A Study on Cancer Patients in the Region of Stockholm by Linking Data from Multiple Sources

Lilja B1,2*, Miranda-Téllez J1, Ljunggren G1,3, Loov SA1, Wettermark B1,2, Lissmats A4 and Henriksson R4,5

1Public Healthcare Services Committee Administration, Stockholm County Council, Stockholm, Sweden
2Centre for Pharmacoepidemiology, Department of Medicine, Karolinska Institutet, Stockholm, Sweden
3Department of Learning, Informatics, Management and Ethics, Medical Management Centre, Karolinska Institutet, Stockholm, Sweden
4Regional Cancer Centre Stockholm Gotland, Stockholm County Council, Stockholm, Sweden
5Department of Radiation Science, Oncology, University of Umeå, Sweden

Abstract

Background: Data from clinical practice have only to a limited extent, been used routinely to monitor cancer patients initiated on new drugs. In this study of patients with cancer, focussing on prostate, breast, and skin cancer, two years of individual data from several registries was used to explore the possibilities to monitor patients with cancer.

Methods: This study is based on a research database with more than 78 million records with person-linked diagnoses, drug treatment, and socioeconomic characteristics from eight national and regional registries, for patients with a recorded cancer diagnosis or treated with cancer drugs during 2001-2011. For this cross-sectional registry study 7,378 patients diagnosed with prostate, breast, or skin cancer during 2009-2010, were selected to assess patient characteristics, comorbidities and drug treatment.

Results: Of the population selected from the Swedish Cancer Register with the three major diseases, 3,581 had prostate cancer, 2,760 had breast cancer, and 1,037 had skin cancer. The income was 70.1%, 62.9%, and 53.3% in the prostate, breast and skin cancer group, respectively. Urogenital- and cardiovascular diseases were common in both prostate (47.8% and 52.7%), and breast cancer (52.4% and 42.6%) patients. In skin cancer patients, other skin diagnoses were most common (50.7%) followed by cardiovascular disorders (48.3%). Cancer drugs, mainly mature, were received by 85.9% of patients with breast cancer, 32.4% of patients with breast cancer, and 41.1% of patients with skin cancer. Additional tumour diagnoses for 5.2% of prostate cancer patients, 4.1% of breast cancer patients, and 17.3% of patients with skin cancer, were found in primary care data.

Conclusion: Access to healthcare data, including primary care, and the opportunity to link records from multiple data sources by the Swedish personal identity number, allow the possibility to study treatment, disease pattern and characteristics in large cancer patient populations.

Keywords: Prostate cancer; Breast cancer; Skin cancer; Drugs; Record linkage study; Pharmacoepidemiology; Healthcare registries

Abbreviations

NBHW: The National Board of Health and Welfare; S-G Region: The Healthcare Region Stockholm and Gotland; ICD-10: The International Statistical Classification of Diseases and Related Health problems Tenth Revision; ATC: The Anatomical Therapeutic Chemical (Classification); SALT: Sjukhusapotekens Läkemedelstillverkning/The Hospital Pharmaceutical Manufacturing Database.

Introduction

The surveillance of drugs newly introduced in clinical practice with regard to efficacy, safety and cost-effectiveness, is of utmost importance for patients, health professionals, pharmaceutical companies, regulators, and payers [1-3]. Therefore systems for monitoring disease pattern, drug utilization and outcomes of the treatment are required [4].

At marketing approval medicines have proved a positive benefit-risk ratio based on pre-clinical and clinical studies. However, there is still concern about the effectiveness and safety in broader patient populations [4]. These challenges are especially important in the cancer field, where the number of patients studied in clinical trials is often limited [5]. Efforts to facilitate approval of novel treatment, including by conditional approval, have been made during the last years [5-7]. This increases the need of post-marketing surveillance to assess safety and effectiveness [8-10]. Pharmacoepidemiological studies on large number of patients may be useful to provide post-approval evidence at a relatively low cost [2]. However, these studies are afflicted with several challenges, including difficulties in assessing complete and valid data [11,12].

Population-based registries in the Nordic countries provide good opportunities for pharmacoepidemiological research due to unique identification numbers for all citizens [13,14]. In a large number of studies in the Nordic countries, prescription registries have been used to assess utilization patterns as well as safety or effectiveness of the therapy [13]. Only a limited number of these studies and studies from other countries with access to similar registers have included oncology drugs [13,15-24], despite the growing expenditure and the large number of new drugs to be introduced in the coming years [25,26]. This could be explained by the fact that many oncology drugs are...
administered in hospital settings and are, therefore, to a limited extent included in ambulatory care prescription registries. Furthermore, to the best of our knowledge, none of the previously published population-based studies on cancer drugs has included data on socioeconomic, diagnoses recorded by other healthcare providers than in the specialist settings, drugs prepared for parenteral administration, or dispensed prescription drugs for other conditions than cancer [15-24].

As part of a project for improvement of the introduction and surveillance of new drugs in Stockholm, Sweden [26], a model of record linkage to assess utilization patterns of cancer drugs was initiated. The aim of the present study was to study the possibility to use our real world research database for follow-up of cancer patients. For this purpose; comorbidities, drug treatment, and socioeconomic status among the three most common cancer diseases were analyzed for patients with a new cancer diagnosis recorded during 2009-2010.

Methods

The research database - Sources and periods

Data from patients with a recorded malignant cancer diagnosis or dispensed cancer drugs during 2001-2011 were selected. Information about comorbidity, other drug treatments, mortality and socioeconomic was added to these patients using the personal identity numbers [14]. For this purpose data was requested, depending among other on availability, from the following organizations: a) The National Board of Health and Welfare (NBHW) – the Swedish Cancer Register (incident cancer cases 2001-2010) [27-29], the National Patient Register (all hospitalizations and outpatient consultations in specialist care with diagnoses 2001-2011) [30,31], the Swedish Prescribed Drug Register (July 2005-2011) [32], and the Cause of Death Register (2001-2011) [33]; b) Statistics Sweden – demographic and socioeconomic data (education, income, civil status and country of birth) (2009-2011) [34]; c) Apoteket AB (the provider of pharmacy services at the time of the study) – cancer drugs prepared for parenteral administration from the Sjukhusapotekens läkemedelstillverkning (SALT)/the hospital pharmaceutical manufacturing database (June 2008-2011) [35]; d) Stockholm County Council – the regional administrative database on all healthcare consumption, including primary care consultations [44]. Both the National Patient Register and the regional healthcare administrative databases (including primary care) were used for linkage to this patient group. The categorization of the two periods used in the study were obtained and shared the key file for the requested data. Applications were approved and confidentiality agreements signed with the data owners before data delivery. Data from the different registries was received as datasets separated according to source.

Study design and setting

This cross-sectional registry study was based on 7,378 patients with prostate, breast or skin cancer recorded in the Swedish Cancer Register of the healthcare region Stockholm during 2009-2010. This S-G region comprises approximately 23% of the Swedish population (9.7 million inhabitants 2014). This area of Sweden includes cities, large rural areas and a sparsely-populated archipelago. The Stockholm County Council and Gotland are both responsible for financing their primary and secondary healthcare, mainly through taxes.

Selection of the study groups

The Swedish Cancer Register, the only source of incident cancer diagnoses, was used to select our study groups. Patients with prostate (ICD code: C61), breast (C50) or skin (C44) cancer (basal cell carcinoma not included) recorded as the only diagnosis during 2009-2010 were selected (Figure 2). Malignant melanoma (C43) was not included in the skin cancer group. Patients with more than one cancer site recorded in the Swedish Cancer Register or in specialist care (in- and out-patient care) registries during (2009-2010) or before (2001-2008) the study period, were excluded. Information about other diagnoses (comorbidity) recorded during the study period (all ICD-10 codes: Chapters A-Q at 3-digit level), drug therapy (all ATC codes except V, various) as well as demographic and socioeconomic data (country of birth, level of education, civil status, and income) was linked to this patient group. The categorization of the two income groups were based on the median year income in the general population in the S-G region on last of December 2009 [44]. Both the National Patient Register and the regional healthcare administrative databases (including primary care) were used for investigating comorbidities. Patients who died during the study period (127 prostate cancer, 106 breast cancer, and 60 skin cancer) were included in the analyses.

Statistics

Descriptive statistics are presented as frequencies, proportions and standard deviations. Data management and descriptive analyses were performed with SAS Enterprise Guide 6.1 (SAS Institute Inc., Cary, NC).
### Figure 1: Registries included in the research database of cancer patients in the region of Stockholm and Gotland (S-G region), Sweden.

| Register                                                                 | Period  |
|--------------------------------------------------------------------------|---------|
| The Swedish Cancer Register                                               |         |
| The National Patient Register (hospitalizations, outpatient consultations in secondary care) |         |
| The Swedish Prescribed Drug Register                                     |         |
| The Cause of Death Register                                              |         |
| Sociodemographics                                                        |         |
| Parenteral drug preparations (SALT)                                       |         |
| The administrative healthcare database of Stockholm County Council (primary care, hospitalizations, outpatient consultations in secondary care) |         |
| The INCA Registry for new cancer drugs                                   |         |

| Year | 2001 | 2002 | 2003 | 2004 | 2005 | 2006 | 2007 | 2008 | 2009 | 2010 | 2011 |
|------|------|------|------|------|------|------|------|------|------|------|------|
| The Swedish Cancer Register                                               |       |      |      |      |      |      |      |      |      |      |      |
| The National Patient Register (hospitalizations, outpatient consultations in secondary care) |       |      |      |      |      |      |      |      |      |      |      |
| The Swedish Prescribed Drug Register                                     |       |      |      |      |      |      |      |      |      |      |      |
| The Cause of Death Register                                              |       |      |      |      |      |      |      |      |      |      |      |
| Sociodemographics                                                        |       |      |      |      |      |      |      |      |      |      |      |
| Parenteral drug preparations (SALT)                                       |       |      |      |      |      |      |      |      |      |      |      |
| The administrative healthcare database of Stockholm County Council (primary care, hospitalizations, outpatient consultations in secondary care) |       |      |      |      |      |      |      |      |      |      |      |
| The INCA Registry for new cancer drugs                                   |       |      |      |      |      |      |      |      |      |      |      |

### Figure 2: Selection of the study groups.

- **Research database**
  - The Swedish Cancer Register
  - Study population
    - Malignant diagnoses Stockholm and Gotland 2009-2010
      - N= 21,733 (20,759 patients)
    - Three main diagnoses:
      - Prostate cancer: 3,942
      - Breast cancer: 3,032
      - Skin cancer: 1,686
      - 8,660 (8,641 patients)
    - 13 men with breast cancer
    - Other than the three most common Cancer diagnoses:
      - N= 12,549 (12,356 patients)
      - With any other cancer diagnoses During 2001-2010:
        - Prostate group: 361 patients
        - Breast group: 272 patients
        - Skin group: 649 patients

- **Other diagnoses (2001-2010)**
  - 1The administrative healthcare database of Stockholm County Council, 2The National Patient Register,
  - 3The Swedish Prescribed Drug Register, 4Parenteral drug preparations, 5Population statistics (2009-2010)* (B: Country of birth, C: Civil status, E: Education, I: Income)
Results

Description of the patient groups

During the study period (2009-2010), 8641 patients were diagnosed with prostate, breast, and skin cancer. According to the selection criteria 1,263 patients were excluded (Figure 2). Out of the 7,378 selected patients 3,581 had prostate cancer, 2,760 breast cancer, and 1037 skin cancer. The majority of patients, 96.8%, were registered in the Stockholm county, and the remaining in Gotland.

Most of the patients in all three groups were born in Sweden. The education level had similar distribution across the three groups. The patients in all three groups had an income above the median in the general population (Table 1).

Comorbidity

For all the three cancer groups studied, cardiovascular disease was one of the two most common comorbidities (Table 2). Hypertension was present in 35.4% of prostate cancer patients, in 26.7% of breast cancer patients, and in 27.3% of patients with skin cancer. Urogenital diagnoses were also common in prostate (27.8% male genital disorders, including prostate hyperplasia) and breast cancer patients (28.5% mammary gland disorders). Of the endocrine disorders diabetes mellitus was the most frequent and present in 11.8% of the prostate cancer patients. Additional tumour diagnoses for 5.2% of prostate cancer patients, 4.1% of breast cancer patients, and 17.3% of patients with skin cancer, were identified in the primary care data (data not shown).

Treatment with cancer drugs

Parenteral preparations or prescribed oncological agents were dispensed to 32.4% of prostate cancer patients, to 85.9% of breast cancer patients, and to 41% of patients with skin cancer (Table 3). The most common treatments were: bicalutamide and leuprolelin in prostate cancer; tamoxifen, cyclophosphamide, and epirubicin in breast cancer; bicalutamide, leuprolelin, and fluorouracil in skin cancer patients. The 13 patients with skin cancer that received bicalutamide or leuprolelin had a prostate cancer diagnosis recorded only in the primary care registry. The patients may have received more than one of the medications during the study period either in combination or sequentially (not analyzed).

Other drug treatments

More than 97% of the patients in all three groups had obtained non-cancer drugs. During the two-year period the most common non-cancer treatments were anti-infective in patients with prostate cancer, drugs for nervous system disorders in patients with breast cancer, and cardiovascular drugs in patients with skin cancer (Table 4). Less than 3% of the patients had no other prescription drugs dispensed in ambulatory care during the period. Among drugs used for nervous system disorders, various analgesics were dispensed to 41.8% of all patients with prostate cancer, 39.8% of patients with breast cancer, and 28.3% of patients with skin cancer. Psychotropic drugs were also dispensed; sedatives to 11.3%, 18.7%, and 21.0%, respectively; antidepressants to 4.2%, 6.8%, and 5.3%, respectively; tranquilizers to 3.8%, 6.3%, and 5.0%, respectively. Neuroleptics were dispensed to 1.1% or less of the patients in all three groups. One fourth (27%) of all men with prostate cancer received agents for erectile dysfunction. Mephrotexate was dispensed to less than 1% of the patients in all three groups of patients. Antiepileptic and leucocyte stimulating drugs (mainly pegfilgrastim), were most frequently received, 5.8% and 23.8%, respectively, by breast cancer patients (data not shown).

Discussion

This study was carried out in line with the increasing interest for real world healthcare data for follow up of patients. After collection of data on individual cancer patients from different sources into a research database we created the three cancer groups for the present study. Data from the Swedish Cancer Register was chosen to select the cancer patients since this is the only registry (except for the quality registry) with verified tumour diagnoses [27]. In order to study oncological drug treatment, patients with more than one cancer recorded between 2001 and 2010 in the Swedish Cancer Register or in specialist care registries were excluded. The cancer diagnoses set in primary care were not considered in the selection of the study groups assuming they had not been confirmed by a specialist.

Results from patients with prostate, breast and skin cancer diagnosed during 2009-2010 are presented as an illustration of the potential of record linkage to monitor health, drug utilisation, effectiveness and safety in cancer patients.

| Country of birth N (%) | Breast N = 2760 | Skin N = 1037** |
|------------------------|----------------|---------------|
| Sweden                 | 3046 (85.1)    | 2192 (79.4)   |
| Other                  | 535 (14.9)     | 568 (20.6)    |

| Education N (%) | Breast N = 2760 | Skin N = 1037** |
|----------------|----------------|---------------|
| > 3 years after high school | 1318 (36.9)    | 1124 (40.7)   |
| High school     | 1435 (40.1)    | 1074 (38.9)   |
| <=9 years       | 774 (21.6)     | 523 (19.0)    |
| Missing         | 54 (1.5)       | 39 (1.4)      |

| Civil status N (%) | Breast N = 2760 | Skin N = 1037** |
|-------------------|----------------|---------------|
| Married           | 2192 (61.2)    | 1165 (42.2)   |
| Single            | 370 (10.3)     | 538 (19.5)    |
| Divorced          | 676 (18.9)     | 600 (21.7)    |
| Widow             | 305 (8.5)      | 429 (15.5)    |
| Missing           | 38 (1.1)       | 28 (1.0)      |

| Income* N (%) | Breast N = 2760 | Skin N = 1037** |
|---------------|----------------|---------------|
| Below median  | 933 (26.0)     | 916 (33.2)    |
| Above median  | 2510 (70.1)    | 1735 (62.9)   |
| Missing       | 138 (3.9)      | 109 (3.5)     |

*Categories are based on the median year income of individuals older than 20 years in the general population, December 2009 (25,000 US dollar approximately) [44].
**53% men
Diabetes mellitus prevalence in men was 25.5% (65-74 years). Data from cancer group seems to be lower than that found in the same study where on the other hand the prevalence of diabetes mellitus in the prostate (women 45-74 years), and 51.5% (both genders 65 years and above).

The prevalence of hypertension was: 43.1% (men 65-74 years), 31.9% general population in Stockholm during 2007-2011 [36]. In that study in all three study groups compared to that reported in a study on the same region [46,47]. It was not clear how the different socioeconomic factors affected this association, and it was suggested that residence area may play a role [46,47]. This needs to be addressed, and the socioeconomic status has shown to be associated with cancer incidence and survival [46,47]. It was not clear how the different socioeconomic factors affected this association, and it was suggested that residence area may play a role [46,47]. This needs to be addressed, and the socioeconomic components in our research database favours such studies. Moreover, the data can be used to investigate inequities in access to medicines, and for safety and effectiveness studies.

Similar conclusions on the potential of record linkage for studies in cancer patients were drawn in a Dutch overview study [45]. We did also show the additional benefit of the Nordic population-based registries with individual level data on comorbidty, drug treatment, and socioeconomic characteristics of the patients. Socioeconomic status has shown to be associated with cancer incidence and survival [46,47]. It was not clear how the different socioeconomic factors affected this association, and it was suggested that residence area may play a role [46,47]. This needs to be addressed, and the socioeconomic components in our research database favours such studies. Moreover, the data can be used to investigate inequities in access to medicines, and for safety and effectiveness studies.

The apparent differences in income and civil status found among prostate cancer patients, in comparison to the other two groups, trigger the need of deeper analysis taking into account other potential factors explaining these findings.

The prevalence of hypertension in our study was apparently higher in all three study groups compared to that reported in a study on the general population in Stockholm during 2007-2011 [36]. In that study the prevalence of hypertension was: 43.1% (men 65-74 years), 31.9% (women 45-74 years), and 51.5% (both genders 65 years and above). On the other hand the prevalence of diabetes mellitus in the prostate cancer group seems to be lower than that found in the same study where diabetes mellitus prevalence in men was 25.5% (65-74 years). Data from that study was recalculated for comparison. Some of the comorbidities might be related to cancer while others represent common conditions in the general population. Further analysis is required to enlighten this issue.

Most of the oncological drugs used by the patients in the study groups were mature drugs available on the Swedish market before the millennium shift [48]. The exceptions were polyestradiolphosphate (approved 2007) for prostate cancer and exemestane (2000), capecitabine (2001), and bevacizumab (2005) for breast cancer. The drugs were used mainly according to their approved indications for prostate cancer or breast cancer. Some exceptions were tamoxifen in prostate cancer patients and carboplatin and cisplatin in breast cancer patients. However, tamoxifen has been used in the preventive treatment of gynecomastia and breast pain in patients with prostate cancer receiving antigonadal treatment [49]. Carboplatin in combination with paclitaxel and trastuzumab has been proposed as an advantageous alternative treatment in patients with breast cancer [50]. Etoposide, unsuccessful as single treatment in patients with breast cancer, has shown better effect when used in combination with cisplatin [51]. Some patients with skin cancer received cisplatin with among other an indication for squamous-cell carcinoma. The skin cancer patients who received anti-androgen treatment (bicalutamide or leuprorelin) had a prostate cancer recorded only in primary care. Anti-androgens may also be used against hirsutism in certain skin cancer types [52].

A Dutch study showed a minimal use of cyclophosphamide,
mehotrexate, and 5-fluorouracil during 2005 to 2008 in early-stage breast cancer. They also reported a decrease of the use of anthracyclines to 68% of the patients, while the use of trastuzumab- and taxane-containing treatments increased to 24% and 34%, respectively during this period [53]. In contrast we found that these oncological drugs were all used to a lower extent in our study while the antiestrogen tamoxifen was the most frequent treatment. These differences may be explained by cross country differences in the determinants behind the introduction of new medicines in healthcare including guidelines, regulations, support structures, participation in clinical trials and pharmaceutical company marketing [54]. Different countries have also in recent years presented various models to optimize the introduction of new medicines including horizon scanning, forecasting, risk-sharing arrangements and health technology assessment post-launch [55].

Despite that cancer diagnoses set in primary care were not used in the selection of the study groups, this data was shown to be important for gathering all the information about diagnoses and contacts in the health care, and to explain the indication for observed treatment. It was found that all three groups had other cancer diagnoses only recorded in specialist care. Some of these diagnoses may have been reported to the national Cancer Register before 2001, or were not confirmed in specialist care.

**Strength and limitations**

The use of person-data to link different data sources is an advantage in this study. Data from the different registries on other diagnoses, recorded in specialist or primary care, deaths, and socioeconomics was included. The comprehensive coverage of the healthcare administrative database in Stockholm including hospitalizations, outpatient specialist care and primary care is an important strength of this study. With the exception of very few private clinics that operate without subsidies, all consultations and diagnoses in Stockholm are recorded in this database. An additional strength is the combination of data on drug treatment from different sources enabling an overview of the cancer treatment. Different methods have been applied in other epidemiological studies to obtain information on drug use in cancer patients. However, to our knowledge, this is the first Swedish study undertaken with individual level data on cancer medication administered in the hospital for three malignant diseases. The registry of drug preparations has previously been used in a Swedish study on castration resistant prostate cancer [35]. Still, it is important to acknowledge that further information on administered drugs in hospital care may be found in the electronic medical records [56]. These data will be incorporated in future studies.

A common limitation in registry studies is the validity and completeness of diagnoses [12]. However, the validity of recorded hospital diagnoses in Sweden in general is well documented as well as the completeness and validity of the Swedish Cancer Register [27,30]. We used diagnoses from both the National Patient Register and from the administrative database in order to retrieve patients care in other regions. Comorbidity data for the patients from registered in Stockholm and Gotland was gathered from the National Patient Register. Currently, the health care is obliged to report hospitalization and out-patient specialist care to this register. The regional administrative database includes only the patients from Stockholm. Therefore, primary care data from Gotland representing 3.2% of the selected population is missing. Another limitation of this study may be the inclusion of patients who died during the two-year period which may have led to underestimation of treatment. However, this would probably have a minor effect on the results since at the most 5.8% of the patients died during the two years.

The main purpose of this study was to describe some of the possibilities for surveillance of cancer patients and their treatment in clinical practice using record linkage of existing databases. The results show that the current research database fulfill the criteria for obtaining information about cancer diagnosis, other diagnoses, drug therapy (including temporal associations between diagnosis and treatment), diagnosis-related procedures, demographics, and socioeconomic status. However, for studies on effectiveness and safety, additional registries and medical records with data on additional drugs administered in the hospital, clinical assessments, and laboratory data need to be linked.

**Acknowledgements**

We thank our co-worker Thomas Cars, pharmacist, for helpful suggestions and support at the beginning of the study. Anders Walander, Centre for Epidemiology and Community Medicine, Stockholm County Council for valuable discussions when selecting variables for population statistics, and the statistician Bengt Sjöborg for SAS programming. This investigation was funded by the Stockholm County Council, Sweden.

---

**Table 4:** Patients with prescription drugs (other than cancer drugs) dispensed at least once during 2009-2010 in the S-G region.

| ATC group by chapter | Prostate (N = 3581) | Breast (N = 2760) | Skin (N = 1037) |
|----------------------|--------------------|-----------------|----------------|
|                      | N  | (%)  | N  | (%)  | N  | (%)  |
| A Alimentary tract and metabolism | 2252 (62.9) | 1979 (71.7) | 634 (61.1) |
| B Blood and blood forming organs | 2178 (60.6) | 1025 (37.1) | 587 (56.6) |
| C Cardiovascular system | 2287 (63.9) | 1417 (51.3) | 717 (69.1) |
| D Dermatological | 1073 (30.0) | 993 (36.0) | 560 (54.0) |
| G Genitourinary system and sex hormones | 1977 (55.2) | 1007 (36.5) | 318 (30.7) |
| H Systemic hormonal prep, excluding sex hormones | 524 (14.6) | 1382 (50.1) | 225 (21.7) |
| J General anti-infective for systemic use | 2966 (82.8) | 1800 (65.2) | 646 (62.3) |
| M Muscle-skeletal system | 1494 (41.7) | 1334 (48.3) | 394 (38.0) |
| N Nervous system | 2340 (65.3) | 2128 (77.1) | 679 (65.5) |
| P Anti-parasite | 177 (4.9) | 155 (5.6) | 52 (5.0) |
| R Respiratory system | 1379 (38.5) | 1394 (50.5) | 434 (41.8) |
| S Sensory organs | 779 (21.7) | 769 (27.9) | 376 (36.2) |
| Any drug (within A-S) | 3547 (99.1) | 2698 (97.8) | 1011 (97.5) |
| No drugs (within A-S) | 34 (0.9) | 62 (2.2) | 26 (2.5) |

**Bold** = Most common treatments

---

ISSN: 2167-1052 APDS, an open access journal

Volume 4 • Issue 4 • 1000187
References

1. Godman B, Paterson K, Malmstrom RE, Selke G, Fagot JP, et al. (2012) Improving the managed entry of new medicines: sharing experiences across Europe. Expert Rev Pharmacoecon Outcomes Res 12: 439-441.

2. Schnereiss S (2007) Developments in post-marketing comparative effectiveness research. Clin Pharmacol Ther 82: 143-156.

3. Jönsson B, Ramsey S, Wilking N (2014) Cost effectiveness in practice and its effect on clinical outcomes. J Cancer Pol 2: 12-21.

4. Eichler HG, Abadie E, Breckenridge A, Flaimon B, Gustafsson LL, et al. (2011) Bridging the efficacy-effectiveness gap: A regulator’s perspective on addressing variability of drug response. Nat Rev Drug Discov 10: 496-506.

5. Pignatti F, Gravanis I, Herold R, Vamvakas S, Jonsson B, et al. (2011) The European Medicines Agency: an overview of its mission, responsibilities and recent initiatives in cancer drug regulation. Clin Cancer Res 17: 5220-5225.

6. European Medicines Agency (2014) Human Medicines Highlights.

7. Rosenfeld H, Kropp T, Benson K, Ricci MS, McGuinn WD, et al. (2010) Regulatory aspects of oncology drug safety evaluation: past practice, current issues, and the challenge of new drugs. Toxicol Appl Pharmaco 243: 125-133.

8. Eichler HG, Oye K, Baird LG, Abadie E, Brown J, et al. (2012) Adaptive licensing: taking the next step in the evolution of drug approval. Clin Pharmacol Ther 91: 426-437.

9. Moore TJ, Furberg CD (2013) Development Times, Clinical Testing, Postmarket

10. Sorensen HT, Sabroe S, Olsen J (1996) A framework for evaluation of issues, and the challenge of new drugs

11. Schneeweiss S, Avorn J (2005) A review of uses of health care utilization databases for epidemiologic research on therapeutics. J Clin Epidemiol 58: 323-337.

12. Sorenson HT, Sabroe S, Olsen J (1996) A framework for evaluation of secondary data sources for epidemiological research. Int J Epidemiol 25: 435-442.

13. Wettermark B, Zoega H, Furu K, Korhonen M, Hallas J, et al. (2013) The Nordic prescription databases as a resource for pharmacoepidemiological research - A literature review. Pharmacoepidemiol Drug Saf 22: 691-699.

14. Ludvigsson JF, Otterblad-Olausson P, Pettersson BU, Ekbohm A (2009) The Swedish personal identity number: Possibilities and pitfalls in healthcare and medical research. Eur J Epidemiol 24: 659-667.

15. Aplenc R, Fisher BT, Huang YS, Li Y, Alonzo TA, et al. (2012) Merging of the National Cancer Institute-funded cooperative oncology group data with an administrative data source to develop a more effective platform for clinical trial analysis and comparative effectiveness research: A report from the Children's Oncology Group. Pharmacoepidemiol Drug Saf 21: 37-43.

16. Chang CS, Yang YH, Hsu CN, Lin MT (2012) Trends in the treatment changes and medication persistence of chronic myeloid leukemia in Taiwan from 1997 to 2007: A longitudinal population database analysis. BMC Health Serv Res 12: 359.

17. Dore DD, Liang C, Ziyadeh N, Norman H, Bayliss M, et al. (2012) Linkage of routinely collected oncology clinical data with health insurance claims data-an example with aromatase inhibitors, tamoxifen, and all-cause mortality. Pharmacoepidemiol Drug Saf 21: 29-36.

18. Grotthuy F, Blick ED, Choll AL, Bekaii-Saab TS, Bendell JC, et al. (2014) Bevacizumab exposure beyond first disease progression in patients with metastatic colorectal cancer: analyses of the ARIEs observational cohort study. Pharmacoepidemiol Drug Saf 23: 726-734.

19. Guerin A, Chen L, Wu EQ, Ponce de Leon D, Griffin JD, et al. (2012) A retrospective analysis of therapy adherence in imatinib resistant or intolerant patients with chronic myeloid leukemia receiving nilotinib or dasatinib in a real-world setting. Curr Med Res Opin 28: 1155-1162.

20. Joergen M, Schaefer-Thuer C, Koedel B, Matter-Walstra K, Gibbons-Mansico J, et al. (2014) Off-label use of anticancer drugs in eastern Switzerland: A population-based prospective cohort study. Eur J Clin Pharmacol 70: 719-725.

21. Oberstein PE, Hershman DL, Khanna LG, Chabot JA, Insel BJ, et al. (2013) Uptake and patterns of use of gemcitabine for metastatic pancreatic cancer: A population-based study. Cancer Invest 31: 316-322.

22. Ronning, PA, Helseth E, Meling TR, Johannessen TB (2012) A population-based study on the effect of temozolomide in the treatment of glioblastoma multiforme. Neuro Oncol 14: 1178-1184.

23. van Herk-Sukel MP, van de Poll-Franse LV, Lemmens VE, Vreugdenhil G, Puij JF, et al. (2010) New opportunities for drug outcomes research in cancer patients: The linkage of the Eindhoven Cancer Registry and the PHARMO Record Linkage System. Eur J Cancer 46: 395-404.

24. Wahlgren T, Hartman A, Sandstrom P, Lundstam S, Kowalski J, et al. (2013) Treatment and overall survival in renal cell carcinoma: a Swedish population-based study (2000-2006). Br J Cancer 108: 1541-1549.

25. Evaluate Pharma (2012) Surveying Tomorrow’s BioPharma Landscape.

26. Wettermark B, Persson ME, Wilking N, Kalin M, Korkmaz S, et al. (2010) Forecasting drug utilization and expenditure in a metropolitan health region. BMC Health Serv Res 10: 128.

27. Barlow L, Westergren K, Holmberg LT, Talbäck M (2009) The completeness of the Swedish Cancer Register: A sample survey for year 1998. Acta Oncol 48: 27-33.

28. National Board of Health and Welfare (2011) Official Statistics Sweden, Statistics - Health and Medical Care Cancer Incidence in Sweden 2010.

29. National Board of Health and Welfare. The Swedish Cancer Registry.

30. Ludvigsson JF, Andersson E, Ekbohm A, Feychting M, Kim JL, et al. (2011) External review and validation of the Swedish national inpatient register. BMC Public Health 11: 450.

31. National Board of Health and Welfare. The National Patient Register.

32. Wettermark B, Hammar N, Fored CM, Leimanis A, Otterblad Olausson P, et al. (2007) The new Swedish Prescribed Drug Register—opportunities for pharmacoepidemiological research and experience from the first six months. Pharmacoepidemiol Drug Saf 16: 726-735.

33. Johansson LA, Bjorkenstam C, Westerling R (2009) Unexplained differences between hospital and mortality data indicated mistakes in death certification: an investigation of 1,094 deaths in Sweden during 1995. J Clin Epidemiol 62: 1202-1209.

34. Statistics Sweden. Longitudinal integration database for health insurance and labour market studies (LISA by Swedish acronym).

35. Lissbrant IF, Garho W, Widmark A, Stattin P (2013) Population-based study on use of chemotherapy in men with castration resistant prostate cancer. Acta Oncol 52: 1593-1601.

36. Carlsson AC, Wandel P, Osby U, Zarrinkoub R, Wettermark B, et al. (2013) High prevalence of diagnosis of diabetes, depression, anxiety, hypertension, asthma and COPD in the total population of Stockholm, Sweden — A challenge for public health. BMC Public Health 13: 670.

37. Wandel P, Carlsson AC, Wettermark B, Lord G, Cars T, et al. (2013) Most common diseases diagnosed in primary care in Stockholm, Sweden, in 2011. Fam Pract 30: 505-513.

38. Zarrinkoub R, Wettermark B, Wandel P, Mejert M, Szulkin R, et al. (2013) The epidemiology of heart failure, based on data for 2.1 million inhabitants in Sweden. Eur J Heart Fail 15: 995-1002.

39. National Board of Health and Welfare (2000) National Health Care Quality Registers in Sweden 1999.

40. National Board of Health and Welfare (2010) International statistical classification of diseases and related health problems (ICD-10-EN).

41. World Health Organization (1992) International Statistical Classification of Diseases and Related Health Problems.

42. World Health Organization (1990) ICD-O International Classification of Diseases for Oncology, Geneva.

43. World Health Organization (2013) Guidelines for ATC classification and DDD assignment.

44. Statistics Sweden (2012) Households economic standard.
46. Danzig MR, Weinberg AC, Ghandour RA, Kotanarti S, McKiernan JM, et al. (2014) The association between socioeconomic status, renal cancer presentation, and survival in the United States: A survival, epidemiology, and end results analysis. Urology 84: 583-589.

47. Hastert TA, Beresford SA, Sheppard L, White E (2014) Disparities in cancer incidence and mortality by area-level socioeconomic status: A multilevel analysis. J Epidemiol Community Health 0: 1-9.

48. Jönsson B, Wilking N (2014) New cancer drugs in Sweden: Assessment, implementation and access. Journal of Cancer Policy 2: 45-62.

49. Perdona S, Autorino R, De Placido S, D’Amiento M, Gallo A, et al. (2005) Efficacy of tamoxifen and radiotherapy for prevention and treatment of gynaecomasia and breast pain caused by bicalutamide in prostate cancer: A randomised controlled trial. Lancet Oncol 6: 295-300.

50. Robert N, Leyland-Jones B, Asmar L, Bell R, Ilegbodu D, et al. (2006) Randomized phase III study of trastuzumab, paclitaxel, and carboplatin compared with trastuzumab and paclitaxel in women with HER-2-overexpressing metastatic breast cancer. J Clin Oncol 24: 2786-2792.

51. Sledge GW Jr (1991) Etoposide in the management of metastatic breast cancer. Cancer 67: 266-270.

52. Zouboulis CC, Chen WC, Thornton MJ, Qin K, Rosenfield R, et al. (2007) Sexual hormones in human skin. Horm Metab Res 39: 85-95.

53. van Herk-Sukel MP, van de Poll-Fransen LV, Creemers GJ, Lemmens VE, van der Linden PD, et al. (2013) Major changes in chemotherapy regimens administered to breast cancer patients during 2000-2008 in the Netherlands. Breast J 19: 394-401.

54. Chauhan D, Mason A (2008) Factors affecting the uptake of new medicines in secondary care - A literature review. J Clin Pharm Ther 33: 339-348.

55. Wettermark B GB, Eriksson C, van Ganse E, Garattini S, Joppi R, et al. (2010) Einfuhrung neuer Arzneimittel in europaische Gesundheitssysteme. [Introduction of new medicines into European healthcare systems]. GGW 10: 24-34.

56. Cars T, Wettermark B, Malmstrom RE, Ekeving G, Vikstrom B.et al,(2013) Extraction of electronic health record data in a hospital setting: Comparison of automatic and semi-automatic methods using anti-TNF therapy as model. Basic Clin Pharmacol Toxicol 112: 392-400.