Systematic Review and Meta-Analysis

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Intravenous compounding robots in pharmacy intravenous admixture services

A systematic review

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Abstract

Background: There is a lack of best evidence of intravenous compounding robots for hospital decision-makers. This study aimed to conduct a systematic review of intravenous compounding robots.

Methods: A comprehensive search of relevant professional health technology assessment websites and electronic databases was conducted from inception to February 3, 2022. Current studies related to intravenous compounding robots were included in this systematic review. Two reviewers independently screened the literature, extracted data, and assessed quality. The results were reported by qualitative description because of heterogeneity in the characteristics of the data in the included studies.

Results: Thirty-three studies were included. Effectiveness: The robots improved production efficiency compared with usual/manual preparation; however, the intravenous preparation process requires further optimization. Additionally, robots reduced the incidence of medicine residues, preparation errors, and preparation failures. The solution properties of intravenous admixture medicines were satisfactory, and the robots also contributed to error recognition. Safety: The robots reduced product pollution and environmental pollution, but vigilance is still required to ensure that pollution stays low. The robots also reduced the incidence of health damage to technicians. Economy: The robots reduced material costs in these studies; however, whether they can reduce labor costs remains unclear. Social suitability: Technicians had a high degree of satisfaction with the robots, but few relevant studies focused on this aspect.

Conclusions: Intravenous compounding robots have certain advantages in terms of effectiveness, safety, economy, and social adaptability.

Abbreviations: HTA = Health Technology Assessment, PIVAS = pharmacy intravenous admixture services, RCTs = randomized controlled trials

Keywords: automation, intravenous admixture medicine, intravenous compounding robot, systematic review

1. Introduction

The pharmacy intravenous admixture service (PIVAS) is an essential department involved in the centralized preparation and supply of intravenous admixture medicines in medical institutions.[1] With the increasing demand for intravenous admixture medicines, completion of the preparation by manual labor alone will result in problems such as low efficiency, numerous errors, and high risks. One systematic review showed that the incidence of an incorrect dose, incorrect concentration, and inadequate aseptic technique in the preparation of intravenous admixture medicines in medical institutions was 32.6%, 88.6%, and 92.7%, respectively.[2] A multicenter study showed that PIVAS staff face severe health risks due to the manual preparation of anti-tumor drugs.[3] Another multicenter survey showed that PIVAS nurses were under great pressure because of the fear of medical accidents and occupational injuries, insufficient sleep, and fatigue.[4]

With the rapid development of electronic information technology, increasingly more intelligent software and equipment are being applied to PIVAS.[5] According to data released by the

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As this manuscript contains no individual personal data, consent for publication is not applicable.

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

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Table 1

Search strategy and results of searching.

1.1 Professional HTA database	
Website name	**Website**
International Network of Agencies for Health Technology Assessment (INAHTA)	http://www.inahta.org/
Health Technology Assessment International (HTAi)	https://htai.org/
International Credential Evaluation Service (ICES)	https://www.bcit.ca/ices/
International Society for Pharmacoeconomics and Outcomes Research (ISPOR)	https://www.ispor.org/
European Health Network for Technology Assessment (EUnetHTA)	https://eunethta.eu/
National Institution for Health Research (NIHR)	https://www.nihr.ac.uk/explore-nihr/funding-programmes/health-technology-assessment.htm
Canadian Agency for Drugs and Technologies in Health (CADTH)	https://www.cadth.ca/
Australian Government Department of Health-Health Technology Assessment (AGDHHTA)	https://www1.health.gov.au/internet/hta/publishing.nsf/Content/home-1
Swedish Agency for Health Technology Assessment and Assessment of Social Services (SBU)	https://www.sbu.se/en/

1.2 English database			
English database	PubMed	Embase	Cochrane
Search strategy	((((intravenous[Title/Abstract]) OR (Infusion*[Title/Abstract])) OR (Infusions, Intravenous[MeSH Terms])) AND ((((((robot*[Title/Abstract]) OR (robotics[MeSH Terms])) OR (Automat*[Title/Abstract])) OR (Automation[MeSH Terms])) OR (Intelligen*[Title/Abstract])) OR (Artificial Intelligence[MeSH Terms])) AND (((((Admixture*[Title/Abstract]) OR (deploy*[Title/Abstract])) OR (compound*[Title/Abstract])) OR (dispens*[Title/Abstract])) OR (prepar*[Title/Abstract]))	#1 exp intravenous drug administration/ or intravenous.mp. #2 exp infusion/ #3 Infusion*.mp. #4 #1 or #2 or #3 #5 robot*.mp. #6 exp robotics/ #7 Automat*.mp. #8 exp automation/ #9 Intelligen*.mp. #10 exp artificial intelligence/ #11 #5 or #6 or #7 or #8 or #9 or #10 #12 Admixture*.mp. #13 deploy*.mp. #14 compound*.mp. #15 dispens*.mp. #16 prepar*.mp. #17 #12 or #13 or #14 or #15 or #16 #18 #4 and #11 and #17	#1 (intravenous):ti.ab.kw #2 (Infusion*):ti.ab.kw #3 MeSH descriptor: [Infusions, Intravenous] explode all trees #4 #1 or #2 or #3 #5 (robot*):ti.ab.kw #6 MeSH descriptor: [robotics] explode all trees #7 (Automat*):ti.ab.kw #8 MeSH descriptor: [automation] explode all trees #9 (Intelligen*):ti.ab.kw #10 MeSH descriptor: [artificial intelligence] explode all trees #11 #5 or #6 or #7 or #8 or #9 or #10 #12 (Admixture*):ti.ab.kw #13 (deploy*):ti.ab.kw #14 (compound*):ti.ab.kw #15 (dispens*):ti.ab.kw #16 (prepar*):ti.ab.kw #17 #12 or #13 or #14 or #15 or #16 #18 #4 and #11 and #17

1.3 Chinese database				
Chinese database	CNKI	WanFang	VIP	CBM
Search strategy	SU=(“静脉”+“静注”+“静滴”+“输液”) AND SU=(“配药”+“配液”+“调配”+“配置”) AND SU=(“机器人”+“智能”+“自动”)	(主题:(“静脉”)+主题:(“静滴”)+主题:(“静注”)+主题:(“输液”))*(主题:(“配药”)+主题:(“配液”)+主题:(“调配”)+主题:(“配置”))*(主题:(“机器人”)+主题:(“智能”)+主题:(“自动”))	(M=静脉 OR R=静脉 OR M=静注 OR R=静注 OR M=静滴 OR R=静滴 OR M=输液 OR R=输液) AND (M=配药 OR R=配药 OR M=配液 OR R=配液 OR M=调配 OR R=调配 OR M=配置 OR R=配置) AND (M=机器人 OR R=机器人 OR M=智能 OR R=智能 OR M=自动 OR R=自动)	(“静脉”[常用字段:智能] OR “静滴”[常用字段:智能] OR “静注”[常用字段:智能] OR “输液”[常用字段:智能] OR “输注, 静脉内”[加权:扩展]) AND (“配药”[常用字段:智能] OR “配液”[常用字段:智能] OR “调配”[常用字段:智能] OR “配置”[常用字段:智能]) AND (“机器人”[常用字段:智能] OR “智能”[常用字段:智能] OR “自动”[常用字段:智能] OR “机器人”[加权:扩展])

HTA = Health Technology Assessment.

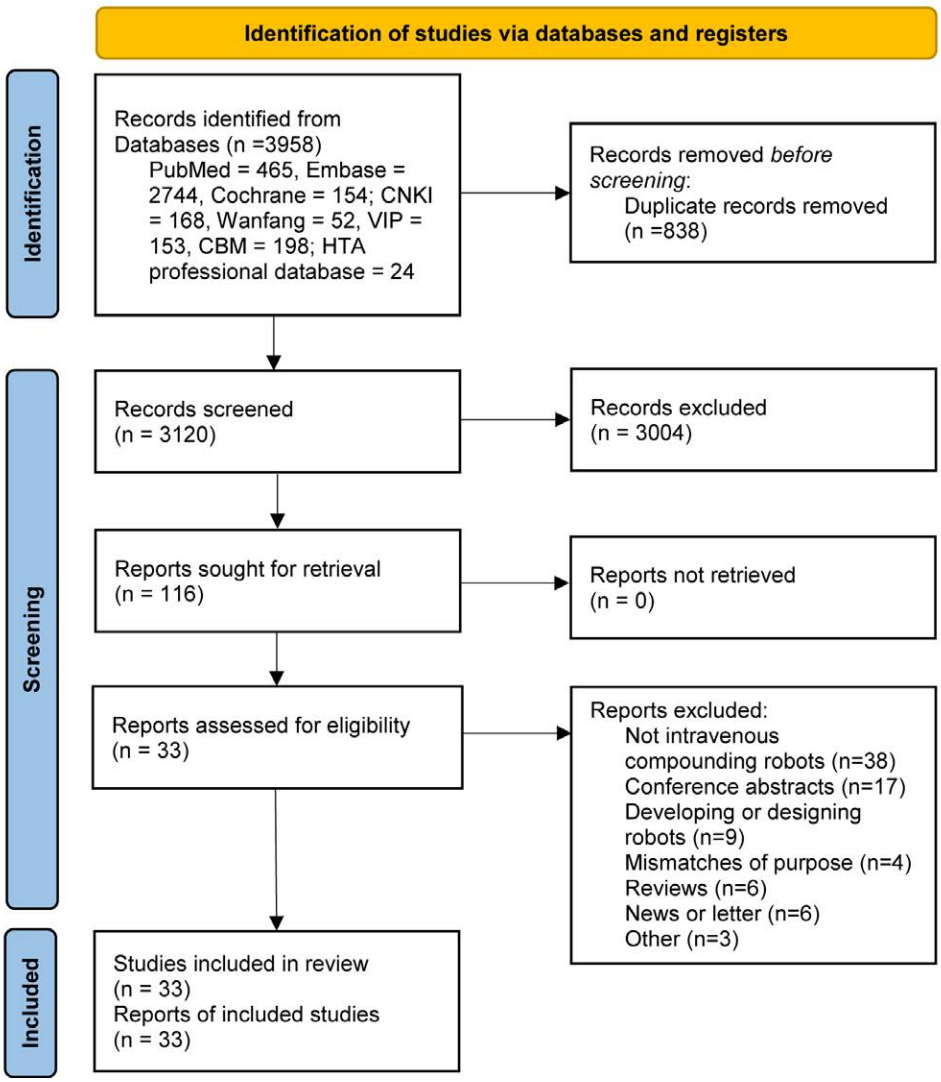

Figure 1. The process of study selection.

American College of Hospital Pharmacists, 0.3% of hospitals have introduced intravenous compounding robots.[6] In 2014, Urbine et al[7] found that the use of the robotic device prevented 5420 medication errors and resulted in an associated savings of $288,350 per year. In 2019, Amodeo et al[8] found that the application of intravenous compounding robots increases precision, improves safety, decreases costs, and saves time.

However, in 2013, Chen et al[9] assessed the human resource cost after applying robot technology and found that robots were unable to improve the full-time equivalents of pharmacists/technicians. In 2015, Nurgat et al[10] reported that robots were used to prepare only 13.79% of anti-tumor drugs in the third year after installation, and 15% of intravenous admixture medicines failed to meet the dose accuracy requirement.

Considering the significant differences in the evaluations of intravenous compounding robots in China and abroad, it is necessary to conduct a systematic review to evaluate the effectiveness, safety, and economy of intravenous compounding robots. Although Health Technology Assessment (HTA) reports on this topic already exist, the number and quality of the included original studies were low,[11,12] and the recent existing review only concentrates on the function of introducing different robots.[5] So we performed the present systematic review to evaluate the application of intravenous compounding robots and thus provide evidence for the introduction of intravenous compounding robots in PIVAS.

2. Methods

2.1. Inclusion and exclusion criteria

The inclusion criteria for this assessment were as follows. Study types: comprehensive HTA reports, systematic reviews/meta-analyses, randomized controlled trials (RCTs), nonRCTs (NRCT), prospective/retrospective observational studies, and economic studies. Study objects: Intravenous admixture medicines that were prepared in the hospital pharmacy. Interventions/comparisons: An intravenous compounding robot was applied in the intervention group, and conventional/traditional manual preparation or other types of intravenous compounding robots were applied in the control group; studies without the control group also were acceptable. Outcomes: Including but not limited to effectiveness outcomes, safety outcomes, economic outcomes, and social suitability outcomes.

The exclusion criteria were as follows: literature without available full texts and conference abstracts; news, subjective views, and editorials; and repeated published literature.

2.2. Search strategy

First, we searched professional HTA databases. Next, we searched English databases including PubMed, Embase, and The Cochrane Library, and Chinese databases including CNKI, VIP, CBM, and Wanfang Database. Table 1 shows the detailed search strategy. The first retrieval period was from database inception to August 11, 2020, and recently we updated the search on February 3, 2022. Finally, we manually searched the references of the included studies as supplements.

2.3. Literature screening and data extraction

Two researchers independently screened the literature and extracted the data. Disagreements were resolved by discussions or a decision by the third researcher. The necessary information with uncertainty was obtained by contacting the authors of the original studies.

2.4. Quality assessment of literature

The quality of the included original studies was assessed independently by 2 researchers. HTA Checklist was used to evaluate the quality of HTAs. The original studies selected different scales (such as the Cochrane Risk of Bias Tool and Risk of Bias in Nonrandomized Studies-of Interventions Tool) for quality assessment according to study types. The quality of pharmacoeconomic studies was assessed by the Quality of Health Economic Studies.

2.5. Data analysis

Meta-analysis is not suitable due to the differences in intravenous admixture medicines, robot models, operating procedures, and other characteristics in the included studies. Therefore, this study only conducts a qualitative analysis of the data.

2.6. Ethics approval and consent to participate

All participants completed and signed an informed consent form before the survey started. This study was approved by the Institutional Review Board of West China Second University Hospital, Sichuan University.

3. Results

3.1. Result of literature search

In total, 3361 studies were obtained from English databases, and 568 studies were obtained from Chinese databases. All studies were screened strictly in accordance with the inclusion and exclusion criteria. Finally, 33 studies[7–39] included 2 HTAs, 16 controlled studies, 13 noncontrolled studies, 1 qualitative study, and 1 economic study. The literature inclusion process and results are shown in Figure 1. The literature excluded in the screening of full text and the reasons for exclusion can be found in Table 2.

3.2. Results of quality assessment

The quality assessment of HTAs showed the quantity of evidence was small and the quality was low. The quality assessment of the economic study showed the quality score (89 points) was relatively high. The description of the methodology in the qualitative study was not clear and it was difficult to assess the quality. In addition, the survey report didn't have an appropriate scale for quality assessment. Details of quality assessments for RCTs, NRCTs, and single-arm studies can be found in Table 3, and the results showed their qualities were acceptable.

3.3. Results of comprehensive analysis

3.3.1. HTAs. Two HTAs[11,12] were included (Table 4); both were published by the Canadian Agency for Drugs and Technologies in Health in 2013 and 2016. The results of these 2 HTAs showed that automation for the preparation of intravenous admixture medicines had certain security and economy. However, because the number and quality of the included original studies were low, it is necessary to update the currently available HTAs or reevaluate the available data. Other HTA databases didn't yet contain any evaluations of intravenous compounding robots.

3.3.2. Original studies. Thirty-one original studies[7–10,13–39] were included and published from 2013 to 2021 by researchers from 11 countries. As classified by study type, these studies comprised 16 controlled studies (4 RCTs, 12 NRCTs), 13 noncontrolled studies (12 single-arm studies, 1 investigation report), 1 qualitative study (in-depth interview), and 1 economic study. Different models of robots were applied in different studies, such as the CytoCare System (Health Robotics), APOTECAchemo System (APOTECA), i.v.STATION System (Aesynt). The sample size of each study ranged from 10 to 11,865, and the observation time ranged from 2 days to 3 years. The main types of intravenous admixture medicines were anti-tumor drugs (16 studies, 51.61%), and other types of medicines included antibiotics, antivirals, traditional Chinese medicine injections, and hemostatics (1 study for each type), and another part of the studies did not classify or report the types of medicines. The basic information of included original studies was detailed in Table 5.

3.3.2.1. Effectiveness.

3.3.2.1.1. Production efficiency. Fifteen studies[7,9,10,13–16,18,19,22,26,28–30,34–37] evaluated production efficiency. Three control studies[13–16,18,35] showed that the number of preparations in the robot groups per unit time was significantly higher than that in the manual group ($P < .05$). One noncontrolled study[30] also showed that the robot had good production efficiency, and one in-depth interview[28] revealed that the robot improved the production efficiency by 3 to 5 times compared with the traditional manual preparation. Four studies showed that with increases in pharmacists' familiarity with robots[10,34] and increases in the quantity of preparations,[7,26,34] the production efficiency of the robot groups was further improved. In one controlled study,[19] the number of preparations by the robot reached 70.4% of the total number of preparations in the inpatient ward, and similarly, another controlled study[37] showed the annual output increased by 50.4% after the introduction of the robot. However, one controlled study[22] showed that the average preparation time in the robot group increased by 47% compared with that in the robot group but that the pharmacists' working time decreased by 76%, and similarly, another controlled study[36] also showed the number of preparations in the robot groups per unit time was significantly lower than that in the manual group ($P < .05$). Similarly, another controlled study[9] showed that the average number of preparations by the robot in 7 hours was comparable with that by the trained and experienced pharmacy staff in 2 to 3 hours. Another noncontrolled study[29] showed that although robots can significantly improve production efficiency, the manual preprocessing and postprocessing steps

were time-consuming and had to be reorganized. The outcomes and conclusions of the included studies were detailed in Table 6, and the detailed tabulated results were detailed in Table 7.

3.3.2.1.2. Medicine residues. Eleven studies[13–16,18,19,28,34–36,39] evaluated medicine residues. Eight controlled studies[13–16,18,19,35,36] conducted a quantitative analysis of medicine residues, and the results of all studies showed that the rates of residues in the robot groups were significantly lower than those in the manual groups ($P < .05$). Two noncontrolled studies [28,39] also showed that the use of robots reduced medicine residues, and another in-depth interview[34] showed that the robots reduced the residual amount of some insoluble medicines and alerted the technicians through an alarm when the residual amount was large. The outcomes and conclusions of the included studies were detailed in Table 6, and the detailed tabulated results were detailed in Table 7.

3.3.2.1.3. Preparation errors or failures. Nine studies[14–17, 19, 23, 29, 35, 37] evaluated the incidence of preparation errors. Seven controlled studies[13–16,18,22,36] conducted a quantitative analysis on the incidence of preparation errors, and all results showed that the incidence of preparation errors in the robot groups was significantly lower than that in the manual group ($P < .05$). One noncontrolled study[28] and one in-depth interview[34] also showed that the robots could reduce the incidence of preparation errors by warning, without interference by factors such as visual fatigue. The outcomes and conclusions of the included studies were detailed in Table 6, and the detailed tabulated results were detailed in Table 7.

Five studies[9,10,25,30,32] evaluated the incidence of preparation failures. The model used in 2 of the studies was the CytoCare, and the incidence of failures was 12% (n = 1028)[10] and 18.7% (n = 4509),[9] respectively. The model used in another study was the APOTECAChemo, and the incidence of failures was 2.44% (n = 11,642).[30] A 3-year real-world study[25] showed that the percentage of actual failed preparations was <1% by RIVA. The reasons for preparation failures included robot shutdowns, mechanical failures, recalibration, and other practical problems.[9] However, as the application time increases, the rate of preparation success might gradually improve. For example, one study[10] showed that the rate of preparation success increased from 76.8% in week 1 to 95.3% in week 10. In addition, 1 noncontrolled study[30] evaluated the robots' role in error recognition and showed that the robot recognized 1.12% (n = 11,865) of errors that would have caused harm to patients. The outcomes and conclusions of the included studies were detailed in Table 6, and the detailed tabulated results were detailed in Table 7.

3.3.2.1.4. Solution properties. One RCT[21] evaluated the properties of the solutions prepared by the robots. By measuring antibody aggregation, the study[21] concluded that robotic compounding of monoclonal antibodies was feasible and that the robot could be used to achieve reproducible high-quality compounding for delicate formulations. The outcomes and conclusions of the included studies were detailed in Table 6.

3.3.2.2. Safety.

3.3.2.2.1. Product pollution. Nine studies[23,24,26,27,29,31,33,34,39] evaluated product pollution. Six studies[23,24,26,27,29,39] did not detect microbial pollution, and one study[31] showed that noncontaminated bags were not contaminated after preparation. One in-depth interview[34] revealed that the robot was cleaner than the biological safety cabinet because it had an air channel cleaning system and a closed negative-pressure environment. However, an investigation showed that microbial contamination might originate from the washing station, which was easily ignored.[33] Another study showed that the technicians' gloves were also key sites of microbial contamination.[23] The outcomes and conclusions of the included studies were detailed in Table 6, and the detailed tabulated results were detailed in Table 7.

3.3.2.2.2. Environmental pollution. Nine studies[17,19,20,23,24,26,27,31,38] evaluated environmental pollution. Two controlled studies[17,20,38] showed that the external pollution of the robots was relatively low through monitoring gloves, infusion bags, and other equipment, indicating that environmental pollution could be improved. One noncontrolled study[26] detected only 1 type of contamination associated with pulling the needle out of the syringe, which was very small (spots of <3 mm) but relatively frequent (11%). Pollution was mainly observed inside the robot,[31] especially in the area of the dosing device.[19,20,27] The robot was able to perform automatic microbial decontamination by ultraviolet radiation.[24] One controlled study and one noncontrolled study showed that the settling plate/contact plate met the recommended limits set for cleanroom Grade A zones,[27] and that the surface and air samples complied with an ISO 5 class environment,[23] indicating that the robots had well-controlled programs. The outcomes and conclusions of the included studies were detailed in Table 6, and the detailed tabulated results were detailed in Table 7.

3.3.2.2.3. Health damage. Eleven studies[13–16,18,19,22,28,31,34,36] assessed health damage to the technical personnel. Six controlled studies[13–16,18,36] performed a quantitative analysis of the incidence of health damage to technical personnel in 2 groups, and all results showed that the incidence of health damage to technical personnel was significantly lower in the robot groups than in the manual groups ($P < .05$). One noncontrolled study[28] also showed that the robot could provide effective occupational protection for nurses. In an in-depth interview,[34] all interviewees were nurses in the oncology ward and daytime chemotherapy center, and they felt strongly about the occupational protection provided by the robots. Two studies[19,31] showed that no contaminant exposure was found in the gloves or on the hands of the technicians after applying the robots. The outcomes and conclusions of the included studies were detailed in Table 6, and the detailed tabulated results were detailed in Table 7.

3.3.2.3. Economy. Four studies[7,8,10,22] conducted an economic evaluation. An economic study[8] showed that robots could reduce healthcare costs by preventing medication errors and reducing adverse drug events, saving an average of $288,350 per year. Two controlled studies[7,22] showed that robots could reduce costs by 8 to 66% by saving materials, and the cost savings might continue to rise with the increase in preparations.[7] However, another study[22] showed that the robots could not reduce labor costs: the mean total pharmacy labor costs per preparation was $5.22 and $5.10 per preparation in the baseline and intervention periods, respectively. Similarly, a study[10] also showed that the robots could not improve the full-time equivalent of a hospital general pharmacist/technician, and even needed additional on-site engineers to help resolve possible breakdowns. The outcomes and conclusions of the included studies were detailed in Table 6.

3.3.2.4. Social suitability. Only one study[25] investigated technicians' satisfaction with robots, and the results showed that responders agreed that the overall impression of robots was "very good." The outcomes and conclusions of the included studies were detailed in Table 6.

4. Discussion

4.1. Statement of principal findings

With respect to effectiveness, based on the currently available evidence, robots could improve production efficiency, but the

Table 2

The literature excluded in the screening of full text and the reasons for exclusion.

Author and year	Title	Reasons
Beels L 2015 [1]	Automated dispensing and injection of 18F-FDG decreases personnel radiation burden	Conference abstract
Cauwenbergh T 2018 [2]	Time savings and improved quality assurance of intravenous cytostatics with semiautomated dose-banding	Conference abstract
Culleton S 2019 [3]	Delivery of 18F-PSMA-1007 through an automatic infusion device	Conference abstract
Dekyndt B 2017 [4]	Assessment of 4 manual infusion devices of [18F]-fluorodeoxyglucose in a nuclear medicine department	Conference abstract
Emery S 2019 [5]	Validation of aseptic filling process of a new automated dispenser, Karl 100	Conference abstract
Federici M 2018 [6]	Media-fill simulation tests of infusion bags prepared in series by the compounding robot APOTE-CAchemo	Conference abstract
Jansson B 2011 [7]	Reduction of the absorbed dose to technologist's fingers from PET-radionuclides using an automatic injection robot	Conference abstract
Larg M I 2015 [8]	Technologist radiation exposure performing PET/CT using F-18-FDG automatic dispenser	Conference abstract
Lima S 2012 [9]	Impact of an automated FDG infusion system in radiation exposure to PET technologists	Conference abstract
Miyaji N 2015 [10]	Quantitative accuracy of F-18 FDG injection compared among 3 automated infusion devices	Conference abstract
Moretti A 2015 [11]	18F-Choline intravenously infusion with an automatic combined dispenser and injector system	Conference abstract
Power L 2012 [11]	Assessing cross-contamination and air contamination in a robotic IV compounder	Conference abstract
Riestra A C 2019 [13]	Productivity analysis of an automated compounding system for intravenous chemotherapy	Conference abstract
Sbaffo M 2017 [14]	Validation of the ultraviolet disinfection efficacy in a new robot for the sterile compounding of intravenous nonhazardous drugs	Conference abstract
Pancisi M 2017 [15]	18F-fluorodeoxyglucose intravenously infusion with an automatic combined dispenser and injector system	Conference abstract
Pugliese S 2017 [16]	Automated intravenous chemotherapy workflow: The added benefit to reduce potential medication errors	Conference abstract
Nurgat Z 2014 [17]	The impact of utilizing intravenous robotic dispensing in oncology pharmacy	Conference abstract
Unluturk M S 2018 [17]	A robotic system to prepare IV solutions	Developing or designing robots
Anonymous 1997 [19]	Automated compounding errors necessitate strict quality-assurance measures	Letter
Bruscolini F 2015 [20]	Evaluation of ultraviolet irradiation efficacy in an automated system for the aseptic compounding using challenge test	Mismatches of purpose – evaluating ultraviolet irradiation efficacy
McIntosh S T 2005 [21]	Using data from automated dispensing units to identify adverse drug reactions	Mismatches of purpose – identifying adverse drug reactions
Chung K 2005 [22]	Microbiologic quality-control study for the purpose of extending the use of transfer sets on the automix 3 + 3 and micromix automated total nutrient admixture compounding pumps	Mismatches of purpose-The use of the disposable transfer sets
Thompson C A 2008 [23]	Robotic workbench to prepare hazardous drugs	News
Lener M E 1987 [24]	The impact of i.v. drug delivery systems on hospital costs: Analysis and one-year followup	Not intravenous compounding robots
Miyaji N 2017 [25]	Comparison of 3 devices for automated infusion of positron-emitting radiotracers	Not intravenous compounding robots
Deng Y 2016 [26]	Risk factors for i.v. compounding errors when using an automated workflow management system	Not intravenous compounding robots
Karanfilovska D 2020 [27]	Use of a radiopharmaceutical multidose dispenser for positron emission tomography: risk assessment and mitigation measures for infection prevention	Not intravenous compounding robots
Lecchi M 2012 [28]	Validation of a new protocol for ^{18}F-FDG infusion using an automatic combined dispenser and injector system	Not intravenous compounding robots
Ybarra J V 2011 [29]	Sterility of pediatric lipid emulsions repackaged by an automated compounding device	Not intravenous compounding robots
Dehmel C 2011 [30]	Do centrally pre-prepared solutions achieve more reliable drug concentrations than solutions prepared on the ward?	Not intravenous compounding robots
Lo A 2014 [31]	Effect of adding piperacillin-tazobactam to automated dispensing cabinets on promptness of first-dose antibiotics in hospitalized patients	Not intravenous compounding robots
Ishimoto K 2001 [31]	Efficiency improvement of dispensing of drugs for injection by a total automatic injection dispenser system including infusion fluids and its evaluation	Not intravenous compounding robots
Cohen M R 1996 [33]	Medication errors associated with automated dispensing modules; Name confusion with new protease inhibitors	Other – full text not found
Cohen M R 2009 [34]	True allergy or other symptom? Too much hydromorphone; patient safety increased in obstetrics; medication patch slips into incorrect automated dispensing cabinet pocket; volume control set safety	Other – full text not found
Yaniv A W 2017 [35]	Robotic i.v. medication compounding: Recommendations from the international community of APOTE-CAchemo users	Other – recommendations
Soumoy L 2019 [36]	Automated compounding of intravenous therapy in European countries: A review in 2019	Reviews
Anonymous 2012 [37]	一种基于激光监测的输液监控及信息管理系统的研究	Developing or designing robots
付雪奇 2015 [37]	输液配药机器人设计及其专家系统控制	Developing or designing robots
李长有 2019 [39]	基于STM32F4的智能配液机设计与实现	Developing or designing robots
刘义刚 2009 [39]	OMRON产品在安瓿输液制剂自动药液调配系统上的应用	Developing or designing robots
吕开广 2004 [41]	医用自动配药系统研究	Developing or designing robots
孙承志 2011 [41]	台达自动化产品在输液贴包装设备上的整合应用	Developing or designing robots
王超 2013 [43]	一种新型智能配药设备的研究	Developing or designing robots
张开 2017 [44]	基于数字图像处理的自动输液设备的设计	Developing or designing robots
黄彩玲 2018 [45]	静配中心机器人配药试运行后工作质量和效率的方法探讨	Mismatches of purpose – how to effectively improve the working quality and efficiency in PIVAS
Anonymous 2016 [46]	医院"机器人护士"1分钟完成配药	News

(*Continued*)

Table 2

(*Continued*)

Author and year	Title	Reasons
Anonymous 2016 [47]	静脉用药配置机器人启用	News
郭潇雅 2018 [48]	静脉药智能调配新样本	News
新华网 2018 [49]	中国机器人亮相美国药学专业会议	News
程宗琦 2015 [50]	苏大附一院静脉药物调配中心信息化与自动化建设的实践	Not intravenous compounding robots
丁亦凡 2018 [51]	自动分拣机在静脉用药调配中心中的应用	Not intravenous compounding robots
董维娜 2005 [52]	多支架静脉输液加药自控装置的临床应用	Not intravenous compounding robots
黄继勋 2017 [53]	我院静脉用药集中调配中心自动化智能建设与实践	Not intravenous compounding robots
金岚 2019 [54]	智能自动化在降低静脉用药调配中心用药风险中的作用	Not intravenous compounding robots
李倚娴 2020 [55]	药品调配与核对智能化工作模式应用与评价	Not intravenous compounding robots
李媛媛 2017 [55]	全自动注药泵在胃肠道肿瘤患者中的应用及护理	Not intravenous compounding robots
连玉菲 2018 [57]	PIVAS自动分拣系统应用效果评价	Not intravenous compounding robots
连玉菲 2017 [58]	DS8000智能分拣系统在我院PIVAS的应用效果	Not intravenous compounding robots
连玉菲 2018 [59]	自动分拣系统的应用对我院PIVAS成品输液分拣工作的影响	Not intravenous compounding robots
刘生杰 2009 [59]	全自动针剂摆药机的引进与应用	Not intravenous compounding robots
刘毅 2014 [61]	我院静脉用药调配中心全自动口服药品摆药机应用体会	Not intravenous compounding robots
沈国荣 2013 [62]	智能摆药系统在静脉用药调配中心的应用	Not intravenous compounding robots
沈国荣 2019 [63]	全自动针剂摆药系统在PIVAS抗肿瘤药物摆药中的应用	Not intravenous compounding robots
沈国荣 2017 [64]	我院PIVAS的自动化建设与实践	Not intravenous compounding robots
邬晓岚 2011 [64]	药品智能存取系统在我院静配中心的应用及实践体会	Not intravenous compounding robots
尤晓明 2016 [66]	智能分拣系统在我院PIVAS中的应用	Not intravenous compounding robots
张永 2016 [67]	关于静脉用药调配中心智能传输分拣系统的探讨	Not intravenous compounding robots
钟丽君 2020 [68]	化疗泵药物输液器配置与传统配置方法的比较	Not intravenous compounding robots
周琴 2019 [69]	静脉输液预调配模式的质量控制和应用	Not intravenous compounding robots
朱米君 2013 [70]	静脉用药调配中心爱朋全自动注药泵的配置及注意事项	Not intravenous compounding robots
郁静 2015 [71]	我院住院药房自动化和信息化建设实践	Not intravenous compounding robots
王建敏 2018 [72]	医用智能配药药机与注射器抽吸药液效果的比较	Not intravenous compounding robots
沈国荣 2020 [73]	静脉输液自动加药混合调配系统在我院静脉用药调配中心的开发与应用	Not intravenous compounding robots
胡蕾 2016 [74]	自动配液机在临床配液中的应用	Not intravenous compounding robots
杨俊 2006 [75]	全自动配液仪对营养液中脂肪乳剂稳定性影响的研究	Not intravenous compounding robots
李新燕 2019 [76]	医院静脉用药调配中心的自动化系统建设与实践	Not intravenous compounding robots
李岩 2019 [77]	双向精密输液配液机在某院PIVAS的应用	Not intravenous compounding robots
宋岚 2019 [78]	新增智能化设备对静脉用药调配中心的影响研究	Not intravenous compounding robots
高天行 2016 [79]	浅谈自动化配置设备在静脉药物配置中心的应用前景和进展	Reviews
耿魁魁 2020 [80]	医疗机构静脉用药调配中心智能化发展现状与展望	Reviews
宫本文 2017 [81]	静脉输液自动化配药系统的研究	Reviews
刘丽萍 2014 [82]	全自动配液设备在数字化药房中的应用	Reviews
刘砚泽 2017 [83]	自动化配置设备在静脉药物配置中心的实际运用及发展前景	Reviews

PIVAS = pharmacy intravenous admixture services.

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Table 2

(Continued)

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intravenous preparation process still requires further optimization; robots could also reduce the incidence of medicine residues, preparation errors, and preparation failures; the solution properties of intravenous admixture medicines prepared by robots were satisfactory and the robots had a role in error recognition. With respect to safety, robots could reduce product pollution and environmental pollution; however, vigilance is still required to ensure that pollution stays low; additionally, robots could reduce the incidence of health damage to technicians. With respect to economic factors, robots could reduce material costs, but whether they could reduce labor costs remains to be further studied. Finally, in terms of social suitability, technicians had a high degree of satisfaction with the robots. However, there are relatively few relevant studies on this aspect at present.

Table 3

Quality assessments of randomized controlled trials, nonrandomized controlled trials, and single-arm studies.

Table 3.1 Results of quality assessment by Cochrane Risk of Bias (RoB) Tool

Randomized controlled trials	Cochrane risk of bias tool						
	Term 1	Term 2	Term 3	Term 4	Term 5	Term 6	Term 7
Wang YJ 2020	L	U	U	U	L	L	U
Cheng XL 2019	U	U	U	U	L	L	U
Jin Z 2018	U	U	U	U	L	L	U
Zhou HZ 2017	L	U	U	U	L	U	U

Table 3.2 Results of quality assessment by Risk of Bias In nonrandomized Studies-of Interventions (ROBINS-I)

Nonrandomized controlled trials and single-arm studies	ROBINS-I						
	Term 1	Term 2	Term 3	Term 4	Term 5	Term 6	Term 7
Werumeus Buning 2020	U	L	L	L	L	L	U
Yang P 2020	L	L	L	L	L	L	U
Amodeo 2019	U	L	L	L	L	L	L
Iwamoto 2017	U	L	L	L	L	L	U
Nurgat 2015	U	L	L	L	L	L	U
Schierl 2014	U	L	L	L	L	L	U
Peters 2013	U	L	L	L	L	L	U
Seger 2012	U	L	L	L	L	L	U
Jobard 2020	H	L	L	L	L	L	U
Sabatini 2019	U	L	L	L	L	L	U
Nurgat 2019	U	L	L	L	L	L	U
Carrez 2018	L	L	L	L	L	L	U
Krämer 2018	H	L	L	L	L	L	U
Zhao Y 2018	U	L	L	L	U	H	H
Chen 2013	H	L	L	L	L	L	U
Schoening 2016	U	L	L	L	L	L	U
De La Ramos 2015	H	L	L	L	L	L	U
Sessink 2014	U	L	L	L	L	L	U
Yaniv 2013	H	L	L	L	L	L	U
Jin TH 2021	U	L	L	L	L	L	U
Chen W 2021	U	L	L	L	L	L	U
Jiang DM 2021	U	L	L	L	L	L	U
Capilli M 2021	U	L	L	L	L	L	U
Hao ML 2021	U	L	L	L	L	L	U

Term 1: Random sequence generation; Term 2: Allocation concealment; Term 3: Blinding (participants and personnel); Term 4: Blinding (outcome assessment); Term 5: Incomplete outcome data; Term 6: Selective reporting; Term 7: Other sources of bias. L = low risk, H = high risk, U = unclear.

Term 1: Bias due to confounding; Term 2: Bias in selection of participants into the study; Term 3: Bias in the classification of interventions; Term 4: Bias due to deviations from intended interventions; Term 5: Bias due to missing data; Term 6: Bias in measurement of outcomes; Term 7: Bias in selection of the reported result. H = high risk, L = low risk, M = medium risk, U = unclear, VH = very high risk of bias.

Table 4

Basic information, evidence, and results of included HTAs.

HTAs	Country	Number of included studies	Intervention group	Control group	Clinical evidence	Economic evidence	Conclusion
CADTH 2013 [11]	Canada	2	Automated (or robotic) equipment	Manual method	Two nonrandomized studies were identified regarding the safety of patients in acute care	No literature identified	Automation for the preparation of intravenous solutions has certain security
CADTH 2016 [12]	Canada	2	Automated (or robotic) equipment	Manual or alternate methods, or no comparator	One nonrandomized study was identified regarding the safety of patients in acute care	One economic evaluation was identified regarding the economy for patients in acute care.	Automation for the preparation of intravenous solutions has certain security and economy

HTA = Health Technology Assessment, CADTH = Canadian Agency for Drugs and Technologies in Health.

4.2. Strengths and limitations

This study has good innovation in research content, focusing on intravenous compounding robots for the first time, and comprehensively evaluating effectiveness, safety, economics, and other aspects through a systematic review. However, this study has 3 main limitations. First, because of our limited access to data, we were unable to obtain the full texts of some studies that met the inclusion criteria. Second, there was great heterogeneity among the studies, preventing the data from being merged; thus, only qualitative analyses could be conducted. Third, most of the original studies involved evaluations of effectiveness and safety and lacked evidence of economy and social adaptability.

4.3. Interpretation within the context of the wider literature

The results of this study are similar to those of 2 existing HTAs, which showed that automation for the preparation of intravenous admixture medicines had certain security and

Table 5

Basic information of included studies.

Included studies	Country	Study type	Robot model	Observation group	Control Group	Sample size (observation group/ control group)	Observation time	Types of intravenous medicines
Controlled study								
Wang YJ 2020	China	RCT	NR	Robot	Manual preparation	480/480	–	Unclassified medicine
Cheng XL 2019	China	RCT	NR	Robot	Manual preparation	300/300	–	Unclassified medicine
Jin Z 2018	China	RCT	NR	Robot	Manual preparation	200/200	–	Unclassified medicine
Zhou HZ 2017	China	RCT	WEINAS-PD160	Robot	Manual preparation	200/200	–	Unclassified medicine
Werumeus Buning 2020	Holland	NRCT	APOTECAchemo	Robot	Manual preparation	80/80	–	Anti-tumor drug (5-fluorouracil, cyclophosphamide)
Yang P 2020	China	NRCT	*P*-006-C Ⅱ, *P*-006-z Ⅱ	Robot	Manual preparation	500/500	–	Unclassified medicine
Amodeo 2019	Italy	NRCT	i.v.Station	Robot	Manual preparation	100/100	–	Unclassified medicine (neonatal intensive care unit)
Iwamoto 2017	Japan	NRCT	APOTECAchemo	Robot	Manual preparation	40/40	–	Anti-tumor drug (fluorouracil, cyclophosphamide)
Nurgat 2015	Saudi Arabia	NRCT	CytoCare	Robot	Manual preparation	3679/134	–	Anti-tumor drug
Schierl 2014	Germany	NRCT	APOTECAchemo	Robot	Manual preparation	50/49	–	Anti-tumor drug (cyclophosphamide)
Peters 2013	Holland	NRCT	i.v.STATION	Robot	Manual preparation	8/6	–	Anti-tumor drug (infliximab, trastuzumab, bevacizumab)
Seger 2012	America	NRCT	CytoCare	Robot	Manual preparation	972/1421	–	Anti-tumor drug
Chen W 2021	China	NRCT	Angel compounding robots	Robot	Manual preparation	200/200	–	Other (Antibiotics and traditional Chinese medicine injections)
Jiang DM 2021	China	NRCT	Bowei AL_x0002_XL-04	Robot	Manual preparation	200/200	6 mo	Unclassified medicine
Capilli M 2021	Italy	NRCT	APOTECAchemo	Robot	Manual preparation	–	3 mo	Anti-tumor drug
Hao ML 2021	China	NRCT	WEINAS	Robot	Manual preparation	30/30	–	Anti-tumor drugs (cyclophosphamide, fluorouracil, gemcitabine)
Noncontrolled study								
Jobard 2020	France	Single-arm study	KIRO Oncology	Robot	–	274	–	Placebo solution
Sabatini 2019	Italy	Single-arm study	APOTECAunit	Robot	–	–	2 mo	Unclassified medicine
Nurgat 2019	Canada	Single-arm study	RIVA	Robot	–	–	36 mo	Unclassified medicine (Small-volume injection preparation)
Carrez 2018	Switzerland	Single-arm study	PharmaHelp	Robot	–	150	–	Anti-tumor drugs (cytotoxic drugs)
Krämer 2018	Germany	Single-arm study	APOTECAchemo	Robot	–	50	–	Other (Ganciclovir)
Zhao Y 2018	China	Single-arm study	Angel compounding robots	Robot	–	115	12 mo	Anti-tumor drug
Chen 2013	China	Single-arm study	CytoCare	Robot	–	1028	2 mo	Anti-tumor drug
Schoening 2016	Germany	Single-arm study	PharmaHelp	Robot	–	–	6 mo	Anti-tumor drug
De La Ramos 2015	France	Single-arm study	APOTECAChemo	Robot	–	11,865	31 mo	Anti-tumor drug

(*Continued*)

Table 5

(*Continued*)

Included studies	Country	Study type	Robot model	Observation group	Control Group	Sample size (observation group/ control group)	Observation time	Types of intravenous medicines
Sessink 2014	Belgium	Single-arm study	CytoCare	Robot	–	–	2 d	Anti-tumor drug
Yaniv 2013	America	Single-arm study	APOTE-CAchemo	Robot	–	7384	13 mo	Anti-tumor drug
Jin TH 2021	China	Single-arm study	Anchong	Robot	–	85	5 d	Other (carbazochrome sodium sulfonate)
Cluck 2012	America	Investigation report	Intellifill i.v.	Robot		–	–	Unclassified medicine
Qualitative Study								
Wang T 2019	China	In-depth interview	NR	Robot		10	–	Anti-tumor drug
Economic Study								
Urbine 2014	America	Economic study	RIVA	Robot	Manual preparation	1000 times simulations	–	Unclassified medicine

NRCT = nonrandomized controlled trial, RCT = randomized controlled trial.

Table 6

Outcomes and conclusions of the included studies.

	Effectiveness		Safety		Economy		Social suitability	
Study	Outcomes	Conclusions	Outcomes	Conclusions	Outcomes	Conclusions	Outcomes	Conclusions
Controlled studies								
Wang YJ 2020[13]	①②③	The robot could significantly improve the dispensing efficiency, and reduce the rate of dispensing errors and medicine residues.	③	The robot could reduce the accidents of injury, playing a protective role for the nurse's health.	–	–	–	–
Cheng XL 2019[14]	①②③	The robot guaranteed the accuracy and safety of infusion and reduced the error rate of disposition.	③	The robot was beneficial to strengthen the occupational protection of personnel.	–	–	–	–
Jin Z 2018[15]	①②③	Robots could effectively ensure the safety and accuracy of infusion, avoiding deployment errors.	③	Robots could reduce the harm of dispensation to nurses.	–	–	–	–
Zhou HZ 2017[16]	①②③	Robots could improve efficiency, reduce medicine residues and dispensing errors, and increase the accuracy of dispensation.	③	Nurses' occupational injury caused by dispensing was reduced.	–	–	–	–
Werumeus Buning 2020[17]	–	–	②	External (cross-) contamination of infusion bags was lower using the robotic system.	–	–	–	–
Yang P 2020[18]	①②③	The robot has higher accuracy and safety, and it could effectively dispense intravenous medicines and reduce the rate of errors.	③	The robot could prevent unnecessary injury to the nurses.	–	–	–	–
Amodeo 2019[7]	①	The benefits of robot included increased precision in drug preparation, improved safety, and saved time.	–	–	①②	The benefits of robot included improved safety.	–	–

(*Continued*)

Table 6

(*Continued*)

	Effectiveness		Safety		Economy		Social suitability	
Study	**Outcomes**	**Conclusions**	**Outcomes**	**Conclusions**	**Outcomes**	**Conclusions**	**Outcomes**	**Conclusions**
Iwamoto 2017[19]	①②	Robotic preparation had substantial advantages in drug compounding for accuracy.	②③	Robotic preparation had substantial advantages in drug compounding for safety.	–	–	–	–
Nurgat 2015[9]	①④	Robots for preparation had a limited efficiency impact in practice. This solution was not yet mature enough for universal adoption.	–	–	–	–	–	–
Schierl 2014[20]	–	–	②	Contamination was lower when the production was carried out by the robot.	–	–	–	–
Peters 2013[21]	⑤	Robotic compounding of mAbs is feasible, indicating it can be used to achieve reproducible high-quality compounding for delicate formulations.	–	–	–	–	–	–
Seger 2012[22]	①③④	Although the robot did not reduce serious medication errors, accuracy of medication preparation was improved significantly.	③	Staff safety was improved significantly by robotically preparing.	①②	Labor costs were similar, although the ancillary material costs decreased.	–	–
Chen W 2021[35]	①②	Although the robot had a relatively long dispensing time, its medicine residues were small.	–	–	–	–	–	–
Jiang DM 2021[36]	①②③	The application of robots in PIVAS could improve production efficiency.	③	The application of robots reduced occupational injury to deployed nurses.	–	–	–	–
Capilli M 2021[37]	①	In an effort to satisfy an ever-increasing workload, computerization and automation are essential instruments to maintain and ensure high standards of quality.	–	–	–	–	–	–
Hao ML 2021[38]	①	Robots could remarkably reduce environmental contamination.	②	The external contamination occurred extensively on some hazardous drug vials.	–	–	–	–
Noncontrolled studies								
Jobard 2020[23]	–	The precision was validated for all preparations.	①②	The samples of surfaces and air complied with ISO 5 class environment, but the gloves of personnel presented microbiological growth.	–		–	
Sabatini 2019[24]	–		①②	The robot met the requirements for advanced aseptic processing in hospital pharmacies and the pharmaceutical industry in general, providing advantages in terms of safety for patients.	–		–	

(*Continued*)

Table 6

(*Continued*)

	Effectiveness		Safety		Economy		Social suitability	
Study	**Outcomes**	**Conclusions**	**Outcomes**	**Conclusions**	**Outcomes**	**Conclusions**	**Outcomes**	**Conclusions**
Nurgat 2019[25]	④	It is feasible to replace some of the manual compoundings of small-volume parenteral preparations through batch compounding using an IV robotic device.	–		–		①	Responses resulted in the agreeance that the overall impression of robot was "very good." The safety features of robot had a median score of being "very safe."
Carrez 2018[26]	①	The automated system was able to produce chemotherapy effectively, delivering appropriate quality with productivity.	①②	Automated systems have the potential to guarantee optimal safety for patients and technicians.	–		–	
Krämer 2018[27]	–	–	①②	The robot revealed an adequate level of sterility and a well-controlled aseptic procedure.	–	–	–	–
Zhao Y 2018[28]	①②③	The robot was safer and more accurate and improved the working efficiency of nurses.	③	The robot could provide effective occupational protection and reduce the incidence of nosocomial infection.	–		–	
Chen 2013[10]	①④	The success rate rose slowly from 76.8 to 95.3% over the 2-mo recording period. The major mechanical problems encountered were air, clamping, and waste bin problems.	–	–	①	Robot was not able to improve the FTE pharmacists/technicians.	–	–
Schoening 2016[29]	①	The automated admixing process of the device showed remarkable effectivity and satisfying accuracy, but the manual preprocessing and postprocessing steps were time-consuming.	①	Validation of the automated preparation process showed no microbiological growth.	–		–	
De La Ramos 2015[30]	①④⑥	The robot allows the identification of errors, promoting safety and quality.	–		–		–	
Sessink 2014[31]	–		①②③	The robot had a low pollution level, with the greatest safety for technical personnel.	–		–	
Yaniv 2013[32]	④	The robot performed compounding tasks safely and accurately.	–		–		–	
Cluck 2012[33]	–		①	Patients revealed no positive blood cultures, and none of the patients developed signs or symptoms of infection when using the robot for intravenous medication preparation.	–		–	

(*Continued*)

Table 6

(*Continued*)

Study	Effectiveness		Safety		Economy		Social suitability	
	Outcomes	Conclusions	Outcomes	Conclusions	Outcomes	Conclusions	Outcomes	Conclusions
Jin TH 2021[39]	②	The robot has a good application prospect.	①	The robot has a good application prospect.	–	–	–	–
Qualitative Study								
Wang T 2019[34]	①②③	Robots have obvious advantages, but it is necessary to strengthen the training in using methods so that nurses can master the operation methods and improve the experience.	①③	Robots have obvious advantages, but it is necessary to strengthen the training in using methods so that nurses can master the operation methods and improve the experience.	–		–	
Economic study								
Urbine 2014[8]	–	The use of a robotic device can prevent errors that can cause adverse drug events.	–		①②	The use of a robotic device can reduce health care costs by preventing errors that can cause adverse drug events.		

Effectiveness: ① Production efficiency ② Medicine residues ③ Preparation errors ④ Preparation failures ⑤ Error recognition ⑥Solution properties; Safety: ① Product pollution ② Environmental pollution ③ Health damage; Economy: ① Labor costs ② Material costs; Social suitability: ① Satisfaction of personnel.
FTE = full-time equivalents, PIVAS = pharmacy intravenous admixture services.

economy.[11,12] There are 2 main reasons for this result. Firstly, in recent years, due to the increasingly rapid development of information technology, robots have been verified can partially or completely replace manual work in various medical activities.[40,41] Secondly, robots don't get tired easily which makes them suitable for repetitive work,[4] and robots can keep pharmacists from occupational injuries.

4.4. Implications for policy, practice, and research

This review showed that high-quality, large-scale, multicenter RCTs or well-designed observational studies are needed for further evaluation. Additionally, more attention should be paid to the economy and social suitability of intravenous compounding robots in future studies to provide more evidence for medical institutions. In addition, PIVAS in medical institutions should cooperate with the manufacturers of intravenous compounding robots to jointly determine how to further optimize intravenous compounding robots.

4.5. Conclusion

Intravenous compounding robots have certain advantages in terms of safety, effectiveness, economy, and social adaptability. High-quality and large-sample RCTs or well-designed observational studies are still needed to further evaluate these robots, especially in terms of economic and social suitability.

Author contributions

Conceptualization: Chunsong Yang, Xiaofeng Ni, Lingli Zhang, Lijuan Peng.
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Table 7

The detailed tabulated results.

Table 7.1 The detailed tabulated results of the effectiveness evaluation

	Production efficiency			Medicine residues		Preparation errors		Preparation failures	
		(mean ± SD)		(The rate of residues) (n, %)		(The incidence of preparation errors) (n, %)		(The incidence of failures) (n, %)	
Study	Outcome	Observation group	Control group	Observation group	Control group	Observation group	Control group	Observation group	Control group
Controlled studies									
Wang YJ 2020	Number of preparations/h	42.86 ± 6.64*	28.26 ± 1.14	5 (1.04%)*	24 (5.00%)	3 (0.60%)*	22 (4.58%)	–	–
Cheng XL 2019	Number of preparations/h	42.26 ± 8.84*	26.68 ± 8.67	2 (0.67%)*	11 (3.67%)	0 (0.00%)*	8 (2.67%)	–	–
Jin Z 2018	Number of preparations/h	43.02 ± 9.71*	27.42 ± 8.81	8 (4.00%)*	26 (13.00%)	4 (0.004%)*	13 (0.019%)	–	–
Zhou HZ 2017	Number of preparations/h	42.13 ± 6.83*	28.69 ± 7.69	9 (4.50%)*	23 (11.50%)	3 (0.003%)*	11 (0.016%)	–	–
Yang P 2020	Number of preparations/h	275 ± 8.52*	26.22 ± 7.52	20 (4.00%)*	65 (13.00%)	1 (0.2%)*	8 (1.6%)	–	–
Jiang DM 2021	Number of preparations/h	53.75 ± 9.12*	28.20 ± 7.74	7 (3.50%)*	18 (9.00%)	5 (0.006%)*	14 (0.017%)	–	–
Amodeo 2019	Influence factor	The time saved ranged from 16 s to 2 h and 57 min and may continue to rise even as the total number of medications prepared to increase.		–	–	–	–	–	–
Iwamoto 2017	Production efficiency	The highest percentage of robotic preparation among total preparation for inpatients was 70.4%.		0 (0.00%)*	2 (50.00%)	–	–	–	–
Capilli M 2021	Production efficiency	Regarding robotic compounding, the annual production increased by 50.4%.		–	–	–	–	–	–
Nurgat 2015	Preparation time	7 h	2–3 h	–	–	–	–	845–4509 (18.7%)	–
Peters 2013	–	–	–	–	–	–	–	–	–
Seger 2012	Preparation time	10 min 51 s*	7 min 24 s	–	–	1 (0.9%)*	23 (12.5%)	1/110 (0.9%)*	23/184 (12.5%)
Noncontrolled studies									
Nurgat 2019	–	–	–	–	–	–	–	<1% (0.21%, 0.15%, and 0.18% in 2015, 2016, and 2017, respectively)	
Carrez 2018	Influence factor	If more than 1 run were to be made, this would create an efficiency gain.		–	–	–	–	–	–
Kramer 2018	–	–	–	–	–	–	–	–	–
Zhao Y 2018	Production efficiency	Compared with the traditional manual infusion configuration, the work efficiency is 3–5 times higher		The use of robots reduced medicine residues.		The robot could reduce the incidence of preparation errors.		–	–

(*Continued*)

Table 7

(*Continued*)

Table 7.1 The detailed tabulated results of the effectiveness evaluation

	Production efficiency			**Medicine residues**		**Preparation errors**		**Preparation failures**	
	(mean ± SD)			**(The rate of residues) (n, %)**		**(The incidence of preparation errors) (n, %)**		**(The incidence of failures) (n, %)**	
Study	**Outcome**	**Observation group**	**Control group**	**Observation group**	**Control group**	**Observation group**	**Control group**	**Observation group**	**Control group**
Chen 2013	Influence factor	Pharmacists' increasing familiarity with the machine.		–	–	–	–	123–1028 (12.0%)	–
Schoening 2016	Influence factor	The manual preprocessing and postprocessing steps are time-consuming.		–	–	–	–	–	–
De La Ramos 2015	Preparation time	5 min 43 s (1 min 34 s-47 min 26 s)	–	–	–	–	–	326–11,642 (2.44%)	–
Qualitative study									
Wang T 2019	Influence factor	The increase in time and frequency of use.		The use of robots reduced medicine residues		The robot could reduce the incidence of preparation errors by warning, without interference by factors such as visual fatigue.		–	–

Table 7.2 The detailed tabulated results of the safety evaluation

Study	Product pollution		Environmental pollution		Health damage	
	Observation group	Control group	Observation group	Control group	Observation group	Control group
Controlled studies						
Wang YJ 2020	–	–	–	–	0%* (chapped fingers: 0, scratched by ampoules: 0, stuck by syringes: 0)	1.25% (chapped fingers: 3, scratched by ampoules: 2, stuck by syringes: 1)
Cheng XL 2019	–	–	–	–	0.33%* (chapped fingers: 0, scratched by ampoules: 0, fatigue: 1, stuck by syringes: 0)	4.67% (chapped fingers: 1, scratched by ampoules: 8, fatigue: 3, stuck by syringes: 2)

(*Continued*)

Table 7
(*Continued*)

Table 7.1 The detailed tabulated results of the effectiveness evaluation

	Production efficiency			Medicine residues		Preparation errors		Preparation failures	
	(mean ± SD)			(The rate of residues) (n, %)		(The incidence of preparation errors) (n, %)		(The incidence of failures) (n, %)	
Study	Outcome	Observation group	Control group	Observation group	Control group	Observation group	Control group	Observation group	Control group
Jin Z 2018	–			–		–		0%* (chapped fingers: 0, scratched by ampoules: 0, fatigue: 0, stuck by syringes: 0)	11.5% (chapped fingers: 1, scratched by ampoules: 11, fatigue: 5, stuck by syringes: 6)
Zhou HZ 2017	–			–		–		0%* (chapped fingers: 0, scratched by ampoules: 0, fatigue: 0, stuck by syringes: 0)	37.5% (chapped fingers: 4, scratched by ampoules: 38, fatigue: 19, stuck by syringes: 14)
Werumeus Buning 2020	–			External contamination: 3.75% External cross-contamination: 1.25%		External contamination: 3.75% External cross-contamination: 2.5%		–	–
Yang P 2020	–			–		–		0.6%* (chapped fingers: 0, stuck by syringes: 3)	11.4% (chapped fingers: 29, stuck by syringes: 28)
Iwamoto 2017	–			The compounding area under the dosing device (CPA, 25 ng/cm^2) The gripper of the robot arm (CPA, 0.04 ng/cm^2)		Biological safety cabinet (fluorouracil, 12.5 ng/cm^2)		No traces of the contaminants were detected in the gloves of operators.	No traces of the contaminants were detected in the gloves of operators.
Schierl 2014	–			Gloves (1 of 8: 0.0007 ng/cm^2) Infusion bags (3 of 20: 0.0005, 0.0019, 0.0094 ng/cm^2) Surfaces under the dosing device (0.0293–0.1603 ng/cm^2)		Gloves (0.0004–0.0967 ng/cm^2) Infusion bags (70%, <0.0004–2.89 ng/cm^2) Environmental pollution (most locations, <0.001 ng/cm^2)		–	–

(*Continued*)

Table 7

(*Continued*)

Table 7.1 The detailed tabulated results of the effectiveness evaluation

	Production efficiency			Medicine residues		Preparation errors		Preparation failures	
	(mean ± SD)			(The rate of residues) (n, %)		(The incidence of preparation errors) (n, %)		(The incidence of failures) (n, %)	
Study	Outcome	Observation group	Control group	Observation group	Control group	Observation group	Control group	Observation group	Control group
Seger 2012	–			–		–		2.9%* (28)	5.1% (73)
Jiang DM 2021	–			–		–		0%* (fatigue: n = 0, scratched by ampoules: n = 0, joint strain: n = 0)	92.86% (fatigue: n = 7, scratched by ampoules: n = 13, joint strain: n = 4)
Noncontrolled studies									
Jobard 2020	No microbiological contamination was detected.			The samples of surfaces and air complied with ISO 5 class environment.				–	–
Sabatini 2019	No microbiological contamination was detected.			After 3 hours, no microorganisms retained viability.				–	–
Carrez 2018	No particles or microbiological contamination were detected.			Neither volatilization nor contamination of isolator surfaces was observed. Only one contamination related to the operation of the automated system was detected (very low contamination (spots < 3mm) but relatively frequent (11%)).				–	–
Kramer 2018	No microbiological contamination was detected.			The environmental monitoring with settle/contact plates matched the recommended limits set for cleanroom Grade A zones, except in the loading area of the robot.				–	–
Zhao Y 2018	–			–		–		The robot could provide effective occupational protection for nurses	
Schoening 2016	No microbiological contamination was detected.			–		–		–	–
Sessink 2014	Low levels of product contamination.			Contamination with cyclophosphamide was mainly observed inside CytoCare, before preparation, after preparation, and after daily routine cleaning. Contamination outside CytoCare was incidentally found.				Almost all outer pairs of gloves used for preparation and daily routine cleaning were contaminated with cyclophosphamide. Cyclophosphamide was not found on the inner pairs of gloves and on the hands of the technicians.	
Cluck 2012	Microbial contamination might originate from the washing station.			–		–		–	–
Qualitative study									
Wang T 2019	The robot was cleaner than the biological safety cabinet			–		–		All interviewees had strong experience with occupational protection provided by the robots.	

CPA = cyclophosphamide.

* The studies reported that the *P* value was <.05.

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