Design of a relative value unit-based tool for the measurement and reimbursement of pharmacy services for clinical trials

Neus Pagès-Puigdemont,[1,2] Glòria Molas,[2,3] Maria Queralt Gorgas,[3] Núria Berga,[1] Carles Codina,[2] Miquel Cruel,[3] Begoña Gómez-Perez,[2] Mercè Espona,[4] Ainhoa Rodríguez-Arias,[1] Esther Salas,[4] Maria Antònia Mangues[1]

[1]Pharmacy Department, Hospital de la Santa Creu i Sant Pau, Barcelona, Spain
[2]Pharmacy Department, Hospital Clínic i Provincial de Barcelona, Barcelona, Spain
[3]Pharmacy Department, Hospital Parc Taulí, Sabadell, Spain
[4]Pharmacy Department, Hospital del Mar, Barcelona, Catalunya, Spain

Correspondence to
Dr Neus Pagès-Puigdemont, Pharmacy Department, Hospital de la Santa Creu i Sant Pau, Barcelona 08025, Spain; npages@clinic.cat

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ABSTRACT

Objective To develop a relative value unit (RVU)-based tool for the measurement and reimbursement of pharmacy services for clinical trials.

Methods A portfolio of activities was agreed by consensus in four tertiary hospitals. Related activities were pooled into several categories or intermediate products. We recorded the duration of each activity by multiple determinations. We then calculated the average time of all determinations. The reference activity was assigned a value of 1. All other activities were compared to the reference activity to obtain the RVU. To establish which items should be invoiced to third parties for the activities performed, we defined the final products (different types of clinical trials according to their complexity).

Results Ten intermediate products and five final products were differentiated. Six intermediate products could be repeated over the course of a clinical trial and seven were performed whether or not the clinical trial had included patients. Each final product consisted of different categories. The total number of RVUs produced for a clinical trial was the sum of each constant category value plus the repetitive category values multiplied by the number of repetitions.

Conclusion The application of RVU methodology in investigational drug services allows a more precise quantification of services performed. After a prospective validation to confirm the applicability of this tool, it may contribute to more appropriate invoicing to third parties for these services.

INTRODUCTION

Investigational drug services (IDS) provide support to ensure that, during the course of a clinical trial, investigational drugs are used safely and in accordance with the protocol specifications and regulatory framework required. These services are invoiced to the principal investigator (PI), who is responsible for the conduct and administration of the clinical trial within the healthcare centre. All funding provided by the sponsor for the development of a clinical trial is managed by the PI.

In Spain and, more specifically in the four hospitals participating in this study, invoices for IDS services are usually calculated as a percentage of a fixed amount. This amount is the payment received by the PI for every participant included in a clinical trial. The percentage invoiced ranges from 2.5% to 15% depending on the complexity of the clinical trial. However, reimbursement based on a percentage of the fee received by a PI does not always match the workload generated in the IDS unit per trial. For this reason, it would be of interest for an IDS unit to develop a more sensitive tool to measure and reimburse its activity in clinical trials.

Several cost accounting systems are used in the field of clinical management, such as the DRG (Diagnosis Related Group), the CCR (Cost to Charge Ratios), the ABC (Activity-Based Costing method) and the RVU systems.[1–4] The RVU system consists of standardised, non-monetary units of measurement assigned individually to specific medical procedures. The value of a procedure in RVUs depends on its complexity and the time and resources used in performing the task.[5 6] The RVU system is widely used for setting physician fee-for-services in the United States.[7–9] We hypothesised that the RVU system could be a more accurate method for measuring activity and calculating costs in IDS. In Spain, the use of the RVU system for the reimbursement of general activities in hospital pharmacies is explained in an official document published by the Spanish Society of Hospital Pharmacy in collaboration with the National Health Institute.[10 11] Nonetheless, detailed information about clinical trial activity in pharmacy services is not specified. The total RVUs assigned to each individual trial is the same in all cases, regardless of complexity or number of services carried out.

The aim of this study is to develop an RVU-based tool for the measurement and reimbursement of pharmacy services for clinical trials.

METHODS

The study was conducted at four tertiary hospitals in the area of Barcelona: Hospital de la Santa Creu i Sant Pau, Hospital Clínic, Hospital Universitari Parc Taulí and Hospital del Mar, all of which have an IDS unit within the hospital pharmacy. A project team including the chief pharmacists and staff from the different IDS units was created. Between March 2014 and October 2014, periodic meetings were organised to establish which tasks were to be performed. Procedures and results were always agreed by all parties.

Initially, each IDS unit developed an internal portfolio of regular activities and services. During team meetings, these portfolios were discussed and a consensus was reached for a common portfolio.

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The primary consideration when including an activity in the common portfolio was that it had to be routinely performed in an IDS unit. Two activities (study drug delivery to other hospitals and preparation of investigational medicinal product (IMP) capsules) were excluded from the shared portfolio, as they were performed by one hospital only.

The next step was to calculate the RVU for each activity. First, we recorded the duration of each activity by measuring, with a chronometer and on multiple occasions, the time taken to perform each activity. We then calculated the average time taken to fulfil a task and the coefficient of variation (CV) of all determinations. If the CV was >1, a second round of measurements was carried out to reduce variability. The next step was to choose a reference activity, which was assigned a value of 1; other activities were then compared to this reference. To calculate the RVU, the average time needed to finish a task was then divided by the average time needed to accomplish the reference activity. For instance, if activity X took an average of 10.86 min and the reference activity took an average of 17.09 min, the RVU of activity X was 0.635.

After obtaining the RVU for all activities, we established a list of final products that indicated what should be invoiced to third parties in relation to the activities performed. In this context, IDS final products are defined as the different types of clinical trials, which are classified according to their complexity. To simplify the calculation, related activities were pooled together into several categories, which in RVU methodology are named intermediate products. It is important to note that different final products have common categories or intermediate products (site selection visit, site initiation visit, receipt of IMP, IMP storage, monitoring visits, site close out, other activities), but they also have some particular activities that are not included in all clinical trials (for example, different types of IMP dispensing or IMP preparation).

RESULTS

Table 1 shows the pharmacy activities and services portfolio agreed on by the four participating hospitals. Writing a protocol summary for the pharmacy services was chosen as the reference activity. Such outlines are written with the objective of summarising all relevant information related to the clinical trial for use within the IDS unit. The decision was based on the fact that every IDS unit drafts these summaries for all clinical trials.

Portfolio activities were grouped in 10 categories: site selection visit, site initiation visit, reception of the IMP, storage and handling of IMP, IMP dispensing, IMP return, IMP preparation (for those drugs that require compounding in the pharmacy department), monitoring visits, study close out and other activities.

The IMP dispensing category was divided into three subtypes: (1) drug block dispensing to the research team (delivery of the study drug takes place just after its reception); (2) drug dispensing to research team for each patient and visit; and (3) drug dispensing directly to the patient. For activities related to study drug preparation, we also differentiated two subtypes: (1) preparation of non-cytotoxic agents in the non-sterile or sterile pharmacy compounding areas; and (2) preparation of cytotoxic agents in the biological safety cabinets (BSCs) within the hazardous drugs compounding area.

Seven of the 10 categories of activities were performed whether or not the clinical trial had included patients (site selection visit, site initiation visit, reception of IMP, storage and handling of IMP, monitoring visits, study close out and other activities). Six categories could be repeated over a clinical trial course (reception of IMP, storage and handling of IMP, IMP dispensing, IMP return, IMP preparation and monitoring visits).

The research team considered that it was not feasible to determine activity time for all tasks that a clinical trial involves in a prospective way, owing to the long duration of most clinical trials. For this reason, every hospital selected several clinical trials of each type and timed activities on multiple occasions. Although some activities such as block dispensing to the research team and site close out were measured fewer than 10 times, none of them resulted in a CV >1, meaning a second round of determinations was not warranted. If CV was found to be >1, a second round of measurements for those activities was then performed. After this second round, a CV>1 remained for only three activities (management of expired stock, telephone calls and emails to clinical research associates, and participation in audits or inspections). However, CV values stayed close to 1, meaning the impact of these measurements on the final value calculated for the whole category or intermediate product was very low. Consequently, the research team considered it unnecessary for a third round of determinations to take place.

RVU values and average activity time for all categories are shown in table 2. We also included the average number of determinations for every activity in each category. This table is the basis for measuring the activities performed within a particular clinical trial calculated in RVUs in an IDS unit.

We established five types of clinical trials (also called final products), which all related to common activities. On the other hand, some intermediate products were specific to a particular final product depending on the type of clinical trial or its complexity. The common activities were the seven categories that can be performed whether or not patients are included in a study. The resulting final products were: a clinical trial with no patients included or that required block dispensing (includes block dispensing to research team), a clinical trial with individual dispensing (includes direct dispensing to patient), a clinical trial with individual dispensing and IMP return, a clinical trial with IMP preparation at the pharmacy department (which can encompass two different types of preparation), and a high complexity clinical trial (includes direct dispensing to patient, IMP preparation and IMP return). Usually, highly complex clinical trials are those in the field of oncology, which handles at least two different IMPs; one of these warrants preparation in the pharmacy compounding areas and the other is dispensed to the research team or to the patient, without requiring preparation.

Calculation of payments based on RVUs for a particular clinical trial is obtained from the sum of the values of each constant intermediate product or category plus the value of each repetitive category multiplied by the number of repetitions.

Table 3 provides an example of an RVU calculation for a particular clinical trial.

DISCUSSION

In this study, an RVU-based tool was designed to measure activity generated in IDS units and optimise invoicing for the services provided through activity quantification.

Although a document has been published in Spain explaining how pharmacy services can develop a portfolio of activities and measure them, it is not sufficiently explicit for application in an IDS unit. At present, the baseline measurement of activity is ‘unit-dose dispensing’ because it is the activity most repeated in hospital pharmacies in our country. In our study, however, we considered that the development of a clinical trial protocol

Table 1 Common activities portfolio

Intermediate products	Activities
Site selection visit	Facilities visit/site qualification Freezers and refrigerators check Calibration certificates check (probes, freezers, refrigerators and thermometers) Review of pharmacy clinical trials SOPs Collection of GCP certificate Management of personal data and curriculum vitae
Site initiation visit	Field monitor initiation visit Review of pharmacy file (pharmacist's manual, investigator's brochure, approval document copies, clinical trial agreement, pharmacy dispensing procedures, pharmacy signature list, monitoring visit log, drug accountability forms, unblinding procedure, key contact details) Providing/receiving training in IWRS/IVRS and protocol specifications Elaboration of protocol summary for pharmacy (including compounding if needed) Modifying the pharmacy protocol summary according to amendments made to it after field monitor consultations Clinical trial logging in electronic prescribing system Label editing (if needed) Training of pharmacy staff on the IMP protocol Review of pharmacy procedures with investigator Password activation Signature logs Signature of trial documents and training records
Receipt of IMP	Reception and recording of the delivery of IMPs (clinical trial identification and downloading of template data logger, shipping temperature review, drug reconciliation with shipping invoice) Safe handling and storage of IMPs Confirmation of reception in electronic prescribing system Confirmation of reception by IWRS, IVRS or fax Organising the return of packaging to the promoter (when needed) Quarantine of IMPs and communication to field monitor in case of temperature excursion
IMP storage	Control of inventory and expiry dates Ordering of IMP kits by phone, email, IVRS or IWRS Temperature monitoring, reporting of temperature excursions to the sponsor and quarantine IMPs (when needed) Management of expired stock (expiry date relabelling or return and disposal of expired IMPs) Database update (due to variations in the expiry date, for example)
Dispensing of IMP ► Block dispensing to research team ► Dispensing to research team for each patient and visit ► Direct dispensing to patient	Patient and trial identification IMP assignment by IWRS/IVRS Check of IMP prescription (IMP data, dose, quantity and patient number) Filling out trial worksheets and labels Drug preparation according to the pharmacy manual Registering every dispensing episode in the electronic prescribing system Patient counselling (on dosing, administration, adverse events, medication safe handling and storage) [only when dispensing directly to the patient]
IMP return	Drug accountability Storage of returned IMP
IMP preparation ► Preparation of non-cytotoxic agents in the non-sterile or sterile pharmacy compounding areas ► Preparation of cytotoxic agents in biological safety cabinets within the hazardous drugs compounding area	Patient and trial identification IMP assignment by IWRS/IVRS Check of IMP prescription (IMP data, dose, quantity and patient number) Filling out trial worksheets and labels Drug preparation according to the pharmacy manual (including blinding, if appropriate) Pharmacy check on final product Registration and management of returns
Monitoring visits	Drug accountability and reconciliation Stock verification IMPs destruction Provision of logs to field monitor Expiry date relabelling Signature of amendments and other trial documents
Site close out	Return and disposal of unused IMPs and their registration in electronic database Archiving stock and dispensing logs Issue resolving (pending queries) Pharmacy and investigator site file merging Study internal closure in electronic database
Other activities	Maintenance of a pharmacy study file (including hard copies of emails and any relevant correspondence) Telephone calls and emails to CRAs Telephone calls and emails to logistics companies for the reception or devolution of IMPs Review of protocol amendments Archiving clinical trial documentation Participation in audits or inspections

CRA, clinical research associate; GCP, good clinical practice; IMP, investigational medicinal product; IVRS, interactive voice response system; IWRS, interactive web response system; SOP, standard operating procedure.

Table 2 Average activity time for intermediate products, relative values and average number of determinations for all activities within the same category

Intermediate products	Average time (minutes)	Relative value	Average number of determinations
Site selection visit	50.0	2.925	13.2
Site initiation visit	238.3	13.943	24.1
Receipt of IMPs	59.2	3.463	51.9
IMP storage	82.1	4.805	25.6
Dispensing of IMPs			
Block dispensing to research team	12.8	0.751	6.0
Dispensing to research team every patient visit	15.6	0.911	19.7
Direct dispensing to patient	26.1	1.525	11.0
IMP return	4.3	0.253	21.5
IMP preparation			
Preparation of non-cytotoxic agents in the non-sterile or sterile pharmacy compounding areas	57.8	3.384	10.8
Preparation of cytotoxic agents in biological safety cabinets within the hazardous drugs compounding area	37.8	2.213	18.1
Monitoring visits	80.0	4.680	25.4
Site close out	57.7	3.375	3.4
Other activities*	114.9	6.721	25.8

*The time invested is the average time required to perform all activities in this category.
IMP, investigational medicinal product.

summary for pharmacy was more appropriate as the baseline activity for an IDS unit. This activity was used as baseline whether or not the clinical trial had finally included patients in that centre. Furthermore, this is one of the first tasks that IDS staff performs when a clinical trial is initiated at the hospital.

Table 2 shows which activities have a greater weight in the management of IMPs in IDS units. Site initiation visit is the activity with the highest score because it requires more staff time. Nevertheless, some activities that have a lower score have a greater impact on final product value because they occur repeatedly during the course of a clinical trial. This would be the case for activities such as dispensing of IMPs and IMP return.

It is important to highlight that in our study the preparation of a non-cytotoxic drug in the non-sterile compounding area or in a BSC in the sterile compounding area has a higher RVU score assigned than the preparation of a cytotoxic agent in a BSC in the hazardous drugs compounding area. This difference is because cytotoxic agents are always prepared in the pharmacy department regardless of trial design (blinded or unblinded design) owing to safety concerns related to their manipulation. The preparation of cytotoxic IMPs takes place during the same work shift as non-clinical trial chemotherapy preparation. This means this process is easily adapted to the daily run of the unit, as staff and equipment are ready to prepare a dose if an IMP is needed. In contrast to cytotoxic drugs, the preparation of an IMP in the non-sterile compounding area or in the non-cytotoxic sterile preparation area in the pharmacy department would take place only when the investigator team is blinded. This implies a longer preparation time than if the nursing staff prepared the IMP on the hospital wards.

This study has designed an RVU-based tool for the measurement and reimbursement of pharmacy services for clinical trials. The monetary cost of an RVU can be established dividing IDS cost (per year) by the amount of RVU produced in the same period of time. The cost for maintaining an IDS unit includes direct costs (human resources and supplies), indirect costs (water and electricity running costs or maintenance service) and structural costs (administration and hospital management). The monetary cost of RVUs can differ between hospitals as they may have different levels of organisation, efficiency and productivity.

Table 3 Example of the formula we use to perform a relative value unit (RVU) calculation for the services we provide within a particular clinical trial

Analysis of the situation at clinical trial close out: a total of three patients were included in a trial where individual dispensing was performed. Reception of IMP and IMP storage were activities performed three times during this clinical trial course. The IDS received two monitoring visits. Direct dispensing occurred a total number of 3, 5 and 6 times for each patient, respectively.

Intermediate product	Relative value	Number of times an activity was performed	Number of RVUs
Site selection visit*	2.925	1	2.925
Site initiation visit*	13.943	1	13.943
Receipt of IMP	3.463	3	10.389
IMP storage	4.805	3	14.415
Direct dispensing to patient	1.525	3+5+6	21.350
Monitoring visits	4.680	2	9.360
Site close out*	2.925	1	2.925
Other activities*	13.943	1	13.943
Total number of RVUs			**89.250**

*This activity can only be repeated once during the clinical trial course.

Although an RVU system permits comparison among hospitals, it does not reflect the quality of the service. If the investment is lower, an RVU can have a lower cost, but this may be at the expense of less quality.

It is not possible to compare our study results with others because, to our knowledge, this is the first time an RVU-based tool in this field has been developed. In other hospital areas or departments, the portfolio of services is more clearly defined, so establishing the RVU value for each service is simpler. For example, in surgery units, final products are the various types of surgical interventions.[12 13] In IDS, it is more difficult to establish the final products and their corresponding value in RVUs. For this reason, we found it more appropriate to create a project team and make all decisions by consensus.

This study is the first step towards implementing a new tool for invoicing of clinical trial activities performed by IDS units. However, a prospective validation process to confirm its reproducibility is required.

Limitations

The main limitation of our study is that some activities were excluded because they were not routinely performed in all the participating IDS (for example, distribution to other healthcare centres or preparation of IMP capsules). Another difficulty in developing the portfolio of services was the difference in organisational and human resources at each IDS unit. In some IDS units, staff who work in the clinical trial area are involved in other hospital pharmacy activities during their working day, while in other centres their dedication is exclusive. Another study limitation is that RVU methodology simplifies reality and workload, so activities can be over- or underestimated. Nonetheless, when quantifying procedures, it is important to use a system that is efficient and not too time-consuming.

What this paper adds

What is already known on this subject?

- Relative value units (RVUs) are non-monetary units used to measure medical procedures in order to calculate productivity and determine costs.
- The value of a procedure in RVUs depends on its complexity and the time and resources used in performing the task.

What this study adds

- The design of an RVU-based tool to measure the activity generated in investigational drug services (IDS) permits a more precise quantification of performed activities.
- A RVU-based tool can help to achieve a more accurate invoice for the services performed in IDS.

CONCLUSIONS

Applying RVU methodology when measuring services performed for clinical trials in IDS allows more precise quantification than the application of a simple percentage of the amount received by the principal investigator for each study patient. The method described here may contribute to more appropriate invoicing to third parties for these services. A prospective validation of this tool is needed to confirm its applicability.

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