-unrelated internal code.

After assignment of the NDP, the total DDD was calculated for each grouped record (patient + AIC pair). We then calculated the total DDD for each group of the Anatomical Therapeutic Chemical (ATC) classification system [6].

Since Lombardy Open Data provides only values as grouping by first ATC group (first letter of the ATC code) the values of the Ada data were grouped in the same way.

The DDD/1000 inhabitants/day (DDD_{id}) was then calculated using formula (1) [7]:

$$DDD_{id} = \frac{NDP \times PP \times 1000}{POP \times RD} \quad (1)$$

Or, in our case, using Formula (2):

$$DDD_{id} = \frac{DDD_{tot} \times 1000}{POP \times RD} \quad (2)$$

where NDP is the number of DDDs per package; PP is the number of packages prescribed; POP is the total population of the area, re-proportioned by age group 18–39 and sex; RD is the number of reference days, i.e., 365 (1 year); DDD_{tot} is the number of total DDDs, obtained from the sum of the DDDs per ATC group of the grouped records.

The choice of the population in the denominator required special attention. In fact, the cohort whose medicine consumption we analyzed in this study was made up of an atypical set of cases, for which the use of the reference standard population for each age group could lead to misleading results. Therefore, we decided to select a population for the denominator that could best represent the whole, calculating it as a re-proportioning of the total population according to the scheme shown in Table 1. Thus, the population in the denominator was derived as a proportion of the total population covered by the CRs, multiplied by the ratio between the number of patients considered in the study and the total incident cases in one year in the coverage areas of the CRs for all ages.

Table 1. Re-proportioning of the reference population.

| | M | F |
|--|-----------|-----------|
| Total cancer cases in the CR areas for all ages in 2012 (a) | 30,671 | 27,322 |
| Ada cohort patients aged 18–39 years in 2012, with medicine consumption in the same year (b) | 3250 | 4900 |
| Ratio between Ada cohort patients and total CR patients (b/a) | 10.6% | 17.9% |
| Total population in the CR coverage area | 4,063,258 | 4,307,101 |
| Reference re-proportioned population for calculation | 430,556 | 772,447 |

CR = cancer registry.

3. Results

From the Ada database, 8150 patients with a cancer diagnosis between 1989 and 2012 and medicine consumption in 2012 were extracted. The group included 4900 females and 3250 males; distribution by life status was available at the most recent follow-up (≤ 31 December 2017), as reported in Table 2. Most patients were diagnosed quite recently (from one to five years, as shown in Table 2), but there was also a sizeable group with a longer period of observation (up to 15 years).

Table 2. Distribution of cases selected for the analysis, by sex, time elapsed since diagnosis, and life status.

| Years Since Diagnosis | 0 | 1–5 | 6–15 | 16–25 | Total | Alive | Dead | % Dead |
|-----------------------|------|------|------|-------|-------|-------|------|--------|
| Males | 387 | 2092 | 745 | 26 | 3250 | 3008 | 242 | 7.4% |
| Females | 637 | 3267 | 965 | 31 | 4900 | 4588 | 312 | 6.4% |
| Total | 1024 | 5359 | 1710 | 57 | 8150 | 7596 | 554 | 6.8% |

In Figures 2–5, the cases considered are presented by cancer type and sex according to the two main classifications in use: ICCC3 (International Classification of Childhood Cancer [8]) and ICD-10 (the WHO *International Classification of Diseases, 10th edition* [9]).

The processing of the pharmaceutical records selected for the analysis is summarized in Table 3.

Table 4 shows the set of values processed with the relative comparisons, where some excesses of consumption can be noted.

ATC group L, specific to cancer medicines, and groups G + V, which contain medicines used in cancer therapy, were excluded as they are outside the scope of this study.

ATC groups A (alimentary tract and metabolism) and C (cardiovascular system) for females, and ATC group N (nervous system) for both sexes showed significant increases.

ATC group J (anti-infectives for systemic use) for males and ATC group M (musculoskeletal system) for females showed intermediate increases, while group H (systemic hormonal preparations) for both sexes showed smaller increases.

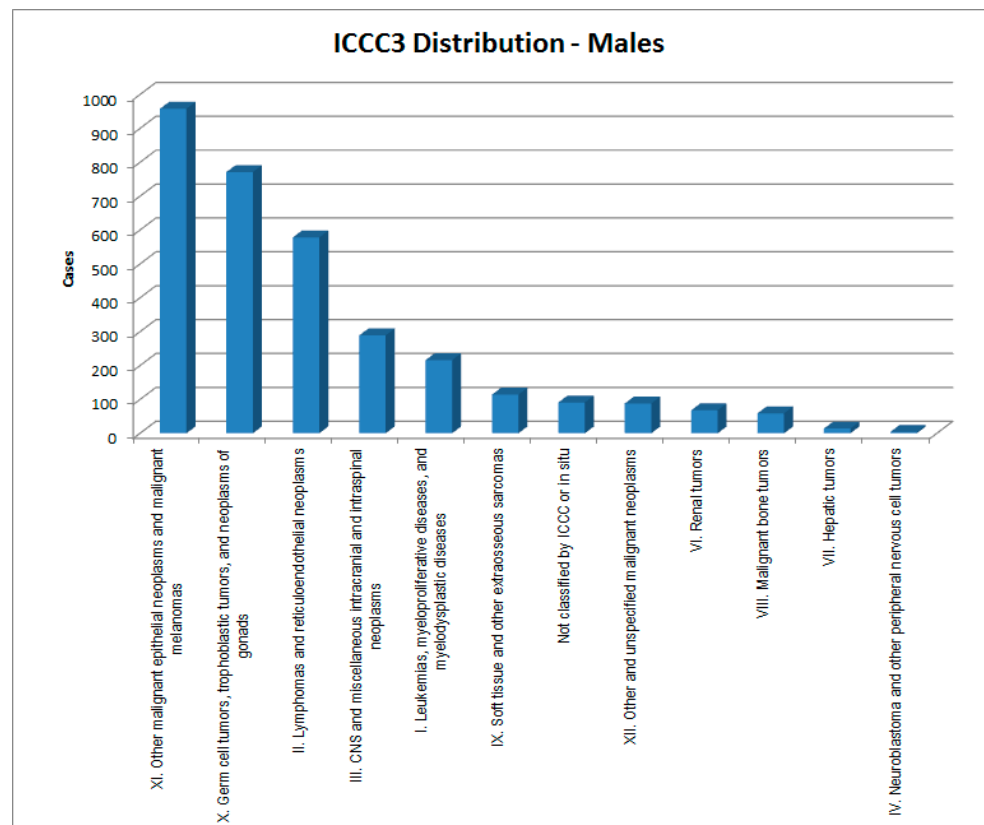


Figure 2. ICC3 (standard) distribution of cases—males.

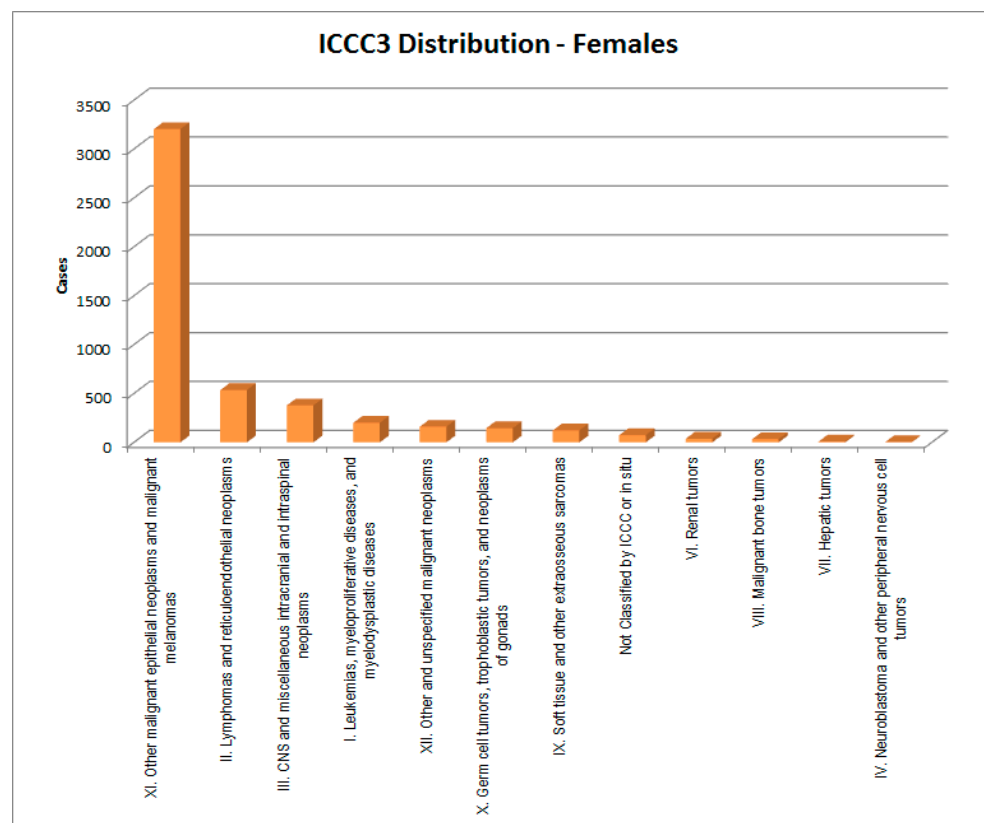


Figure 3. ICC3 (standard) distribution of cases—females.

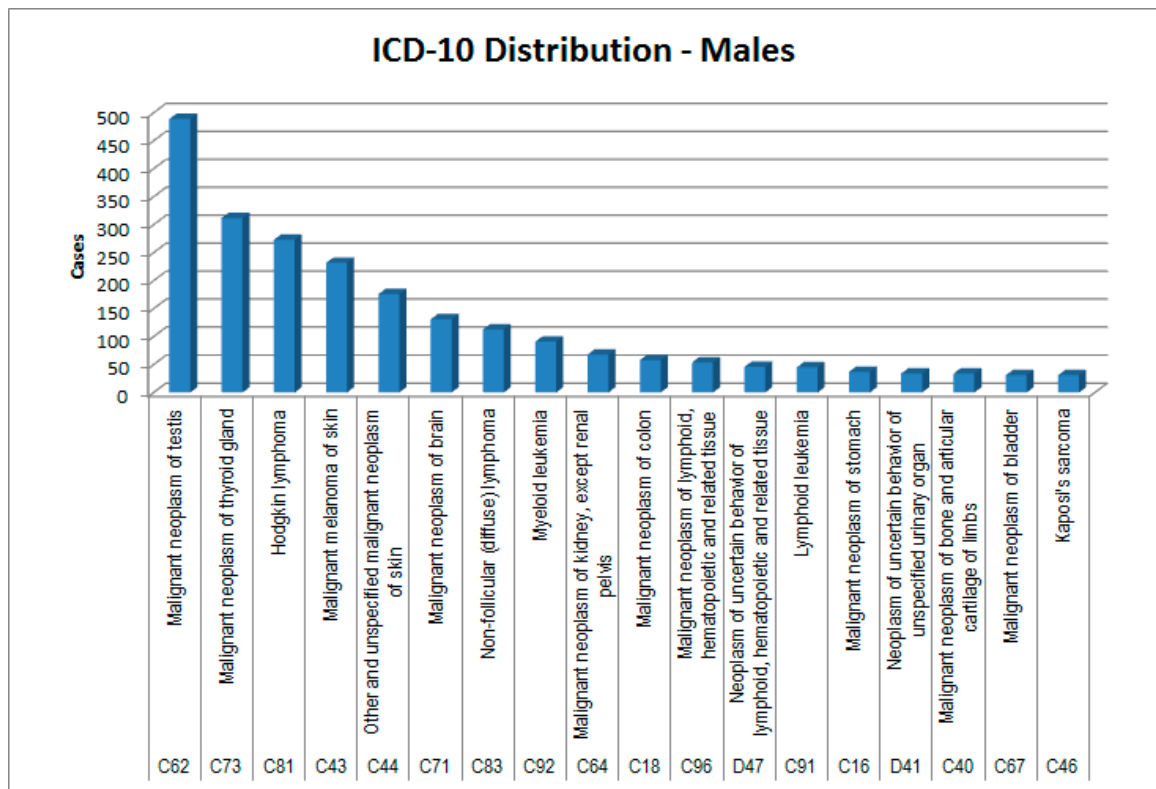


Figure 4. ICD-10 distribution of cases—males.

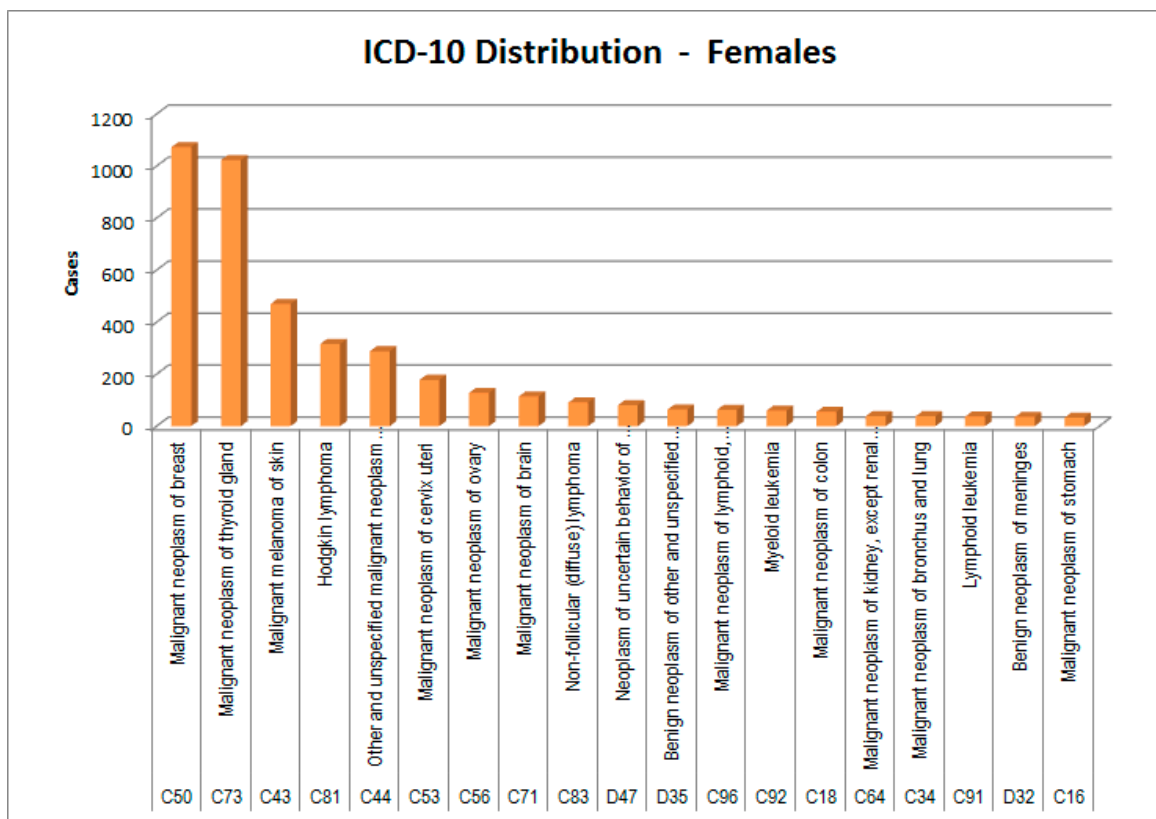


Figure 5. ICD-10 distribution of cases—females.

Table 3. Summary of elaborations on pharmaceutical records extracted from Ada database.

| Description | Number of Records | Initial Year, Incident Cases | Final Year, Incident Cases | Notes |
|---|-------------------|------------------------------|----------------------------|----------------------------|
| Patients with cancer and medicine consumption in 2012, aged between 18 and 39 years | 8150 | 1989 | 2012 | 4900 females 3250 males |
| Records of medicines, 2012 | 632,675 | 2012 | 2012 | |
| Records grouped by patient and AIC (a) | 139,931 | 2012 | 2012 | |
| Grouped records with invalid AIC | 17,931 | | | 12.8% of total (a) |
| Grouped records not connectable to NDP or null NDP | 1935 | | | 1.4% of total (a) |
| Total valid grouped records | 120,065 | | | |

AIC = marketing authorization number; NDP = number of defined daily doses.

It should be noted that, for both sexes, ATC group R, relating to medicinal products for the respiratory system, presented a decrease in consumption.

The consumptions of ATC groups that showed significant increases was then analyzed by ATC subgroups (to the third and fourth digits). The results, shown in Figures 6–13, are expressed as the total number of DDDs prescribed for each group or subgroup and divided into three age groups.

The analysis of the relationship between cancer type, total DDDs of ATC group C, and age did not show significant associations, as shown in Table 5, in which an extract of this sub-analysis is presented. Normally, higher consumption is attributed to the older age group, although for lymphoid and ovarian diseases, the higher consumption is attributable to the intermediate age group (25–32 years).

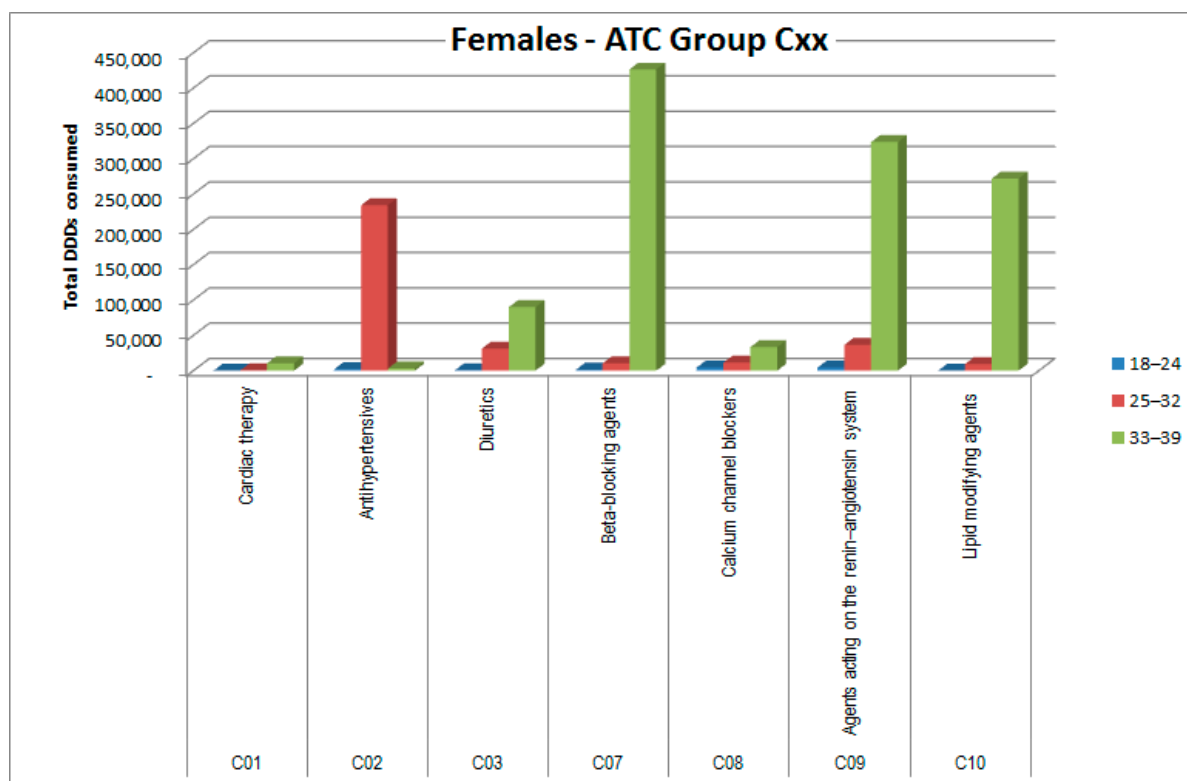
**Figure 6.** DDD consumption for females, ATC group Cxx.

Table 4. Comparisons between Ada cohort and Lombardy Open Data for ATC groups in 2012.

| | | Alimentary Tract and Metabolism | Blood and Blood-Forming Organs | Cardiovascular System | Dermatologicals | Genito-Urinary System and Sex Hormones | Systemic Hormonal Preparations, Excluding Sex Hormones and Insulins | Anti-Infectives for Systemic Use | Antineoplastic and Immunomodulating Agents | Musculoskeletal System | Nervous System | Antiparasitic Products, Insecticides and Repellents | Respiratory System | Sensory Organs | Various | |
|------------------------------------|--------|--|--------------------------------|-----------------------|-----------------|--|---|----------------------------------|--|------------------------|----------------|---|--------------------|----------------|---------|-------|
| ↓Origin ATC Group→ | | A | B | C | D | G | H | J | L | M | N | P | R | S | V | |
| Year 2012 Males, age 18–39 | 1 | Lombardy OPEN DATA 2012 M (DDD/1000 inhabitants/day) | 20.18 | 4.99 | 23.92 | 2.63 | 0.86 | 6.28 | 12.6 | 1.00 | 3.5 | 24.86 | 0.15 | 22 | 1.07 | 0.14 |
| | 2 | Consumption 2012, Ada DB M patients (DDD/1000 inhabitants/day) | 20.04 | 8.33 | 12.19 | 0,32 | 0.59 | 17.58 | 88.40 | 3564.54 | 2.13 | 366.26 | 0.03 | 3.33 | 0.36 | 2.13 |
| | 3 | Increase % (2 vs. 1) | −1% | 67% | −49% | −88% | −31% | 180% | 601% | 356,354% | −39% | 1373% | −80% | −85% | −66% | 1421% |
| Year 2012 Females, age 18–39 | 4 | Lombardy OPEN DATA 2012 F (DDD/1000 inhabitants/day) | 19.34 | 14.6 | 11.59 | 1.57 | 36.54 | 15.40 | 16.90 | 1.76 | 3.61 | 27.78 | 0.62 | 22 | 0.75 | 0.10 |
| | 5 | Consumption 2012, Ada DB F patients (DDD/1000 inhabitants/day) | 327.01 | 34.80 | 649.13 | 0.43 | 1275.91 | 51.64 | 23.08 | 2444.78 | 35.82 | 938.37 | 0.43 | 7.90 | 1.42 | 1.46 |
| | 6 | Increase % (5 vs. 4) | 1591% | 138% | 5501% | −73% | 3392% | 235% | 37% | 138,808% | 892% | 3278% | −31% | −64% | 89% | 1360% |
| | | Excluded for use in cancer therapy | | | | | | | | | | | | | | |
| | | 100–300% | | | | | | | | | | | | | | |
| | | 300–1000% | | | | | | | | | | | | | | |
| | >1000% | | | | | | | | | | | | | | | |

DDD = defined daily dose; ATC = Anatomical Therapeutic Chemical classification; M = male; F = female.

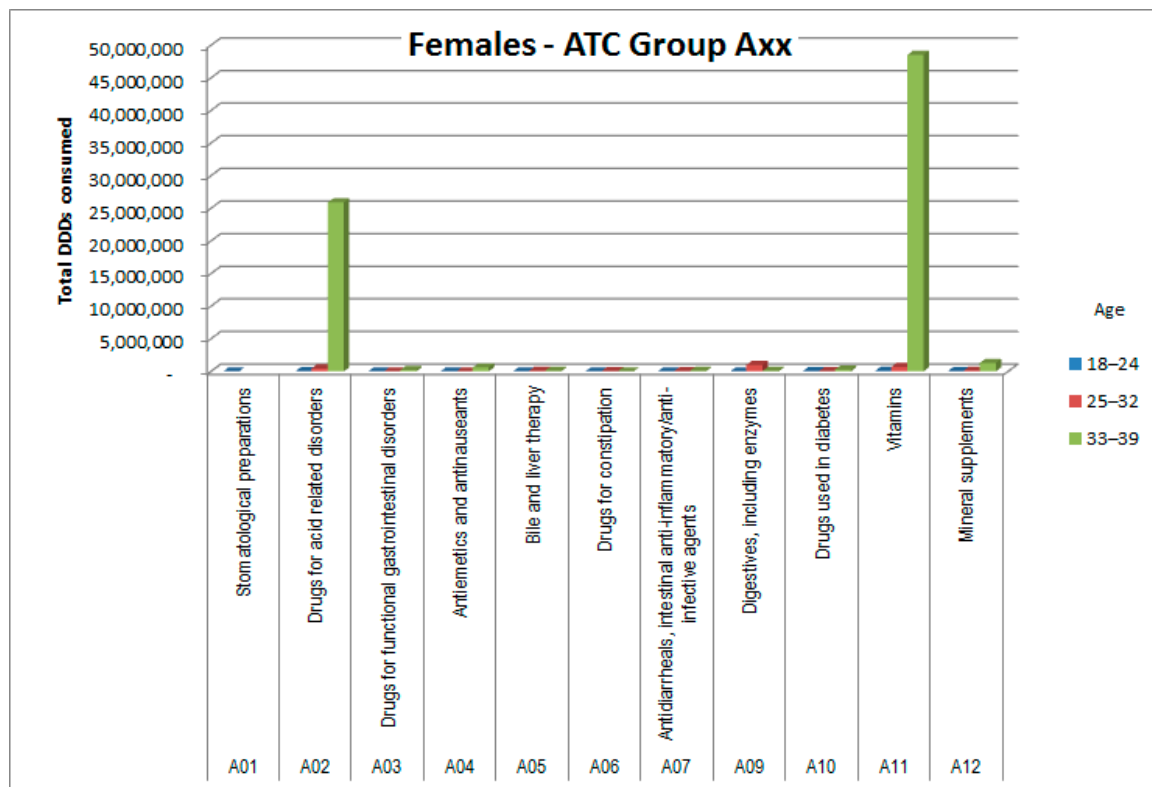


Figure 7. DDD consumption for females, ATC group Axx.

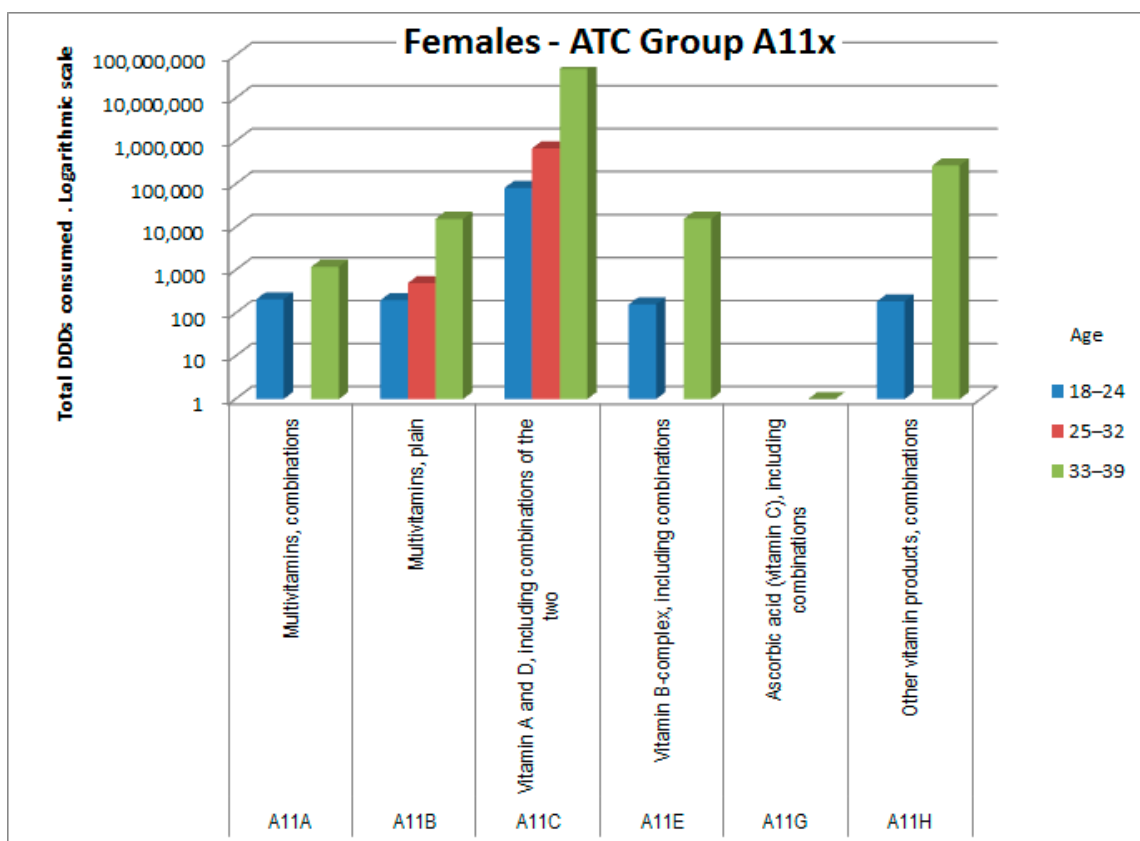


Figure 8. DDD consumption for females, ATC subgroup A11x (vitamins).

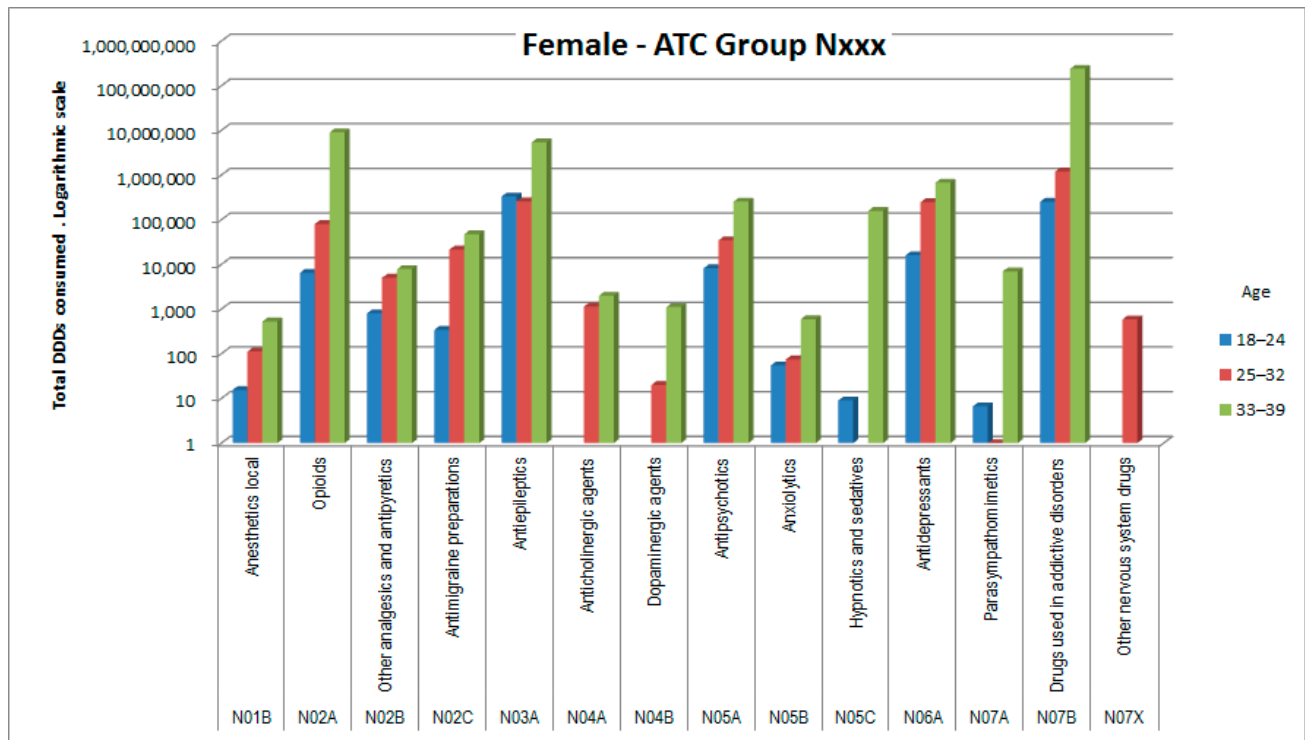


Figure 9. DDD consumption for females, ATC group Nxxx.

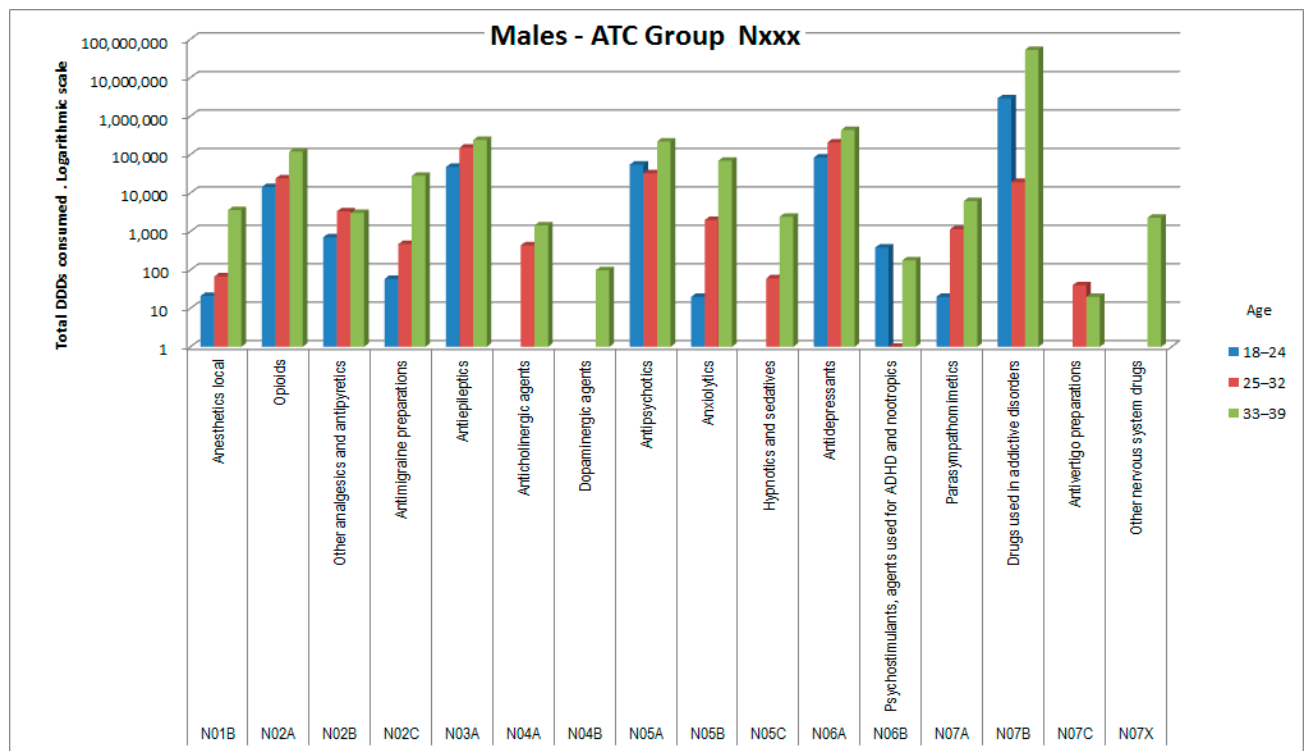


Figure 10. DDD consumption for males, ATC group Nxxx.

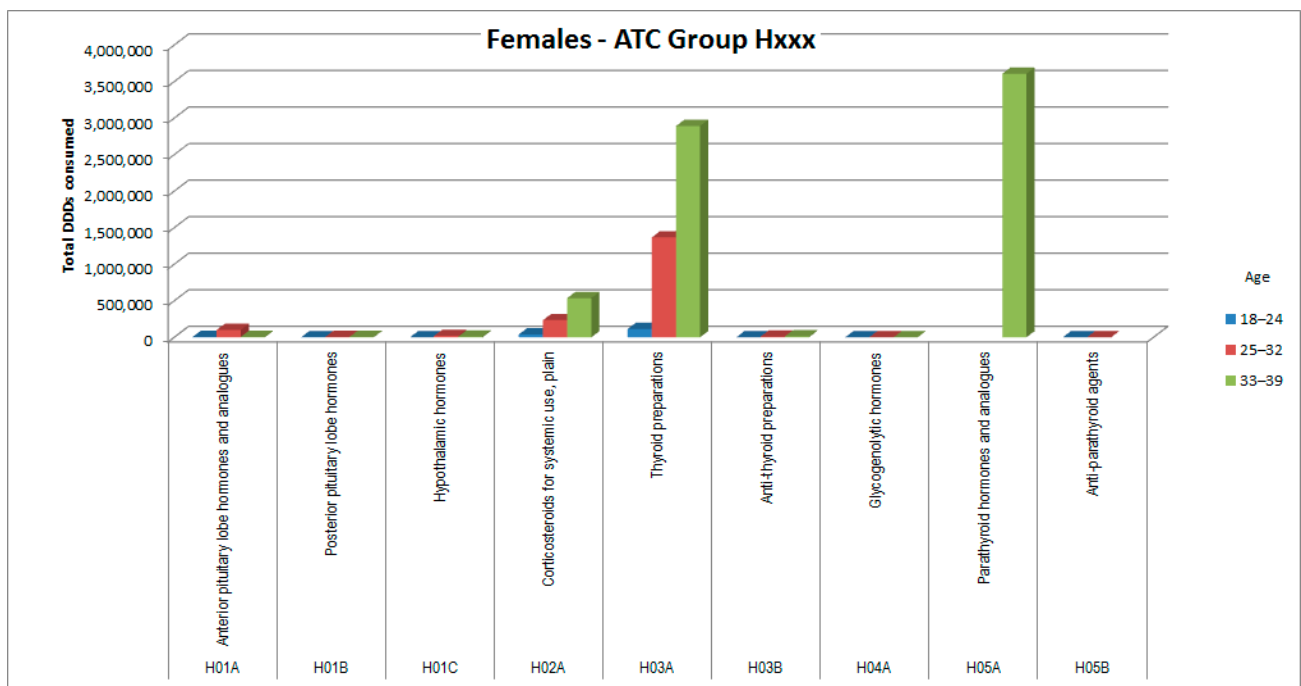


Figure 11. DDD consumption for females, ATC group Hxxx.

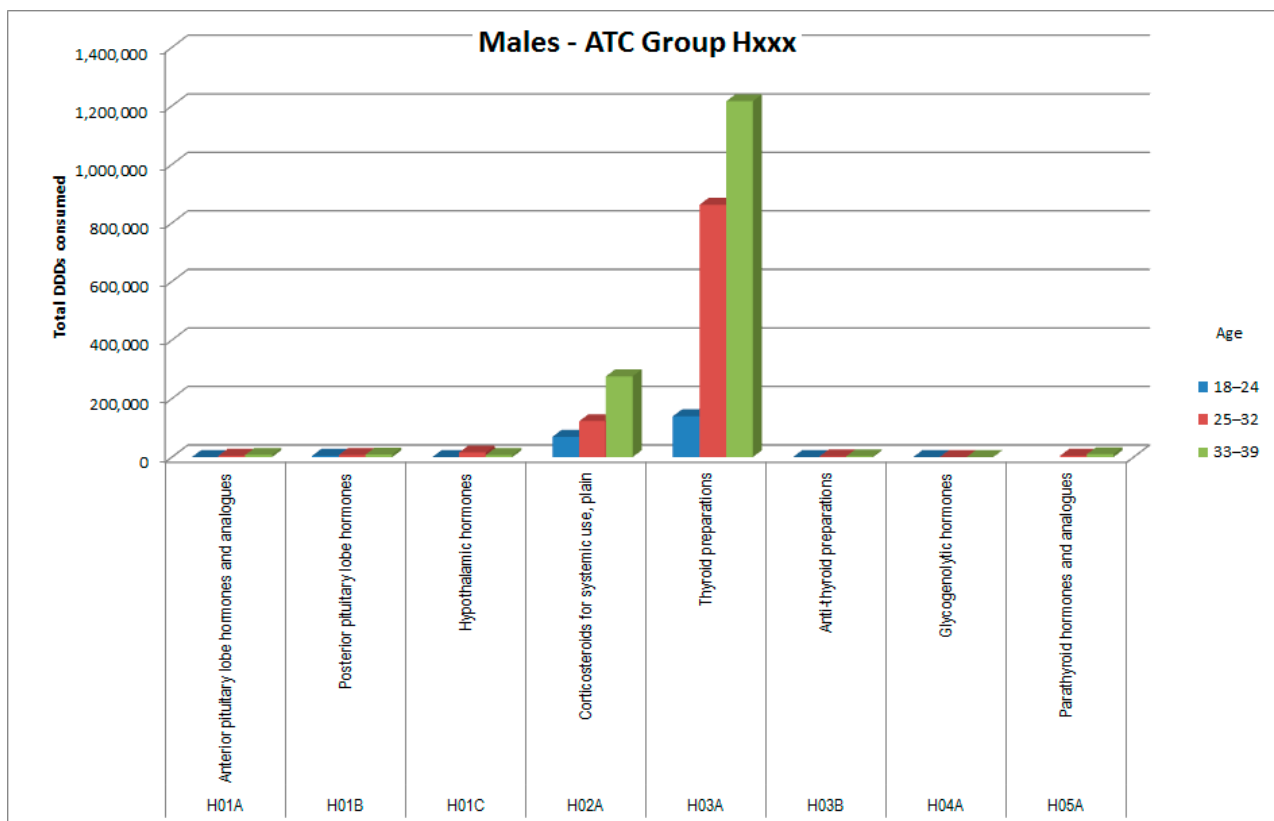


Figure 12. DDD consumption for males, ATC group Hxxx.

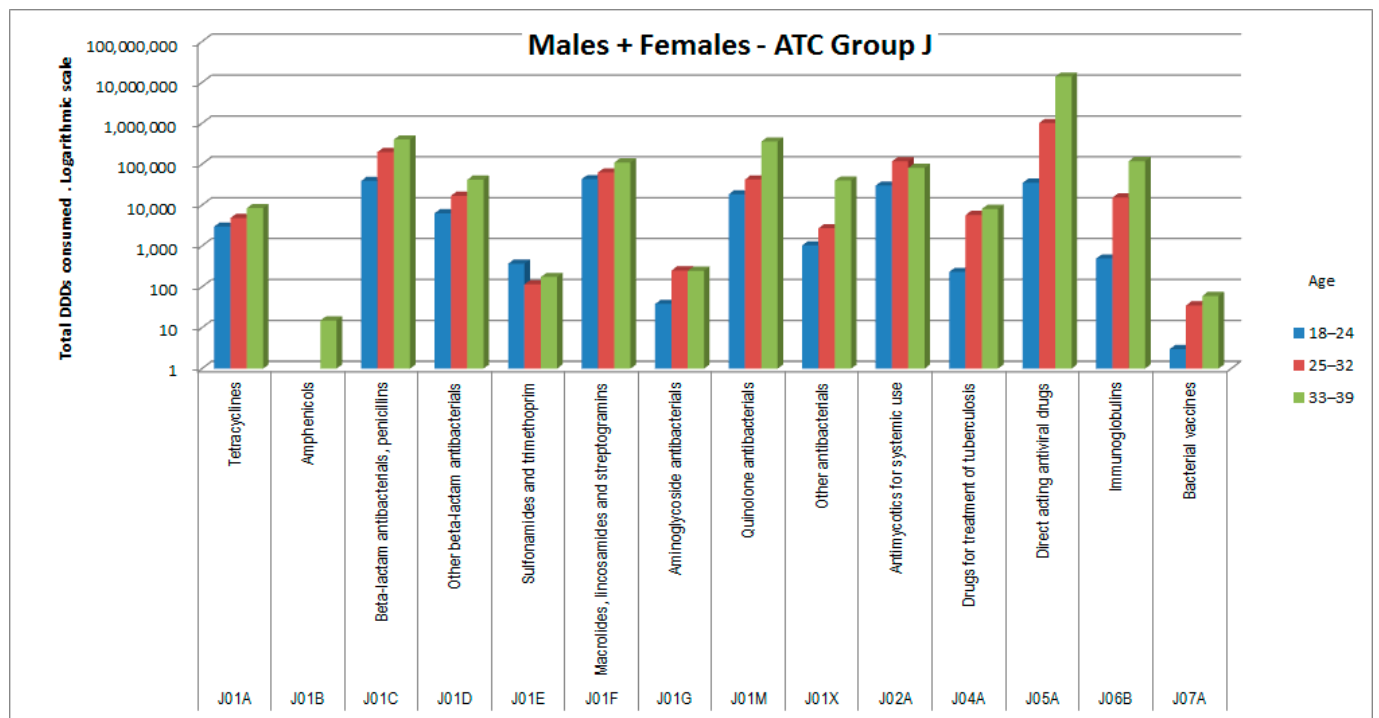


Figure 13. DDD consumption for males + females, ATC group Jxxx.

Table 5. Total DDDs for ATC group Cxx (females).

| ICD-10 | Description | Age | Total DDDs |
|--------|--|-------|------------|
| C81 | Hodgkin disease | 33–39 | 306,236 |
| C50 | Malignant neoplasm of breast | 33–39 | 256,674 |
| C96 | Malignant neoplasm of lymphoid, hematopoietic and related tissue | 25–32 | 231,672 |
| C73 | Malignant neoplasm of thyroid gland | 33–39 | 164,893 |
| C83 | Non-follicular lymphoma | 33–39 | 126,998 |
| C22 | Malignant neoplasm of liver and intrahepatic bile ducts | 33–39 | 100,059 |
| C56 | Malignant neoplasm of ovary | 25–32 | 27,132 |
| D46 | Myelodysplastic syndrome | 33–39 | 25,468 |
| C49 | Malignant neoplasm of connective and soft tissue | 33–39 | 24,477 |
| C44 | Other and unspecified malignant neoplasm of skin | 33–39 | 21,156 |
| C53 | Malignant neoplasm of cervix uteri | 33–39 | 16,263 |

DDD = defined daily dose; ATC = Anatomical Therapeutic Chemical classification.

In Table 6, the consumption of H03A (thyroid preparations) and H05A (parathyroid hormones) medicines is analyzed, comparing patients with thyroid cancer (ICD-10 C73) and patients with other cancers (ICD-10 not C73), who showed substantial differences.

In Table 7, a detail of total DDD for subgroup N07B (medicines used in addictive disorders) is shown.

Table 6. Analysis of DDDs for thyroid preparations (H03A) and parathyroid hormones (H05A).

| ICD10 | ATC | TOTAL DDD |
|-----------------|------|-----------|
| C73 | H03A | 5,617,183 |
| All but not C73 | H03A | 984,064 |
| C73 | H05A | 3,606,180 |
| All but not C73 | H05A | 0 |

DDD = defined daily dose; ATC = Anatomical Therapeutic Chemical classification.

Table 7. Total DDDs for ATC subgroup N07B (males + females).

| ATC Group | Description | Use | Total DDDs |
|-----------|--------------------------------------|--------------------------------------|-------------|
| N07BA02 | Medicines used in smoke dependence | Medicines used in smoke dependence | 30 |
| N07BB | Medicines used in alcohol dependence | Medicines used in alcohol dependence | 172,422 |
| N07BC01 | Betahistine | Medicines for nausea and vomiting | 75,161 |
| N07BC02 | Methadone | Severe pain syndromes (dependence) | 295,004,425 |
| N07BC51 | Buprenorphine, combinations | Buprenorphine, combinations | 1,170,013 |

DDD = defined daily dose; ATC = Anatomical Therapeutic Chemical classification.

4. Discussion

Cancer patients have a need for more medicines of some of the ATC groups compared with a general patient population, as we found in our pilot study [10]. The cohort of cancer patients considered in this study, which was extrapolated from the Ada database, had particular characteristics, especially given the young age of the patients (18–39 years), but also given the specific peculiarity of the cancer types that most affect these patients [11]. This can greatly influence the consumption of medicines not directly involved in cancer treatment.

We performed analyses of some of the ATC groups that showed consumption increases, evaluating the ratios, gender differences, and clinical aspects of medicine prescriptions. The ATC groups L (antineoplastic), G (sex hormones), and V (miscellaneous) were excluded from the analysis because medicines belonging to these groups are normally used in cancer treatment.

ATC group C (cardiovascular system) showed excess consumption among female patients (Figure 6), to be attributed mainly to blood pressure and lipid regulators in the older age group (33–39 years). As shown in Table 5, this excess was not attributable to any particular cancer type, except as expected in the case of hormone replacement therapy in thyroidectomized patients.

Consumption of ATC group A medicines (alimentary tract and metabolism) was also higher in female patients (Figure 7). The increase was mainly related to subgroup A02 (antacids) and subgroup A11 (vitamins), with substantial consumption of vitamin D, as shown in Figure 8.

Both sexes, albeit with small differences between them, showed increased consumption of medicines belonging to ATC group N (nervous system), with the greatest increase observed for subgroup N07B (substances against abuse, listed in Table 6). In this group methadone (ATC N07BC02) was the agent with the greatest consumption, followed by opioids (N02A), antiepileptics (N03A), and antidepressants (N06A).

H03A (thyroid preparations) represented the subgroup with the highest consumption for ATC group H (systemic hormonal preparations); among female patients there was also a conspicuous peak for the H05A subgroup (parathyroid hormones). Comparative analysis of consumption in these two ATC subgroups between patients with thyroid cancer (ICD-10 C73) and patients with other cancers (ICD-10 not C73) revealed substantial differences, as shown in Table 6.

Additionally, ATC group J (anti-infectives for systemic use) showed a significant increase in consumption, due essentially to antibiotic and antiviral medicines.

4.1. Outline of Clinical Pharmacology

In ATC group A (alimentary tract and metabolism), the significantly higher prescription rate among women, almost exclusively in the older age group, was mainly attributable to the A11 subgroup (vitamins) and to a lesser extent to the A02 subgroup (antacids and analogues). Further sub-analysis of A11, also by age group, showed that vitamins are often prescribed in combination, and most prescriptions focus on vitamin A, E, and D combinations, probably because of their antioxidant (E) and anti-osteoporosis (D) effects, and on those of the B complex, probably for their effects on nerve fibers; these three aspects may be useful in counteracting some frequent side effects of cancer chemotherapy. The benefits of vitamin supplementation in cancer patients when not undergoing chemotherapy cycles are less clear and still debated [12,13]. Furthermore, although the increased use of vitamin D in the older age group of females appears consistent with the risk of osteoporosis, especially if they use corticosteroids, it is not clear how gender medicine can justify the other differences. It could be hypothesized that these medicines are used as placebo, and the appropriateness of prescribing them needs evaluation [14].

For ATC group C (cardiovascular system), the gender difference was even more pronounced. Males have a basal consumption in the reference population that is about double that of females, but in the observed cohort, their consumption halved (−49%), while for females a 55-fold increase in consumption was observed. As shown in Figure 6, these are mainly beta-blocking agents (C07) but also real antihypertensives (C02, C09) and anti-dyslipidemics (C10). Additionally, for this ATC group, gender medicine can provide some explanation, given that the hormone blockade in some oncology protocols can have opposite effects in the two sexes as regards the cardiovascular system, but the difference between the sexes was so high that this consideration appears insufficient, and again, the question of prescription appropriateness arises.

In ATC group H (systemic hormonal preparations), females tend to have a 2.5 times higher basal consumption than males, but in the patients of the Ada cohort, consumption almost tripled in both sexes. Disaggregating by ATC subgroup, we observed that females, in whom thyroid neoplasms have a double incidence compared with males (Figures 4 and 5), showed a prescription value of thyroid replacement therapy that was quadruple compared with males. It should be considered that in females there is a higher incidence of autoimmune thyroiditis; however, females have a specificity: unlike males, they also take replacement therapy for iatrogenic hypoparathyroidism, probably in consideration of the fact that they are at greater risk of osteoporosis than males, even before menopause [15].

Additionally, in ATC group J (anti-infectives for systemic use), there was an increase in consumption, modest in females but very marked in males. This increase was attributable to antibacterial medicines (bactericides more than bacteriostatics), antifungals, and antivirals, which are widely used in these patients who are often immunosuppressed as a result of the demanding cancer treatments [16].

In ATC group N (nervous system), females showed an overall triple consumption compared with males, indicating their greater propensity for medicine consumption in general [17–19]. The most commonly used medicines by both males and females in our cohort were those classified in the subgroup for substance abuse cessation, but which in these patients are used to treat chronic pain (methadone in 99.5% of cases, buprenorphine in 0.4%). Second in use were other subgroups of specific medicines for the treatment of painful symptoms, which appear relevant and diversified in pathogenesis [20]. These include substances with different mechanisms of action, such as N01B, N02A, N02B, and N02C, but also N06A and sometimes N03A. Last in this category were medicines used, together with non-medicinal techniques, to treat the psychological distress of these patients [21], which in addition to being frequent can in some cases reduce adherence to therapy [22] and sometimes lead to overt mental health issues (N05A, N05B, N05C, and again N06A) [23].

4.2. Observations and Limitations

- (1) For a more effective analysis it would be preferable to use an internal standard, in the event that records of all prescriptions were available, as the references used (OsMed [24], Open Data, etc.) often have non-compliant characteristics or can limit the calculation needs.
- (2) It is necessary to have a sufficiently large cohort to avoid a small number of individuals with diseases related to specific ATC groups or subgroups from skewing the results. With a sufficient number of data (not available in this study), the method could make it possible to stratify the excess consumption of medicines based on the time from diagnosis. In this way, possible differences between patients with the most recent diagnoses and other subgroups of patients could be detected, which would allow us to ascertain whether to associate the observed results with the side effects of specific therapies or with the distant outcomes of therapeutic interventions.
- (3) The groupings of greater detail than the first ATC grouping (first character) are distorting because, although they belong to the same ATC subgroup, the medicines have different characteristics and therefore very different weights in DDD. Evaluating differences in DDD / 1000 inhabitants / day among these medicine subgroups makes no sense. Based on our experience, we have indicated the absolute value of DDD prescribed for some subgroups in order to identify the medicines that most influenced the changes in consumption within the primary group. The evaluation of consumption differences in the ATC subgroups can be performed by comparing the individual subgroups between cohorts with different characteristics, or between a cohort and a reference standard (as expressed in point 1).
- (4) It is important to carry out appropriate quality control of the pharmaceutical sources, particularly regarding the correct attribution of AIC and ATC codes, which can be problematic when internal codes not corresponding to the official nomenclature are used.

5. Conclusions

The analysis of medicine consumption using DDD allows interesting observations to be made on consumption in specific patient populations. Fragile populations, such as the one considered for this study, consisting of cancer patients of the Ada database, show increases in consumption of specific ATC groups and significant differences between the sexes.

These findings can be used for better patient care, and they could be preparatory to actions to prevent and reduce the side effects of therapies and the sequelae of the primary disease, often present in this group of patients.

This technique can be implemented, with appropriate adaptations, for similar analyses in different patient groups. Moreover, if used in the context of the population and in comparison with exposure to environmental agents or adverse events, it can be employed as a sentinel event for monitoring situations of discomfort or suffering.

Author Contributions: G.B. contributed to study conception, designed the study, managed the Ada database to extract the data, performed the analyses, and wrote the first draft of the paper; G.T. contributed to study conception and writing the paper; S.F., A.B. and V.P. performed statistical controls; A.T. (Annalisa Trama) contributed to writing the paper; C.T. contributed to the clinical pharmacology analysis and to writing the paper; A.T. (Andrea Tittarelli) helped in managing the Ada database and in writing the paper. All authors read and approved the final manuscript.

Funding: This research received no external funding.

Institutional Review Board Statement: The study was conducted according to the guidelines of the Declaration of Helsinki, and approved by the Institutional Review Board (or Ethics Committee) of Fondazione IRCCS Istituto Nazionale Tumori (protocol code INT 134/17, date of approval 20 July 2017).

Informed Consent Statement: The data contained in the Ada database were collected with the approval of the related cancer registries. Each registry provided patient data in an anonymous format. Data collection was approved by the competent ethics committee. All data used in this study were processed and treated anonymously. The authors state that no informed consent nor further ethical approval was needed for the study.

Data Availability Statement: The data will be provided upon request.

Acknowledgments: The authors thank Marije de Jager for proofreading and correcting the English. Ada Working Group: Veneto Cancer Registry (CR) (Massimo Rugge), Milano CR (Maria Teresa Greco), Tuscany CR (Gianfranco Manneschi), Romagna CR (Stefania Giorgetti), Catania-Messina-Enna CR (Salvatore Sciacca), Liguria CR (Rosa Angela Filiberti), Brescia CR (Cinzia Gasparotti), Modena CR (Giuliano Carrozzi), Palermo CR (Walter Mazzucco), Reggio-Emilia CR (Lucia Mangone), Latina CR (Silvia Iacovacci), Napoli 3 Sud CR (Mario Fusco), Umbria CR (Fabrizio Stracci), Trento CR (Roberto Vito Rizzello), Ragusa CR (Giuseppe Cascone), Taranto CR (Sante Minerba), Bergamo CR (Giuseppe Sampietro), Lecce CR (Anna Melcarne), Mantova CR (Paolo Ricci, Luciana Gatti), Pavia CR (Lorenza Boschetti), Como CR (Maria Letizia Gambino), Monza-Brianza CR (Elisabetta Merlo), Barletta-Andria-Trani CR (Rossella Bruni), Caserta CR (Alessandra Sessa), Napoli 2 Nord CR (Giancarlo D’Orsi), Sondrio CR (Anna Clara Fanetti), Brindisi CR (Emma Cozzi), Trapani CR (Tiziana Scuderi), Campania Childhood CR (Francesco Vetrano), Marche CR (Iolanda Grappasonni), Valle D’Aosta CR (Salvatore Bongiorno), Emilia-Romagna Mesothelioma CR (Antonio Romanelli).

Conflicts of Interest: The authors declare no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

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