

# Frequency, nature and determinants of pharmacy compounded medicines in Dutch community pharmacies

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## Key words

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## Abstract

**Aims:** To examine the frequency, nature and determinants of pharmacy compounded medicines in Dutch community pharmacies

**Methods:** A prospective nested case-control study comparing prescriptions for pharmacy compounded medicines (cases) with non-pharmacy compounded medicines (controls) was carried out in 79 Dutch community pharmacies. 991 Prescriptions for compounded medicines (cases), dispensed by the pharmacy on a predetermined day in a specific period (29 March until 11 April 2001), and 993 prescriptions for non-compounded medicines (controls) randomly selected on the same day, were studied. The nature and frequency of compounded medicines as well as patient, drug and prescriber related determinants were assessed. In addition, some organisational characteristics, like compounding site and use of protocols, were investigated. Also, the value of compounded medicines in terms of the availability of an industrially compounded equivalent and patient specific reasons, as perceived by the participating pharmacists, was evaluated.

**Results:** The overall frequency of prescriptions for pharmacy compounded medicines in relation to the total number of prescriptions was 3.4%. This means 12.5 compounded medicines per pharmacy per day on average, but there was a large variation between pharmacies. Excluding the products purchased from specialised compounding companies (28.4%) and the small part of medicines coming from other pharmacies (5.2%), we found an overall frequency of 2.3% of actual compounding in the pharmacy itself.

On average, approximately one employee was needed for compounding activities with a large variation between pharmacies. More than 13% of the pharmacists stated that they delivered more than 25% of their compounded medicines to other pharmacies. In 2 pharmacies (2.6%) no actual compounding took place. For 58% of the products manufactured in the pharmacy itself or coming from other pharmacies a (semi-) standardised protocol was used.

Compared to non-compounded medicines we found a huge share of dermatological dosage forms among compounded medicines (62.1% versus 5.3%). Oral solutions and ear-nose-throat (ENT) products were also found relatively often. While no ATC class was very pronounced in the control group, the group of dermatologicals was prominently present in the case group (57%) followed by CNS agents (8.4%). The dermatologist was a very strong determinant of compounded medicines compared to GPs (OR<sub>adj</sub> 12.2 [6.3–23.6]). Patients of 12 years or younger received a significantly higher rate of compounded medicines than persons older than 12 years of age (OR<sub>adj</sub> 3.4 [2.5–4.8]). Compounding occurred almost twice as often when a medicine was prescribed for the first time compared to a repeat prescription (OR<sub>adj</sub> 1.8 [1.5–2.2]). In about 63% of the cases the pharmacist judged that an industrially produced medicine could not substitute for the compounded medicine. In about 33% of the compounded products they indicated a patient specific reason. In about 10% this reason concerned a strictly defined pharmaceutical care issue.

**Conclusions:** Based upon our research, all Dutch community pharmacies compound more than 13,000 medicines per day (2.3% of all prescriptions). They consist mainly of dermatological preparations. Younger children (< 12 yr) receive a significantly higher rate of compounded medicines than other people. At least 1.2 compounded prescriptions per pharmacy per day have a specific pharmaceutical care reason according to the pharmacists.

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## Introduction

For centuries compounding was an elementary task of the pharmacist: the pharmacist as an artisan. Since World War II the situation has gradually changed. As more industrialised preparations became available the importance of compounding decreased and the profession shifted towards a more patient oriented role in the optimal choice and use of medicines. In several Western countries compounding by individual pharmacies even ceased to exist or was dramatically minimised. In the Netherlands, however, it remained substantially until today. At the beginning of the nineties the share of pharmacy compounded products in the Netherlands was still estimated at 10 to 15% of all dispensed drugs<sup>1</sup>. According to the Dutch National Health Insurance it declined from 5.5% in 1994 to 3.7% in 2000<sup>2</sup>. Data from the Foundation for Pharmaceutical Statistics (SFK; Stichting Farmaceutische Kengetallen, The Hague) confirm that there is a decline during these years, but not as strong: from 6.6% in 1995 to 5.5% in 2000<sup>3,4</sup>.

Since the middle of the 1980s, every now and then there has been a national debate about compounding in Dutch pharmacies. The arguments against are mainly related to the quality of compounded products. It has been suggested that the quality of compounded products can only be guaranteed by adherence to GMP rules, including the use of standardised protocols, in process controls, validation and laboratory controls<sup>5–9</sup>. Co-operation between pharmacies as to compounding of specific products and more consultation between pharmacists and prescribers about (ir)rational extemporaneous prescribing have been

proposed as measures to ameliorate conditions to reach higher compounding quality<sup>8–11</sup>. In addition, pharmacy compounded medicines are far less studied and documented than their industrial equivalents with respect to biopharmaceutical aspects and safety, but in particular with respect to efficacy. While for standardised pharmacy compounded products (bio) pharmaceutical issues are to some extent sufficient and for safety a certain amount of experience can be built up, the real problem is with the efficacy issue. Formal clinical trials are hardly executed mainly due to costs. The arguments in favour of today's pharmacy compounding are primarily found in the realm of pharmaceutical care. It has been suggested that compounded products are needed in certain patient specific situations and can contribute to patient tailored pharmacotherapy, e.g., a product is needed but not commercially available (e.g., 'orphan drug' situations), or a special dosage form or strength is required, for instance, for children. In some instances this means 'off-label use', which can also occur when a drug is used experimentally. This 'off-label use' can also be considered a reason against pharmacy compounding. Other pharmaceutical care arguments in favour are improved patient compliance and an existing contraindication or allergy for an ingredient of the speciality<sup>9,11,12</sup>. Another argument in favour of pharmacy compounding is that these medicines are often cheaper<sup>1,9,12</sup>. Some of the pros and cons are also found in international literature<sup>13–16</sup>.

We carried out this study into the frequency, nature and determinants of compounded medicines in Dutch community pharmacies, because of conflicting data about the frequency of compounding and the lack of detailed information about its nature and aspects related to their pros (e.g., patient tailoring) and cons (e.g., less stringent quality assurance).

## Methods

### Setting and design

In 1999 we received a positive response from 470 Dutch community pharmacies to our invitation to participate in a previous study about prescription modifications<sup>17</sup>. Of the 60% of pharmacies ( $n = 282$ ) that did not participate in that study, we asked 50% ( $n = 141$ ) to join this prospective nested case-control study about pharmacy compounding. 84 Pharmacies were enrolled in the study, but five had to be excluded because they did not adhere to the study protocol, leaving 79 pharmacies (almost 5% of all Dutch pharmacies) for evaluation. Each participating pharmacy had to collect all dispensed prescriptions for pharmacy compounded medicines (cases) during one predetermined study day between 29 March and 11 April 2001. They had to sample at random an equal number of non-pharmacy compounded medicines (controls) that were dispensed on the study day. All participating pharmacies received a pre-tested study protocol and three types of registration forms: one for the documentation of each dispensed prescription for a pharmacy compounded medicine (case), one for each non-pharmacy compounded medicine (control) and one general form concerning basic characteristics of the pharmacy on the study day. The protocol advised

to contact a telephone help desk in case of any uncertainty.

### Selection of cases

All prescriptions for medicines that were compounded and dispensed in the pharmacy on the study day, had to be included. A broad definition of a pharmacy compounded product was employed to measure the full magnitude of compounding. Following the Dutch national prices list, our definition comprised not only medicines compounded by the pharmacy itself, but also products compounded by other (hospital) pharmacies or by specialised compounding companies. The latter produce and deliver medicines to pharmacies in a finished or almost finished state without any assessment by the Dutch regulatory authorities. A protocol and an 'inclusion scheme' with eight examples were sent to help the pharmacists to select cases.

### Selection of controls

The pharmacists had to provide an equal number of non-pharmacy compounded medicines (controls) by selecting this number at random from all prescriptions of the same day. This random selection was performed by blind drawing of the required number of prescriptions from a box containing all prescriptions for non-compounded medicines of that day. When there was more than one medicine on the same prescription the first medicine had to be chosen. Non-medicine prescriptions had to be excluded.

### Validation of the cases

To check the reliability of the registered data, pharmacists were asked to send not only their registration forms but also anonymized copies of each underlying prescription to the co-ordinating study centre. When data in the registration form appeared to be incorrect compared with the prescription copy, it resulted in exclusion (which was rarely needed) or in an alteration by the research team.

### Classification of prescriptions

All compounded products were classified into therapeutic groups using the Anatomical Therapeutic Chemical (ATC) classification of the WHO Collaborating Centre for Drug Statistics Methodology<sup>18</sup>. When no classification could be found in the official ATC system, we assigned an ATC-like code to the product within the rules and spirit of this classification. When we could not assign such a code, the product was classified as V03AX (other therapeutical products). In addition, the following variables of each prescription were registered: gender and age of patient, type of prescriber, repeat or first prescription, and dosage form.

For all cases, except for the products compounded by specialised compounding companies, the origin of protocols used for compounding purposes was requested (different kinds exist in Dutch community pharmacies). In the first place, national standard protocols are used for the compounding of standard products, the so-called FNA (Formularium Nederlandse Apothekers = Formulary Dutch Pharmacists) formulas. These products are well investigated and documented, both technically (e.g., shelf life) and pharmacotherapeutically (rationality). The LNA (Labo-

ratorium van Nederlandse Apothekers = Laboratory of Dutch Pharmacists) is responsible for these formulas and compounding protocols. Another category is the semi-standard protocol, which is less well investigated and documented. They are found in specific locations, where local pharmacists have made them for specific products. Another type of semi-standardised protocols concern an FNA-protocol, which is no longer updated by the LNA. Finally, it is possible to make a protocol at the moment of manufacturing. In most cases these non-standardised protocols are not or at best only slightly documented.

In addition, the pharmacist was asked to determine the value of each compounded medicine in terms of the availability of an industrially compounded product and patient specific reasons.

#### Data analysis

After inspection, data from the registration forms were entered in a database (Microsoft Access) and statistically analysed using standard descriptive data analysis (SPSS version 10.0). Logistic regression analysis was used to estimate the association between characteristics and compounding.

#### Results

The basic characteristics of the participating pharmacies are presented in Table 1. There was a large variation in the total number of prescriptions and the number of pharmacists and assistants per pharmacy, which probably reflects the fact that both small and very large pharmacies participated in the study. Compared to the average Dutch pharmacy the enrolled

pharmacies processed more prescriptions per day but had a lower number of personnel. The workload of assistants was consequently higher.

In 2 of 78 enrolled pharmacies (2.6%) compounding of medicines did not take place by the pharmacy itself. On average approximately one employee, mainly an assistant, was needed for compounding. In relation to the total number of personnel this means that a Dutch pharmacy uses almost 15% of its qualified personnel for compounding related tasks. However, there was a large variation in the mean number of personnel deployed for compounding. Six pharmacies (8.0%) stated that more than 25% of their compounded medicines were delivered to other pharmacies and this share was more than 50% in four pharmacies (5.3%).

On the study day, the overall frequency of compounded medicines relative to all dispensed prescriptions was 3.4% (991 cases out of 28,711 prescriptions; Table 2). The number of cases per pharmacy varied from 2 to 35 with a mean of 12.5 compounded medicines per pharmacy per day. The frequency of compounded prescription only medicines (= POM) as to the total number of POM prescriptions was 5.1% (range between pharmacies from 0.5 to 14.1%).

The majority of all dispensed compounded medicines was compounded in the pharmacy itself (657; 66.3%). Almost half of the latter was prepared extemporaneously (302; 30.5%), while the other half (343; 34.6%) was kept as stock (Table 3). A large part (28.4%) of the so-called pharmacy compounded products was purchased from special companies, leaving a small part of products coming from other pharmacies, like the hospital pharmacy (52; 5.2%).

**Table 1** Characteristics of the included pharmacies (n = 79)

	Mean	Range	Mean data of Dutch pharmacies (n = 1602) <sup>a</sup>
<i>Prescription characteristics</i>			
• number of prescriptions per day	372.9	164–753	325 <sup>a</sup>
• number of POM <sup>b</sup> prescriptions per day	297.7	26–654	
<i>Personnel characteristics</i>			
• number of pharmacists	1.4	0.5–2.5	1.63
• number of assistants	4.7	2.0–8.5	5.90
• number of personnel <sup>c</sup>	6.1		7.53
• workload per assistant <sup>d</sup>	79.3		55.1
• workload per personnel	61.1		43.2
<i>Compounding characteristics</i>			
• number of non-compounding pharmacies (n = 78)	2 (2.6%)		
• mean number of personnel deployed for compounding	0.9	0.1–3.0	
• share of compounding for other pharmacies (n = 75)			
• 0–25%	65 (86.7%)		
• 26–50%	6 (8.0%)		
• 51–75%	4 (5.3%)		
• 76–100%	0 (0.0%)		

<sup>a</sup> Data obtained from SFK (Stichting Farmaceutische Kengetallen = Foundation for Pharmaceutical Statistics, The Hague) concerning the first quarter of 2001. Estimation of number of prescriptions per day based upon a total of 21000 prescriptions in first quarter of 2001.

<sup>b</sup> POM = prescription only medicine(s).

<sup>c</sup> Personnel = number of pharmacists plus number of pharmacy assistants (full-time equivalents).

<sup>d</sup> Workload assistants = number of prescriptions per full-time assistant per day.

**Table 2** Frequency of pharmacy compounded medicines in Dutch community pharmacies

	Total number	Number of cases	Frequency <sup>a</sup>	Range <sup>b</sup>
All prescriptions	28711	991	3.4%	0.4–6.8%
POM prescriptions <sup>c</sup>	19347	991	5.1%	0.5–14.1%

$$^a \text{ Frequency} = \frac{\text{Number of all cases} \times 100\%}{\text{Total number of prescriptions}}$$

<sup>b</sup> Range concerns the frequency per pharmacy.

<sup>c</sup> POM = prescription only medicine(s).

The use of protocols was considered for the products manufactured in the pharmacy itself and those coming from other pharmacies. In 58% of the cases the pharmacy used a standardised or semi-standardised protocol.

The data of drug related variables like dosage form and type of drug (ATC-code) are presented in Figures 1 and 2, respectively. There was a large share of dermatological dosage forms in the case group (62.1% versus 5.3% in the control group). Oral solutions and ENT (ear, nose, throat) products were also found relatively more often among compounded medicines (7.4 and 7.1%, respectively).

The large share of dermatological dosage forms is also reflected in the distribution of ATC codes (D; 57%). All other ATC classes within the group of compounded medicines had a relatively small share with the nervous system products as the highest (N; 8.4%). In the control group nervous system medicines were prescribed most frequently (19.6%), followed by cardiological preparations (C; 14.9%) and alimentary tract and metabolism medicines (A; 10.7%).

In Table 4 the determinants of compounded medicines are summarised. Compounding occurred almost twice as often when a medicine was prescribed for the first time compared to a repeat prescription (OR<sub>adj</sub> 1.8 [1.5–2.2]). With respect to patient-related factors we found that children (12 years or younger) received a considerably higher rate of compounded medicines than people older than 12 years of age (OR<sub>adj</sub> 3.4 [2.5–4.8]). Correspondingly, the mean age in the case group was somewhat lower than that in the control group (43.1 [s.d. 26.3] versus 51.5 [s.d. 21.7]). With

respect to other patient related factors, gender did not appear to be significant.

With regard to prescriber related determinants, dermatologists were the most important: the chance of getting a compounded medicine from a dermatologist was more than twelve times as high as that for a general practitioner (OR<sub>adj</sub> 12.2 [6.3–23.6]). Other prescribers like paediatricians had an impact similar to that of GPs.

In Table 5 the value of pharmacy compounded products according to the participating pharmacists is shown. In 63.4% of the cases the pharmacist believed an industrially produced medicine could not substitute for the compounded product.

The participating pharmacists indicated patient specific reasons in 33.2% (330 of 991 cases) of the pharmacy compounded products: intolerance or contraindication were mentioned in 0.8% of the cases, convenience to use in 4.4%, and special demand of the prescriber or patient in 8.5% (6.1% and 2.4% respectively). The reason 'special dose needed' was mentioned in 4.2% of the cases. In almost 7% of the cases the product was compounded to avoid (partial) payment by the patient. Some specialities are not remunerated at all or are partially remunerated because of remuneration limits within ATC clusters. In both situations pharmacy compounded medicines may be alternatives for specialities. In 3.3% of the cases ( $n = 33$ ) there was more than one reason to dispense a pharmacy compounded product, a combination of the reasons mentioned above. In 8.5% there was 'another reason' to compound in the pharmacy. With respect to the patient specific reasons for compounding, the

**Table 3** Characteristics of pharmacy compounded medicines in Dutch community pharmacies (cases): compounding site and use of protocols<sup>a</sup>

	Number of cases ( $n = 991$ )
<i>Compounding site</i>	
Compounded by the pharmacy itself (A)	657 (66.3%)
– Extemporaneous manufacturing	302 (30.5%)
– Product in stock	343 (34.6%)
Compounded by other (hospital) pharmacy (B)	52 (5.2%)
Compounded by special company (C)	281 (28.4%)
<i>Use of protocols (A + B)</i>	
– Standardised protocol used	218 (30.7%)
– Semi standardised protocol used	194 (27.3%)
– Non standardised protocol, or no protocol used	296 (41.7%)

<sup>a</sup> Not all data count up to 100% because of missing values.

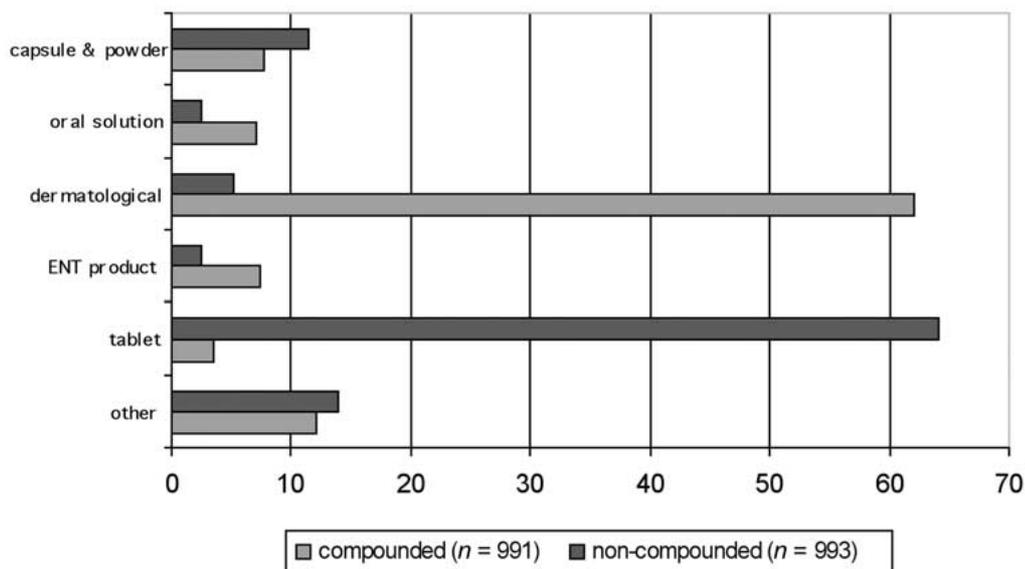
overall picture did not clearly change, when the results were considered without products coming from special companies.

### Discussion

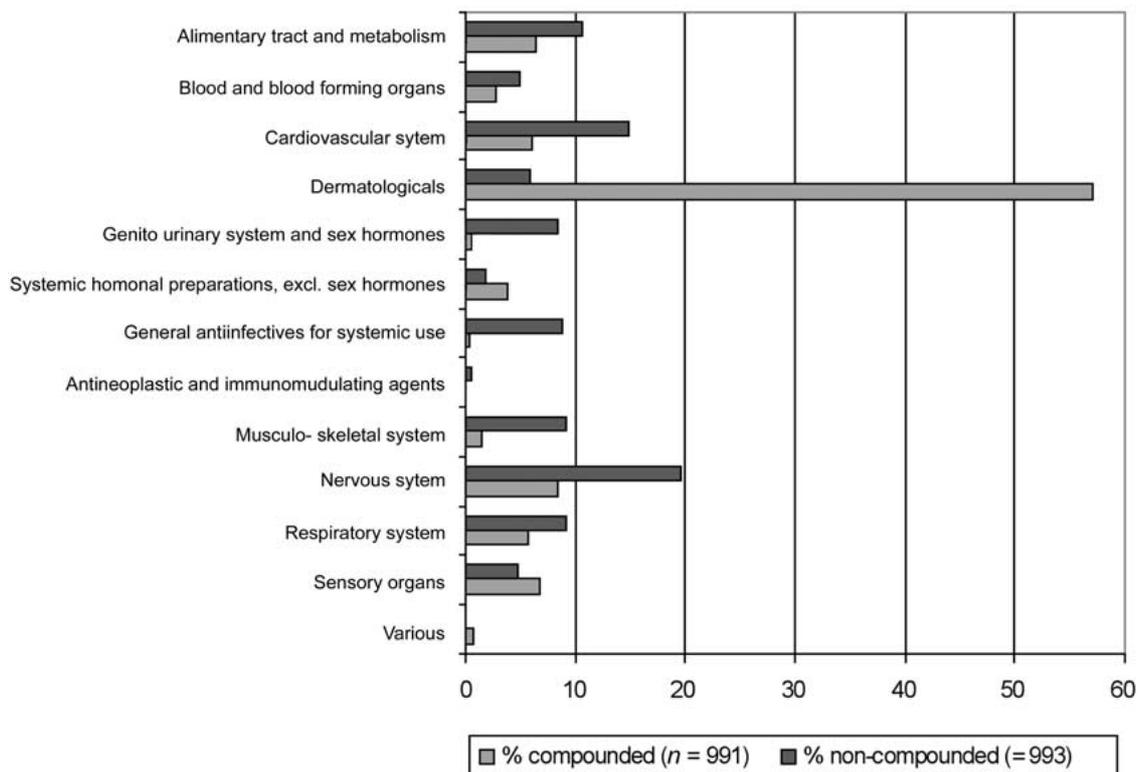
In this study we found that 3.4% of all dispensed prescriptions in Dutch pharmacies concern a compounded medicine, which means an average number of 12.5 compounded medicines per pharmacy per day. Two-thirds of these medicines are still manufactured in the pharmacy itself. In comparison with non-compounded medicines, compounded medicines were significantly more often prescriptions for chil-

dren, dermatological dosage forms and products, prescriptions by dermatologists and first prescriptions. Participating pharmacists estimated that at least 10% of the compounded medicines had a pharmaceutical care reason.

Two other Dutch sources for drug utilisation data give conflicting figures for the year 2000 concerning the frequency of compounded medicines: 3.7% according to the Dutch National Health Insurance<sup>2</sup> and 5.5% according to SFK (Foundation for Pharmaceutical Statistics, The Hague)<sup>3,4</sup>. Both figures are based on remuneration data, which are based on the Dutch national pricing list. These data do not differentiate between the origin of pharmacy compounded products.



**Figure 1** Frequency (%) of dosage forms in pharmacy compounded and non-compounded medicines



**Figure 2** Frequency (%) of ATC groups in pharmacy compounded and non-compounded medicines. Data do not sum to 100% because of missing values or data not shown (low frequency of antiparasitics)

**Table 4** Determinants of pharmacy compounded medicines in Dutch community pharmacies<sup>a</sup>

Characteristic	Cases n = 991 (100%)	Controls n = 993 (100%)	OR [95% CI] Crude	OR [95% CI] Adjusted <sup>b</sup>
<i>Patient related</i>				
<i>Gender</i>				
Male			1 (ref.)	
Female	57.5%	60.9%	0.95 [0.87–1.04]	
<i>Age</i>				
< 12 years	15.7%	5.1%	3.44 [2.47–4.80]	3.43 [2.46–4.80]
12–75 years	70.8%	79.6%	1 (ref.)	1 (ref.)
> 75 years	13.4%	15.3%	0.98 [0.76–1.27]	0.99 [0.87–1.04]
<i>Prescriber related</i>				
General Practitioner	75.1%	81.7%	1 (ref.)	1 (ref.)
Dermatologist	10.9%	1.0%	11.66 [6.06–22.39]	12.23 [6.33–23.60]
Paediatrician	1.3%	0.8%	1.77 [0.73–4.30]	0.65 [0.25–1.68]
Other prescribers	12.7%	16.5%	0.84 [0.65–1.08]	0.86 [0.67–1.11]
<i>Drug related</i>				
Repeat prescription	46.9%	61.9%	1 (ref.)	1 (ref.)
First prescription	52.5%	36.6%	1.89 [1.58–2.27]	1.80 [1.50–2.16]

<sup>a</sup> Not all data count up to 100% because of missing values.

<sup>b</sup> Adjusted for all other characteristics.

They represent not only pharmacy made products, but also products defined as pharmacy manufactured but coming from other pharmacies or specialised companies. As presented in the introduction, both the Dutch National Health Insurance and the SFK show in percentage terms a decline in compounding. As shown by us, the actual compounding by pharmacies is even lower (2.3%).

The considerable proportion (28.4%) of preparations coming from specialised companies is of concern, since the availability of these products on the Dutch medicines market is controversial. Until now these specialised firms have been able to avoid any formal medicine approval procedure. In the United States

this phenomenon caused the FDA to issue guidance regarding pharmacy compounding<sup>19</sup>. Among others, Dutch specialised companies present a large part of their products as semi-manufactured or almost finished articles so that the pharmacy itself has to finish the product, often in a very easy way. The rise of these firms is a consequence of shortage of personnel in the pharmacies and a call among pharmacists for more centralised compounding. Consequently, these firms compound those preparations that are more broadly needed. Patient tailored products are probably more often extemporaneously compounded and remain in the pharmacy itself.

**Table 5** Value of pharmacy compounded medicines (cases) as perceived by the participating pharmacists: commercial availability of equivalent products and patient specific reasons<sup>a</sup>

	number of compounded medicines/cases (n = 991, 100%)
<i>Equivalent product commercially available</i>	
Positive judgement	237 (23.9%)
Negative judgement	628 (63.4%)
Unknown to pharmacist	115 (11.6%)
<i>Preparations with one patient specific reason</i>	
Intolerance/contraindication	8 (0.8%)
Inconvenient to use	44 (4.4%)
Special dose needed	42 (4.2%)
Demand of patient	24 (2.4%)
Demand of prescriber	60 (6.1%)
Prevention of (partial) payment by patient or other cost reason	68 (6.9%)
Other reason	84 (8.5%)
<i>Preparations with a combination of two or more patient specific reasons</i>	33 (3.3%)

<sup>a</sup> Not all data count to 100% because of missing values.

Our study also revealed that pharmacy compounding consists for a large part of dermatological products and dermatological dosage forms (Figures 1 and 2). Correspondingly, the dermatologist is relatively strongly represented within the group of compounded preparations compared with the GP. Although not exactly similar, these data confirm results from others<sup>4,20</sup>.

With respect to patient related determinants, children below 12 years of age received relatively more compounded medicines than other age groups. In a study by Crawford et al., who evaluated frequently extemporaneously compounded drug formulations, the group of infants and children was considerable<sup>21</sup>. This might be explained by the fact that children need patient tailored therapy more frequently, for which commercial products are not available, because a special dose or dosage form is needed<sup>22</sup>. On the one hand there is the benefit that pharmacy compounding makes patient-tailored dosage forms or dose strengths available for children. On the other hand there is the risk that pharmacy compounding thereby supports use of drugs in children which have not yet been evaluated in an appropriate way and which may give rise to considerable adverse drug reactions<sup>23,24</sup>.

With respect to drug related determinants we found that compounded medicines are less chronically prescribed than non compounded medicines: first prescriptions occur twice as often as repeat prescriptions. This might be related to the fact that some ATC groups (e.g. C and N), for which continuous use is normal, are more pronounced in the control group. (Figure 2). Furthermore young people, who generally use medicines less chronically, are more represented in the case group than in the control group. (Table 4).

The pharmacies did not use a standardised or semi-standardised protocol in 42% of the cases (Table 3). We have not investigated to what extent the pharmacies were unable to use any protocol, and when they were unwilling to do so. Most likely, both mechanisms have played a role in our sample. When a patient requires a special composition, dosage form or strength that is not commercially available, extemporaneous compounding is needed to provide this patient with an individually tailored medicine<sup>9,15,16</sup>. This type of compounding cannot always be based on the application or adjustment of an existing protocol. We found that younger patients (< 12 yr) used significantly more compounded medicines, and it is well established that this age group has a larger need for special dosage forms and strengths than adult patients<sup>22</sup>. We also found other reasons, why medicines were sometimes compounded for individual patients, e.g. because this increased the convenience to use, or because the prescriber or patient insisted on a particular medicine (Table 5).

There were some limitations regarding our study. Although we used a random sample from volunteering community pharmacies throughout the country, we found some differences, like a higher workload, between the average enrolled and average Dutch pharmacy (Table 1). To reduce the risk of overestimation, every reported case was checked on the basis of anonymous copies of the original prescription. But underestimation cannot be totally ruled out, because some cases may not have reached us due to pressure of time or inappropriate handling. Another limitation of our

study was that it occurred in a short time period and that it cannot predict possible (but unknown) seasonal variations. Fluctuating patterns within a week however were ruled out by assigning all days of the week equally in the study period.

In the debate with respect to pharmacy compounding one may find several pros and cons. As described in the introduction, the arguments in favour of pharmacy compounding are related to pharmaceutical care suggesting that compounded products are needed in certain patient specific situations<sup>9,11,12</sup>. However, this statement has never been properly investigated. In this study we did a preliminary estimate based upon the opinion of the participating pharmacists (Table 5). In 33.2% of the pharmacy compounded products pharmacists indicated patient specific reasons. Specific pharmaceutical care issues like intolerance or contraindication, convenience to use and special dose needed, were mentioned in 9.5% of all cases. Therefore, at least 1.2 compounded prescriptions per pharmacy per day had a specific pharmaceutical care reason. A closer look at the category 'combination of reasons' revealed more (1,1%) such indications. It cannot be ruled out that in the other categories mentioned, like 'demand of prescriber', pharmaceutical care issues may have been present. At the same time, we have to emphasise that the opinion of prescribing doctors was not investigated explicitly. One may argue that while prescribing these preparations, they almost certainly had a positive opinion about their value for the individual patient. Cost represented a considerable share (6.9%) of patient specific reasons indicating that the price of compounded medicines is lower in some instances<sup>1,9</sup>. It remains debatable whether avoidance of cost for the patient is a pharmaceutical care issue.

This study gives some indication regarding the value of compounding for the Dutch outpatient. A more in depth analysis is needed to assess the potential clinical relevance of compounded medicines which we intend to do by presenting representative samples of cases of this study and/or other to multidisciplinary rating panels<sup>25,26</sup>.

## Conclusion

Based upon our research, more than 13,000 medicines per day are compounded in Dutch community pharmacies (2.3% of all prescriptions). A remaining part of compounded products (1.1% of all prescriptions) is coming from other pharmacies but in particular from specialised companies. Pharmacy compounded products consist mainly of dermatological preparations. Younger children (< 12 yr) receive a significantly higher rate of compounded medicines than others. At least 1.2 compounded prescriptions per pharmacy per day have a specific pharmaceutical care reason according to the pharmacists. It could be that compounding for Dutch outpatients will continue to decline due to external reasons, like the growing availability of the controversial (half-) products from the above-mentioned specialised compounding firms, changes in the remuneration system and a growing pressure in our evidence-based medicine era to rationalise dispensing and compounding<sup>8,9</sup>. Also organisational aspects like shortage of personnel and efforts of pharmacists to cooperate with prescribers – especially dermatologists –

and colleagues to rationalise compounding, will contribute to a further decline<sup>4</sup>. We believe nevertheless that compounding for Dutch outpatients will hold a place, especially because it offers a potentially valuable tool to provide pharmaceutical care to individual patients.

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### Possible conflict of interests

None.

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