An orchestra in need of a conductor

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DOI:
10.33612/diss.165632361

CHAPTER 3A

A survey of practices related to drug monographs in parenteral drug guides in the Netherlands

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Submitted

Supplementary material

Abstract
Parenteral drug guides (PDGs) are used as a reference for medical professionals in Dutch hospitals. PDGs contain individual monographs on each drug with instructions for the preparation, storage and administration of parenteral solutions. Currently, Dutch hospital organizations maintain their own PDGs independently. We assessed the similarities and dissimilarities in the management and content of PDGs in the Netherlands with a semi-structured survey and an analysis of drug monographs. A total of 49 participants involved in PDG management in different hospitals agreed to participate in the survey and 109 monographs were collected and analyzed. We found that the majority of data in Dutch PDGs is extracted from the same four literature sources and databases, resulting in largely similar monographs. A major difference between monographs is the number of drug-drug compatibilities listed, for example ranging from 0 to 125 compatibilities for vancomycin monographs, underscoring the difficulty in compatibility data management. Thirty-two (65%) participants indicated that their PDG was not up-to-date. The possibility of a joint Dutch PDG must be examined as it may both reduce redundant PDG maintenance work and associated costs and it may facilitate safe concurrent administration of intravenous drugs.

Introduction

Hospitals in the Netherlands commonly use parenteral drug guides (PDGs) as a reference for medical professionals how to handle parenteral drugs safely. PDGs consist of multiple monographs that contain instructions for the preparation, storage, and administration of parenteral drug solutions. A PDG is commonly embedded in a designated document management software package that allows a content manager to track, review and submit changes to a monograph. Simultaneously, medical professionals are able to consult the most recent version of that monograph at the bedside. An example of a monograph is provided in the supplementary material (Supplementary material: File S1).

At this time dozens of Dutch PDGs are locally maintained by hospital pharmacists which is also common practice in many European countries. To our knowledge joint nationwide PDGs are available to medical professionals in Belgium, Denmark, France, Norway, and in the United Kingdom.[1–5] The main provider of drug stability and preparation data for Dutch PDGs is the Royal Dutch Association for the Advancement of Pharmacy (in Dutch: KNMP) with support from the Dutch Association of Hospital Pharmacists (in Dutch: NVZA). Data that are not present in this database, but are relevant for clinical practice (e.g. drug compatibilities), are often retrieved from other databases such as Micromedex and Stabilis.[6,7] It is the responsibility of the local pharmacists within each hospital to assess which databases and which levels of evidence suit their local information needs.

The degree of overlap in Dutch PDGs is currently unknown. Although a large proportion of drug data is provided by the KNMP there is no way to verify how much of this information is used in a local PDG, nor from which sources additional data is retrieved. The different sources may vary in quality, and as they are processed manually there also is a risk of transcription or interpretation errors.[8–11] As a result this could affect the quality of PDGs, which in turn may affect treatment decisions and patient safety. We therefore aim to provide an overview of practices related to the management and content of PDGs in different Dutch hospitals.

Materials and methods

Ethical approval for this study was waived by the Institutional Review Board of the University Medical Center Groningen, the Netherlands (METc.2020/093). A semi-structured survey was conducted by telephone interviews to assess the current practice in terms of the use and maintenance of PDGs in Dutch hospitals. Two researchers were involved in contacting participants between January and March 2020. When a survey could not be conducted over the telephone (e.g. when a participant was occupied), the survey was conducted via e-mail. All 71 Dutch hospital organizations were asked to participate in this study.

The questions of the survey are listed in the supplementary material (Supplementary material: Table S1).

Following the survey questions, participants were asked to share the monographs of three common drugs (vancomycin, flucloxacillin, and furosemide) from their PDG.

Data processing
Numeric survey responses were summarized using the mean ±SD when they were normally distributed. The median and interquartile range (IQR) was used for non-normal data. Qualitative survey responses were processed and summarized in text by a researcher.

The content of each monograph was read and the unique components (e.g. document version number, preparation instructions, Y-site compatibility) were listed. Frequencies of occurrence were determined for each component, as were the number of items within a certain component type when applicable (e.g. number of different Y-site compatibilities).

Results
Participants
A total of 49 representatives from different Dutch hospitals involved in the maintenance of, with responsibility for the content of their local PDG, agreed to participate. Forty-seven (96%) participants were hospital pharmacists and two (4%) were pharmacy-technicians.

A total of 4 (8%) university hospitals, 13 (27%) top-clinical hospitals, and 32 (65%) general hospitals were represented by the participants. The mean ±standard deviation (SD) bed count was 510 ±241.

Questionnaire responses
Questionnaire responses are summarized in Table 1. The iProva software suite (Infoland B.V., Veldhoven, the Netherlands) was used in 43 (88%) hospitals. Other data management systems used were Manual Master (ManualMaster International, Papendrecht, the Netherlands) as well as an Access database (Microsoft inc., Redmond, WA, United States of America). One hospital stored their collection of monographs as Word documents, of which the content was copy-pasted into iProva when a drug was used in clinical practice.

The median [IQR] number of persons directly involved in the maintenance of local PDGs was 2 [2-3]. Persons who were involved were hospital pharmacists, pharmacy-technicians, residents, quality assurance officers, interns, and medical doctors.

Some hospitals use separate drug monographs per patient group (e.g. neonates, children, and adults), and others used a single monograph to accommodate drug data for all patient groups. Likewise, dosing protocols can be part of a drug monograph and sometimes they are stored in a separate document within the PDG.

The update frequency varied considerably between hospitals. The majority of hospitals (92%) set a predefined time after which monographs became outdated and required revision. This period varied from 1 to 5 years. In 4 (8%) cases revisions were only performed upon request by clinicians.

Estimated maintenance time varied from 1 to 20 hours per week. In most cases there was no time specifically reserved for the maintenance of the PDG, which had to be performed ad hoc in addition to other tasks.

Almost all participants (94%) indicated that (in)compatibilities were included in their PDG. In some cases incompatibilities were omitted from the PDG. When this was the case, a statement was added saying all combinations that were not explicitly listed as compatible, must be considered to be incompatible. One hospital used custom software and a database for the storage and retrieval of compatibility data. Compatibilities in this database were updated annually in collaboration with an external software manufacturer. Another hospital provided a clickable link within each monograph from which a separate compatibility chart could be accessed.

Twenty (41%) participants indicated that compatibility charts were used in some departments of their hospital, most frequently in critical care, gynecology and anesthesiology departments. In some cases these charts were created or supported by the local hospital pharmacy, in other cases they were created and maintained by the departments that used them. A common reason not to endorse the use of compatibility charts is that they are frequently not updated together with their corresponding monographs, hence they are not always up to date.

Eighteen (37%) participants indicated that monographs were shared occasionally with other hospitals. This was often the case when a patient is transferred to another hospital that was not familiar with one of the patient's drugs. Four (8%) participants indicated that there was a structural exchange of PDG data with another hospital.

In 41 (85%) cases the backlog in monographs up for revision was known. Although most document management systems allow setting a revision due date for a monograph, this functionality was not always used. Therefore, it was not always possible to assess the number of monographs eligible for revision. In 17 (35%) cases the PDG was up-to-date.

The KNMP database was the only resource that was used in all hospitals.[12] Other commonly used resources of drug data were the drugs' Summaries of Product Characteristics (SmPCs), Micromedex®, and Stabilis® databases, which were used in 40 (82%), 36 (74%), and 33 (67%) cases, respectively.[6,7] Table 2 lists the frequencies of data sources consulted by the participants.

Figure 1 shows boxplots that illustrate the diversity in the number of Y-site and IV-bag (in)compatibilities for vancomycin. Figure S1 (Supplementary material) shows boxplots with item counts within selected monograph components for vancomycin. Boxplots with item counts and (in)compatibilities for flucloxacillin and furosemide monographs are available in in the supplementary material (Supplementary material: Figures S2-S5).

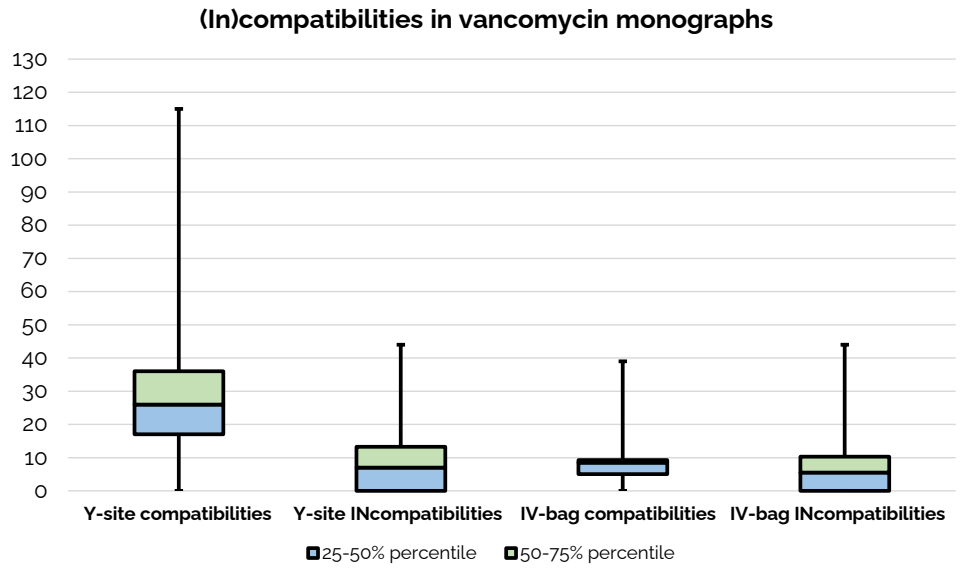

Figure 1. Boxplots with the number of Y-site and IV-bag (in)compatibilities within 36 vancomycin monographs. Boxes indicate the second (blue; 25-50%) and third (green; 0-75%) quartile. Whiskers indicate minimal and maximal values.

Constituents of drug monographs

A total of 109 drug monographs was received. Table S2 (Supplementary material) lists the frequencies of occurrence of the different components in the drug monographs. Note that document metadata such as the next revision date were only counted when they were printed on the monograph. In some cases metadata were accessible through a separate menu within the document management system, but not in the document itself. General remarks included special considerations for the administration of a drug (e.g. whether a drug is photosensitive or has an unusual color). Administration categories ranged from A to D, indicating that a drug must be administered:

[A] manually using a syringe

[B] using a manually operated IV system (without a pump)

[C] using only a volumetric pump

[D] using only a syringe pump

Dosing instructions often included different administration rates depending on the prescribed daily dose and drug concentration. Acute side-effects included side-effects that could occur immediately during administration, such as pain during injection or allergic reactions. Examples of later side-effects are phlebitis and fever.

Table 1. Characteristics of PDG maintenance

Variable	N = 49
PDG software	
iProva, n (%)	43 (88)
ManualMaster, n (%)	2 (4)
MS Access, n (%)	1 (2)
MS Word, n (%)	1 (2)
Other, n (%)	2 (4)
Persons involved in maintenance, median [IQR]	2 [2-3]
Monographs in PDG, mean ±SD	367 ±141
Update cycle	
1 year, n (%)	1 (2)
2 years, n (%)	9 (18)
3 years, n (%)	25 (51)
4 years, n (%)	3 (6)
5 years, n (%)	7 (14)
no fixed date, n (%)	4 (8)
Estimated update duration[a], median [IQR] hours	0.5 [0.3 – 1.0]
Maintenance time available	
Total available time, mean ±SD (hours/week)	4.2 ±4.8
Are compatibilities included in monographs?	
yes, n (%)	46 (94)
Are compatibility charts used in hospital?	
yes, n (%)	20 (41)
Are monographs exchanged with another hospital?	
never, n (%)	24 (51)
occasionally, n (%)	18 (37)
structurally, n (%)	4 (8)
unknown, n(%)	2 (4)
Backlog[b], mean ±SD	30 ±46

[a]Of a typical monograph
[b]Number of monographs due for revision
SD: standard deviation, IQR: Interquartile range

Table 2. Data sources used to update parenteral drug guides

Data source	Used for[a]	Frequency (%)
KNMP Kennisbank[13]	dosing, stability, interactions, preparation, side-effects, shelf-life	49 (100)
Summary of product characteristics	dosing, stability, interactions, preparation, compatibilities, side-effects	40 (82)
Micromedex®[6]	compatibilities	36 (74)
Stabilis®[7]	compatibilities, interactions, shelf-life	33 (67)
Trissel's Handbook on Injectable Drugs[14]	compatibilities	16 (33)
PDG from another hospital[15]	dosing, stability, interactions, preparation, compatibilities, side-effects	9 (18)
Lexicomp/UpToDate Drug Database[16,17]	dosing, interactions, side-effects	9 (18)
Farmacotherapeutisch Kompas[18]	interactions, side-effects	5 (10)
King Guide to Parenteral Admixtures[19]	compatibilities	2 (4)
Pediatric Injectable Drugs[20]	dosing, preparation, side-effects	2 (4)
Extended Stability for Parenteral Drugs[21]	preparation, stability	1 (2)
Kinderformularium[22]	dosing, preparation, interactions	1 (2)

[a]As reported by participants in this study. Data sources may contain more types of information than mentioned in this column.
PDG: parenteral drug guide

Discussion

In this study we assessed the similarities in the management and content of PDGs in the Netherlands. We used a semi-structured survey to assess the diversity in maintenance procedures. We also obtained monographs of vancomycin, flucloxacillin, and furosemide and analyzed their contents.

We observed considerable overlap both in the maintenance procedures and in the components within PDGs. Although many components were present in the majority of monographs, the number of items within these components was quite different. For example, for vancomycin the median number of mentioned side-effects within the monographs was 3, but up to 8 different side-effects were mentioned in a single monograph (Supplementary material: Figure S1). Likewise, the number of (in)compatibilities varied greatly between monographs of the same drug, for example ranging from 0 to 125 compatibilities for vancomycin monographs (Figure 1). This highlights the difference in available information on the same drug between PDGs.

The majority of our participants (88%) used the same software to store and maintain their PDG. We also found that the majority of data in Dutch PDGs is based on the same literature sources and databases, rendering a large degree of overlap in their constituents and redundancy in maintenance procedures throughout the country (Figure 2A). At the same time, many hospitals have a sizable backlog of monographs that require revision. We therefore believe that a joint PDG maintained by hospital pharmacists would not only markedly improve the efficiency of maintenance procedures, but may also lead to a higher quality up to date PDG in the Netherlands (Figure 2B).

An example of a joint PDG in use today is the Injectable Medicines Guide (IMG), or Medusa, which is used in the United Kingdom.[1] The IMG contains over 400 drug monographs and is maintained by National Health Service hospital pharmacists. Locally produced drug data and guidelines can be linked to individual drug monographs in the IMG. Likewise, organizations that produce their own monographs for specific drugs can also upload and view them in the IMG. Most organizations gain access to the IMG by providing and updating monographs which can be used by others.[23] Such a subscription model may also be considered for a joint PDG in the Netherlands.

Y-site (in)compatibilities are relevant for clinical practice as incompatibilities are known to cause inactivation of drugs, precipitation and embolism.[24–26] Nurses who require compatibility data to safely co-administer two drugs through a single intravenous (IV) line are required to look up both relevant monographs. When these are inconsistent, the most recently updated monograph must be followed. In intensive care units (ICUs) where patients receive twice the number of different drugs compared to a regular ward, the number of drug pairs adds complexity to this already cumbersome process.[27] Therefore, compatibility charts are often derived from a PDG as they allow nurses to identify (in)compatibilities more efficiently.[25,28,29]

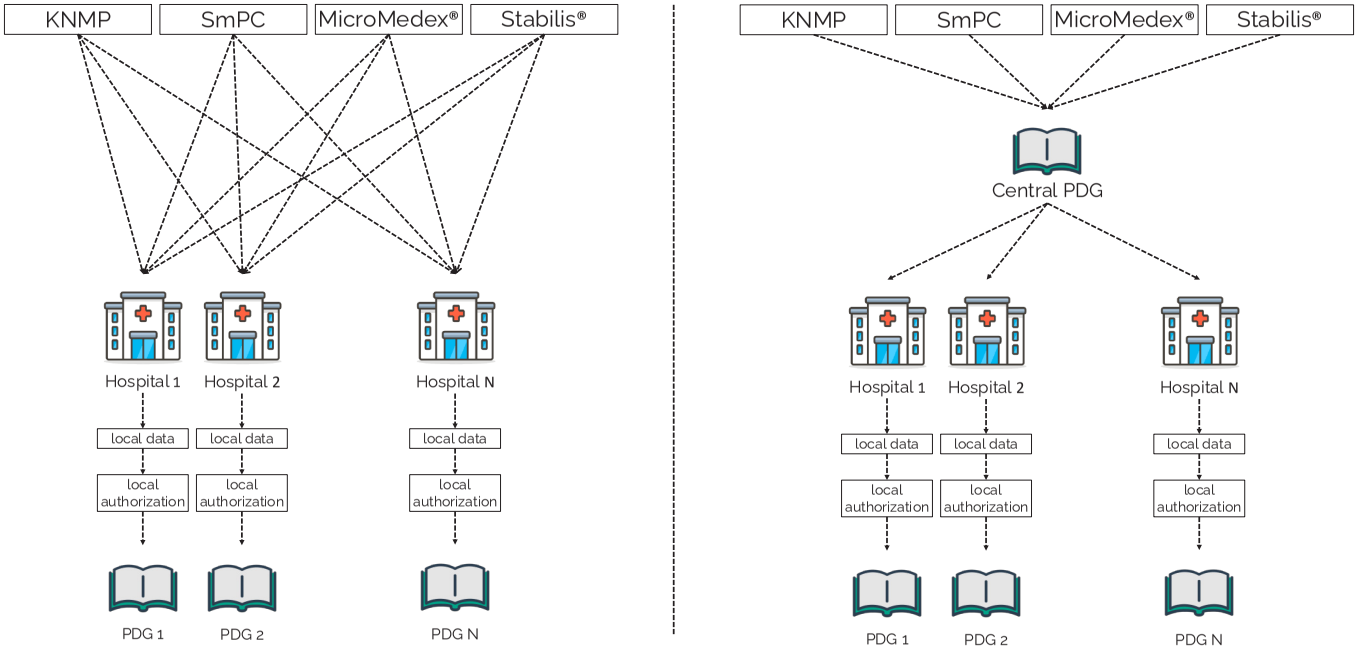

Figure 2. In the current situation (panel A) each hospital consults all data sources by itself. In a possible future scenario (panel B) a joint PDG contains the data relevant to all hospitals, improving efficiency in PDG maintenance. Hospital and book icons were created by Vincent Le Moign and are available under the CC Attribution License.[31]

When the compatibility of one drug pair has changed, the two relevant drug monographs must be updated to be consistent. However, as monographs are usually updated only one at a time, inconsistencies can easily arise within a single PDG. Participants in our study indicated that including compatibility data in monographs is often a difficult process. Multiple participants indicated that they did not update compatibilities data at all unless it was requested by clinicians.

Currently we are developing a collaboration model where hospitals in the Netherlands can contribute to a publically accessible compatibility database. We therefore developed a digital Y-site compatibility chart that interfaces with our local PDG so that it is updated automatically on a daily basis. Hospitals are able to tailor the chart to their local needs and can submit compatibilities that are missing in the chart. These additions are reviewed by local experts before publication. A public proof-of-concept version of this chart can be found online and is available in both the Dutch and English language.[30] In the future more drug data and functionalities may be added. For now it provides an example how drug data may be accessed in a centralized manner.

A limitation of this study is that it was not possible to compare the content of complete PDGs. Hence in this study we asked participants to share drug monographs of a few commonly used drugs. We investigated the constituents of these monographs but we did not compare their overall agreement, quality or correctness. Although we expect that a joint PDG would improve efficiency and reduce costs in the long term, the costs and benefits of a joint PDG must be investigated in a future study. The responsibility for the development and maintenance of a joint PDG monographs in the Netherlands should lie in the hands of a professional organization such as the KNMP or the NVZA.

Conclusions

The majority of data in Dutch PDGs is based on the same literature sources and databases, rendering a large degree of overlap in their content and redundancy in maintenance procedures. Most Dutch PDGs are not up to date and drug compatibility data in particular are difficult to maintain. We therefore recommend examining the cost and benefits of a potential joint Dutch PDG as it may eliminate redundant maintenance work as well as associated costs.

Acknowledgments

The authors would like to acknowledge Kees Neef, Petr Horak, Alison Thomson, and Patrick van Vreeswijk for their valuable assistance in this project.

Supplementary material

Supplementary material can be downloaded from https://ivcompatibility.org/thesis/supplements.html.

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