Report nr. C13:04

Comparison of costs of different methods of administering Herceptin (trastuzumab)

December 2013

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Introduction

This report, which was commissioned by Icepharma/Roche in Iceland, compares the costs of administering Herceptin (trastuzumab) in two different ways: intravenous injection or subcutaneous injection.

The report was compiled by Dr. Sveinn Agnarsson, associate professor at the School of Business, University of Iceland, and Hugrún Jónsdóttir, BS, research assistant at the Institute of Economic Studies, University of Iceland. We are very thankful for the expert help and valuable information provided by Þórunn Sævarsdóttir, head of the nursing department at day ward unit 11B, Landspítali, Inga Jakobína Arnardóttir, at the Landspítali pharmacy and Helga Þ. Bjarnadóttir, division of finance and information, Landspítali.

December 1st 2013

Dr. Gunnar Haraldsson
Director of the Institute of Economic Studies

Summary

In 2012, 65 women received treatment with Herceptin (trastuzumab) for HER2-positive breast cancer at day ward unit 11B at Landspítali (LUH) in Reykjavik. The medicine was administered to the patients by means of intravenous infusion, which has up to now been the standard method. On average, it took qualified nurses at day ward unit 11B 90-112 minutes to administer Herceptin (trastuzumab) to first-time patients, but 40-62 minutes to administer the medicine to patients on subsequent visits. The patients themselves spent 80-145 minutes on first-time visits and 50-115 minutes on the following visits.

Changing the method of administering Herceptin (trastuzumab) from intravenous injection to subcutaneous injection would result in considerable time and cost savings. The analysis undertaken in this report reveals that the total time spent by hospital staff and patient on each visit could be reduced by 154-205 minutes in the case of first visits, and 74-125 minutes in the case of subsequent visits. This increased efficiency would enable staff at day ward 11B to improve the overall level of service provided. The associated cost savings are estimated at €60-70 for each first visit and €40-48 for subsequent visits. Total costs in 2012 could have been reduced by €38,400-45,000.

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1 Introduction

HER2-positive breast cancer is caused by overexpression or amplification of the human epidermal growth factor receptor 2 (HER2), which is a protein. This type of breast cancer is treated through biological therapy with the humanized monoclonal antibody Herceptin (trastuzumab) which binds to growth factor receptors on the surface of the tumor cells, thus obstructing the proliferation of cancer cells. Standard administration of Herceptin (trastuzumab) is by intravenous infusion, but a newly developed formulation of the drug makes subcutaneous injection possible.

The subcutaneous administration of Herceptin (trastuzumab) is considered less invasive and less time-consuming than the standard intravenous administration. Because of the time savings involved, the subcutaneous injection is believed to offer more convenience for patients and health care professionals. Furthermore, the new type of administration may reduce health care costs in general. In Iceland, the administration of Herceptin (trastuzumab) takes place at The National University Hospital of Iceland (Landspítali Háskólasjúkrahús, hereafter referred to as LUH) in Reykjavík, the capital of Iceland, and Akureyri Hospital, in Akureyri in the north of the country. This analysis is based on evidence gathered from day ward unit 11B at LUH, where most of the patients receive treatment.

The aim of this analysis is to estimate the explicit and implicit cost savings generated by altering the administration of Herceptin (trastuzumab) from intravenous infusion to subcutaneous injection at LUH. Each administration process will be described as accurately as possible. The cost comparison consists of analysis of the underlying factors of the process, such as preparation and administration, and the time it takes to carry out each individual task. This will allow for a greater understanding of the subject and lead to a better evaluation of the cost differences involved. The following analysis is a health economic analysis that is based on a micro-economic approach.

2 General information

Intravenous administration is an injection into a vein. Subcutaneous administration, however, is an injection under the skin. With intravenous administration, the administered

drug can produce effects within a few seconds, while subcutaneous administration of a drug normally results in effects within a few minutes depending on the local blood flow in the injected area (Encyclopædia Britannica, 2013a). A phase III, randomized, international, open-label, multicentre study in women with HER2-positive early breast cancer, called the HannaH study, has shown comparable pharmacokinetics, efficacy and overall safety profile for the two ways of administering Herceptin (trastuzumab) (Ismael et al., 2012). In the HannaH study, efficacy was based on pathological complete response. The subcutaneous formulation demonstrated non-inferior pharmacokinetics and pathological complete response rate, and a safety profile consistent with that of the intravenous formulation. Therefore, the potential benefits of altering the administration are embodied in better use of resources and greater convenience followed by the time savings the new formulation offers (Ismael et al., 2012).

A currently ongoing study, PrefHer, evaluates patient preference and health care professional satisfaction with subcutaneous administration of Herceptin (trastuzumab) (Pivot, X., et al., 2013). This study is designed to evaluate overall preference of patients with HER2-positive early breast cancer regarding the route of Herceptin (trastuzumab) administration in the adjuvant therapy. According to Pivot et al. (2013), 91.5% of patients preferred the subcutaneous administration of Herceptin (trastuzumab) over the standard intravenous one. In an exploratory analysis, the patients' most common reason for preferring the subcutaneous formulation was time saving (90.3% of the patients who preferred subcutaneous administration) and reduced pain or discomfort (40.7%) compared with the intravenous administration (De Cock, 2013).

A parallel PrefHer sub-study evaluates the utilization of medical resources. According to its results, patient infusion chair-time would be reduced substantially, as up to five times more chair-time is required with the intravenous infusion than the subcutaneous injection. Pharmacy preparation time would also be reduced substantially. The time that health care professionals dedicate to the administration would also be reduced by 30-51% and could be reduced even further with increased experience. As a result, the overall time savings from replacing intravenous administration with subcutaneous administration increase efficiency of the health care centre and its staff (De Cock, 2013).
Before calculating possible cost savings, explicit or implicit, of changing the administration from intravenous infusion to subcutaneous injection, it is appropriate to

briefly discuss HER2-positive, Herceptin (trastuzumab) and the institution treating HER2-positive individuals in Iceland (predominantly LUH).

2.1 HER2-positive and Herceptin (trastuzumab)

The most frequent symptom of breast cancer is an unusual lump or swelling in the breast area, caused by growth of malignant cells in the mammary glands. Breast cancer is the most common type of cancer among women (WHO, 2013). In high-income countries, breast cancer is the leading cause of cancer-related death among women aged 20 to 59. The likelihood of breast cancer grows with age; 75% of all diagnosed women are diagnosed after the age of 50. Both environmental and genetic factors can cause breast cancer, although the exact causes of breast cancer are generally unknown. Treatment for breast cancer may entail surgery, radiation, chemotherapy or biological treatment (Encyclopædia Britannica, 2013c).

HER2-positive (human epidermal growth factor receptor 2) is a type of breast cancer caused by mutation in a specific gene that produces the protein HER2. Other mutations in genes that have been connected with breast cancer are BRCA1, BRCA2, CHEK2, and p53 (Encyclopædia Britannica, 2013c). HER2-positive breast cancer is identified by overexpression, or amplification, of the human epidermal growth factor receptor 2 (HER2), which leads to increased quantities of HER2 on the surface of the tumor cells. Approximately 15-20% of women with breast cancer have HER2-positive breast cancer (Wolff et al., 2007). HER2 is found on the surface of the cancer cells in 20-30% of invasive breast cancers (Landspítali Háskólasjúkrahús, 2012; Hudis, 2007). HER2-positive tumors tend to be hostile and unresponsive to most chemotherapy agents (Encyclopædia Britannica, 2013b).

HER2-positive breast cancer is treated through biological therapy with Herceptin (trastuzumab). In biological therapy, chemical inhibitors are used to obstruct the hormones that stimulate growth of cancer cells. Herceptin (trastuzumab) is a humanized monoclonal antibody that inhibits the proliferation of cancer cells by binding to growth factor receptors on the surface of the cells (Encyclopædia Britannica, 2013c). The drug obstructs the overexpression of HER2 along with encouraging antibody-dependent cellular cytotoxicity (Hudis, 2007; Landspítali Háskólasjúkrahús, 2012). Herceptin (trastuzumab) has been used since 1998, first to extend survival in women with advanced breast cancer and later in combination with or following standard chemotherapy (Encyclopædia

Britannica, 2013b.). Herceptin (trastuzumab) is primarily intended to treat advanced HER2-positive breast cancer and for adjuvant therapy of early-stage HER2-positive breast cancer. Herceptin (trastuzumab) can also be used, along with other drugs, for the treatment of HER2-positive metastatic gastric cancer and gastro-esophageal junction cancer. Research in pathology by the University of Iceland indicates that 15% of patients diagnosed with breast cancer in Iceland are HER2-positive (Landspítali Háskólasjúkrahús, 2012).

2.2 National University Hospital

The National University Hospital of Iceland (LUH) (Landspítali Háskólasjúkrahús), which is the main hospital in Iceland, was established in March 2000 with the merger of two hospitals – Ríkisspítalar and Sjúkrahús Reykjavíkur - that had by then come under state management. The main obligations of LUH are patient service, clinical education and training, and scientific research. LUH supplies primary and specialized care for both short-term and long-term diseases. The various clinical services provided by the hospital occur in outpatient clinics, day patient units, inpatient wards and clinical laboratories. Furthermore, LUH's support offices provide services involving human resources, economics and finance, information technology and operations (Landspítali Háskólasjúkrahús. Landspitali University Hospital, n.d.; Landspítali Háskólasjúkrahús. Stefna og hlutverk, n.d.).

LUH, which is the only university hospital in Iceland, is an important educational institution in the field of health sciences. An overwhelming majority of students in health sciences gets their clinical training at the hospital, which consequently is of tremendous importance for the future of the health care system in Iceland. More than 250 students study at the hospital on a daily basis and over 1.300 students are educated and trained there annually. Furthermore, many employees of LUH also have teaching posts at the University of Iceland and other universities, which facilitates the collaboration between LUH and the academy. Most students who receive training at LUH are studying medicine or nursing at the University of Iceland, but trainees are also drawn from the fields of pharmacology, physiotherapy, dentistry, psychology, and social counselling (Landspítali Háskólasjúkrahús. Vísindi og menntun, n.d.; Landspítali Háskólasjúkrahús. Menntun heilbigðisstétta, n.d.).

Clinical services at LUH are divided into six different fields. The largest field is the department of internal medicine (icel. lyflækningasvið), which provides general and specialized care in medicine and nursing. The operations of internal medicine are diverse and the majority of its patients are short-term patients. Internal medicine operates in four different locations in the Reykjavík area: Fossvogur við Hringbraut, Landakot, Grensás and Kópavogur. Many of the services provided by internal medicine are not available anywhere else in Iceland. Internal medicine provides care for many of the most common and most serious health problems the hospital faces, including treatment for cancer-related ailments. Other specialties include general medicine, hematology, rehabilitation, arthritis, heart disease, skin and venereal disease, neurological disease, and geriatrics (Landspíali Háskólasjúkrahús. Klínísk þjónusta, n.d.).

2.2.1 Day ward unit 11B

The department of internal medicine at LUH has twelve day patient units, including day ward unit 11B, which is a clinic for blood and cancer related medicine/diseases (Dagdeild blóð- og krabbameinslækninga 11B) (Landspítali Háskólasjúkrahús. Dagdeildir, n.d.). HER2 -positive breast cancer patients who are being treated with Herceptin (trastuzumab), receive their treatment at ward unit 11B (Landspítali Háskólasjúkrahús. Dagdeild blóð- og krabbameinslækninga, n.d.).

Day ward unit 11B is situated in the main building of LUH at Hringbraut and is open daily from 8:00 to 16:00. The ward primarily provides medication, symptomatic and supportive treatment, and supervision for patients with cancer or hematological diseases. In 2012, there was a total of 8,104 visits to ward 11B, and 919 were for administration of Herceptin (trastuzumab) (H.E. Bjarnadóttir, personal communication, September 27, 2013).

3 Intravenous infusion

Herceptin (trastuzumab) is usually administered for one year to patients with early-stage breast cancer. If the cancer is metastatic, the drug is administered until disease progression (European Medicines Agency, n.d.). Herceptin (trastuzumab) can be administered every three weeks or weekly. Pharmacokinetic research has demonstrated analogous serum concentrations of Herceptin (trastuzumab) in the blood for either type of administration. In cases where the administration occurs every three weeks, the recommended initial loading dose is 8mg/kg, with subsequent doses of 6 mg/kg. For weekly administration, the

recommended initial loading dose is 4mg/kg and 2mg/kg thereafter. Recommended infusion time is 90 minutes for both cases. If the initial loading dose is well tolerated by the patient, the infusion time can be shortened to 30 minutes after the first administration (European Medicines Agency, n.d; Landspítali Háskólasjúkrahús, 2012). Each administration arrangement gives a yearly total of 106 mg/kg for the individual patient, but the total time of the treatment depends on the frequency of administration.

Since the Herceptin (trastuzumab) dosage is adjusted according to each patient's body weight, the annual amount administered to patients also varies. The amount of Herceptin (trastuzumab) used by the hospital therefore also fluctuates. Furthermore, because the dosage depends on body weight, the dosage for each patient needs to be specially prepared by the hospital pharmacy. Before the patient arrives for infusion, the medicine needs to be removed from its vial and reconstituted before it is put into the infusion bag. In cases where a patient cannot attend the scheduled administration, the blend is discarded and the medicine goes to waste.

3.1 Administration processes

Many different tasks are involved in the process of administering Herceptin (trastuzumab). Each task performed contributes to the total administration time and costs. Within the hospital, these consist of tasks undertaken at the pharmacy and day ward 11B, while the costs for the patient can be broken into travel costs and time-use cost.

3.1.1 Hospital pharmacy

The process begins when orders for Herceptin (trastuzumab) are submitted to the hospital pharmacy. There, pharmacological technicians prepare the dosage for each patient. The work is supervised by experienced pharmacists who also sign off on each bag of reconstituted Herceptin (trastuzumab). Information about time spent on preparing each order is not available, but staffers from the pharmacy and the division of finance and information have estimated the average cost of preparing the dosage (I. J. Arnardóttir, personal communication, September 9, 2013).

3.1.2 Day ward 11B

Information about the time it takes to carry out the various tasks associated with the administration of Herceptin (trastuzumab) at day ward 11B was gathered directly from staff at the ward. A questionnaire was submitted to Þórunn Sævarsdóttir, the head of the

nursing department, which she and other qualified nurses at the ward filled out jointly (Þ. Sævarsdóttir, personal communication, August 14, 2013).

In general, it takes staff at day ward 11B 5 minutes to order Herceptin (trastuzumab), while 15 minutes are spent on preparing for the arrival of the next patient. Upon arrival at 11B, a patient reports to the reception desk, and then goes to the waiting lounge. The wait is usually short. However, if an order for Herceptin (trastuzumab) has not been placed in advance, the patient must wait for up to 60 minutes while the hospital pharmacy processes the order. During that time, however, nurses can attend to other duties. The patient is next prepared for the infusion, which will normally take 60 minutes for first-time patients. Qualified nurses always attend to patients throughout the first infusion, and also spend around 15 minutes with patients after the infusion is completed. Removing needles, booking the next appointment etc. takes an additional 5 minutes, and cleaning up after the patient has left takes another 2 minutes. In all, nurses at day ward 11B spend on average 112 minutes on preparing for the visit of patients and administering Herceptin (trastuzumab) for the first time. This time is, however, considerably shorter if the patient is having other injections or infusions during the same visits. In Table 1, it is assumed that in such cases, time spend on preparation at the day ward before the patient arrives, as well as time spent on removing needles, cleaning up after the patient has left, etc., can be attributed to the administration of other medicines. Taking this into account, the minimum time spent on administering Herceptin (trastuzumab) to first-time patients is set at 90 minutes.

Table 1 Time spent on administering Herceptin (trastuzumab) at day ward 11B to first-time patients. Minutes.

Activity	Minutes	
	Min.	Max.
Placing an order for Herceptin	5	5
Preparation at day ward	0	15
Preparing patient for infusion	10	10
Time spent with patient during infusion	60	60
Time spent with patient after infusion	15	15
Removing needles, book next appointment etc.	0	5
Cleaning up after patient has left	0	2
Total time	90	112

For subsequent visits, the infusion time is only 30 minutes, and nurses will generally spend 15 minutes with patients while the infusion is taking place. Other activities and tasks take the same amount of time as during the first visit. On average, nurses will therefore spend 40-62 minutes preparing for the subsequent visits and administering Herceptin (trastuzumab) to patients.

Table 2 Time spent on administering Herceptin (trastuzumab) at day ward 11B for subsequent visits. Minutes.

Activity	Minutes	
	Min.	Max.
Placing an order for Herceptin	5	5
Preparation at day ward	0	15
Preparing patient for infusion	10	10
Time spent with patient during infusion	15	15
Time spent with patient after infusion	10	10
Removing needles, book next appointment etc.	0	5
Cleaning up after patient has left	0	2
Total time	40	62

3.1.3 Patients

Because of the assumption that the price of treatment will be homogeneous for intravenous and subcutaneous administration, the difference in the patient's cost is embodied in the opportunity cost of the treatment. In addition to time spent at day ward 11B, the patient must travel to and from the hospital and possibly also spend time on doctor's appointments. However, in this analysis it is assumed that time spent on travelling and appointments is the same regardless of whether the treatment involves intravenous or subcutaneous administration. As explained below, this assumption is though unlikely to hold for all patients.

As revealed in Table 3, patients can on average expect to spend 80-145 minutes at day ward 11B when receiving Herceptin (trastuzumab) for the first time, with the difference depending on whether the medicine has been ordered from the LUH pharmacy before their arrival or if they have to wait while the order is processed.

Table 3 Time spent by first-time patients in day ward 11B. Minutes

Activity	Minutes	
	Min.	Max.
Waiting for Herceptin to arrive fromLHS pharmacy	0	60
Preparing patient for infusion	10	10
Infusion	60	60
Recovering from infusion	10	10
Removing needles, book next appointment etc.	0	5
Total time	80	145

Subsequent visits to day ward 11B are considerably shorter, with patients spending on average 50-115 minutes per visit.

Table 4 Time spent in day ward 11B for subsequent visits. Minutes.

Activity	Minutes	
	Min.	Max.
Waiting for Herceptin to arrive fromLHS pharmacy	0	60
Preparing patient for infusion	10	10
Infusion	30	30
Recovering from infusion	10	10
Removing needles, book next appointment etc.	0	5
Total time	50	115

3.2 Administration costs

As mentioned above, no data exists regarding the average time it takes staff at the hospital pharmacy of LUH to process orders of Herceptin (trastuzumab). However, it has been estimated that the average costs of processing the orders is € 21 (I. J. Arnardóttir, personal communication, September 9, 2013).[1]

Costs incurred at day ward 11B may be divided into wage costs and cost of materials. Average hourly wages per qualified nurse, including social security contributions, amounted in 2012 to € 23. In Table 5, the average labour costs are multiplied with the average time spend on preparing and administrating Herceptin (trastuzumab) to patients. The cost of materials involves all direct costs, but does not include depreciation, etc. Average costs per first time visit were thus € 62-81.

In this analysis, the costs to patients is estimated as the decrease in contribution to gross national income that results from women having to spend time at day ward unit 11B

[1] Accoding to the Central Bank of Iceland, the average exchange rate in 2012 was 1 € = ISK 161.2.

instead of taking part in some productive market activity. In order to assess this loss, it is first necessary to estimate hourly labour costs, and then account for the fact that not all women are employed.

According to Statistics Iceland, medium earnings for women working full-time in the private sector were € 1,950 per month in 2012, or € 2,720 including all social security contributions. As women worked on average 40.7 hours a week, average wage costs per hour amounted to € 15.

In general, none of the patients receiving treatment with Herceptin (trastuzumab) are able to work during the first half of the treatment period, but some work at least part-time during the second half. In 2012, the employment rate of women aged 55-74 was 55.1% in Iceland. This study assumes that at most, a similar proportion of women being treated with Herceptin (trastuzumab) worked during the second half of the treatment period. As a minimum, it is assumed that none of the women worked. This yields an employment rate range of 0-27.6% which is then used to scale down average labour costs per hour.

As shown in Table 5, total costs per first-time visit of patients receiving intravenous infusion treatment with Heceptin (trastuzumab) ranged between € 62 and € 81. The difference between the minimum and maximum is solely due to the fact that in the former case, it is assumed that patients do not have to wait for the university pharmacy to process the orders for Herceptin (trastuzumab), while in the latter it is assumed that such a delay occurs.

Table 5: Average cost of administering Herceptin (trastuzumab) to first-time patients. Euros.

Activity	Min	Max
Costs incurred at pharmacy	21	21
Costs incurred at day ward 11B		
Average wages per hour	23	23
Average time per first time visit	90	112
Labour costs	35	43
Materials	6	6
Total	41	49
Time-use cost of patients		
Average wages per hour	0	4
Average time per first time visit	0	1
Opportunity cost	0	10
Total costs	62	81

In Table 6, the costs associated with subsequent visits have been compiled in a similar manner. Here, total costs range between € 42 and 59.

Table 6: Average cost of administering Herceptin (trastuzumab) for subsequent visits. Euros.

Activity	Min	Max
Costs incurred at pharmacy	21	21
Costs incurred at day ward 11B		
Average wages per hour	23	23
Average time per subsequent visits	40	62
Labour costs	16	24
Materials	6	6
Total	21	30
Time-use cost of patients		
Average wages per hour	0	4
Average time per subsequent visits	50	115
Opportunity cost	0	8
Total costs	42	59

4 Subcutaneous injection

The subcutaneous formulation of Herceptin (trastuzumab) has been developed as an alternative to the intravenous infusion. Subcutaneous injection of the drug does not require

adjustments for body weight. The drug is administered with a fixed dose of 600 mg injected under the skin, and a loading dose in not needed. The new formulation additionally contains recombinant human hyaluronidase PH-20 (rHuPH-20) as an excipient, which enables a larger volume of Herceptin (trastuzumab) to be administered in shorter time. This newly developed technology (EnhanzeTM) allows injected volumes to distribute over a broader range of molecular weights than before, without distorting the tissue (Bookbinder et al., 2006). The subcutaneous injection simplifies the administration of Herceptin (trastuzumab), with an injection taking 3-5 minutes. General administration time at the hospital would be reduced, along with observation time and pharmacy preparation time. With subcutaneous injection, the Herceptin (trastuzumab) dosage is fixed. Since the formulation does not require reconstitution before it is used, it does not have to be discarded if the patient misses the scheduled administration.

4.1 Administration process and costs involved

Subcutaneous administration involves many tasks similar to intravenous administration. However, with subcutaneous administration, the same tasks may take a different form or require less time. While some tasks become unnecessary, e.g. preparation of the infusion bag, other tasks change considerably, e.g. monitoring and disposal of materials. The greatest change involved in the transition is perhaps in the tasks performed in the hospital's pharmacy, as reconstitution of Herceptin (trastuzumab) is not required for the subcutaneous formulation.

As shown in Table 7, it is estimated that on average, administrating Herceptin (trastuzumab) in a subcutaneous manner will take 3-22 minutes.

Table 7: Time spent on administering Herceptin (trastuzumab) subcutaneously in day ward 11B. Minutes.

Activity	Minutes	
	Min.	Max.
Preparation at day ward	0	10
Injection	3	5
Removing needles, book next appointment etc.	0	5
Cleaning up after patient has left	0	2
Total time	3	22

Subcutaneous administration also reduces the duration of time patients must spend in the ward. As shown in Table 8, it is estimated that the administration will take 20 minutes on

average. The new form of Herceptin (trastuzumab) will be prescribed to patients, but not provided by the hospitals where the medicine is administered. Patients will therefore have to fetch the medicine from the hospital drug store on their way to day ward unit 11B, which is estimated to take 10 minutes.

Table 8: Time spent by patients receiving subcutaneous administration in day ward 11B. Minutes.

	Minutes	
Activity	Min.	Max.
Fetching medicine from drug store	10	10
Preparation at day ward	0	10
Injection	3	5
Removing needles, book next appointment etc.	0	5
Total time	13	30

Presently, Herceptin (trastuzumab) is only administered in Iceland at LUH or á Akureyri Hospital. All patients receiving this treatment must therefore visit one of these hospitals, regardless of where they reside. As subcutaneous administration could conceivably be carried out at othe hospitals in Iceland, patients could receive the treatment closer to home. No attempt is made to estimate those individual cost- and time- savings in this analysis, but these could easily be substantial.

The average cost of subcutaneous administration can be estimated by using the same estimates of wage costs at day ward 11B and the opportunity costs of patients as noted above. As revealed in Table 9, the average cost incurred at day ward 11B is estimated as € 2-9, while the average opportunity costs of patients are estimated as € 0-2. Average total cost is thus estimated as € 2-9.

Table 9: Average cost of administering Herceptin (trastuzumab)) subcutaneously. Euros.

Activity	Min.	Max.
Costs incurred at day ward 11B		
Average wages per hour	23	23
Average time per visit	3	22
Labour costs	1	9
Materials	0	0
Total	1	9
Time-use cost of patients		
Average wages per hour, adjusted for labour participation rate	0	4
Average time per visit	13	30
Opportunity cost	0	2
Total costs	1	11

5 Cost comparison

Having estimated the costs associated with administrating Herceptin (trastuzumab) subcutaneously and through intravenous infusion, it is now possible to assess the potential cost savings the former method implies, both on average and for a whole year. The annual savings are calculated using patient data for the year 2012. In that year, 65 patients received Herceptin (trastuzumab) treatment at day ward 11B. These patients accounted for 919 visits to the ward, of which 27 are defined as first-time visits and 892 as subsequent visits.

The results from this cost comparison are presented in Table 10. The top panel shows the costs associated with the first and subsequent visits of patients receiving intravenous infusion, and subcutaneous injection respectively. These are costs per patient. The middle panel shows estimated average savings 1 and average savings 2. The former represents the difference in costs between first-time administration through intravenous infusion and subcutaneous injection, while the latter shows the difference in costs between subsequent intravenous infusions and subcutaneous injection. Average savings 1 range between € 60 and 70, while average savings 2 are estimated as € 40-48. This represents cost savings of 82-97%.

The lower panel shows first the number of cancer patients treated with Herceptin (trastuzumab) at daily ward 11B in 2012. The 65 patients treated that year accounted for

919 ward visits. It is assumed that Herceptin (trastuzumab) was administered slowly the first time each patient received intravenous infusion, but that subsequent administration took place at a faster rate. On the basis of these premises, it is estimated in the bottom half of Table 10 that potential savings could in 2012 have amounted to € 38,400-45,000. Most of these savings are expected to occur because of the difference in costs associated with subsequent visits of patients receiving intravenous infusion and subcutaneous injections, with only a small portion of the costs savings due to differences in costs between first-time intravenous infusions and subcutaneous injections.

Table 10: Comparison of costs associated with administrating Hereptin (trastuzumab) through intravenous infusion and subcutaneous injection. Euros.

Administration	Min	Max
Intravenous infusion, first visit	62	81
Intravenous infusion, subsequent visits	42	59
Subcutaneous injection	1	11
Average savings 1	61	70
Average savings 2	41	48
Average savings 1, in %	98%	87%
Average savings 2, in %	97%	82%
Number of administrations at day ward 11B in 2012		
Intravenous infusion, first visit	27	27
Intravenous infusion, subsequent visits	892	892
Total savings 1	1.636	1.886
Total svaings 2	36.737	43.128
Total savings	38.373	45.014

As shown in Table 11, it is estimated that, on average, administrating Herceptin (trastuzumab) in a subcutaneous manner will take 16-52 minutes, which represents a time savings of 154-205 minutes when Herceptin (trastuzumab) is administered to a patient for the first time, and time savings of 74-125 minutes on subsequent visits. The new method of administering Herceptin (trastuzumab) could thus result in considerably time savings. This increased efficiency would enable staff at day ward 11B to improve the overall level of service. As discussed above, it is also assumed that this form of administration will not require any input from the hospital pharmacy, which would also result in time savings.

Table 11: Comparison of time associated with administrating Hereptin (trastuzumab) through intravenous infusion and subcutaneous injection. Minutes.

	Minutes	
Administration	Min	Max
Intravenous infusion, first visit	170	257
Intravenous infusion, subsequent visits	90	177
Subcutaneous injection	16	52
Average savings 1	154	205
Average savings 2	74	125
Average savings 1, in %	91%	80%
Average savings 2, in %	82%	71%

It must be stressed that the above analysis assumes that the cost of each dose of Hereptin (trastuzumab) remains the same, regardless of whether the drug is administered through intravenous infusion and subcutaneous injection.

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