Robotic reconstitution of cytostatic drugs and monoclonal antibodies: transforming aseptic drug compounding in hospital pharmacies

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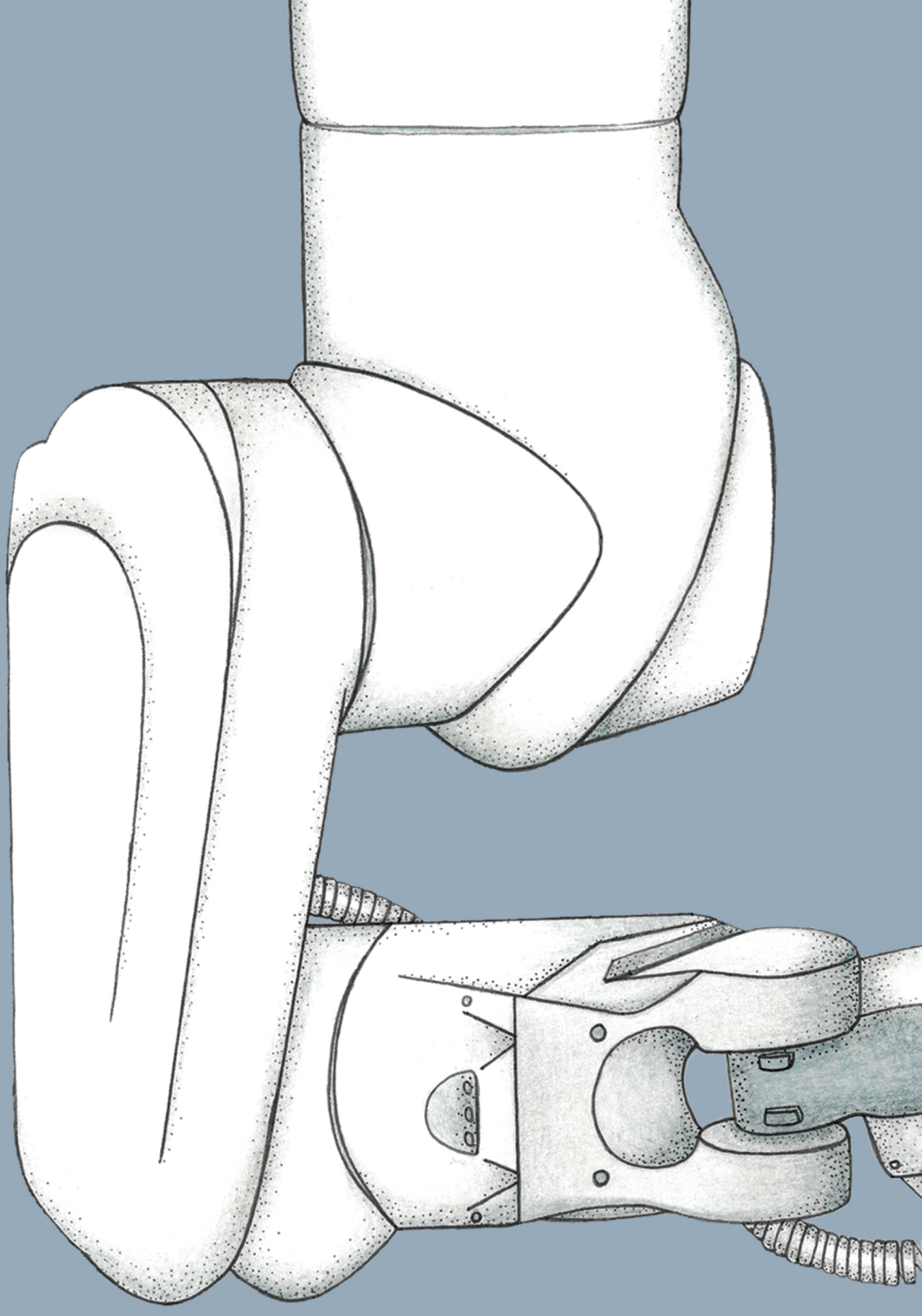
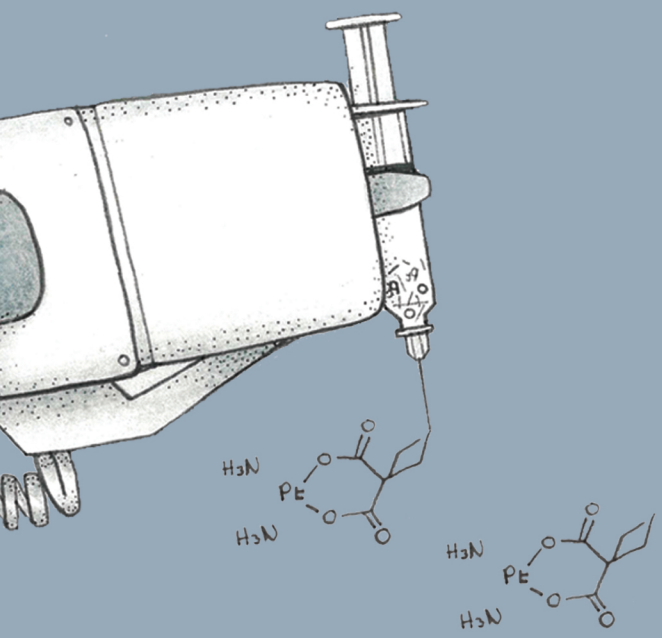
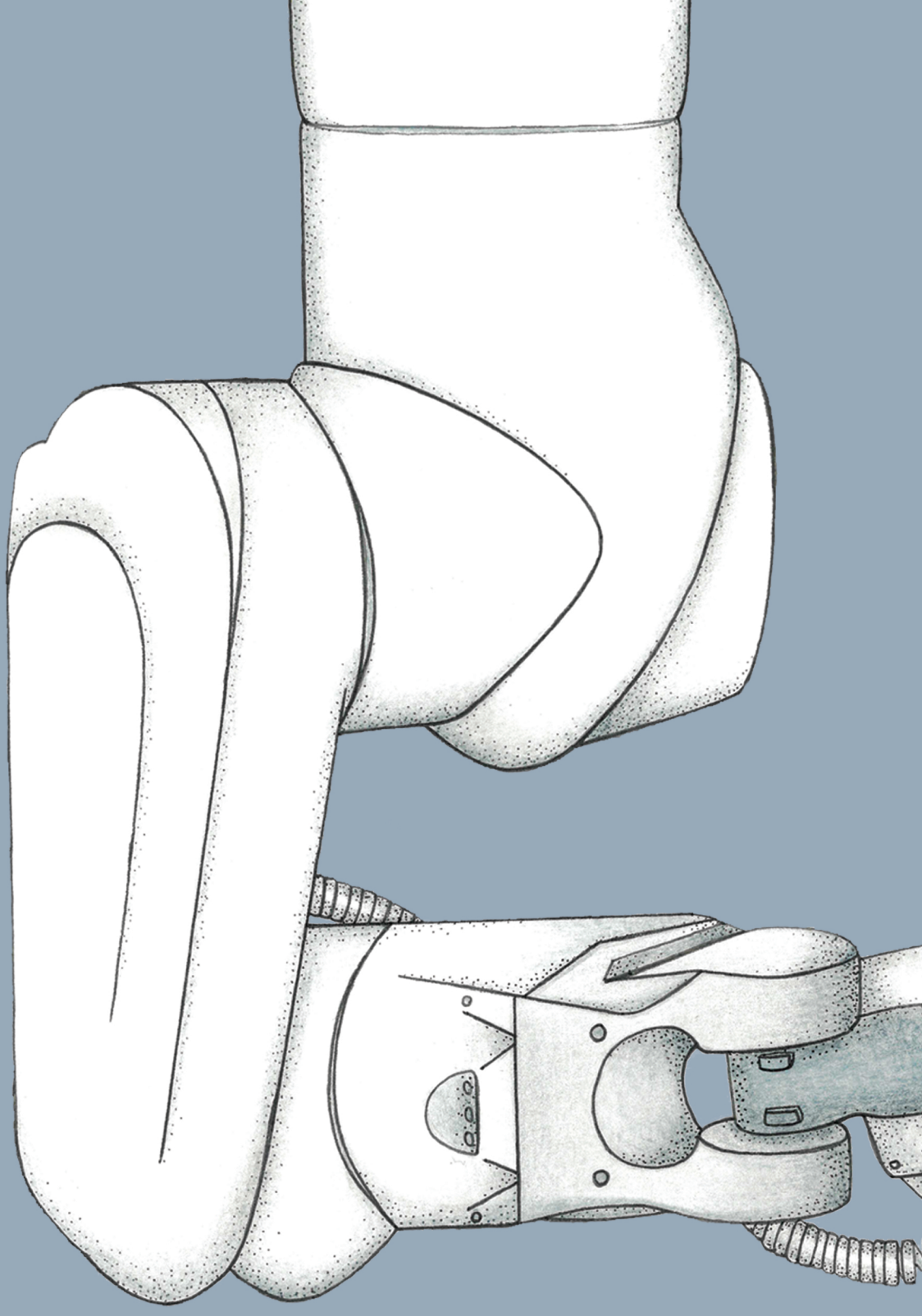


Section III

Robotic reconstitution and cost-effectiveness





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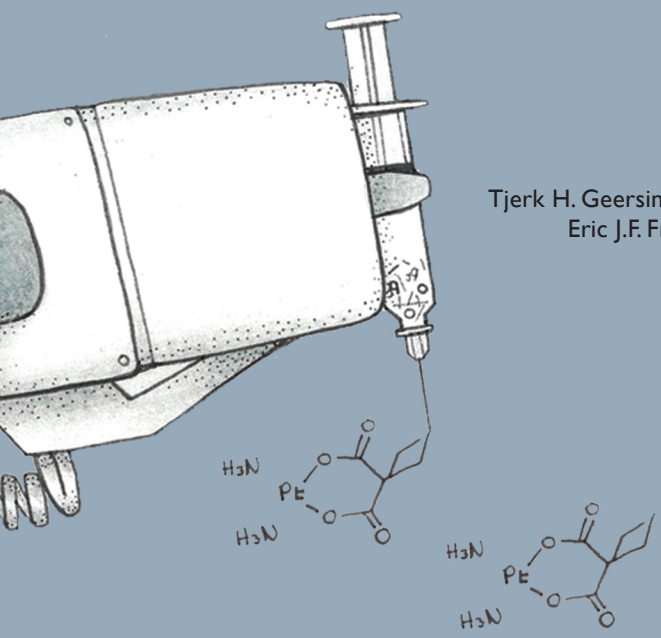
Analysis of production time and capacity for manual and robotic compounding scenarios for parenteral hazardous drugs



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ABSTRACT

Background The increasing amount of hazardous preparations in combination with shortages leads to a call for more efficient compounding methods. This research aims to evaluate the required amount of time, production capacity and direct labour costs of the manual, manual software-supported and robotic compounding of parenteral hazardous drugs.

Methods This multicentre study was conducted at the clinical pharmacy departments of three Dutch hospitals with different compounding methods: St. Antonius hospital (manual software-supported compounding), Amsterdam University Medical Centre (Amsterdam UMC) (both robotic compounding and manual compounding without software support) and OLVG (robotic compounding). Time measurements of individual hazardous drugs were performed in all three hospitals. At Amsterdam UMC and St. Antonius hospital, the times per compounding phase, the production capacity and the direct labour costs per preparation were also determined. To reflect real-world situations, the combination of robotic and manual compounding was also studied.

Results The total compounding process, including the actions before compounding and the release-time and cleaning time, lasted 6:44 min with robotic compounding and was faster than manual compounding with and without software support (6:48 and 9:48 min, respectively). The production capacity of one full-time equivalent (FTE) on 1 day (P1FTE1day) was 15 preparations per FTE per day with manual compounding with and without software support, and 57 preparations per FTE per day with only robotic compounding. If manual and robotic compounding were combined, the production capacity was 30 preparations per FTE per day. In this setting, the direct labour costs per preparation were €5.21, while these costs were €13.18 with only manual compounding.

Conclusion Compared with manual compounding, robotic compounding was faster over the total compounding process. A combination of manual compounding and robotic compounding could lead to 100% more preparations per FTE and 2.5 times lower direct labour costs compared with manual compounding.

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INTRODUCTION

Hospital pharmacies are facing a continuous growth in clinical and logistic demands, often accompanied by limitations in budget and human resources. In 2019, the incidence of oncology patients was around 23.9 million across over 204 countries, and this statistic is expected to increase each year.[1] Therefore, more chemotherapy bags and syringes must be compounded through hospital pharmacies, even though there is a great shortage of pharmacy technicians.[2] More efficient compounding methods are necessary, which became even more visible during the COVID-19 pandemic when many hospital personnel were on sick leave.

Currently, there are three commonly used aseptic compounding methods for parenteral hazardous drugs: manual, manual with software support and robotic. Manual compounding is associated with multiple repetitive strain injuries among pharmacy technicians, which may exacerbate the problem of staff shortages.[3] Gravimetric manual compounding systems with software support provide improved accuracy and precision compared with conventional manual compounding.[4] Robotic systems can take over repetitive compounding actions from pharmacy technicians, providing a solution for staff shortages and injuries caused by repetitive strains.[5] Other advantages of robotic systems are full traceability, less drug waste, proven accuracy and reduced exposure to cytotoxic drugs during compounding.[6-9]

Batson *et al* and Masini *et al* showed that robotic compounding was associated with longer compounding times compared with manual compounding.[5,10] Most other literature also compared the time needed to compound one single preparation of a hazardous drug. This data can be used to consider which drugs should be selected to compound by hand or by a robot. However, compounding robots have a significant influence on the workflow of the total compounding process. Therefore, it is more important to determine the time of the total compounding process. Capilli *et al* showed that after the implementation of a robot, the number of resources dedicated to the compounding activities remained unchanged at 7.5 full-time equivalent (FTE), while the production increased by 22%.[7] However, no studies have compared the time and FTE required for the preparation of cytostatics between three different compounding methods: manual, manual with software support and robotic.

Time saving for pharmacy technicians is highly desirable and is an important factor for hospitals in deciding whether to switch to the purchase of a robot. Therefore, we evaluated the required amount of time for the compounding subprocesses, the production capacity and the direct labour costs of the manual, manual software-supported and robotic compounding of parenteral hazardous drugs. Moreover, it is not possible to compound 100% of all the preparations using a robotic system. For example, robots cannot compound complex preparations such as loaded beads, experimental cytotoxics or intrathecal administration systems. Therefore, the combination of robotic and manual compounding will be compared with simple manual compounding.

This study aims to evaluate the required amount of time, production capacity and direct labour costs of the manual, manual software-supported and robotic compounding of parenteral hazardous drugs.

METHOD

Study design, setting and data collection

This multicentre study of compounding parenteral hazardous drugs includes data from three Dutch hospitals: St. Antonius hospital, Amsterdam University Medical Centre (Amsterdam UMC) and OLVG. Fig. 1 shows the included hospitals, the compounding methods and the topics studied. St. Antonius hospital has two locations in Nieuwegein and Utrecht. We collected data from both locations using the manual software-supported compounding method via Careflow Chemotherapy (CMS) version 6.1.0 from Careflow Medicines Management (Basildon, England). Amsterdam UMC has two locations in Amsterdam, called AMC and VUmc. Data were collected from AMC using the manual volumetric compounding method, while data were collected from VUmc using both the manual volumetric compounding method and the APOTECAchemo version 2021 robotic system from Loccioni (Ancona, Italy). In OLVG hospital, also located in Amsterdam, we collected data using the same robotic system (APOTECAchemo version 2017 from Loccioni). All robot compounding times were extracted from 1 November 2021 to 31 December 2021 to obtain a realistic case mix.

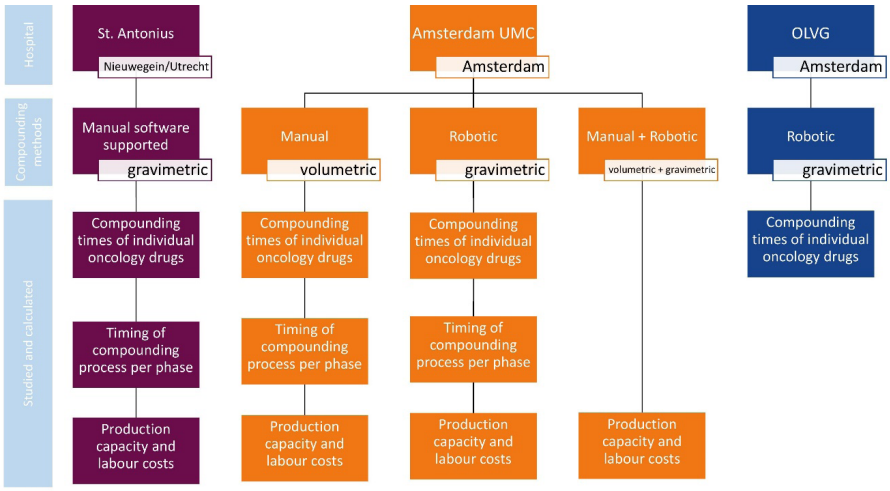

Fig. 1 Included hospitals, their methods of compounding parenteral hazardous drugs and the topics studied.

To compare the total compounding process in the different hospitals, all compounding process activities were divided into four phases: preparation before the start of the compounding, actual compounding, the release of the preparation and the cleaning procedure. These four phases and the exact start and stop moments are given in table 1. In total, nine different drugs were included in this research to determine their compounding times. The inclusion criterium for a drug was that it was used in oncology and that it could be compounded both manually and robotically. We included the powdered drugs cyclophosphamide, paclitaxel and pemetrexed and the diluted drugs carboplatin, cisplatin, cytarabine, doxorubicin, fluorouracil, irinotecan and oxaliplatin. A minimum of three preparations were timed for each drug to provide a realistic average compounding time per drug.

Table 1. Number of time measurements per compounding phase, including the operators involved and the start and stop moments for time measurements

Phase	Start and stop moments for time measurements	Operators	No of measurements
Activities before compounding	Start: the moment when the operator is selecting the specific order. Stop: the moment when all the materials and vials were placed in the lock to the cleanroom.	PE/PT	A minimum of 3 preparations per drug compounded by a minimum of 3 different colleagues.
Manual or robotic compounding	Start: the moment when an operator takes the specific materials and vials out of the lock. Stop: the moment when the compounded preparation is placed in the lock for release.	PE/PT/ Robot	A minimum of 3 preparations per drug compounded by a minimum of 3 different colleagues.
Release of preparation	Start: the moment when the preparation is taken out of the lock for release. Stop: the moment when the preparation has been released.	PT/Ph	A minimum of 3 preparations per drug released by a minimum of 3 different colleagues.
Cleaning	Start: the moment when the operator(s) are done compounding and start collecting the cleaning equipment. Stop: the moment the cleaning is done and the operator(s) are leaving the cleanroom.	PE/PT	3 different colleagues

PE, pharmaceutical employee; Ph, pharmacist; PT, pharmacy technician.

At OLVG, we were only able to determine the compounding of the individual hazardous drugs. In the other settings, all four phases of the compounding process were determined. All activities were timed at least three times and executed by at least three different staff members to obtain reliable real-world data. Because the hospitals have slightly different workflows, tasks and responsibilities for their staff, an overview of all tasks was created to compare the data (table 2). Furthermore, this overwiew indicates how many staff members worked on the activity, including their functions.

Table 2. The number and functionality of staff involved in the activities of the different compounding processes

Phase	Activity	Manual compounding St. Antonius hospital	Manual compounding Amsterdam UMC	Robotic compounding Amsterdam UMC
Activities before compounding	Authorization of prescription	1 Ph	1 Ph	1 Ph
	Printing the protocol and performing all calculations	1 PE	1 PT	n.a.
	Collect materials necessary for the compounding process	1 PE	1 PT	n.a.
	Scanning barcodes of all materials and entering in CMS/EPIC	1 PE	1 PT	n.a.
	Placing all materials in the lock to the compounding area	1 PE	1 PT	n.a.
Manual or robotic compounding	Verification of incoming materials necessary for the compounding process	1 PT+ 1 PE	1 PT + 1 PE	Robot + 1 PT/ PE
	Disinfection of materials necessary for the compounding process	1 PT + 1 PE	1 PT + 1 PE	1 PT/PE
	Compounding process	1 PT + 1 PE	1 PT + 1 PE	Robot + 1 PT/ PE
	Checking the weight of the preparation	1 PT + 1 PE	1 PT + 1 PE	Robot + 1 PT/ PE
	Checking the labels	1 PT + 1 PE	1 PT + 1 PE	1 PT/PE
	Labeling, packaging, and placing it in the lock for release	1 PT + 1 PE	1 PT + 1 PE	1 PT/PE
Release of preparation	Provisional release of the preparation	1 PT	n.a.	n.a.
	The final release of the preparation	1 Ph	1 Ph	1 Ph
Cleaning	Cleaning of workbench and working areas	1 PT/PE	1 PT/PE	Robot + 1 PT/ PE

n.a., not applicable; PE, pharmacy employee; Ph, pharmacist; PT, pharmacy technician.

In St. Antonius hospital, prescriptions were automatically sent from Epic, the electronic patient dossier (EPD), to CMS, the software for manual preparations. All instructions were digital and did not have to be printed on paper. In both of the Amsterdam UMC hospitals, the compounding instructions were printed on paper for manual preparations. The robots on location at VUmc and OLVG automatically sent all prescriptions from Epic to the APOTECA robot software. After the release, a message was sent back from the APOTECA software to Epic.

Definitions

To determine the impact on production capacity and direct labour costs, a comparison was made between manual, manual software-supported and robotic compounding by comparing data from St. Antonius hospital and Amsterdam UMC. We calculated the production of one compounding day (Pday) by dividing the total number of annual preparations by the total number of compounding days (260). For the Pday for manual compounding in Amsterdam UMC, the total number of annual manual preparations before implementation of the robot was used. The number of FTEs was based on the daily occupancy that is needed in the total compounding process to compound the Pday. The production capacity (P1FTE1day) was calculated by dividing the Pday by the number of FTEs. Because it seems that it is not possible to compound 100% of the preparations with a robotic system, we added a combined scenario of manual and robotic preparations. This scenario corresponds to the current situation in Amsterdam UMC. The total daily production capacity was estimated for each setting. Moreover, we determined the total amount of FTE (with a working week of 36 hours) needed per day for pharmacy employees, pharmacy assistants and pharmacists for each setting. By using the average salaries from the collective labour agreement for hospitals, we calculated the direct labour costs per day for each staff member. We used the these direct labour costs per FTE to estimate the costs per preparation in order to determine the difference between the three compounding methods. Pharmacy technicians (PTs) were in possession of a PT diploma and had higher salaries than pharmacy employees (PEs). Therefore, they were described as separate functionaries in tables 1 and 2. However, in both St. Antonius hospital and Amsterdam UMC, the PEs can be trained internally to perform (some of) the same tasks as PTs in the cleanroom.

RESULTS

Compounding times of individual drugs

The compounding times of the individual hazardous drugs are shown in table 3. In total, 121 manual preparations were measured in two hospitals, St. Antonius hospital and Amsterdam UMC. In addition, 2069 robotic compounding times were extracted from APOTECAchemo over 2 months. The manual compounding in St. Antonius hospital was the fastest compounding method, at 3:31 min (SD 2:00). This compounding method, which used software support, was 1:03 and 1:26 min faster than robotic compounding at OLVG (4:34 min, SD 1:46) and Amsterdam UMC (5:57 min, SD 2:33), respectively, and 1:33 min faster than the manual compounding method without software support in Amsterdam UMC (5:04 min, SD 2:18). Pemetrexed manual compounding times are missing in Amsterdam UMC because this preparation completely switched to robotic compound-

ing during the measurement period. Cyclophosphamide is the only drug where robotic compounding was faster than manual software-supported compounding.

Table 3. Compounding times measured per hazardous drug per location

Hospital	**St. Antonius hospital**		**Amsterdam UMC**				**OLVG**	
Name drug	**Manual compounding, software-supported**		**Manual compounding**		**Robotic compounding**		**Robotic compounding**	
	N	Average compounding time, min (SD)	N	Average compounding time, min (SD)	N	Average compounding time, min (SD)	N	Average compounding time, min (SD)
Carboplatin	8	2:29 (SD 0:53)	11	4:37 (SD 1:25)	113	5:18 (SD 1:54)	157	6:15 (SD 2:24)
Cisplatin	4	2:23 (SD 0:08)	7	3:21 (SD 0:25)	122	6:22 (SD 3:39)	35	5:31 (SD 2:37)
Cyclophospha-mide	5	8:14 (SD 1:02)	9	8:17 (SD 0:59)	112	7:46 (SD 4:12)	141	5:25 (SD 1:45)
Cytarabine	4	2:42 (SD 0:59)	7	3:38 (SD 2:08)	94	3:36 (SD 1:39)	94	3:36 (SD1:39) *
Doxorubicin	9	3:25 (SD 1:37)	8	4:20 (SD 1:30)	131	4:37 (SD (1:19) **	131	4:37 (SD 1:19)
Irinotecan	5	2:17 (SD 0:25)	7	3:93 (SD 0:50)	51	4:00 (SD 1:06)	95	4:00 (SD 1:03)
Oxaliplatin	5	3:20 (SD 1:04)	9	4:41 (SD 1:19)	137	4:31 (SD 0:57)	160	4:35 (SD 1:16)
Paclitaxel	8	3:41 (SD 1:53)	12	4:17 (SD 1:08)	197	3:42 (SD 1:00)	369	3:46 (SD 1:14)
Pemetrexed	3	3:04 (SD 0:49)	-	- ***	75	5:57 (SD 0:54)	80	4:39 (SD 0:55)
Total average compounding time	51	3:31 (SD 2:00)	70	5:04 (SD 2:18)	1032	5:57 (SD 2:33)	1262	4:34 (SD 1:46)

*Cytarabine time and SD from Amsterdam UMC taken over due to missing data
**Doxorubicin time and SD of OLVG taken over due to missing data
***Pemetrexed manual compounding is missing in Amsterdam UMC due to the switch to robotic compounding

Times per compounding phase

The total compounding process, including the actions before compounding and the release and cleaning time lasted 6:44 min with robotic compounding, and 6:48 and 9:48 min with manual compounding with and without software support, respectively (fig. 2). In the phase before compounding, the robot time measurement was 0:00 min, while the manual compounding time measurements were 2:20 min (SD 0:17) at St. Antonius hospital and 3:36 min (SD 1:44) at Amsterdam UMC. The compounding itself was faster when using the manual compounding settings: 3:31 min (SD 2:00) at St. Antonius hospital and 5:04 min (SD 2:18) at Amsterdam UMC versus 5:57 min (SD 2:33) with robotic compounding. The time required for releasing the preparation was not much

different between robotic and manual compounding at Amsterdam UMC, and manual compounding at St. Antonius hospital, 0:44 min (SD 0:37), 0:56 min (SD 0:34) and 0:45 min (SD 0:11), respectively. One cleaning of a robot takes more time than the cleaning of a safety cabinet used for manual compounding (21:08 min vs 13:17 min, respectively). However, APOTECAchemo robots only need to be cleaned once a week instead of every day, so the cleaning time per preparation was more favourable to the robot (0:03 min) compared with manual preparation at Amsterdam UMC (0:15 min) and St. Antonius hospital (0:12 min).

Production capacity and direct labour costs

The production capacity of one FTE on 1 day (P1FTE1day) was 15 preparations with manual compounding with and without software support, and 57 preparations per PTE

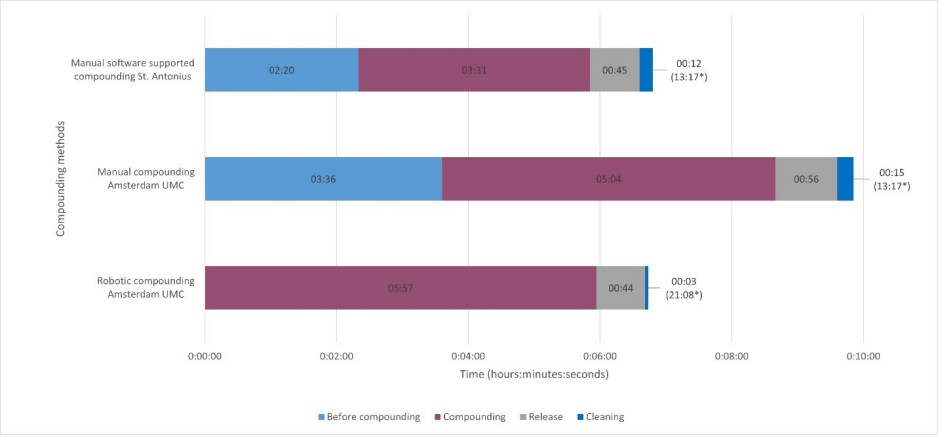

Fig. 2 Compounding and cleaning times per phase and per preparation for all different compounding processes. *Average cleaning time of one cleaning, used to calculate the cleaning time per preparation. Hereby taking into account that the robot was cleaned once a week and the safety cabinets for manual preparations every day.

per day with only robotic compounding (table 4). This implies that the P1FTE1day of robotic compounding is over three times higher compared with manual compounding. When manual and robotic compounding were combined, reflecting a more real-world situation, the P1FTE1day was 30 at Amsterdam UMC, which is two times higher than only manual compounding (P1FTE1day = 15) at the same centre. More specifically, when manual and robotic compounding were combined, the direct labour costs per preparation were €5.21, while these costs were €13.18 with only manual compounding.

Table 4. Production capacity and direct labour costs analysis per location.

		St. Antonius hospital	Amsterdam UMC		
Type of compounding →		**Manual software supported**	**Manual**	**Robotic**	**Manual + robotic**
Production and FTE	P_{day}	125	105	70	35 (manual) + 70 (robot)
	FTE	5.56 PE 2.99 PT 0.07 Ph 8.62 in total	2.22 PE 4.44 PT 0.23 Ph 6.89 in total	0.56 PE 0.56 PT 0.12 Ph 1.23 in total	1.08 PE 2.17 PT 0.20 Ph 3.45 in total
	$P_{1FTE1day}$	15	15	57	30
Labour costs per preparation (euro)	C_{1prep}	€ 12.66	€ 13.18	€ 3.73	€ 5.21

P_{day} = production of one compounding day = number of preparations compounded on one day at the hospital concerned.
FTE = Full-Time Equivalent (with 36 hours working week) staff required for compounding.
$P_{1FTE1day}$ = production capacity of one FTE on one day = the number of preparations that one FTE can compound on one day; W_{day} / FTE.
C_{1prep} = labour costs per preparation = labour costs of all staff for one day divided by the workload of one compounding day (P_{day}). Salaries of staff were based on average salaries for the relevant positions according to the Collective Labor Agreement for Hospitals.
PE, pharmacy employee; Ph, pharmacist; PT, pharmacy technician.

DISCUSSION

This study evaluated the amount of time, production capacity and direct labour costs required by manual volumetric, manual software-supported and robotic compounding of parenteral hazardous drugs. It is relevant to compare these different compounding methods owing to the increase in requested chemotherapy and the growing shortage of qualified personnel. We show that the use of an APOTECAchemo robot can cope with the growing shortage of personnel. More specifically, robotic compounding was faster over the total compounding process and provided a higher production capacity of the staff and lower direct labour costs compared with manual compounding.

When analysing only the actual compounding times, the manual compounding of individual drugs was faster for most drugs compared with robotic compounding, which is in line with earlier studies.[10-13] A 2014 study at a cancer centre in Italy comparing the APOTECAchemo robot with manual preparations in terms of quality, economic sustainability and compounding time found that robotic compounding always takes more time than manual compounding. Six of the same drugs were included in our study. The only difference among our results was that we found that cyclophosphamide was compounded faster by the robot. This can be explained by a difference in measuring methods between

the two studies. We did not include the dissolution time of the vial in our study because the robot arm can continue with the next preparation while dissolving the vial(s).

When comparing both hospitals that used manual compounding, St. Antonius had an average compounding time of 3:31 min (SD 2:00), which was faster than Amsterdam UMC (5:04 min, SD 2:18). This difference could be attributed to the software support available during compounding for the pharmacy technicians at St. Antonius hospital. The software received the prescription via a link with the electronic patient file, which prevented the overwriting of data and manual calculations and ensured that printing of preparation prescriptions was not necessary.

Comparing the average compounding time in both settings with robotic compounding, there is a difference of 1:23 min in favour of OLVG. This may be because the employees at OLVG gained more experience with working with the robot. After all, their robot was implemented in 2017, 4 years earlier than Amsterdam UMC. Other factors that influenced work efficiency after the implementation of a robot were the size of the drug vials used and the drug volumes required for the preparations.[14]

In contrast to the actual compounding time of individual hazardous drugs, the total time of the compounding process was shorter during robotic compounding. Robotic compounding saved time in the phases before compounding and cleaning. With robotic compounding, no time was required to get the supplies ready, because all supplies were already present in the cleanroom and the robot itself carried out the security checks. The time for loading and unloading the supplies was not measured, because the robot arm can continue the compounding of another preparation during these actions. In addition, robotic compounding led to less cleaning time because the robot was cleaned once a week and the safety cabinets for manual compounding were cleaned every day. After the introduction of the robot in Amsterdam UMC, the cleaning frequency was reduced in phases from daily to weekly based on extensive microbiological monitoring results, wipe tests and research from a hospital pharmacy in Mainz.[15] Daily cleaning activities in robotic compounding only involved turning on the ultraviolet lamps overnight and cleaning the pump that withdraws liquid from an infusion bag. These results are in line with Capilli *et al*,[7] who showed that automation of the compounding process could meet the growing demand for treatments without a parallel increase in staff. While their production increased by 22%, the number of resources dedicated to the compounding activities remained unchanged at 7.5 FTE.[7]

Our study is the first multicentre study to evaluate the required amount of time and production capacity of three different compounding methods for parenteral hazardous

drugs: manual, manual software-supported and robotic compounding. Whereas most previous comparative studies only evaluated the actual time of compounding, we evaluated the total compounding process.[5,10,16,17] By also carrying out an evaluating at a process level, we determined how many preparations one FTE can produce in a day using the different compounding methods. This demonstrates that each staff member can compound half of the preparations with the manual compounding process compared with a process where manual compounding is combined with an APOTECAchemo robot.

Clearly, there are several limitations to the present study. First, the pharmacy technicians knew that they were being timed during the manual compounding process, which may have influenced them to work faster or slower. To prevent this, we instructed the technicians to work at their usual pace. Second, direct labour costs differ per country, compounding processes differ per institute and the results of our study are specific for APOTECAchemo robots. Therefore, the results cannot directly apply to pharmacies in different countries or institutions that use another robot.

Third, the number of manual preparations, which depended on the prescriptions within our measurement period, was much lower than for robot preparations. This could cause bias, as different drug doses and associated drug volumes correlate with the compounding time of individual preparations. Finally, we assumed a robotic compounding process in which loading, unloading and dissolving are not included in the time measurements because the robot arm can work on another preparation at that time. However, the employees that work with the robot must be properly trained to load and unload at the right time; namely, at moments when the robot arm does not need any new materials from the loading area. This prevents the loss of time waiting for the robot arm on completion of the loading process. If these actions do not take place as instructed, this can positively influence the results in favour of the robot. To solve this limitation, we recommend using the mean preparations per hour in order to describe the overall speed of the robot in follow-up research. This was also advised in a recently published multicenter study.[14] In doing so, any time lost owing to the robot employee not working 100% efficiently is also included in the time measurements. We also advise hospitals considering robotic compounding to study the satisfaction of the pharmacy technicians before and after the implementation of a robot. Staff is scarce, which makes it important to know whether robotic compounding can contribute to work satisfaction; for example, through fewer health and safety complaints, more involvement in innovations and more task differentiation.

CONCLUSION

Compared with manual compounding, robotic compounding was faster over the total compounding process owing to the time saved in the phases before compounding and cleaning. A combination of manual compounding and robotic compounding could lead to 100% more preparations per FTE and 2.5 times lower direct labour costs compared with manual compounding.

REFERENCES

1. Kocarnik JM, Compton K, Dean FE, et al. Cancer Incidence, Mortality, Years of Life Lost, Years Lived With Disability, and Disability-Adjusted Life Years for 29 Cancer Groups From 2010 to 2019: A Systematic Analysis for the Global Burden of Disease Study 2019. *JAMA oncology* 2022; **8**(3): 420-44.
2. Schneider PJ, Pedersen CA, Ganio MC, Scheckelhoff DJ. ASHP national survey of pharmacy practice in hospital settings: Workforce-2018. *Am J Health Syst Pharm* 2019; **76**(15): 1127-41.
3. Zamani M, Chan K, Wilcox J. Pharmacy Technicians' Perceptions of Risk Reduction Strategies Implemented in Response to the Repetitive Strain Injury Associated with Sterile Compounding. *International journal of pharmaceutical compounding* 2021; **25**(3): 182-6.
4. Pang B, Earl M, Knoer S, Yaniv A, Willner M, Boyd A. Comparison of IV oncology infusions compounded via robotics and gravimetrics-assisted workflow processes. *Am J Health Syst Pharm* 2021; **78**(2): 122-34.
5. Batson S, Mitchell SA, Lau D, et al. Automated compounding technology and workflow solutions for the preparation of chemotherapy: a systematic review. *European journal of hospital pharmacy : science and practice* 2020; **27**(6): 330-6.
6. Baan SD, Geersing TH, Crul M, Franssen EJF, Klous MG. An economic evaluation of vial sharing of expensive drugs in automated compounding. *International journal of clinical pharmacy* 2022; **44**(3): 673-9.
7. Capilli M, Enrico F, Federici M, Comandone T. Increasing pharmacy productivity and reducing medication turnaround times in an Italian comprehensive cancer center by implementing robotic chemotherapy drugs compounding. *J Oncol Pharm Pract* 2021: 1078155221992851.
8. Geersing TH, Klous MG, Franssen EJF, van den Heuvel JJG, Crul M. Robotic compounding versus manual compounding of chemotherapy: Comparing dosing accuracy and precision. *Eur J Pharm Sci* 2020; **155**: 105536.
9. Werumeus Buning A, Geersing TH, Crul M. The assessment of environmental and external cross-contamination in preparing ready-to-administer cytotoxic drugs: a comparison between a robotic system and conventional manual production. *Int J Pharm Pract* 2020; **28**(1): 66-74.
10. Masini C, Nanni O, Antaridi S, et al. Automated preparation of chemotherapy: quality improvement and economic sustainability. *Am J Health Syst Pharm* 2014; **71**(7): 579-85.
11. Iwamoto T, Morikawa T, Hioki M, Sudo H, Paolucci D, Okuda M. Performance evaluation of the compounding robot, APOTECAchemo, for injectable anticancer drugs in a Japanese hospital. *J Pharm Health Care Sci* 2017; **3**: 12.
12. Nurgat Z, Faris D, Mominah M, et al. A three-year study of a first-generation chemotherapy-compounding robot. *Am J Health Syst Pharm* 2015; **72**(12): 1036-45.
13. Yaniv AW, Knoer SJ. Implementation of an i.v.-compounding robot in a hospital-based cancer center pharmacy. *Am J Health Syst Pharm* 2013; **70**(22): 2030-7.
14. Riestra AC, López-Cabezas C, Jobard M, et al. Robotic chemotherapy compounding: A multicenter productivity approach. *J Oncol Pharm Pract* 2021: 1078155221992841.
15. Krämer I, Federici M, Kaiser V, Thiesen J. Media-fill simulation tests in manual and robotic aseptic preparation of injection solutions in syringes. *J Oncol Pharm Pract* 2016; **22**(2): 195-204.
16. Palma E, Bufarini C. Robot-assisted preparation of oncology drugs: the role of nurses. *Int J Pharm* 2012; **439**(1-2): 286-8.
17. Palma E, Bufarini C. Robotized compounding of oncology drugs in a hospital pharmacy. *International journal of pharmaceutical compounding* 2014; **18**(5): 358-64.