

BMJ Open is committed to open peer review. As part of this commitment we make the peer review history of every article we publish publicly available.

When an article is published we post the peer reviewers' comments and the authors' responses online. We also post the versions of the paper that were used during peer review. These are the versions that the peer review comments apply to.

The versions of the paper that follow are the versions that were submitted during the peer review process. They are not the versions of record or the final published versions. They should not be cited or distributed as the published version of this manuscript.

BMJ Open is an open access journal and the full, final, typeset and author-corrected version of record of the manuscript is available on our site with no access controls, subscription charges or pay-per-view fees (<u>http://bmjopen.bmj.com</u>).

If you have any questions on BMJ Open's open peer review process please email <u>info.bmjopen@bmj.com</u>

## Clinical pharmacist-led medication reconciliation supplemented with medication review in chronic kidney disease admitted patients: a cost-benefit analysis

Journal:	BMJ Open
Manuscript ID	bmjopen-2024-087232
Article Type:	Original research
Date Submitted by the Author:	04-Apr-2024
Complete List of Authors:	Altawalbeh, Shoroq ; Jordan University of Science and Technology, Department of Clinical Pharmacy Sallam, Nahlah M.; Jordan University of Science and Technology, Department of Clinical Pharmacy Al-Khatib, Minas; Jordan University of Science and Technology, Department of Clinical Pharmacy Alshogran, Osama Y.; Jordan University of Science and Technology, Department of Clinical Pharmacy Bani Amer, Mohammad S.; Jordan University of Science and Technology, Department of Internal Medicine
Keywords:	Medication Reconciliation, Health Services, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health & safety < HEALTH SERVICES ADMINISTRATION & MANAGEMENT





I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

terez oni

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

1 2		
2 3		
4	1	Research Article
5	2	
6	2	
7	3	Clinical pharmacist-led medication reconciliation supplemented with
8 9	Ū	Cinitan bini manana an mananan a contenuntan sabbianan di han
10	4	medication review in chronic kidney disease admitted patients: a cost-benefit
11	4	incurcation review in chrome kiuney disease admitted patients. a cost-benefit
12		<b>,</b> ,
13 14	5	analysis
14		
16	6	Shoroq M. Altawalbeh, PharmD, PhD, <sup>1</sup> Nahlah M. Sallam, M.S <sup>1</sup> , Minas Al-Khatib, PharmD, <sup>1</sup> Osama Y.
17		
18	7	Alshogran, M.S, PhD, <sup>1</sup> Mohammad S. Bani Amer, MD <sup>2</sup>
19 20		
20	8	<sup>1</sup> Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan University of Science and Technology, Irbid,
22	9	Jordan. <sup>2</sup> Department of Internal Medicine, Faculty of Medicine, Jordan University of Science and Technology,
23	10	Irbid, Jordan.
24 25	-	
25 26	11	
27		
28	12	Shoroq M. Altawalbeh, PharmD, PhD, Department of Clinical Pharmacy, Faculty of Pharmacy,
29	13	Jordan University of Science and Technology, Irbid 22110, Jordan. Email address:
30 31	14	smaltawalbeh@just.edu.jo
32	15	ORCID: 0000-0001-8345-4048
33		
34	16	
35 36	17	Nahlah M. Sallam, Msc, Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan
37	18	University of Science and Technology, Irbid 22110, Jordan. Email address:
38	19	nmsallam20@ph.just.edu.jo
39		
40 41	20	ORCID: 0000-0001-9311-600X
41	21	Minas Al-Khatib PharmD, Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan
43	22	University of Science and Technology, Irbid 22110, Jordan. Email address:
44	23	makhatib@just.edu.jo
45	24	
46 47	24	
48	25	Osama Y. Alshogran, Msc, PhD, Department of Clinical Pharmacy, Faculty of Pharmacy,
49	26	Jordan University of Science and Technology, Irbid 22110, Jordan. Email address:
50	27	oyalshogran@just.edu.jo
51 52	20	
52 53	28	ORCID: 0000-0002-2466-4763
54		
55		
56		
57 58		
59		1
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1 2		
3	29	Mohammad S. Bani Amer, MD, Department of Internal Medicine, Faculty of Medicine, Jordan
4 5	30	University of Science and Technology, Irbid 22110, Jordan. Email address:
6 7	31	m.baniamer1997@gmail.com
7 8	32	
9 10	33	*Corresponding Author:
11	34	Shoroq M. Altawalbeh, PharmD, PhD
12 13	35	Associate Professor
14 15	36	Department of Clinical Pharmacy
16 17	37 38	Jordan University of Science and Technology; Faculty of Pharmacy
18 19	39	P.O.Box 3030, Irbid 22110, Jordan
20 21 22	40 41	Tel.:+962(0)27201000 Fax : + 962 (0) 2 7095123
23	42	E-mail: <u>smaltawalbeh@just.edu.jo</u>
24 25	43	ORCID: 0000-0001-8345-4048
26 27	44	
28 29	45	Running Title: Cost-benefit of medication reconciliation in CKD
30 31 32	46	Number of Tables: 2
33 34	47	Number of Figures: 3
35 36	48	Keywords: Medication reconciliation, clinical pharmacist, cost-benefit, chronic kidney disease,
37 38 39	49	Jordan.
40 41 42	50	
43 44	51	
45 46	52	
47 48 49	53	
50 51	54	
52 53 54	55	
55 56	56	
57 58		
59 60		2 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

BMJ Open

2		
3 4	57	
5 6 7	58	Abstract
, 8 9	59	<b>Objective:</b> Chronic kidney disease (CKD) is associated with a high economic burden, which is
10 11	60	exacerbated by the high susceptibility to drug-related problems (DRPs) in this patient population
12 13 14	61	This study aimed to evaluate the cost-benefit ratio of medication reconciliation supplemented
15 16 17	62	with medication review among inpatients with CKD.
17 18 19	63	Design: This was a cost-benefit analysis conducted along with a prospective interventional
20 21 22	64	study.
23 24 25	65	Setting: The study was conducted at two hospitals in Jordan between February and May 2023.
26 27 28	66	Participants: The prospective interventional study included 142 admitted patients with CKD.
29 30	67	Method: Patients received medication reconciliation at admission and discharge as well as
31 32 33	68	medication review throughout admission. A cost-benefit analysis was conducted from the
34 35	69	healthcare system perspective by assessing the cost of the service (the pharmacist time required
36 37 29	70	to complete the service per patient) and the economic benefit in terms of cost savings and cost
38 39 40	71	avoidance. The primary outcome measures were the net benefit and the benefit-to-cost ratio of
41 42	72	the intervention.
43 44 45	73	<b>Results:</b> The total estimated cost of all DRPs in the absence of interventions (cost avoidance)
46 47	74	was \$83,052.4; among which \$20,623.19 was attributed to medication discrepancies. The cost
48 49 50	75	savings were estimated at -\$467.5. The supplemented medication reconciliation service was
51 52	76	estimated to cost \$713.7. Accordingly, the estimated net benefit was \$81,871.15 over the 4-
53 54 55 56 57 58	77	month study period.

#### **BMJ** Open

	ИЈ Оре
Conclusion: Delivering a supplemented medication reconciliation service by a clinical	n: first
pharmacist for CKD patients is cost beneficial from the healthcare perspective in Jordan, an	publis
example of a low- and middle-income country (LMIC). This finding further confirms the pivotal	hed as
role of clinical pharmacists in multidisciplinary healthcare teams.	10.1136/bmjc Protected b
Keywords: Medication reconciliation, clinical pharmacist, cost-benefit, chronic kidney disease,	open-2( y copy
Jordan.	MJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.
4 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	ie de l

1 2		
2 3 4	104	
5 6	105	
7	106	
8 9 10	107	Strengths and limitations of this study
10 11 12	108	• The study was conducted along with a prospective interventional study.
13 14	109	• Evaluation of the probability scores of drug related problems (DRPs) was
15 16 17 18 19	110	conducted by an expert panel composed of five independent evaluators.
	111	• The exact real cost of adverse events resulting from drug DRPs could not be
20 21	112	measured.
22 23 24	113	• The study relied on admission charges, medication prices, and lab prices rather than
24 25 26 27 28 29 30 31 32 33 34	114	actual costs.
	115	
	116	
	117	
	118	
35	119	
36 37 38	120	• The study relied on admission charges, medication prices, and tab prices rather than actual costs.
39	121	
40 41	122	
42 43	123	
44 45 46 47 48 49 50 51	124	
	125	
	126	
	127	
52 53	128	
53 54 55	129	
55 56 57 58	130	
59 60		5 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1 2		
2 3 4	131	
5	132	
6 7	133	
8 9 10	134	Introduction
11 12	135	Chronic kidney disease (CKD) is associated with high financial burden globally, exceeding
13 14	136	expenditures incurred by other highly burdened patients such as those with stroke and cancer. <sup>1, 2</sup>
15 16 17	137	CKD is a complex medical state accompanied by multiple concurrent illnesses, which inflate the
18 19	138	cost of management. Around \$18 billion had been spent by the national US Department of
20 21	139	Veterans Affairs for the care of patients with CKD without renal replacement therapy (RRT), with
22 23	140	expenditures increased across the advanced stages of CKD. <sup>3, 4</sup> In Jordan, the Ministry of Health
24 25 26	141	expended approximately \$17.7 Million per year for hemodialysis patients management in 2010,
27 28	142	with an average of annual cost of \$9,979 per patient. <sup>5</sup> A study conducted in Lebanon reported the
29 30	143	median cost for all CKD stages per year of \$4,764.02 (IQR \$2,475.24 - \$23,455.61) in 2019 from
31 32 33	144	a society perspective. <sup>6</sup> Studies highly recommend implementing programs and policies to reduce
34 35	145	progression and complications of CKD to mitigate the growing disease burden especially in
36 37	146	countries with limited resources. <sup>7</sup>
38 39 40	147	Interestingly, many serious Drug related problems (DRPs) are preventable in CKD
40 41 42	148	patients.8 Patients with CKD are very vulnerable to medication discrepancies and other DRPs.9, 10
43 44	149	Developing DRPs increased the exposure to re-hospitalization, extended length of hospital stays,
45	450	

and early death, and therefore expanded the cost.<sup>11-13</sup> Clinical pharmacy services have revealed a positive economic impact on healthcare organizations across the literature.<sup>14</sup> Medication reconciliation is a healthcare service directed primarily by a clinical pharmacist and aimed at preventing and resolving DRPs and proposed to reduce health expenditures.<sup>15</sup> The economic burden of medication discrepancies and other DRPs is understudied, particularly in developing 

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) .

and

data mining, AI training, and similar technologies

Protected by copyright, including for uses related to text

countries, including Jordan. Moreover, there is a dearth of data regarding the efficiency of clinical
pharmacy services implemented in patients with CKD, especially in low-income to middle-income
countries. Therefore, this study aimed to evaluate the cost-benefits of implementing a clinical
pharmacist-led service for supplemented medication reconciliation among admitted patients with
CKD in Jordan.

### 160 Methods

161 Study design

The cost-benefit analysis was developed along with a prospective interventional clinical study that involved patients with stages 2-5 CKD, who were admitted to two healthcare hospitals in Jordan: King Abdullah Hospital (KAUH) and Princess Basma Hospital (PBH). A clinical pharmacist was responsible for providing supplemented medication reconciliation to CKD-admitted patients over four months (from February to May 2023). The costs and benefits over the study period were calculated. The primary outcome measure was the net benefit generated by the supplemented medication reconciliation service provided to CKD patients during the study period. The net benefit was estimated according to the following equation: [net benefit = total benefits (cost avoidance + cost saving)-service cost]. In addition, the benefit-to-cost ratio was estimated. The health care system perspective was adopted in the current study. Base case calculations were performed using Excel software. The cost-benefit analysis model is depicted in Figure 1. The demographic and clinical characteristics of the study sample are summarized in the Supplementary Material (Table S1).

175 Description of supplemented medication reconciliation

Patients received a supplemented medication reconciliation service across the transitionsof care during their admission to the internal medicine ward, in addition to a medication review

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Page 9 of 33

#### BMJ Open

for possible DRPs. The procedure of supplemented medication reconciliation consisted of medication reconciliation at admission, medication review throughout admission, and medication reconciliation at discharge. At admission, demographic, clinical, and medical data for each enrolled patient were collected from the medical records, followed by interviews with the patients or their caregivers to verify the patients' demographics, medical history, and pre-admission medication list. The pre-admission drug lists were also confirmed using all other available sources, such as bottles, prescriptions, and previous medical records, to obtain the best possible medication history (BPMH). The BPMH was compared with the current hospital medication sheet (admission medication orders) to extract discrepancies at admission. Medication reviews and clinical case analyses were conducted regarding dose adjustments, drug interactions, missing medications, inappropriate medications, unnecessary medications, and monitoring after admission and during the hospitalization period to identify the DRPs. At discharge, the best possible discharge medication plan (BPMDP) was created from the BPMH, the last medication list during index hospitalization, and new medications planned to be started upon discharge. The BPMDP was compared with discharge prescription and summary. Patient education was provided to willing patients before discharge. All identified discrepancies and other DRPs were discussed with the resident responsible for the resolution as accessible.

195 Estimation of costs

196 Input costs in the current study include the resources used to provide the supplemented 197 medication reconciliation, that is, the pharmacists' time. The time taken by the pharmacist to 198 deliver the supplemented medication reconciliation per patient (in hours) was recorded for each 199 admission. The cost of the medication reconciliation service was estimated by multiplying the 200 service time by the average hourly wage rate for clinical pharmacists, as obtained from the

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES)

and

data mining, AI training, and similar technologies

Protected by copyright, including for uses related to text

**BMJ** Open

financial department at KAUH. The average annual wage rate was converted to the hourly wagerate based on 240 working days per year and 8 working hours per day.

203 Estimation of benefits

The economic benefits associated with the potential prevention of DRPs through interventions recommended by clinical pharmacists were evaluated in terms of "cost savings" and "cost avoidance."

207 Cost saving

In the cost-saving analysis, the decreased medication costs due to interventions and the increased medication costs and costs attributed to requesting labs were estimated. The cost of any medication (increased or decreased) was estimated as the cost of medication per unit multiplied by the frequency per day and then by the duration of therapy.<sup>16</sup> Acute therapy duration was estimated based on the clinical scenario, while chronic medication use was calculated over three months' time horizon. Public per-unit prices of drugs were obtained from the Jordan Food and Drug Administration (JFDA).<sup>17</sup> For interventions that included the addition of a laboratory test, the increased cost for each intervention was estimated using the prices of laboratory tests obtained from KAUH laboratory department. Both drug and lab prices were converted to costs by multiplying them by an assumed Ratio of Cost to Charge (RCC). The net cost saving was estimated by subtracting the total increased cost from the decreased cost resulting from the implementation of the supplemented medication reconciliation services.

*Cost avoidance* 

Cost avoidance was estimated for each intervention recommended by the clinical pharmacist in the current study as the cost avoided by potential prevention of DRPs. The probability of DRP in the absence of intervention was determined according to the Nesbit et al Page 11 of 33

#### **BMJ** Open

scale <sup>18</sup> which has five levels of risk of causing DRPs: 0 (none), 0.01 (very low), 0.1 (low), 0.4 (medium), or 0.6 (high). The DRP probability in the absence of the intervention was estimated for all identified discrepancies and other DRPs by a team of experts, comprising four clinical pharmacists and one physician. Examples of the studied clinical cases with potential probabilities of DRPs are presented in Supplementary Material (Table S2). The cost avoidance attributed to each intervention was calculated by multiplying the corresponding DRP probability by the DRP cost. The cost of a DRP was assumed to be the cost of an additional 2 days of hospital stay.<sup>19</sup> Admission charges were retrieved from the billing system for all admissions included in the study, and the average charge per day was calculated for these CKD patients. The average charge per day was adjusted using the assumed RCC to estimate the RCC cost of DRPs. Cost avoidance was estimated in total and by the Pharmaceutical Care Network Europe (PCNE) Classification for Drug-Related Problems V9.1 based on the cause,<sup>20</sup> and the Medication Discrepancy Taxonomy (MedTax) system.<sup>21</sup> All financial data were extracted in Jordanian Dinar currency unit (JOD) and converted to United States Dollars (USD) at a rate of (1 JOD = 1.41 USD). The RCC value was assumed to be 0.8 throughout the base case analysis and varied in the sensitivity analysis. 

239 Sensitivity analysis

One-way sensitivity analysis was conducted to account for the variability in the key model parameters. DRP probabilities were varied using the minimum and maximum probabilities assigned by the expert panel. All costs were varied over a range of  $\pm$  20% of the base case cost. The average service time was varied over two SD of the mean, as calculated in this study. RCC was varied in the range (0.7 to 0.9). Probabilistic sensitivity analysis was conducted, in which the input variables were varied simultaneously over 10,000 Monte Carlo simulations. Beta distribution

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) .

and

data mining, AI training, and similar technologies

Protected by copyright, including for uses related to text

#### **BMJ** Open

was used for DRP probabilities, uniform distribution for RCC and hourly wage rate, normaldistribution for service time in minutes, and gamma distribution for cost.

- **Results** 
  - 250 Cost of supplemented medication reconciliation

The average time required to perform a supplemented medication reconciliation service (medication reconciliation plus medication review during admission) was 43.38 (SD= 6.65) minutes, ranging from 26 to 60.5 minutes. The total time spent by the clinical pharmacist on the supplemented medication reconciliation over the four-month intervention period was 6117.1 minutes (101.95 hours). The average duration to accomplish a primary medication reconciliation service at admission was  $15.79 \pm 1.74$  minutes. Though, the average time for medication review during the admission was  $21.6 \pm 4.30$  minutes (ranged from 11.6 to 35.5 minutes) per patient. Medication reconciliation time at discharge averaged  $3.58 \pm 1.55$  minutes per patient. Based on the reported average monthly salary of the clinical pharmacist at KAUH, the wage per hour was \$7 assuming 8 hours per day. Taking this into account, the total intervention cost over 4-month study period was \$713.7 ( $$7 \times 101.95$  hours). 

- 262 Benefits of supplemented medication reconciliation
  - 263 Estimated cost saving

The total increased medication cost was estimated to be \$9,349 and lab needed total cost was estimated at \$5,248. The decrease in medication costs owing to the intervention was \$14,012. Total cost saving (after being adjusted with RCC of 0.8) = \$11,210[\$14,012\*0.8] - \$7,479[\$9,349 \*0.8] - \$4,198[\$5,248\*0.8] = -\$467.5.

*Estimated cost avoidance* 

The average admission charge for patients with CKD enrolled in the study was \$2811 (SD= \$2172), and the average admission charge per day was \$340.20 (SD= \$199.48). The assumed cost of a DRP was the estimated cost of two additional hospitalization days for patients with CKD in the current study [\$680.4 multiplied by 0.8 RCC = \$483.1]. The estimated probabilities of DRPs in the absence of intervention were averaged using a panel of five expert evaluators. The majority of DRPs (73.4%; N=735) were in the low-to medium-risk category (0.1-0.4), while 21.2% (N=212) were in the low-risk category (<0.1), and 5.4% (N=54) were in the moderate-to high-risk category (>0.4). The average cost of a potential DRP, estimated by multiplying the average DRP probability by the estimated RCC cost for two additional hospitalization days was \$82.96 (SD=\$57.7). The total estimated cost of all DRPs in the study was \$83,052.4 (the cost avoidance). Patient transfer related DRPs (medications discrepancies) were found to be the third most expensive cause-based domain in the PCNE classification of DRPs (V9.1), contributing to around 25% of the total cost avoidance (\$20,623.19). The greatest weight of discrepancies' cost avoidance was attributed to "drug omission" category (\$12,693.54) followed by "discrepancy in frequency/strength/dose" (\$4,612.56) and "drug addition" (\$2,399.36), Table 1. A detailed summary of the cost avoidance per PCNE cause-based domains is presented in Table 1. 

285 Cost benefit analysis

The net benefit was calculated by subtracting the total cost of intervention from total cost avoidance and saving [cost avoidance (\$83,052.4) + cost saving (- 467.5) - cost of the intervention (\$713.7) = \$81,871.15]. The benefit-to-cost ratio estimated in this study was (115.7:1). Table 2.

289 Sensitivity analyses

The study conclusion was insensitive to uncertainty in any of the input variables including
DRP probabilities, DRP cost, RCC, per-unit cost of drugs and labs, hourly wage rate, and average

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

service time. The main driver of the outcome was the DRP probability, followed by the DRP cost,
as depicted in Figure 2. However, the net benefit was positive over all plausible ranges of the input
variables. The minimum estimated net benefit was \$50,203 based on varying DRP probability. In
probabilistic sensitivity analysis, the average expected value of the net benefit was \$90,451(SD =
\$126,294). Only 866 out of 100,000 iterations (8.7%) showed a negative net benefit (Figure 3).

299 Discussion

The major findings of the current study emphasize the substantial economic burden of medication discrepancies and other DRPs in patients with CKD. In addition, the results showed that the estimated economic benefit was remarkable compared to the estimated cost of the medication reconciliation service. Overall, the results indicate that supplemented medication reconciliation services mediated by clinical pharmacists are cost beneficial.

The majority of DRPs in the current study were classified as having a medium risk of DRPs. Despite the different scales used to evaluate the clinical significance of DRPs in patients with CKD, most studies have found that the majority of DRPs in this high-risk population were with moderate to significant clinical impact. In a study conducted in Jordan among hospitalized patients with CKD, the majority of DRPs (62%) were classified among the significant category. however, the study used a different scale (extremely significant, much significant, significant, and slightly significant).<sup>22</sup> In a study conducted in Canada, approximately half of the observed DRPs were moderate in severity in terms of causing harm to CKD patients.<sup>23</sup> The different scales used in severity assessment across the literature makes the comparison seems challenging. Overall, most 

> l For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

recognized DRPs were considered clinically important in the current study and potentiallypreventable.

This study revealed the beneficial effect of clinical pharmacist medication reconciliation intervention on CKD patients in terms of the cost-benefits associated with this service. A recent review of 47 studies among CKD patients also supports this finding; 7 studies approved the significant cost savings and 15 studies reported improvement in clinical outcomes due to clinical pharmacy care, including blood pressure, anemia, length of hospital stay, readmissions, kidney function, and other laboratory tests (i.e., PTH, calcium, uric acid, cholesterol, and HbA1c).<sup>14</sup>

The average time needed for full supplemented medication reconciliation services provided for each CKD admission in the current study was  $43.38 \pm 6.65$  minutes. This is comparable to other studies that measured the time needed for medication reconciliation services:  $44.4 \pm 21.8$ ,<sup>24</sup>  $40 \pm 17.2$  minutes,<sup>25</sup> and 48 minutes.<sup>26, 27</sup> In addition, the total time to deliver a primary medication reconciliation service at all transitions of care per patient was estimated with a median of 24 minutes (IQR 20-30 minutes).<sup>28</sup> The specific time for medication reconciliation at admission was roughly similar to our finding (15 minutes (IQR 10–21)) in two previous studies.<sup>29, 30</sup> Moreover, medication reconciliation at discharge after conducting medication reconciliation at admission was previously estimated to need approximately 3.5 minutes,<sup>31</sup> which is also comparable to the estimated time in the current study. However, a recent systematic review reported a wider range of the mean time for medication reconciliation implementation across nine studies with an average of 34.5 ( $\pm$ 39.4) minutes.<sup>32</sup> This variability could be originated from the diverse models and services involved across the pooled studies and variations in study population. 

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

335 CKD has been associated with a high economic burden.<sup>3, 33-35</sup> DRPs have been associated
336 with high costs that affect patient safety and healthcare expenditures.<sup>36</sup>. Our study estimated the

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

net benefit attributed to avoiding and resolving DRPs to be \$81,871.15 over 4 months for a cumulative number of 142 CKD patients. Such remarkable benefit confirms the need of implementing supplemented medication reconciliation in CKD patients. Likewise, a recent retrospective cohort in the US among hemodialysis patients estimated cost saving from preventing DRPs to be \$447,355 over a 6-month period of observation, attributing this benefit to performing medication reconciliation with medication review.<sup>37</sup> A Malaysian study measured the cost saving resulted from only dose adjustment in CKD inpatients to be \$2,250 for 212 dose related recommendations over 4 months, in which the clinical pharmacist worked within a multidisciplinary rounds with the nephrology team to adjust the doses as needed.<sup>38</sup> This saved cost is considered much lower than the avoided cost resulting from renal dose adjustment in our study (\$14,756 for 4 months, 94 dose adjustment interventions). An earlier prospective study conducted medication therapy evaluation by pharmacist found that the ratio of pharmaceutical care cost to healthcare system saving is \$1 to \$3.98 among end-stage renal disease patients in the USA.<sup>39</sup> This is much smaller compared to the benefit to cost ratio estimated in the current study (115:1). This variability might be related in part to the relatively lower wage rates of clinical pharmacists in Jordan than in the USA. However, the estimated cost of a DRP is also expected to be higher in terms of admission-day costs in the USA. Another study found annual direct cost savings of more than \$780,000 after implementing supplemented medication reconciliation with patient education in internal medicine wards in Kansas ascribed to reducing readmissions.<sup>40</sup> A Chinese trial found cost saving attributed to antimicrobial dose adjustment (number of adjusted doses= 183) by a clinical pharmacist of \$3,525 per patient with sepsis undergoing continuous dialysis in the ICU.<sup>41</sup> Wage rates and the cost of health care may differ widely across regions and institutions which make the comparison in cost is not sufficiently clear/straightforward. This also highlights the need

Page 17 of 33

#### **BMJ** Open

to obtain relevant data from local or regional studies to better support the decisions of policy makers based on information from relevant settings. 

In Jordan, the role of clinical pharmacists appears to be economically effective for other populations. Among outpatients with chronic diseases, the estimated cost avoidance per month due to pharmacist interventions (number of interventions = 79 among 48 patients) was 6.422.41.42In another study conducted in Jordan, clinical pharmacist intervention in the ICU reduced the total cost of drugs consumption by \$211,574.90 over 10 months.<sup>43</sup> Still, the cost benefit of medication reconciliation among CKD patients has not been well addressed in Jordan and other developing countries. The results of the current study strongly support the need to implement medication reconciliation supplemented with continuous medication review during hospital admission in patients with CKD. 

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

The current study has some limitations. We did not evaluate the actual adverse events resulting from DRPs or the actual role of interventions in decreasing these events. Furthermore, the exact real cost of adverse events resulting from DRPs could not be measured; however, the method of calculating cost avoidance in the current study has considered uncertainty and was implemented in previous studies.<sup>44</sup> In addition, the evaluation of the probability score of each DRP was conducted by an expert panel composed of five independent evaluators. Besides, the assessment of DRP probability scores was conducted independently by the study panel using a validated scale.<sup>18</sup> Another limitation is that we relied on admission charges, medication prices, and lab prices rather than actual costs. However, charges are widely used as a proxy for costs in the literature because of accessibility issues. Furthermore, we used an assumed RCC ratio to approach the actual costs, and this RCC was varied in the sensitivity analysis.

Conclusions

For peer review only - http://bmjopen.bmj.com/site/about/quidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) .

ning, Al training, and similar technologies

Protected by copyright, including for uses related to text

Pharmacist-led medication reconciliation supplemented with contentious medication review is very cost beneficial in CKD admitted patients, with substantial cost avoidance compared to the cost of implementing this service. The results clearly showed that activating the role of clinical pharmacists in providing medication reconciliation with a comprehensive medication review contributed positively to the safety of admitted patients with CKD and had a remarkable economic impact in clinical settings. The net benefit of this intervention could be enhanced by designing an efficient collaborative approach with physicians in hospital settings, and future studies should be directed toward evaluating the cost-benefit of such approaches. Funding: This work was supported by the Deanship of Scientific Research at the Jordan University of Science and Technology [grant number: 20220257]. The funding agency was not involved in the study design, conduct, writing, or decision to submit this article for publication. Competing Interests: The Authors declare that they have no conflicts of interest to disclose. Ethical approval This study was approved by the Institutional Review Board (IRB) Committee at KAUH (Ref number: 123/147/2022) and the Ministry of Health (Ref number: 13902). Author contributions 

60

## BMJ Open

on,	BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.
ng-	hed as 10.1136/bmjop Protected by o
nd	10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http: Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining,
	6 February 2025. Dow Enseignement Si for uses related to tex
	bruary 2025. Downloaded from http://t Enseignement Superieur (ABES) . uses related to text and data mining, A
	//bmjopen.bmj.com/ on June 8, 2025 Al training, and similar technologies
	ı June 8, 2025 at Age ' technologies.
	nce Bibliographique (
	de l

1 2		
2 3 4	403	Altawalbeh S: Conceptualization, Methodology, Data curation, Formal analysis, Supervision
5 6	404	Project administration, Funding acquisition, Writing- Original draft preparation, Writing-
7 8 9	405	Reviewing and Editing.
10 11	406	Nahlah M. Sallam: Conceptualization, Methodology, Data curation, Formal analysis, Writin
12 13 14	407	Original draft preparation, Writing- Reviewing and Editing.
15 16 17	408	Minas Al-Khatib, Osama Y. Alshogran: Conceptualization, Methodology, Data curation, and
18 19	409	Writing- Reviewing and Editing.
20 21 22	410	Mohammad S. Bani Amer, MD: Data curation, and Writing- Reviewing and Editing.
23 24 25	411	Data availability statement
26 27 28	412	All data underlying this article are presented in the manuscript.
29 30 31	413	
32 33 34 35	414	
36 37 38		
39 40 41		
42 43		
44 45 46		
47		
48 49		
50		
51		
52 53		
55 54		
55		
56 57		
57 58		

# **References**

- Small C, Kramer HJ, Griffin KA, et al. Non-dialysis dependent chronic kidney disease is associated 1. with high total and out-of-pocket healthcare expenditures. BMC Nephrol 2017; 18: 3. 2017/01/07. DOI: 10.1186/s12882-016-0432-2. Silva Junior GBD, Oliveira JGR, Oliveira MRB, et al. Global costs attributed to chronic kidney 2. disease: a systematic review. Rev Assoc Med Bras (1992) 2018; 64: 1108-1116. 2018/12/21. DOI: 10.1590/1806-9282.64.12.1108. 3. Golestaneh L, Alvarez PJ, Reaven NL, et al. All-cause costs increase exponentially with increased chronic kidney disease stage. Am J Manag Care 2017; 23: S163-S172. 2017/10/06. Saran R, Pearson A, Tilea A, et al. Burden and Cost of Caring for US Veterans With CKD: Initial 4. Findings From the VA Renal Information System (VA-REINS). Am J Kidney Dis 2021; 77: 397-405. 2020/09/06. DOI: 10.1053/j.ajkd.2020.07.013. Al-Shdaifat EA and Manaf MR. The economic burden of hemodialysis in Jordan. Indian J Med Sci 5. 2013; 67: 103-116. 2013/12/12. Aoun M, Helou E, Sleilaty G, et al. Cost of illness of chronic kidney disease in Lebanon: from the 6. societal and third-party payer perspectives. BMC Health Serv Res 2022; 22: 586. 2022/05/04. DOI: 10.1186/s12913-022-07936-0. Rizk R, Hiligsmann M, Karavetian M, et al. A societal cost-of-illness study of hemodialysis in 7. Lebanon. J Med Econ 2016; 19: 1157-1166. 2016/06/29. DOI: 10.1080/13696998.2016.1207653. Laville SM, Gras-Champel V, Moragny J, et al. Adverse Drug Reactions in Patients with CKD. Clin J 8. Am Soc Nephrol 2020; 15: 1090-1102. 2020/07/03. DOI: 10.2215/CJN.01030120. Chia BY, Cheen MHH, Gwee XY, et al. Outcomes of pharmacist-provided medication review in 9. collaborative care for adult Singaporeans receiving hemodialysis. Int J Clin Pharm 2017; 39: 1031-1038. 20170821. DOI: 10.1007/s11096-017-0528-1. Song YK, Jeong S, Han N, et al. Effectiveness of Clinical Pharmacist Service on Drug-Related 10. Problems and Patient Outcomes for Hospitalized Patients with Chronic Kidney Disease: A Randomized Controlled Trial. J Clin Med 2021; 10 20210420. DOI: 10.3390/jcm10081788. 11. Bishop MA, Cohen BA, Billings LK, et al. Reducing errors through discharge medication reconciliation by pharmacy services. Am J Health Syst Pharm 2015; 72: S120-126. 2015/08/15. DOI: 10.2146/sp150021. Ernst FR and Grizzle AJ. Drug-related morbidity and mortality: updating the cost-of-illness model. 12. J Am Pharm Assoc (Wash) 2001; 41: 192-199. 2001/04/12. DOI: 10.1016/s1086-5802(16)31229-3. Alrugayb WS, Price MJ, Paudyal V, et al. Drug-Related Problems in Hospitalised Patients with 13. Chronic Kidney Disease: A Systematic Review. Drug Saf 2021; 44: 1041-1058. 2021/09/13. DOI: 10.1007/s40264-021-01099-3. Al Raiisi F, Stewart D, Fernandez-Llimos F, et al. Clinical pharmacy practice in the care of Chronic 14. Kidney Disease patients: a systematic review. Int J Clin Pharm 2019; 41: 630-666. 2019/04/10. DOI: 10.1007/s11096-019-00816-4. 15. Onatibia-Astibia A, Malet-Larrea A, Mendizabal A, et al. The medication discrepancy detection service: A cost-effective multidisciplinary clinical approach. Aten Primaria 2021; 53: 43-50. 2020/10/01. DOI: 10.1016/j.aprim.2020.04.008. Houso A, Hamdan M and Falana H. Cost benefit analysis of clinical pharmacist interventions in 16. medical intensive care unit in Palestine medical complex: Prospective interventional study. Saudi Pharm J 2022; 30: 1718-1724. 2023/01/06. DOI: 10.1016/j.jsps.2022.09.017. Jordan Food and Drug Administration (JFDA) http://jfda.jo/Pages/viewpage.aspx?pageID=336 17. (accessed July 2023).

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

# BMJ Open

2		
3	461	18. Nesbit TW, Shermock KM, Bobek MB, et al. Implementation and pharmacoeconomic analysis of a
4	462	clinical staff pharmacist practice model. Am J Health Syst Pharm 2001; 58: 784-790. DOI:
5	463	10.1093/ajhp/58.9.784.
6 7	464	19. Chen CC, Hsiao FY, Shen LJ, et al. The cost-saving effect and prevention of medication errors by
8	465	clinical pharmacist intervention in a nephrology unit. Medicine (Baltimore) 2017; 96: e7883. DOI:
9	466	10.1097/MD.00000000007883.
10	467	20. Pharmaceutical Care Network Europe, The PCNE CLassification V 9.1. Pharmaceutical Care
11	468	Network Europe, p Classification for Drug related problems. 2020.
12	469	21. Almanasreh E, Moles R and Chen TF. The medication discrepancy taxonomy (MedTax): The
13	470	development and validation of a classification system for medication discrepancy discrepancies identified through
14	470	medication reconciliation. <i>Res Social Adm Pharm</i> 2020; 16: 142-148. 20190414. DOI:
15		
16	472	10.1016/j.sapharm.2019.04.005.
17	473	22. AbuRuz SM, Alrashdan Y, Jarab A, et al. Evaluation of the impact of pharmaceutical care service
18	474	on hospitalized patients with chronic kidney disease in Jordan. Int J Clin Pharm 2013; 35: 780-789.
19	475	20130725. DOI: 10.1007/s11096-013-9806-8.
20	476	23. Quintana-Barcena P, Lord A, Lizotte A, et al. Prevalence and Management of Drug-Related
21	477	Problems in Chronic Kidney Disease Patients by Severity Level: A Subanalysis of a Cluster Randomized
22 23	478	Controlled Trial in Community Pharmacies. J Manag Care Spec Pharm 2018; 24: 173-181. DOI:
23 24	479	10.18553/jmcp.2018.24.2.173.
24	480	24. Buckley MS, Harinstein LM, Clark KB, et al. Impact of a clinical pharmacy admission medication
26	481	reconciliation program on medication errors in "high-risk" patients. The Annals of pharmacotherapy 2013;
27	482	47: 1599-1610. 20131015. DOI: 10.1177/1060028013507428.
28	483	25. Mendes AE, Lombardi NF, Andrzejevski VS, et al. Medication reconciliation at patient admission:
29	484	a randomized controlled trial. Pharm Pract (Granada) 2016; 14: 656. 20160315. DOI:
30	485	10.18549/PharmPract.2016.01.656.
31	486	26. Cadman B, Wright D, Bale A, et al. Pharmacist provided medicines reconciliation within 24 hours
32	487	of admission and on discharge: a randomised controlled pilot study. BMJ Open 2017; 7: e013647.
33	488	20170316. DOI: 10.1136/bmjopen-2016-013647.
34	489	27. Neeman M, Dobrinas M, Maurer S, et al. Transition of care: A set of pharmaceutical interventions
35	490	improves hospital discharge prescriptions from an internal medicine ward. <i>Eur J Intern Med</i> 2017; 38: 30-
36	491	37. 20161125. DOI: 10.1016/j.ejim.2016.11.004.
37 38	492	28. Cornu P, Steurbaut S, Leysen T, et al. Effect of medication reconciliation at hospital admission on
30 39	492 493	medication discrepancies during hospitalization and at discharge for geriatric patients. <i>The Annals of</i>
40		
41	494	pharmacotherapy 2012; 46: 484-494. 20120313. DOI: 10.1345/aph.1Q594.
42	495	29. Sebaaly J, Parsons LB, Pilch NA, et al. Clinical and Financial Impact of Pharmacist Involvement in
43	496	Discharge Medication Reconciliation at an Academic Medical Center: A Prospective Pilot Study. <i>Hospital</i>
44	497	<i>pharmacy</i> 2015; 50: 505-513. DOI: 10.1310/hpj5006-505.
45	498	30. Vira T, Colquhoun M and Etchells E. Reconcilable differences: correcting medication errors at
46	499	hospital admission and discharge. Qual Saf Health Care 2006; 15: 122-126. DOI:
47	500	10.1136/qshc.2005.015347.
48	501	31. Al-Jazairi AS, Al-Suhaibani LK, Al-Mehizia RA, et al. Impact of a medication reconciliation program
49	502	on cardiac surgery patients. Asian Cardiovasc Thorac Ann 2017; 25: 579-585. 20171012. DOI:
50	503	10.1177/0218492317738382.
51 52	504	32. Fernandes BD, Almeida P, Foppa AA, et al. Pharmacist-led medication reconciliation at patient
52 53	505	discharge: A scoping review. Res Social Adm Pharm 2020; 16: 605-613. 20190801. DOI:
53 54	506	10.1016/j.sapharm.2019.08.001.
55	507	33. Centers for Disease Control and Prevention. Chronic Kidney Disease
56		
57		
58		
59		
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

**BMJ** Open

1		
2 3		
4	508	in the United States, 2023. Atlanta, GA: US Department of Health and Human
5	509	Services, Centers for Disease Control and Prevention; 2023. Available at:
6	510	https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html
7	511	34. prevention Cfdca. Chronic Kidney Disease in the United States, 2021. 2021.
8	512	35. Nguyen-Thi HY, Le-Phuoc TN, Tri Phat N, et al. The Economic Burden of Chronic Kidney Disease in
9	513	Vietnam. <i>Health Serv Insights</i> 2021; 14: 11786329211036011. 20210728. DOI:
10 11	514	10.1177/11786329211036011.
12	515	36. Slawomirski L, Auraaen A and Klazinga NS. The economics of patient safety: strengthening a value-
13	516	based approach to reducing patient harm at national level. 2017.
14	517	37. Daifi C, Feldpausch B, Roa PA, et al. Implementation of a Clinical Pharmacist in a Hemodialysis
15	518	Facility: A Quality Improvement Report. Kidney Med 2021; 3: 241-247 e241. 20210210. DOI:
16	519	10.1016/j.xkme.2020.11.015.
17	520	38. Hassan Y, Al-Ramahi RJ, Aziz NA, et al. Impact of a renal drug dosing service on dose adjustment
18	521	in hospitalized patients with chronic kidney disease. <i>The Annals of pharmacotherapy</i> 2009; 43: 1598-1605.
19 20	522	20090923. DOI: 10.1345/aph.1M187.
20 21	523	39. Manley HJ and Carroll CA. The clinical and economic impact of pharmaceutical care in end-stage
22	524	renal disease patients. <i>Semin Dial</i> 2002; 15: 45-49. DOI: 10.1046/j.1525-139x.2002.00014.x.
23	525	40. Anderegg SV, Wilkinson ST, Couldry RJ, et al. Effects of a hospitalwide pharmacy practice model
24	526	change on readmission and return to emergency department rates. Am J Health Syst Pharm 2014; 71:
25	527	1469-1479. DOI: 10.2146/ajhp130686.
26	528	41. Jiang SP, Zhu ZY, Ma KF, et al. Impact of pharmacist antimicrobial dosing adjustments in septic
27	529	patients on continuous renal replacement therapy in an intensive care unit. Scand J Infect Dis 2013; 45:
28	530	891-899. 20130912. DOI: 10.3109/00365548.2013.827338.
29 30	531	42. Al-Qudah RA, Al-Badriyeh D, Al-Ali FM, et al. Cost-benefit analysis of clinical pharmacist
31	532	intervention in preventing adverse drug events in the general chronic diseases outpatients. J Eval Clin
32	533	Pract 2020; 26: 115-124. 20190624. DOI: 10.1111/jep.13209.
33	534	43. Aljbouri TM, Alkhawaldeh MS, Abu-Rumman AE, et al. Impact of clinical pharmacist on cost of
34	535	drug therapy in the ICU. Saudi Pharm J 2013; 21: 371-374. DOI: 10.1016/j.jsps.2012.12.004.
35	536	44. Abushanab D, Gulied A, Hamad A, et al. Cost savings and cost avoidance with the inpatient clinical
36	537	pharmacist interventions in a tertiary cancer care hospital. J Oncol Pharm Pract 2023:
37	538	10781552231160275. 20230322. DOI: 10.1177/10781552231160275.
38 39		
40	539	
41		
42	540	
43		
44	541	
45	542	
46	542	
47	543	
48 49		
50	544	
51	545	
52	545	
53	546	
54		
55	547	
56		
57 59		
58 59		2
60		2 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

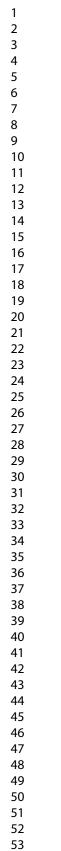
1 2		
3 4	548	Figure Legends:
5 6	549	
7 8	550	
9 10	551	Figure 1: The cost-benefit analysis model.
10 11 12	552	Figure 2: Tornado diagrams of one-way sensitivity analyses.
13	553	Figure 3: Probabilistic sensitivity analysis for the net benefit of supplemented medication
14 15	554	reconciliation service.
16 17 18	555	
19 20 21	556	
22 23	557	
24 25	558	
26 27 28	559	
29 30	560	
31 32 33	561	
34 35	562	
36 37	563	
38 39 40	564	
41 42	565	
43 44 45	566	
45 46 47	567	
48 49	568	
50 51 52	569	
53 54	570	
55 56 57	571	
58 59 60		2; For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

2
3
4
5
6
7
8
9
10
11
12
13
14
15
16
17
18
19
20
20 21
21 22
22
23
24
25
26
27
28
29
29 30
31
21
32
33
34
35
36 37
37
38
39
40
41
41
42 43
44
45
46
47
48
49
50
51
52
52 53
55 54
55
56
57
58
50

	Cause	Cost avoidance (\$)	Total (\$)
Drug selection	Inappropriate drug according to	12,480.17	25,588.49
	guidelines/formulary	0.645.00	-
	No or incomplete drug treatment despite	8,645.98	
	existing indication		-
	No indication for drug	2,295.94	-
	Inappropriate combination of drugs or drugs and dietary supplements	1,916.01	
	Too many different drugs/active ingredients	250.39	-
	prescribed for indication		-
	Inappropriate duplication of therapeutic group or active ingredient	250.38	
Dose selection	Drug dose of a single active ingredient too high	13,710.33	21,141.39
	Dosage regimen too frequent	5,284.26	-
	Drug dose too low	2,146.80	-
Patient transfer	Drug omission	12,693.54	20,623.2
related	Discrepancy in the strength and/or	4,612.57	-
(discrepancies)	frequency and/or number of units of dosage	,	
	form and/or total daily dose		
	Drug addition	2,399.36	-
	Therapeutic class substitution	436.54	-
	Drug duplication	337.48	-
	Discrepancy in the dosage form/route of administration	143.70	-
Drug use process	Inappropriate timing of administration or	2,624.71	2,777.12
	dosing intervals by a health professional		
	Drug administered via wrong route by a	152.41	-
	health professional		
Treatment	Duration of treatment too long	273.25	469.21
duration	Duration of treatment too short	195.96	-
F <b>able 1:</b> Cost avoid	lance per cause-based domains in the PCNE cla	ssification of DI	RPs (V9.1).

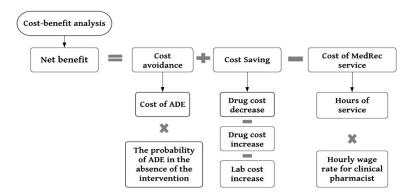
	Drug form	Inappropriate drug form/formulation	114.30	114.30
	Other	Addition of a lab test	10,531.5	12,088.25
	Total	No or inappropriate outcome monitoring	1,556.75	83,052.34
577 578				05,052.54
579 580 581	Table 2: Re	esults of cost-benefit analysis		
		Outcome	Value (\$)	
		Intervention cost over 4 months	713.70	
		Cost avoidance of all DRPs	83,052.4	
		Total cost saving	- 467.5	
		Net benefit over the study period (4 months)	81,871.15	
		Benefit to cost ratio	115.7:1	
32		E.		
83				

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.



58 59

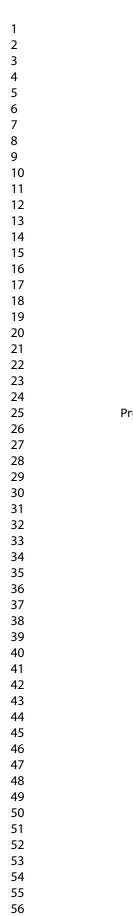
60



The cost-benefit analysis model.

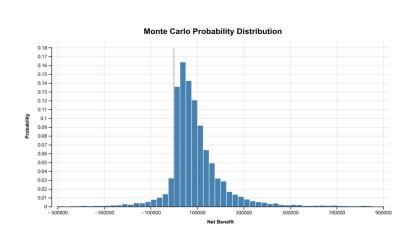
338x190mm (96 x 96 DPI)

1 age 27 of 55	bib open	
1         2         3         4         5         6         7         8         9         10         11         12         13         14         15         16         17         18         19         20         21         22         23         24         25         26         27         28         29         30         31         32         33         34         35         36         37         38         39         40         41         42         43         44         45         46         47         48         49         50         51         52	<figure></figure>	BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.
45 46 47 48 49 50 51	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	n June 8, 2025 at Agence Bibliographique de I r technologies.



57 58 59

60



Probabilistic sensitivity analysis for the net benefit of supplemented medication reconciliation service

338x190mm (96 x 96 DPI)

1	
2	
3	
4	
5	
6	
7	
8	
3 4 5 6 7 8 9 10	
10	
11	
12	
13	
14	
15	
11 12 13 14 15 16 17	
17	
18	
19	
20	
21	
22	
23	
24	
25	
20	
27	
19 20 21 22 23 24 25 26 27 28 29 30 31	
30	
30	
32	
33	
34	
32 33 34 35 36	
36	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49 50	
50	
51 52	
52 53	
53 54	
54 55	
55 56	
56 57	
57	

60

## **Research Article**

# Title: Clinical pharmacist-led medication reconciliation supplemented with medication

review in chronic kidney disease admitted patients: a cost-benefit analysis

Journal: BMJ Open.

to beet terien only

1 2
2 3
4 5
6
7
7 8 9 10 11 12
9
10
11
12
13 14
14 15
15
10 17
17 18
<ol> <li>16</li> <li>17</li> <li>18</li> <li>19</li> <li>20</li> <li>21</li> <li>22</li> <li>23</li> <li>24</li> <li>25</li> <li>26</li> <li>27</li> <li>28</li> <li>29</li> <li>30</li> </ol>
20
21
22
23
24
25
26
27
28
29
30
31 32
32 33
27
34 35
36
27
37 38
39
40
41
42
43
44
45
46 47
47 48
40 49
49 50
50 51
52
53
54
55
56
57
58
59
60

# Table S1: Patient demographics and clinical characteristics of the study sample.

	Study sample
Variable	N(%) N = 142
$C_{\text{outdown}}(0/)$	N = 142
Gender n (%)	52 (27 22)
Female	53 (37.32)
Male	89 (62.68)
Age, years (M± SD)	57.16±15.96
BMI n (%)	
<18.5	6 (4.23)
18.5 -24.9	41 (28.87)
25-29.9	42 (29.58)
> 29.9	53 (37.32)
Marital status	
Married	109 (76.76)
Not married	33 (23.24)
Smoking status	
Yes	43 (30.28)
No	75 (52.82)
Ex-smoker	24 (16.90)
Educational level	
Not educated	20 (14.08)
School	93 (65.49)
University/higher education	29 (20.42)
Employment status	
Employed	26 (18.31)
Retired	32 (22.54)
Unemployed	84 (59.15)
Occupation	
Medical	3 (2.11)
Non-medical	64 (45.07)
No	75 (52.82)
Monthly income	
<500	110 (77.46)
500 -1000	29 (20.42)
>1000	3 (2.11)

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

AKI on Top of CKD related problems	42 (29.58)
CKD/dialysis related problems	71 (50.0)
Others	29 (20.42)
CKD stage	
Stage 2	2 (1.41)
Stage 3a	3 (2.11)
Stage 3b	12 (8.45)
Stage 4	32 (22.54)
Stage 5	93 (65.5)
Years of dialysis (M± SD)	$2.33 \pm 3.66$
Years of CKD (M± SD)	$5.02 \pm 6.80$
Number of comorbidities (M± SD)	$6.36 \pm 2.18$
$CCI (M \pm SD)$	$6.08 \pm 2.93$
Number of medications at admission	9.58 (3.07)
Number of medications at discharge	9.24 (4.34)
Death at discharge	5 (3.52)

Abbreviation: BMI: Body Mass Index, M± SD: Mean ± Standard deviation, CKD: Chronic Kidney Disease, AKI: Acute Kidney Disease. CCI: Charlson Comorbidity Index.

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

#### **BMJ** Open

A patient had a recent myocardial infarction (MI) and had previously	High
undergone stent placement for the main coronary artery. She was taking	(0.6)
febuxostat for gout. The clinical pharmacist recommended switching from	
febuxostat to allopurinol. (Black box warning)	
A female patient on hemodialysis, has a hemoglobin (Hb) level of 12 and a	High
history of stroke. She was on alpha epoetin 4000 units prescribed every	(0.6)
other day (EOD). (Black box warning)	
A 91-year-old female patient with CKD stage 5 (baseline serum creatinine	Medium
is 500 mmol/l). Dialysis was delayed due to her age. The patient is	(0.4)
experiencing uremia, including vomiting symptoms. She was prescribed	
metoclopramide 10 mg intravenously every 8 hours, which is a high dose	
considering her condition. Additionally, she is taking trimetazidine, which	
has a serious interaction with metoclopramide (category X). It is important	
to note that trimetazidine is contraindicated in patients with a GFR <30.	
A patient has osteoporosis and is undergoing hemodialysis. Initially, she	Medium
was prescribed alendronate, but the clinical pharmacist recommended	(0.4),
switching to denosumab. The physician stopped the alendronate as advised	Low
but could not provide denosumab due to economic issues. Subsequently,	(0.1)
the patient visited the outpatient clinic (OPC) due to bone pain, and there	
she received denosumab treatment.	
A patient has a CrCl (Creatinine Clearance) of 13, and he is currently taking	Medium
fenofibrate. Additionally, the triglyceride level is less than 250 mg/dL.	(0.4)
A patient underwent upper endoscopy, which revealed mild gastritis. There	Medium
were no available tests for H. pylori, and the patient's serum creatinine level	(0.4)
was 500 mmol/l (CrCl <15). Nevertheless, upon discharge, the patient was	
prescribed amoxicillin 1g twice daily and clarithromycin 500mg twice	
daily without renal adjustment and without confirming the diagnosis.	
	<u> </u>

A patient has AKI on top of CKD and has been experiencing severe	Medium
vomiting for over a week. Upon admission, the patient's home medication	(0.4)
included metoclopramide 10 mg three times daily taken orally. However,	
after admission, the route was changed to intravenous 10 mg TID (not renal	
dose) without improvement, the dose was changed to metoclopramide	
intravenously at 20 mg three times daily, which is considered too high. The	
clinical pharmacist recommended discontinuing metoclopramide and	
administering ondansetron as an alternative.	
A patient is undergoing hemodialysis and was diagnosed with deep vein	Medium
thrombosis (DVT). Upon discharge, she was prescribed a therapeutic dose	(0.4)
of Enoxaparin. The clinical pharmacist recommended switching to	
apixaban.	
A patient was admitted for liver cirrhosis, baseline CrCl 32, AKI, diabetes	Medium
mellitus (DM), and recently diagnosed depression. He was initially	(0.4)
admitted while taking metformin 500mg once daily. However, upon	
discharge, his medication regimen included metformin 850mg three times	
daily, mirtazapine, spironolactone, and hydrochlorothiazide. The clinical	
pharmacist was unable to reach the responsible physician to discuss the	
changes. Consequently, the patient was readmitted after 5 days due to	
diarrhea and hyponatremia.	
A patient has a UTI and is currently taking ciprofloxacin, calcium	Low
carbonate, and ferrous gluconate twice daily, both at 6 pm and 6 am, all by	(0.1)
oral route.	
A patient admitted with severe hypophosphatemia; the physician initially	Low
recorded that the patient was on calcium carbonate 500mg BID. With	(0.1)
medication reconciliation we found that the actual home dose was calcium	
carbonate 1g TID, along with sevelamer TID, which was obtained from	
outside the hospital (and was not known by the physician). Resolving these	
discrepancies with the physician led to a change in the diagnosis.	
A patient has been taking Combivent® every 8 hours for over than 2 weeks	Low
without any valid indication.	(0.1)

A 32-year-old patient has type 1 diabetes mellitus (DM1), end-stage renal	
	Low
disease (ESRD), partial retinopathy, and uncontrolled DM with recurrent	(0.1)
hypoglycemia. Upon admission, she was using pre-mixed insulin. The	
clinical pharmacist suggested switching to a basal-bolus insulin regimen.	
A patient was discharged without some of his hypoglycemic and	Low
antihypertensive agents unintentionally.	(0.1)
A patient on HD, was on famotidine 40mg once daily at home. Was not	Very
documented.	low
	(0.01)

# **BMJ Open**

#### Clinical pharmacist-led medication reconciliation supplemented with medication review in chronic kidney disease admitted patients: a cost-benefit analysis

Journal:	BMJ Open
Manuscript ID	bmjopen-2024-087232.R1
Article Type:	Original research
Date Submitted by the Author:	27-Sep-2024
Complete List of Authors:	Altawalbeh, Shoroq ; Jordan University of Science and Technology, Department of Clinical Pharmacy Sallam, Nahlah M.; Jordan University of Science and Technology, Department of Clinical Pharmacy Al-Khatib, Minas; Jordan University of Science and Technology, Department of Clinical Pharmacy Alshogran, Osama Y.; Jordan University of Science and Technology, Department of Clinical Pharmacy Bani Amer, Mohammad S.; Jordan University of Science and Technology, Department of Internal Medicine
<b>Primary Subject Heading</b> :	Epidemiology
Secondary Subject Heading:	Medical management, Health services research, Health economics
Keywords:	Medication Reconciliation, Health Services, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health & safety < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

SCHOLARONE<sup>™</sup> Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

terez oni

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

BMJ Open

1		
2		
3 4	1	Research Article
5		
6	2	
7	-	
8	3	Clinical pharmacist-led medication reconciliation supplemented with
9		
10	4	medication review in chronic kidney disease admitted patients: a cost-benefit
11 12		
13	5	analysis
14	5	
15		
16	6	Shoroq M. Altawalbeh, PharmD, PhD, <sup>1</sup> Nahlah M. Sallam, M.S <sup>1</sup> , Minas Al-Khatib, PharmD, <sup>1</sup> Osama Y.
17	-	
18 19	7	Alshogran, M.S, PhD, <sup>1</sup> Mohammad S. Bani Amer, MD <sup>2</sup>
20		
21	8	<sup>1</sup> Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan University of Science and Technology, Irbid,
22	9	Jordan. <sup>2</sup> Department of Internal Medicine, Faculty of Medicine, Jordan University of Science and Technology,
23	10	Irbid, Jordan.
24		
25 26	11	
20		
28	12	Shoroq M. Altawalbeh, PharmD, PhD, Department of Clinical Pharmacy, Faculty of Pharmacy,
29	13	Jordan University of Science and Technology, Irbid 22110, Jordan. Email address:
30	14	smaltawalbeh@just.edu.jo
31	45	
32 33	15	ORCID: 0000-0001-8345-4048
34	16	
35		<u> </u>
36	17	Nahlah M. Sallam, Msc, Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan
37	18	University of Science and Technology, Irbid 22110, Jordan. Email address:
38 39	19	nmsallam20@ph.just.edu.jo
40	20	ORCID: 0000-0001-9311-600X
41	20	
42	21	Minas Al-Khatib PharmD, Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan
43	22	University of Science and Technology, Irbid 22110, Jordan. Email address:
44	23	<u>makhatib@just.edu.jo</u>
45 46	24	
47	27	
48	25	Osama Y. Alshogran, Msc, PhD, Department of Clinical Pharmacy, Faculty of Pharmacy,
49	26	Jordan University of Science and Technology, Irbid 22110, Jordan. Email address:
50	27	oyalshogran@just.edu.jo
51 52	20	
52 53	28	ORCID: 0000-0002-2466-4763
54		
55		
56		
57		
58 59		1
59 60		ا For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
~~		

1 2			
3 4	29	Mohammad S. Bani Amer, MD, Department of Internal Medicine, Faculty of Medicine, Jordan	
5 6	30 31	University of Science and Technology, Irbid 22110, Jordan. Email address: <u>m.baniamer1997@gmail.com</u>	
7 8	32		
9	33	*Corresponding Author:	
10 11	34	Shoroq M. Altawalbeh, PharmD, PhD	
12 13	35	Associate Professor	
14 15	36	Department of Clinical Pharmacy	
16 17	37 38	Jordan University of Science and Technology; Faculty of Pharmacy	
18 19	39	P.O.Box 3030, Irbid 22110, Jordan	
20 21 22	40 41	Tel.:+962(0)27201000 Fax : + 962 (0) 2 7095123	
23 24	42	E-mail: <u>smaltawalbeh@just.edu.jo</u>	
25	43	ORCID: 0000-0001-8345-4048	
26 27	44		
28 29	45	Running Title: Cost-benefit of medication reconciliation in CKD	
30 31 32	46	Number of Tables: 2	
33 34	47	Number of Figures: 3	
35 36	48	Keywords: Medication reconciliation, clinical pharmacist, cost-benefit, chronic kidney disease,	
37 38	49	Jordan.	
39 40 41	50		
42 43	51		
44 45	52		
46 47	52		
48	53		
49 50	54		
51 52	0.		
53 54	55		
55 56 57	56		
58			
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

BMJ Open

2		
3 4	57	
5 6 7	58	Abstract
8 9	59	<b>Objective:</b> Chronic kidney disease (CKD) is associated with a high economic burden, which is
10 11 12	60	exacerbated by the high susceptibility to drug-related problems (DRPs) in this patient population.
12 13 14	61	This study aimed to evaluate the cost-benefit ratio of medication reconciliation supplemented
15 16	62	with medication review among inpatients with CKD.
17 18 19	63	Design: This was a cost-benefit analysis conducted along with a prospective interventional
20 21 22	64	study.
23 24 25	65	Setting: The study was conducted at two hospitals in Jordan between February and May 2023.
26 27 28	66	Participants: The prospective interventional study included 142 admitted patients with CKD.
29 30 31	67	Method: Patients received medication reconciliation at admission and discharge as well as
32 33	68	medication review throughout admission. A cost-benefit analysis was conducted from the
34 35	69	healthcare system perspective by assessing the cost of the service (the pharmacist time required
36 37 38	70	to complete the service per patient) and the economic benefit in terms of cost savings and cost
39 40	71	avoidance. The primary outcome measures were the net benefit and the benefit-to-cost ratio of
41 42 43	72	the intervention.
44 45	73	<b>Results:</b> The total estimated cost of all DRPs in the absence of interventions (cost avoidance)
46 47 48	74	was \$83,052.4; among which \$20,623.19 was attributed to medication discrepancies. The cost
49 50	75	savings were estimated at -\$467.5. The supplemented medication reconciliation service was
51 52	76	estimated to cost \$713.7. As a result, the estimated net benefit amounted to \$81,871.15, with a
53 54 55 56 57 58 59	77	benefit-to-cost ratio of 115.7:1 over the 4-month study period.

3 4

6

### BMJ Open

78	Conclusion: Delivering a supplemented medication reconciliation service by a clinical
79	pharmacist for CKD patients is cost beneficial from the healthcare perspective in Jordan, an
80	example of a low- and middle-income country (LMIC). This finding further confirms the pivotal
81	role of clinical pharmacists in multidisciplinary healthcare teams.
82	role of clinical pharmacists in multidisciplinary healthcare teams. Keywords: Medication reconciliation, clinical pharmacist, cost-benefit, chronic kidney disease, Jordan.
83	Keywords: Medication reconciliation, clinical pharmacist, cost-benefit, chronic kidney disease,
84	Jordan.
85	inclu
86	
87	or use
88	
89	ted to
90	
91	and da
92	atar B
93	níng,
94	
95	training, and similar technologies
96	and s
97	imilar ar
98	techr
99	
100	а С
101 102	
102	
100	
	4 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

Enseignement Superieur (ABES). Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.	BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de
--	--

1		
2 3		
4	104	
5 6	105	
7	106	
8 9 10	107	Strengths and limitations of this study
10 11 12	108	• The study was conducted along with a prospective interventional study.
13 14	109	• Evaluation of the probability scores of drug related problems (DRPs) was
15 16	110	conducted by an expert panel composed of five independent evaluators.
17 18 19	111	• The exact real cost of adverse events resulting fromDRPs could not be measured.
19 20 21	112	• The study relied on admission charges, medication prices, and lab prices rather than
22 23	113	The study relied on admission charges, medication prices, and lab prices rather than actual costs.
24 25 26	114	
27	115	
28 29 30	116	
31	117	
32 33	118	
34 35	119	
36 37	120	
38 39	121	
40 41	122	
42 43	123	
44 45	124	
46 47	125	
48 49	126	
50	127	
51 52 53	128	
54	129	
55 56 57 58	130	
59 60		5 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1 2		
2 3 4	131	
5	132	
6 7	133	
8 9 10	134	Introduction
11 12	135	Chronic kidney disease (CKD) is associated with high financial burden globally, exceeding
13 14	136	expenditures incurred by other highly burdened patients such as those with stroke and cancer. <sup>1, 2</sup>
15 16 17	137	CKD is a complex medical state accompanied by multiple concurrent illnesses, which inflate the
18 19	138	cost of management. Around \$18 billion had been spent by the national US Department of
20 21	139	Veterans Affairs for the care of patients with CKD without renal replacement therapy (RRT), with
22 23	140	expenditures increased across the advanced stages of CKD. <sup>3, 4</sup> In Jordan, the Ministry of Health
24 25 26	141	expended approximately \$17.7 Million per year for hemodialysis patients management in 2010,
27 28	142	with an average of annual cost of \$9,979 per patient. <sup>5</sup> A study conducted in Lebanon reported the
29 30	143	median cost for all CKD stages per year of \$4,764.02 (IQR \$2,475.24 - \$23,455.61) in 2019 from
31 32 33	144	a society perspective. <sup>6</sup> Studies highly recommend implementing programs and policies to reduce
33 34 35	145	progression and complications of CKD to mitigate the growing disease burden especially in
36 37	146	countries with limited resources. <sup>7</sup>
38 39	147	Patients with CKD are very vulnerable to medication discrepancies and other Drug related
40 41 42	148	problems (DRPs).8, 9 Interestingly, many serious DRPs are preventable in CKD patients.10
43 44	149	Developing DRPs increased the exposure to re-hospitalization, extended length of hospital stays,
45		

and early death, and therefore expanded the cost.<sup>11-13</sup> Clinical pharmacy services targeting DRPs
have revealed a positive economic impact on healthcare organizations across the literature.<sup>14</sup>
Medication reconciliation and medication review, primarily led by a clinical pharmacist, are vital
services focused on preventing and resolving medication discrepancies and other drug-related
problems (DRPs). These processes play a key role in enhancing patient outcomes and reducing

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

#### **BMJ** Open

healthcare costs. <sup>15</sup> Medication reconciliation ensures that the patient's medication list is accurate
 and up-to-date during transitions of care, while medication review involves a thorough and
 structured assessment of the patient's medications to ensure they are receiving the most appropriate
 treatment regimen. <sup>16</sup>

The economic burden of medication discrepancies and other DRPs is understudied, particularly in developing countries, including Jordan. Moreover, there is a dearth of data regarding the efficiency of clinical pharmacy services implemented in patients with CKD, especially in low-income to middle-income countries. Although medication reconciliation has the potential to be beneficial in this population, it also incurs costs, highlighting the need for a health economic analysis to determine whether this service can deliver clinical benefits at a reasonable cost, providing a solid rationale for its clinical application. Efforts to evaluate the cost-benefit of medication reconciliation provide essential evidence for healthcare providers and policymakers regarding the value of implementing this clinical service particularly in CKD patients. Examining the costs associated with drug-related problems (DRPs) during CKD hospitalizations will further emphasize the burden of the disease and support efforts to reduce the significant healthcare expenses related to CKD. These insights will underscore the crucial role clinical pharmacists play as part of the multidisciplinary hospital team in alleviating the financial impact of CKD on the healthcare system. Therefore, this study aimed to evaluate the cost-benefits of implementing a clinical pharmacist-led service for supplemented medication reconciliation among admitted patients with CKD in Jordan.

175 Methods

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

#### **BMJ** Open

#### Study design

The cost-benefit analysis was developed along with a prospective interventional clinical study that involved patients with stages 2-5 CKD, who were admitted to two healthcare hospitals in Jordan: King Abdullah Hospital (KAUH) and Princess Basma Hospital (PBH). A clinical pharmacist was responsible for providing supplemented medication reconciliation to CKD-admitted patients over four months (from February to May 2023). The costs and benefits over the study period were calculated relative to absence of this intervention. The primary outcome measure was the net benefit generated by the supplemented medication reconciliation service provided to CKD patients during the study period. The net benefit was estimated according to the following equation: [net benefit = total benefits (cost avoidance + cost saving)-service cost]. In addition, the benefit-to-cost ratio was estimated. The health care system perspective was adopted in the current study. Base case calculations were performed using Excel software. The cost-benefit analysis model is depicted in Figure 1. The demographic and clinical characteristics of the study sample are summarized in the Supplemental Material (Table S1). 

#### **Description of supplemented medication reconciliation**

Patients received a supplemented medication reconciliation service across the transitions of care during their admission to the internal medicine ward, in addition to a medication review for possible DRPs. The procedure of supplemented medication reconciliation consisted of medication reconciliation at admission, medication review throughout admission, and medication reconciliation at discharge. At admission, demographic, clinical, and medical data for each enrolled patient were collected from the medical records, followed by interviews with the patients or their caregivers to verify the patients' demographics, medical history, and pre-admission medication list. The pre-admission drug lists were also confirmed using all other available sources,

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES)

and

data mining, AI training, and similar technologies

Protected by copyright, including for uses related to text

such as bottles, prescriptions, and previous medical records, to obtain the best possible medication history (BPMH). The BPMH was compared with the current hospital medication sheet (admission medication orders) to extract discrepancies at admission. Medication reviews and clinical case analyses were conducted regarding dose adjustments, drug interactions, missing medications, inappropriate medications, unnecessary medications, and monitoring after admission and during the hospitalization period to identify the DRPs. At discharge, the best possible discharge medication plan (BPMDP) was created from the BPMH, the last medication list during index hospitalization, and new medications planned to be started upon discharge. The BPMDP was compared with discharge prescription and summary. Patient education was provided to willing patients before discharge. All identified discrepancies and other DRPs were discussed with the resident responsible for the resolution as accessible. 

#### 210 Estimation of costs

Input costs in the current study include the resources used to provide the supplemented medication reconciliation, that is, the pharmacists' time. The time taken by the pharmacist to deliver the supplemented medication reconciliation per patient (in hours) was recorded for each admission. The cost of the medication reconciliation service was estimated by multiplying the service time by the average hourly wage rate for clinical pharmacists, as obtained from the financial department at KAUH. The average annual wage rate was converted to the hourly wage rate based on 240 working days per year and 8 working hours per day.

218 Estimation of benefits

The economic benefits associated with the potential prevention of DRPs through interventions recommended by clinical pharmacists were evaluated in terms of "cost savings" and "cost avoidance."

#### **BMJ** Open

#### Cost saving

In the cost-saving analysis, the decreased medication costs due to interventions and the increased medication costs and costs attributed to requesting labs were estimated. The cost of any medication (increased or decreased) was estimated as the cost of medication per unit multiplied by the frequency per day and then by the duration of therapy.<sup>17</sup> Acute therapy duration was estimated based on the clinical scenario, while chronic medication use was calculated over three months' time horizon. Public per-unit prices of drugs were obtained from the Jordan Food and Drug Administration (JFDA).<sup>18</sup> For interventions that included the addition of a laboratory test, the increased cost for each intervention was estimated using the prices of laboratory tests obtained from KAUH laboratory department. Both drug and lab prices were converted to costs by multiplying them by an assumed Ratio of Cost to Charge (RCC). The net cost saving was estimated by subtracting the total increased cost from the decreased cost resulting from the implementation of the supplemented medication reconciliation services. 

Cost avoidance

Cost avoidance was estimated for each intervention recommended by the clinical pharmacist in the current study as the cost avoided by potential prevention of DRPs. The probability of DRP in the absence of intervention was determined according to the Nesbit et al scale <sup>19</sup> which has five levels of risk of causing DRPs: 0 (none), 0.01 (very low), 0.1 (low), 0.4 (medium), or 0.6 (high). The DRP probability in the absence of the intervention was estimated for all identified discrepancies and other DRPs by a team of experts, comprising four clinical pharmacists and one physician. Examples of the studied clinical cases with potential probabilities of DRPs are presented in Supplemental Material (Table S2). The cost avoidance attributed to each intervention was calculated by multiplying the corresponding DRP probability by the DRP cost.

The cost of a DRP was assumed to be the cost of an additional 2 days of hospital stay.<sup>20</sup> Admission charges were retrieved from the billing system for all admissions included in the study, and the average charge per day was calculated for these CKD patients. The average charge per day was adjusted using the assumed RCC to estimate the RCC cost of DRPs. Cost avoidance was estimated in total and by the Pharmaceutical Care Network Europe (PCNE) Classification for Drug-Related Problems V9.1 based on the cause,<sup>21</sup> and the Medication Discrepancy Taxonomy (MedTax) system.<sup>22</sup> All financial data were extracted in Jordanian Dinar currency unit (JOD) and converted to United States Dollars (USD) at a rate of (1 JOD = 1.41 USD). All cost data were reported in 2023 values. The RCC value was assumed to be 0.8 throughout the base case analysis and varied in the sensitivity analysis. 

#### 255 Sensitivity analysis

One-way sensitivity analysis was conducted to account for the variability in the key model parameters. DRP probabilities were varied using the minimum and maximum probabilities assigned by the expert panel. All costs were varied over a range of  $\pm 20\%$  of the base case cost. The average service time was varied over two SD of the mean, as calculated in this study. RCC was varied in the range (0.7 to 0.9). Probabilistic sensitivity analysis was conducted, in which the input variables were varied simultaneously over 10,000 Monte Carlo simulations. Beta distribution was used for DRP probabilities, uniform distribution for RCC and hourly wage rate, normal distribution for service time in minutes, and gamma distribution for cost.

#### 264 Public and patient involvement

Patients and the public were not actively involved in the design, conduct, reporting, ordissemination plans of this research.

#### 267 Ethics approval and consent to participate

This study was approved by the Institutional Review Board (IRB) Committee at KAUH (Ref number: 123/147/2022) and the Ministry of Health (Ref number: 13902). Written informed consent was obtained from the participants after they were given comprehensive information about the study's purpose and details. 

**Results** 

### Cost of supplemented medication reconciliation

The average time required to perform a supplemented medication reconciliation service (medication reconciliation plus medication review during admission) was 43.38 (SD= 6.65) minutes, ranging from 26 to 60.5 minutes. The total time spent by the clinical pharmacist on the supplemented medication reconciliation over the four-month intervention period was 6117.1 minutes (101.95 hours). The average duration to accomplish a primary medication reconciliation service at admission was  $15.79 \pm 1.74$  minutes. Though, the average time for medication review during the admission was  $21.6 \pm 4.30$  minutes (ranged from 11.6 to 35.5 minutes) per patient. Medication reconciliation time at discharge averaged  $3.58 \pm 1.55$  minutes per patient. Based on the reported average monthly salary of the clinical pharmacist at KAUH, the wage per hour was \$7 assuming 8 hours per day. Taking this into account, the total intervention cost over 4-month study period was \$713.7 ( $$7 \times 101.95$  hours). 

- Benefits of supplemented medication reconciliation
- Estimated cost saving

The total increased medication cost was estimated to be \$9,349 and lab needed total cost was estimated at \$5,248. The decrease in medication costs owing to the intervention was \$14,012. Total and

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

cost saving (after being adjusted with RCC of 0.8) = \$11,210[\$14,012\*0.8] - \$7,479[\$9,349 \*0.8] - \$4,198[\$5,248\*0.8] = -\$467.5. Table 2 presents cost saving values in total and at the patient level. *Estimated cost avoidance* 

The average admission charge for patients with CKD enrolled in the study was \$2811 (SD= \$2172), and the average admission charge per day was \$340.20 (SD= \$199.48). The assumed cost of a DRP was the estimated cost of two additional hospitalization days for patients with CKD in the current study [680.4 multiplied by 0.8 RCC = 483.1]. The estimated probabilities of DRPs in the absence of intervention were averaged using a panel of five expert evaluators. The majority of DRPs (73.4%; N=735) were in the low-to medium-risk category (0.1-0.4), while 21.2% (N=212) were in the low-risk category (<0.1), and 5.4% (N=54) were in the moderate-to high-risk category (>0.4). The average cost of a potential DRP, estimated by multiplying the average DRP probability by the estimated RCC cost for two additional hospitalization days was \$82.96 (SD=\$57.7). The total estimated cost of all DRPs in the study was \$83,052.4 (the cost avoidance). Patient transfer related DRPs (medications discrepancies) were found to be the third most expensive cause-based domain in the PCNE classification of DRPs (V9.1), contributing to around 25% of the total cost avoidance (\$20,623.19). The greatest weight of discrepancies' cost avoidance was attributed to "drug omission" category (\$12,693.54) followed by "discrepancy in frequency/strength/dose" (\$4,612.56) and "drug addition" (\$2,399.36), Table 1. A detailed summary of the cost avoidance per PCNE cause-based domains is presented in Table 1. Average cost avoidance per patient across the cause-based domains of DRPs (at the patient level) is detailed in the Supplemental Material (Table S3).Cost benefit analysis

#### **BMJ** Open

The net benefit was calculated by subtracting the total cost of intervention from total cost avoidance and saving [cost avoidance (\$83,052.4) + cost saving(-467.5) - cost of the intervention(\$713.7) = \$81,871.15]. The benefit-to-cost ratio estimated in this study was (115.7:1). Table 2. Sensitivity analyses The study conclusion was insensitive to uncertainty in any of the input variables including DRP probabilities, DRP cost, RCC, per-unit cost of drugs and labs, hourly wage rate, and average service time. The main driver of the outcome was the DRP probability, followed by the DRP cost, as depicted in Figure 2. However, the net benefit was positive over all plausible ranges of the input variables. The minimum estimated net benefit was \$50,203 based on varying DRP probability. In probabilistic sensitivity analysis, the average expected value of the net benefit was 90,451(SD =\$126,294). Only 866 out of 100,000 iterations (8.7%) showed a negative net benefit (Figure 3). Discussion The major findings of the current study emphasize the substantial economic burden of medication discrepancies and other DRPs in patients with CKD. In addition, the results showed that the estimated economic benefit was remarkable compared to the estimated cost of the medication reconciliation service. Overall, the results indicate that supplemented medication reconciliation services mediated by clinical pharmacists are cost beneficial. The majority of DRPs in the current study were classified as having a medium risk of DRPs. Despite the different scales used to evaluate the clinical significance of DRPs in patients with CKD, most studies have found that the majority of DRPs in this high-risk population were with moderate to significant clinical impact. In a study conducted in Jordan among hospitalized 

#### Page 16 of 37

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

#### **BMJ** Open

> patients with CKD, the majority of DRPs (62%) were classified among the significant category, however, the study used a different scale (extremely significant, much significant, significant, and slightly significant).<sup>23</sup> In a study conducted in Canada, approximately half of the observed DRPs were moderate in severity in terms of causing harm to CKD patients.<sup>24</sup> The different scales used in severity assessment across the literature makes the comparison seems challenging. Overall, most recognized DRPs were considered clinically important in the current study and potentially preventable.

> This study revealed the beneficial effect of clinical pharmacist medication reconciliation intervention on CKD patients in terms of the cost-benefits associated with this service. A recent review of 47 studies among CKD patients also supports this finding; 7 studies approved the significant cost savings and 15 studies reported improvement in clinical outcomes due to clinical pharmacy care, including blood pressure, anemia, length of hospital stay, readmissions, kidney function, and other laboratory tests (i.e., PTH, calcium, uric acid, cholesterol, and HbA1c).<sup>14</sup>

The average time needed for full supplemented medication reconciliation services provided for each CKD admission in the current study was  $43.38 \pm 6.65$  minutes. This is comparable to other studies that measured the time needed for medication reconciliation services:  $44.4 \pm 21.8$ .<sup>25</sup>  $40 \pm 17.2$  minutes,<sup>26</sup> and 48 minutes.<sup>27, 28</sup> In addition, the total time to deliver a primary medication reconciliation service at all transitions of care per patient was estimated with a median of 24 minutes (IQR 20-30 minutes).<sup>29</sup> The specific time for medication reconciliation at admission was roughly similar to our finding (15 minutes (IQR 10–21)) in two previous studies.<sup>30, 31</sup> Moreover, medication reconciliation at discharge after conducting medication reconciliation at admission was previously estimated to need approximately 3.5 minutes,<sup>32</sup> which is also comparable to the estimated time in the current study. However, a recent systematic review reported a wider range

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

of the mean time for medication reconciliation implementation across nine studies with an average of 34.5 ( $\pm$ 39.4) minutes.<sup>33</sup> This variability could be originated from the diverse models and services involved across the pooled studies and variations in study population. 

CKD has been associated with a high economic burden.<sup>3, 34-36</sup> DRPs have been associated with high costs that affect patient safety and healthcare expenditures.<sup>37</sup>. Our study estimated the net benefit attributed to avoiding and resolving DRPs to be \$81,871.15 over 4 months for a cumulative number of 142 CKD patients. Such remarkable benefit confirms the need of implementing supplemented medication reconciliation in CKD patients. Likewise, a recent retrospective cohort in the US among hemodialysis patients estimated cost saving from preventing DRPs to be \$447,355 over a 6-month period of observation, attributing this benefit to performing medication reconciliation with medication review.<sup>38</sup> A Malaysian study measured the cost saving resulted from only dose adjustment in CKD inpatients to be \$2,250 for 212 dose related recommendations over 4 months, in which the clinical pharmacist worked within a multidisciplinary rounds with the nephrology team to adjust the doses as needed.<sup>39</sup> This saved cost is considered much lower than the avoided cost resulting from renal dose adjustment in our study (\$14,756 for 4 months, 94 dose adjustment interventions). An earlier prospective study conducted medication therapy evaluation by pharmacist found that the ratio of pharmaceutical care cost to healthcare system saving is \$1 to \$3.98 among end-stage renal disease patients in the USA.<sup>40</sup> This is much smaller compared to the benefit to cost ratio estimated in the current study (115:1). This variability might be related in part to the relatively lower wage rates of clinical pharmacists in Jordan than in the USA. However, the estimated cost of a DRP is also expected to be higher in terms of admission-day costs in the USA. Another study found annual direct cost savings of more than \$780,000 after implementing supplemented medication reconciliation with patient education

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

in internal medicine wards in Kansas ascribed to reducing readmissions.<sup>41</sup> A Chinese trial found cost saving attributed to antimicrobial dose adjustment (number of adjusted doses= 183) by a clinical pharmacist of \$3,525 per patient with sepsis undergoing continuous dialysis in the ICU.<sup>42</sup> Wage rates and the cost of health care may differ widely across regions and institutions which make the comparison in cost is not sufficiently clear/straightforward. This also highlights the need to obtain relevant data from local or regional studies to better support the decisions of policy makers based on information from relevant settings.

In Jordan, the role of clinical pharmacists appears to be economically effective for other populations. Among outpatients with chronic diseases, the estimated cost avoidance per month due to pharmacist interventions (number of interventions = 79 among 48 patients) was  $6,422.41.^{43}$ In another study conducted in Jordan, clinical pharmacist intervention in the ICU reduced the total cost of drugs consumption by \$211,574.90 over 10 months.<sup>44</sup> Still, the cost benefit of medication reconciliation among CKD patients has not been well addressed in Jordan and other developing countries. The results of the current study strongly support the need to implement medication reconciliation supplemented with continuous medication review during hospital admission in patients with CKD. 

The current study has some limitations. We did not evaluate the actual adverse events resulting from DRPs or the actual role of interventions in decreasing these events. Furthermore, the exact real cost of adverse events resulting from DRPs could not be measured; however, the method of calculating cost avoidance in the current study has considered uncertainty and was implemented in previous studies.<sup>45</sup> In addition, the evaluation of the probability score of each DRP was conducted by an expert panel composed of five independent evaluators. Besides, the assessment of DRP probability scores was conducted independently by the study panel using a Page 19 of 37

#### BMJ Open

validated scale.<sup>19</sup> Another limitation is that we relied on admission charges, medication prices, and lab prices rather than actual costs. However, charges are widely used as a proxy for costs in the literature because of accessibility issues. Furthermore, we used an assumed RCC ratio to approach the actual costs, and this RCC was varied in the sensitivity analysis. **Conclusions** Pharmacist-led medication reconciliation supplemented with contentious medication review is very cost beneficial in CKD admitted patients, with substantial cost avoidance compared to the cost of implementing this service. The results clearly showed that activating the role of clinical pharmacists in providing medication reconciliation with a comprehensive medication review contributed positively to the safety of admitted patients with CKD and had a remarkable economic impact in clinical settings. The net benefit of this intervention could be enhanced by designing an efficient collaborative approach with physicians in hospital settings, and future studies should be directed toward evaluating the cost-benefit of such approaches. Funding: This work was supported by the Deanship of Scientific Research at the Jordan University of Science and Technology [grant number: 20220257]. The funding agency was not involved in the study design, conduct, writing, or decision to submit this article for publication. Competing Interests: The Authors declare that they have no conflicts of interest to disclose. Author contributions 

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

425	SA contributed to conceptualization, methodology, data curation, formal analysis, supervision,
426	project administration, funding acquisition, and writing original draft. NS contributed to
427	conceptualization, methodology, data curation, formal analysis, and writing original draft. MA
428	and OA contributed to conceptualization, methodology, data curation, and writing- reviewing
429	and editing. MB contributed to data curation and writing- reviewing and editing. SA is the
430	guarantor for the manuscript and accepts full responsibility for the overall content.
431	
432	Data availability statement
433	All data underlying this article are presented in the manuscript.
434	
435	
436	
437	
438	
439	
440	
441	
442	
443	
	10

#### **References**

- 451 1. Small C, Kramer HJ, Griffin KA, et al. Non-dialysis dependent chronic kidney disease is associated
  452 with high total and out-of-pocket healthcare expenditures. *BMC Nephrol* 2017; 18: 3. 2017/01/07. DOI:
  453 10.1186/s12882-016-0432-2.
- 454
   2.
   Silva Junior GBD, Oliveira JGR, Oliveira MRB, et al. Global costs attributed to chronic kidney

   28
   455
   disease: a systematic review. Rev Assoc Med Bras (1992) 2018; 64: 1108-1116. 2018/12/21. DOI:

   29
   456
   10.1590/1806-9282.64.12.1108.
- 457 3. Golestaneh L, Alvarez PJ, Reaven NL, et al. All-cause costs increase exponentially with increased chronic kidney disease stage. *Am J Manag Care* 2017; 23: S163-S172. 2017/10/06.

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES)

data mining, AI training, and similar technologies

Protected by copyright, including for uses related to text and

- 459 4. Saran R, Pearson A, Tilea A, et al. Burden and Cost of Caring for US Veterans With CKD: Initial 460 Findings From the VA Renal Information System (VA-REINS). *Am J Kidney Dis* 2021; 77: 397-405. 461 2020/09/06. DOI: 10.1053/j.ajkd.2020.07.013.
- 462 5. Al-Shdaifat EA and Manaf MR. The economic burden of hemodialysis in Jordan. *Indian J Med Sci* 463 2013; 67: 103-116. 2013/12/12.
- 464
   465
   465
   465
   466
   466
   466
   467
   466
   466
   466
   467
   468
   469
   469
   460
   460
   460
   460
   461
   462
   462
   463
   464
   465
   465
   465
   465
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
   466
- 467 7. Rizk R, Hiligsmann M, Karavetian M, et al. A societal cost-of-illness study of hemodialysis in
   468 Lebanon. J Med Econ 2016; 19: 1157-1166. 2016/06/29. DOI: 10.1080/13696998.2016.1207653.
- 469 8. Chia BY, Cheen MHH, Gwee XY, et al. Outcomes of pharmacist-provided medication review in
   470 collaborative care for adult Singaporeans receiving hemodialysis. *Int J Clin Pharm* 2017; 39: 1031-1038.
   471 20170821. DOI: 10.1007/s11096-017-0528-1.
- 47 472 9. Song YK, Jeong S, Han N, et al. Effectiveness of Clinical Pharmacist Service on Drug-Related
  48 473 Problems and Patient Outcomes for Hospitalized Patients with Chronic Kidney Disease: A Randomized
  49 474 Controlled Trial. *J Clin Med* 2021; 10 20210420. DOI: 10.3390/jcm10081788.
- 475 10. Laville SM, Gras-Champel V, Moragny J, et al. Adverse Drug Reactions in Patients with CKD. *Clin J* 476 *Am Soc Nephrol* 2020; 15: 1090-1102. 2020/07/03. DOI: 10.2215/CJN.01030120.
- 477 11. Bishop MA, Cohen BA, Billings LK, et al. Reducing errors through discharge medication reconciliation by pharmacy services. *Am J Health Syst Pharm* 2015; 72: S120-126. 2015/08/15. DOI: 10.2146/sp150021.

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

#### BMJ Open

Ernst FR and Grizzle AJ. Drug-related morbidity and mortality: updating the cost-of-illness model. 12. J Am Pharm Assoc (Wash) 2001; 41: 192-199. 2001/04/12. DOI: 10.1016/s1086-5802(16)31229-3. Alrugayb WS, Price MJ, Paudyal V, et al. Drug-Related Problems in Hospitalised Patients with 13. Chronic Kidney Disease: A Systematic Review. Drug Saf 2021; 44: 1041-1058. 2021/09/13. DOI: 10.1007/s40264-021-01099-3. 14. Al Raiisi F, Stewart D, Fernandez-Llimos F, et al. Clinical pharmacy practice in the care of Chronic Kidney Disease patients: a systematic review. Int J Clin Pharm 2019; 41: 630-666. 2019/04/10. DOI: 10.1007/s11096-019-00816-4. 15. Onatibia-Astibia A, Malet-Larrea A, Mendizabal A, et al. The medication discrepancy detection service: A cost-effective multidisciplinary clinical approach. Aten Primaria 2021; 53: 43-50. 2020/10/01. DOI: 10.1016/j.aprim.2020.04.008. World Health Organization, Medication safety in transitions of care: technical report, 2019. 16. 17. Houso A, Hamdan M and Falana H. Cost benefit analysis of clinical pharmacist interventions in medical intensive care unit in Palestine medical complex: Prospective interventional study. Saudi Pharm J 2022; 30: 1718-1724. 2023/01/06. DOI: 10.1016/j.jsps.2022.09.017. Jordan Food and Drug Administration (JFDA) http://jfda.jo/Pages/viewpage.aspx?pageID=336 18. (accessed July 2023). 19. Nesbit TW, Shermock KM, Bobek MB, et al. Implementation and pharmacoeconomic analysis of a clinical staff pharmacist practice model. Am J Health Syst Pharm 2001; 58: 784-790. DOI: 10.1093/ajhp/58.9.784. 20. Chen CC, Hsiao FY, Shen LJ, et al. The cost-saving effect and prevention of medication errors by clinical pharmacist intervention in a nephrology unit. Medicine (Baltimore) 2017; 96: e7883. DOI: 10.1097/MD.00000000007883. Pharmaceutical Care Network Europe, The PCNE CLassification V 9.1. Pharmaceutical Care 21. Network Europe, p Classification for Drug related problems. 2020. Almanasreh E, Moles R and Chen TF. The medication discrepancy taxonomy (MedTax): The 22. development and validation of a classification system for medication discrepancies identified through medication reconciliation. *Res Social Adm Pharm* 2020; 16: 142-148. 20190414. DOI: 10.1016/j.sapharm.2019.04.005. AbuRuz SM, Alrashdan Y, Jarab A, et al. Evaluation of the impact of pharmaceutical care service 23. on hospitalized patients with chronic kidney disease in Jordan. Int J Clin Pharm 2013; 35: 780-789. 20130725. DOI: 10.1007/s11096-013-9806-8. Quintana-Barcena P, Lord A, Lizotte A, et al. Prevalence and Management of Drug-Related 24. Problems in Chronic Kidney Disease Patients by Severity Level: A Subanalysis of a Cluster Randomized Controlled Trial in Community Pharmacies. J Manag Care Spec Pharm 2018; 24: 173-181. DOI: 10.18553/jmcp.2018.24.2.173. 25. Buckley MS, Harinstein LM, Clark KB, et al. Impact of a clinical pharmacy admission medication reconciliation program on medication errors in "high-risk" patients. The Annals of pharmacotherapy 2013; 47: 1599-1610. 20131015. DOI: 10.1177/1060028013507428. Mendes AE, Lombardi NF, Andrzejevski VS, et al. Medication reconciliation at patient admission: 26. a randomized controlled trial. Pharm Pract (Granada) 2016; 14: 656. 20160315. DOI: 10.18549/PharmPract.2016.01.656. 27. Cadman B, Wright D, Bale A, et al. Pharmacist provided medicines reconciliation within 24 hours of admission and on discharge: a randomised controlled pilot study. BMJ Open 2017; 7: e013647. 20170316. DOI: 10.1136/bmjopen-2016-013647. Neeman M, Dobrinas M, Maurer S, et al. Transition of care: A set of pharmaceutical interventions 28. improves hospital discharge prescriptions from an internal medicine ward. Eur J Intern Med 2017; 38: 30-37. 20161125. DOI: 10.1016/j.ejim.2016.11.004. 

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

29.

1 2 3

#### **BMJ** Open

Cornu P, Steurbaut S, Leysen T, et al. Effect of medication reconciliation at hospital admission on

Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.		MJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bib
--	--	--

4 529 medication discrepancies during hospitalization and at discharge for geriatric patients. The Annals of 5 530 pharmacotherapy 2012; 46: 484-494. 20120313. DOI: 10.1345/aph.1Q594. 6 531 30. Sebaaly J, Parsons LB, Pilch NA, et al. Clinical and Financial Impact of Pharmacist Involvement in 7 532 Discharge Medication Reconciliation at an Academic Medical Center: A Prospective Pilot Study. Hospital 8 533 *pharmacy* 2015; 50: 505-513. DOI: 10.1310/hpj5006-505. 9 10 534 Vira T, Colquhoun M and Etchells E. Reconcilable differences: correcting medication errors at 31. 11 535 hospital admission and discharge. Qual Saf Health Care 2006; 15: 122-126. DOI: 12 536 10.1136/qshc.2005.015347. 13 537 Al-Jazairi AS, Al-Suhaibani LK, Al-Mehizia RA, et al. Impact of a medication reconciliation program 32. 14 538 on cardiac surgery patients. Asian Cardiovasc Thorac Ann 2017; 25: 579-585. 20171012. DOI: 15 539 10.1177/0218492317738382. 16 540 33. Fernandes BD, Almeida P, Foppa AA, et al. Pharmacist-led medication reconciliation at patient 17 541 discharge: A scoping review. Res Social Adm Pharm 2020; 16: 605-613. 20190801. DOI: 18 542 10.1016/j.sapharm.2019.08.001. 19 20 543 Centers for Disease Control and Prevention. Chronic Kidney Disease 34. 21 544 in the United States, 2023. Atlanta, GA: US Department of Health and Human 22 23 545 Services, Centers for Disease Control and Prevention; 2023. Available at: 24 https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html. 546 25 547 prevention Cfdca. Chronic Kidney Disease in the United States, 2021. 2021. 35. 26 27 548 36. Nguyen-Thi HY, Le-Phuoc TN, Tri Phat N, et al. The Economic Burden of Chronic Kidney Disease in 28 549 Serv Insights 2021; 14: 11786329211036011. Vietnam. Health 20210728. DOI: 29 550 10.1177/11786329211036011. 30 551 Slawomirski L, Auraaen A and Klazinga NS. The economics of patient safety: strengthening a value-37. 31 552 based approach to reducing patient harm at national level. 2017. 32 553 38. Daifi C, Feldpausch B, Roa PA, et al. Implementation of a Clinical Pharmacist in a Hemodialysis 33 554 Facility: A Quality Improvement Report. Kidney Med 2021; 3: 241-247 e241. 20210210. DOI: 34 555 10.1016/j.xkme.2020.11.015. 35 556 39. Hassan Y, Al-Ramahi RJ, Aziz NA, et al. Impact of a renal drug dosing service on dose adjustment 36 37 557 in hospitalized patients with chronic kidney disease. The Annals of pharmacotherapy 2009; 43: 1598-1605. 38 558 20090923. DOI: 10.1345/aph.1M187. 39 559 Manley HJ and Carroll CA. The clinical and economic impact of pharmaceutical care in end-stage 40. 40 560 renal disease patients. Semin Dial 2002; 15: 45-49. DOI: 10.1046/j.1525-139x.2002.00014.x. 41 561 Anderegg SV, Wilkinson ST, Couldry RJ, et al. Effects of a hospitalwide pharmacy practice model 41. 42 change on readmission and return to emergency department rates. Am J Health Syst Pharm 2014; 71: 562 43 563 1469-1479. DOI: 10.2146/ajhp130686. 44 564 Jiang SP, Zhu ZY, Ma KF, et al. Impact of pharmacist antimicrobial dosing adjustments in septic 42. 45 46 565 patients on continuous renal replacement therapy in an intensive care unit. Scand J Infect Dis 2013; 45: 47 891-899. 20130912. DOI: 10.3109/00365548.2013.827338. 566 48 567 43. Al-Qudah RA, Al-Badriyeh D, Al-Ali FM, et al. Cost-benefit analysis of clinical pharmacist 49 568 intervention in preventing adverse drug events in the general chronic diseases outpatients. J Eval Clin 50 Pract 2020; 26: 115-124. 20190624. DOI: 10.1111/jep.13209. 569 51 570 Aljbouri TM, Alkhawaldeh MS, Abu-Rumman AE, et al. Impact of clinical pharmacist on cost of 44. 52 drug therapy in the ICU. Saudi Pharm J 2013; 21: 371-374. DOI: 10.1016/j.jsps.2012.12.004. 571 53 572 45. Abushanab D, Gulied A, Hamad A, et al. Cost savings and cost avoidance with the inpatient clinical 54 pharmacist interventions in a tertiary cancer care hospital. J Oncol Pharm Pract 2023: 55 573 56 574 10781552231160275. 20230322. DOI: 10.1177/10781552231160275. 57 58 59 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml 60

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

1		
2		
3 4	575	
5 6	576	
7 8	577	
9 10	578	
11 12	579	
13 14	580	
15 16	581	
17 18	582	Figure Legends:
19 20	583	
21 22	584	Figure Legends:
23 24	585	
25 26	586	
27 28	587	Figure 1: The cost-benefit analysis model.
29 30 31	588	Figure 2: Tornado diagram illustrating the impact of various parameters on the net benefit of
32 33	589	supplemented medication reconciliation service (one-way sensitivity analysis).
34 35 36	590	Figure 3: Probabilistic sensitivity analysis evaluating the net benefit of supplemented medication
37 38	591	reconciliation service.
39 40 41	592	
42 43	593	
44 45 46	594	
40 47 48	595	
49 50	596	
51 52	597	
53 54		
55 56	598	
57		
58 59		22
60		$^{23}$ For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1		
1 2		
3	599	
4	555	
5	600	
6 7	000	
8	601	
9	001	
10	602	
11	002	
12 13	603	
14	005	
15	604	
16		
17 18	605	
19		
20	606	
21		
22 23	607	Table 1: Cost avoidance per cause-based domains in the PCNE classification of DRPs (V9.1).
25 24	608	
25		
26	609	
27 28		
28 29	610	
30		
31	611	
32 33		
33 34		
35		
36		
37 38		
39		
40		
41		
42 43		
44		
45		
46		
47 48		
49		
50		
51 52		
52 53		
54		
55		
56 57		
57 58		
59		24
60		24 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

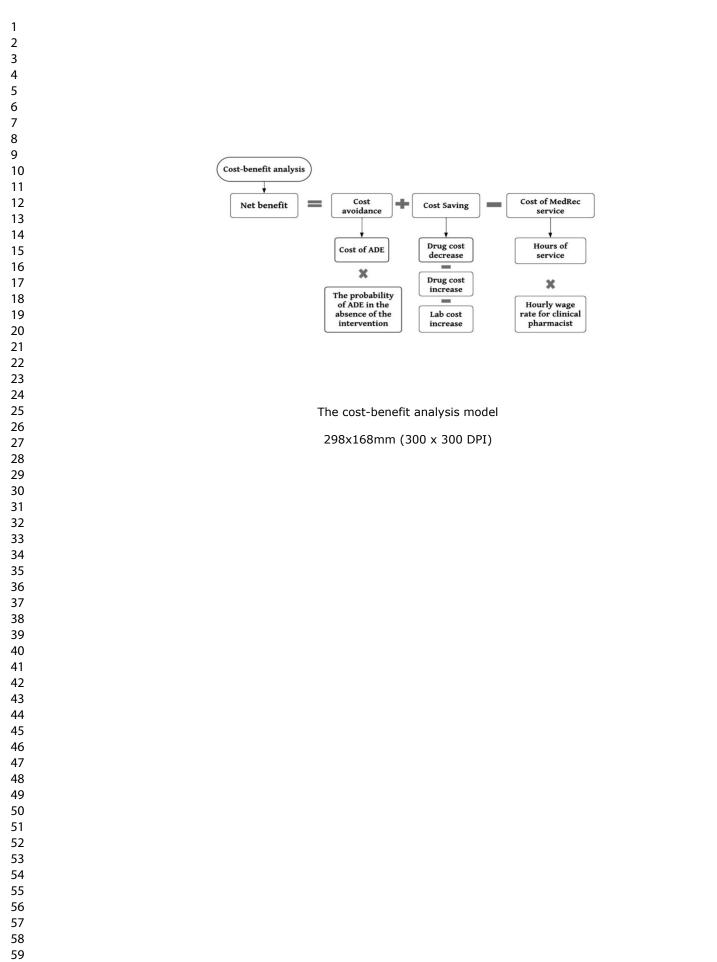
2	
3	
4	
4 5 6 7	
6 7	
/	
8	
9	
10	
11	
12	
13	
14	
15	
10	
17	
10	
עו 20	
20 21	
∠ı 22	
∠∠ 2२	
23 24	
8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30	
25	
20	
28	
20	
30	
31	
31 32	
33	
34	
35	
34 35 36 37 38 39	
37	
38	
39	
40	
41	
42	
43	
44	
45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	
59	
60	

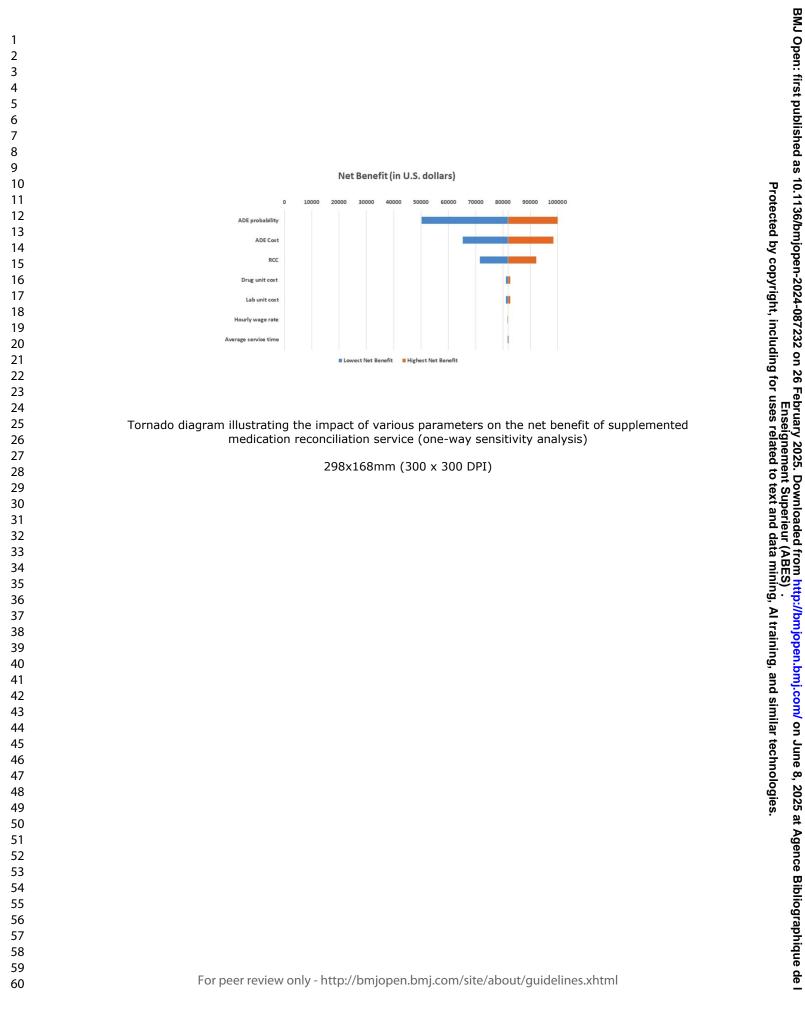
Primary domain	Cause	Cost	Total (\$)
		avoidance (\$)	
Drug selection	Inappropriate drug according to guidelines/formulary	12,480.17	25,588.49
	No or incomplete drug treatment despite existing indication	8,645.98	-
	No indication for drug	2,295.94	-
	Inappropriate combination of drugs or drugs and dietary supplements	1,916.01	
	Too many different drugs/active ingredients prescribed for indication	250.39	
	Inappropriate duplication of therapeutic group or active ingredient	250.38	
Dose selection	Drug dose of a single active ingredient too high	13,710.33	21,141.39
	Dosage regimen too frequent	5,284.26	-
	Drug dose too low	2,146.80	-
Patient transfer	Drug omission	12,693.54	20,623.2
related	Discrepancy in the strength and/or	4,612.57	-
(discrepancies)	frequency and/or number of units of dosage form and/or total daily dose		
	Drug addition	2,399.36	-
	Therapeutic class substitution	436.54	
	Drug duplication	337.48	-
	Discrepancy in the dosage form/route of administration	143.70	
Drug use process	Inappropriate timing of administration or dosing intervals by a health professional	2,624.71	2,777.12
	Drug administered via wrong route by a health professional	152.41	-
Treatment	Duration of treatment too long	273.25	469.21
duration	Duration of treatment too short	195.96	-
Drug form	Inappropriate drug form/formulation	114.30	114.30
Other	Addition of a lab test	10,531.5	12,088.25
	No or inappropriate outcome monitoring	1,556.75	
Total			83,052.34

## 615 Table 2: Results of cost-benefit analysis616

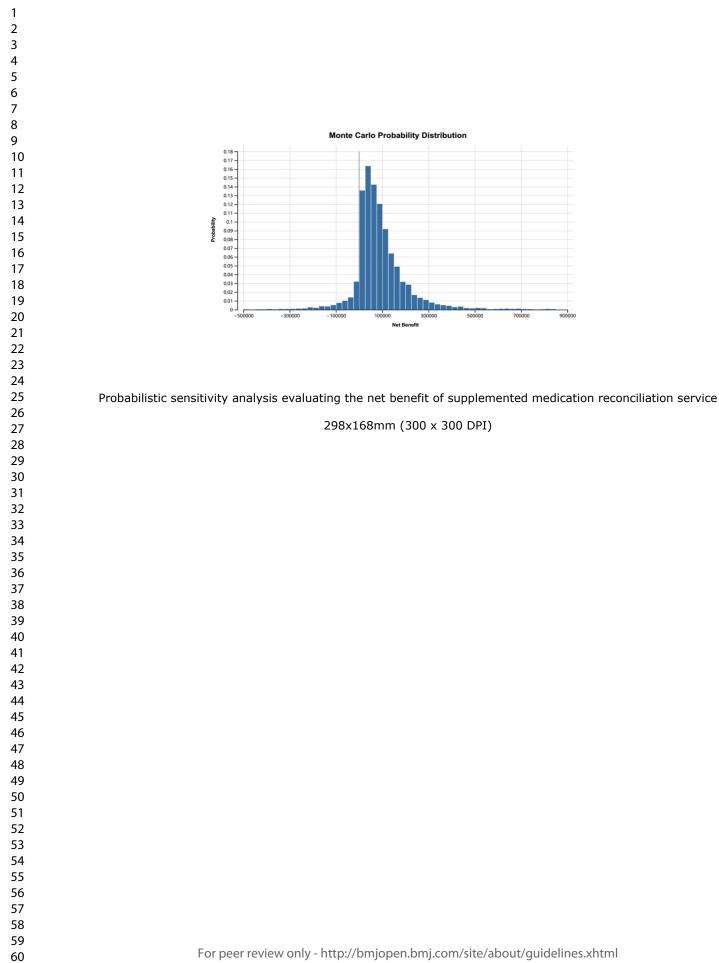
## 

	Outcome	Total (\$)	Average per patient \$ (M± SD)	Number of patients
	Intervention cost over 4 months	713.7	5.03± 0.77	142
	Cost avoidance of all DRPs	83,052.40	584.88± 307.5	142
	Total cost saving	-467.5		
	Drug cost decrease	14012.85	$98.68 \pm 105.7$	142
	Drug cost increase	9349.08	65.84± 83.3	142
	Lab cost increase Net benefit over the study period (4 months)	5248.02 81,871.15	50.95± 32.7	103
	Benefit to cost ratio	115.7:1		
18	$M \pm SD$ : Mean $\pm$ Standard deviation			





BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.



1 2	
3 4	Research Article
5 6	Title: Clinical pharmacist-led medication reconciliation supplemented with medication
7 8 9	review in chronic kidney disease admitted patients: a cost-benefit analysis
10 11 12	Journal: BMJ Open.
13 14	
15 16 17	
18 19	
20 21 22	
23 24	
25 26 27	
28 29	
30 31 32	
33 34 35	
36 37	tor peet terien on
38 39 40	
41 42	
43 44 45	
46 47 48	
49 50	
51 52 53	
54 55 56	
57 58	1
59 60	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

1	
2 3	
5 4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18 19	
20	
20 21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32 33	
33 34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44 45	
45 46	
46 47	
47 48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	
59	
60	

1

## Table S1: Patient demographics and clinical characteristics of the study sample.

X7 · 11	Study sample
Variable	N(%) N = 142
Gender n (%)	N = 142
Female	52 (27 22)
Male	53 (37.32)
	89 (62.68) 57.16 ±15.96
Age, years (M $\pm$ SD)	<i>37.</i> 10 ±13.90
BMI n (%) <18.5	6 (1 22)
18.5 -24.9	6 (4.23)
25-29.9	41 (28.87)
> 29.9	42 (29.58)
Marital status	53 (37.32)
Married	109 (76.76)
Not married	33 (23.24)
Smoking status	55 (25.24)
Yes	43 (30.28)
No	75 (52.82)
Ex-smoker	24 (16.90)
Educational level	
Not educated	20 (14.08)
School	93 (65.49)
University/higher education	29 (20.42)
Employment status	
Employed	26 (18.31)
Retired	32 (22.54)
Unemployed	84 (59.15)
Occupation	
Medical	3 (2.11)
Non-medical	64 (45.07)
No	75 (52.82)
Monthly income (JOD)	
<500	110 (77.46)
500 -1000	29 (20.42)
>1000	3 (2.11)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

AKI on Top of CKD related problems	42 (29.58)
CKD/dialysis related problems	71 (50.0)
Others	29 (20.42)
CKD stage	
Stage 2	2 (1.41)
Stage 3a	3 (2.11)
Stage 3b	12 (8.45)
Stage 4	32 (22.54)
Stage 5	93 (65.5)
Years of dialysis (M± SD)	$2.33 \pm 3.66$
Years of CKD (M± SD)	$5.02 \pm 6.80$
Number of comorbidities (M± SD)	$6.36 \pm 2.18$
$CCI (M \pm SD)$	$6.08 \pm 2.93$
Number of medications at admission (M± SD)	$9.58 \pm 3.07$
Number of medications at discharge ( $M \pm SD$ )	$9.24 \pm 4.34$
Death at discharge	5 (3.52)
Length of stay	$8.94 \pm 8.59$

Abbreviation: BMI: Body Mass Index, M± SD: Mean ± Standard deviation, JOD: Jordanian Dinar, CKD: Chronic Kidney Disease, AKI: Acute Kidney Disease, CCI: Charlson Comorbidity Index. SD).

One JOD is equivalent to 1.41 US Dollars (USD).

**Table S2:** Examples of the studied clinical cases with the probability score to cause ADEs.

A patient had a recent myocardial infarction (MI) and had previously	High
undergone stent placement for the main coronary artery. She was taking	(0.6)
febuxostat for gout. The clinical pharmacist recommended switching from	
febuxostat to allopurinol. (Black box warning)	
A female patient on hemodialysis, has a hemoglobin (Hb) level of 12 and a	High
history of stroke. She was on alpha epoetin 4000 units prescribed every	(0.6)
other day (EOD). (Black box warning)	
A 91-year-old female patient with CKD stage 5 (baseline serum creatinine	Medium
is 500 mmol/l). Dialysis was delayed due to her age. The patient is	(0.4)
experiencing uremia, including vomiting symptoms. She was prescribed	
metoclopramide 10 mg intravenously every 8 hours, which is a high dose	
considering her condition. Additionally, she is taking trimetazidine, which	
has a serious interaction with metoclopramide (category X). It is important	
to note that trimetazidine is contraindicated in patients with a GFR <30.	
A patient has osteoporosis and is undergoing hemodialysis. Initially, she	Medium
was prescribed alendronate, but the clinical pharmacist recommended	(0.4),
switching to denosumab. The physician stopped the alendronate as advised	Low
but could not provide denosumab due to economic issues. Subsequently,	(0.1)
the patient visited the outpatient clinic (OPC) due to bone pain, and there	
she received denosumab treatment.	
A patient has a CrCl (Creatinine Clearance) of 13, and he is currently taking	Medium
fenofibrate. Additionally, the triglyceride level is less than 250 mg/dL.	(0.4)
A patient underwent upper endoscopy, which revealed mild gastritis. There	Medium
were no available tests for H. pylori, and the patient's serum creatinine level	(0.4)
was 500 mmol/l (CrCl <15). Nevertheless, upon discharge, the patient was	
	1

prescribed amoxicillin 1g twice daily and clarithromycin 500mg twice	
daily without renal adjustment and without confirming the diagnosis.	
A patient has AKI on top of CKD and has been experiencing severe	Medium
vomiting for over a week. Upon admission, the patient's home medication	(0.4)
included metoclopramide 10 mg three times daily taken orally. However,	
after admission, the route was changed to intravenous 10 mg TID (not renal	
dose) without improvement, the dose was changed to metoclopramide	
intravenously at 20 mg three times daily, which is considered too high. The	
clinical pharmacist recommended discontinuing metoclopramide and	
administering ondansetron as an alternative.	
A patient is undergoing hemodialysis and was diagnosed with deep vein	Medium
thrombosis (DVT). Upon discharge, she was prescribed a therapeutic dose	(0.4)
of Enoxaparin. The clinical pharmacist recommended switching to	
apixaban.	
A patient was admitted for liver cirrhosis, baseline CrCl 32, AKI, diabetes	Medium
mellitus (DM), and recently diagnosed depression. He was initially	(0.4)
admitted while taking metformin 500mg once daily. However, upon	
discharge, his medication regimen included metformin 850mg three times	
daily, mirtazapine, spironolactone, and hydrochlorothiazide. The clinical	
pharmacist was unable to reach the responsible physician to discuss the	
changes. Consequently, the patient was readmitted after 5 days due to	
diarrhea and hyponatremia.	
A patient has a UTI and is currently taking ciprofloxacin, calcium	Low
carbonate, and ferrous gluconate twice daily, both at 6 pm and 6 am, all by	(0.1)
oral route.	
A patient admitted with severe hypophosphatemia; the physician initially	Low
recorded that the patient was on calcium carbonate 500mg BID. With	(0.1)
medication reconciliation we found that the actual home dose was calcium	
carbonate 1g TID, along with sevelamer TID, which was obtained from	
outside the hospital (and was not known by the physician). Resolving these	
discrepancies with the physician led to a change in the diagnosis.	

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES)

Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies

A patient has been taking Combivent® every 8 hours for over than 2 weeks	Low
without any valid indication.	(0.1)
A 32-year-old patient has type 1 diabetes mellitus (DM1), end-stage renal	Low
disease (ESRD), partial retinopathy, and uncontrolled DM with recurrent	(0.1)
hypoglycemia. Upon admission, she was using pre-mixed insulin. The	
clinical pharmacist suggested switching to a basal-bolus insulin regimen.	
A patient was discharged without some of his hypoglycemic and	Low
antihypertensive agents unintentionally.	(0.1)
A patient on HD, was on famotidine 40mg once daily at home. Was not	Very
documented.	low
	(0.01)

## **Table S3:** Average cost avoidance per patient across cause-based domains in the PCNE classification of DRPs (Version 9.1).

Primary domain	Cause	Cost avoidance (\$) Average per patient	Numl of patier
	Inappropriate drug according to guidelines/formulary	195.0	64
	No or incomplete drug treatment despite existing indication	139.5	62
	No indication for drug	71.7	32
Drug selection	Inappropriate combination of drugs or drugs and dietary supplements	174.2	11
	Too many different drugs/active ingredients prescribed for indication	83.5	3
	Inappropriate duplication of therapeutic group or active ingredient	83.5	3
	Drug dose of a single active ingredient too high	207.7	66
Dose selection	Dosage regimen too frequent	83.9	63
	Drug dose too low	89.4	24
	Drug omission	133.6	95
Patient transfer related (discrepancies)	Discrepancy in the strength and/or frequency and/or number of units of dosage form and/or total daily dose	118.3	39
	Drug addition	150.0	16
	Therapeutic class substitution	24.3	18

2 3 4 5 6	
7 8 9 10 11	
12 13 14 15 16	
17 18 19 20 21	
22 23 24 25 26	
20 27 28 29 30 31	
32 33 34 35 36	
37 38 39 40 41	
42 43 44 45	
46 47 48 49 50	
51 52 53 54 55	
56 57 58 59 60	

	Drug duplication	84.4	4
	Discrepancy in the dosage form/route of administration	71.9	2
Drug use process	Inappropriate timing of administration or dosing intervals by a health professional	77.2	34
	Drug administered via wrong route by a health professional	152.4	1
Treatment duration	Duration of treatment too long	91.1	3
Treatment duration	Duration of treatment too short	65.3	3
Drug form	Inappropriate drug form/formulation	38.1	3
	Addition of a lab test	118.3	89
Others	No or inappropriate outcome monitoring	91.6	17

# **BMJ Open**

## Clinical pharmacist-led medication reconciliation supplemented with medication review in chronic kidney disease admitted patients: a cost-benefit analysis

Journal:	BMJ Open
Manuscript ID	bmjopen-2024-087232.R2
Article Type:	Original research
Date Submitted by the Author:	07-Dec-2024
Complete List of Authors:	Altawalbeh, Shoroq ; Jordan University of Science and Technology, Department of Clinical Pharmacy Sallam, Nahlah M.; Jordan University of Science and Technology, Department of Clinical Pharmacy Al-Khatib, Minas; Jordan University of Science and Technology, Department of Clinical Pharmacy Alshogran, Osama Y.; Jordan University of Science and Technology, Department of Clinical Pharmacy Bani Amer, Mohammad S.; Jordan University of Science and Technology, Department of Internal Medicine
<b>Primary Subject Heading</b> :	Epidemiology
Secondary Subject Heading:	Medical management, Health services research, Health economics
Keywords:	Medication Reconciliation, Health Services, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health & safety < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

SCHOLARONE<sup>™</sup> Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

terez oni

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

1		
2		
3 4	1	Research Article
5		
6	2	
7	-	
8	3	Clinical pharmacist-led medication reconciliation supplemented with
9		
10	4	medication review in chronic kidney disease admitted patients: a cost-benefit
11 12		
13	5	analysis
14	0	
15		
16	6	Shoroq M. Altawalbeh, PharmD, PhD, <sup>1</sup> Nahlah M. Sallam, M.S <sup>1</sup> , Minas Al-Khatib, PharmD, <sup>1</sup> Osama Y.
17	-	
18 19	7	Alshogran, M.S, PhD, <sup>1</sup> Mohammad S. Bani Amer, MD <sup>2</sup>
20		
21	8	<sup>1</sup> Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan University of Science and Technology, Irbid,
22	9	Jordan. <sup>2</sup> Department of Internal Medicine, Faculty of Medicine, Jordan University of Science and Technology,
23	10	Irbid, Jordan.
24		
25 26	11	
27		
28	12	Shoroq M. Altawalbeh, PharmD, PhD, Department of Clinical Pharmacy, Faculty of Pharmacy,
29	13	Jordan University of Science and Technology, Irbid 22110, Jordan. Email address:
30	14	smaltawalbeh@just.edu.jo
31 32	1 5	OB CID: 0000 0001 0245 4040
33	15	ORCID: 0000-0001-8345-4048
34	16	
35		
36	17	Nahlah M. Sallam, Msc, Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan
37	18	University of Science and Technology, Irbid 22110, Jordan. Email address:
38 39	19	nmsallam20@ph.just.edu.jo
40	20	ORCID: 0000-0001-9311-600X
41	20	
42	21	Minas Al-Khatib PharmD, Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan
43	22	University of Science and Technology, Irbid 22110, Jordan. Email address:
44 45	23	makhatib@just.edu.jo
45 46	24	ORCID::0000-0003-0209-1578
47		
48	25	
49	26	Osama Y. Alshogran, Msc, PhD, Department of Clinical Pharmacy, Faculty of Pharmacy,
50	20 27	Jordan University of Science and Technology, Irbid 22110, Jordan. Email address:
51 52		
52	28	<u>oyalshogran@just.edu.jo</u>
54	29	ORCID: 0000-0002-2466-4763
55		
56		
57 58		
58 59		1
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1 2			
3 4	30	Mohammad S. Bani Amer, MD, Department of Internal Medicine, Faculty of Medicine, Jordan	
5 6	31 32	University of Science and Technology, Irbid 22110, Jordan. Email address: m.baniamer1997@gmail.com	
7	33		
8 9	34	*Corresponding Author:	
10 11	35	Shoroq M. Altawalbeh, PharmD, PhD	
12 13 14	36	Associate Professor	
	37	Department of Clinical Pharmacy	
15 16 17	38 39	Jordan University of Science and Technology; Faculty of Pharmacy	
18 19	40	P.O.Box 3030, Irbid 22110, Jordan	
20 21 22	41 42	Tel.:+962(0)27201000 Fax : + 962 (0) 2 7095123	
23	43	E-mail: <u>smaltawalbeh@just.edu.jo</u>	
24 25	44	ORCID: 0000-0001-8345-4048	
26 27	45		
28 29	46	Running Title: Cost-benefit of medication reconciliation in CKD	
30 31	47	Number of Tables: 2	
32 33 34	48	Number of Figures: 3	
35 36	49	Keywords: Medication reconciliation, clinical pharmacist, cost-benefit, chronic kidney disease,	
37 38 39	50	Jordan.	
40 41 42	51		
43	52		
44 45	53		
46 47	55		
48 49	54		
50	55		
51 52			
53 54	56		
55 56 57	57		
58			
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	

## Page 4 of 37

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) .

data mining, AI training, and similar technologies

Protected by copyright, including for uses related to text

#### **BMJ** Open

Abstract **Objective:** Chronic kidney disease (CKD) is associated with a high economic burden, which is exacerbated by the high susceptibility to drug-related problems (DRPs) in this patient population. This study aimed to evaluate the cost-benefit ratio of medication reconciliation supplemented with medication review for inpatients with CKD, compared to the absence of this intervention. Design: This was a cost-benefit analysis conducted along with a prospective interventional study. Setting: The study was conducted at two hospitals in Jordan between February and May 2023. Participants: The prospective interventional study included 142 admitted patients with CKD. Interventions: Patients received medication reconciliation at admission and discharge as well as medication review throughout admission. Primary and secondary outcome measures: The primary outcome measures were the net benefit and the benefit-to-cost ratio of the intervention. A cost-benefit analysis was conducted from the healthcare system perspective by assessing the cost of the service (the pharmacist time required to complete the service per patient) and the economic benefit, including total and per-patient cost savings and cost avoidance. **Results:** The total estimated cost of all DRPs in the absence of interventions (cost avoidance) was \$83,052.4 (average of \$584.88± 307.5 per patient); among which \$20,623.19 was attributed to medication discrepancies. The cost savings were estimated at -\$467.5. The supplemented medication reconciliation service was estimated to cost \$713.7. As a result, the estimated net 

benefit totaled \$81,871.15, averaging \$576.56 per patient, with a benefit-to-cost ratio of 115.7:1

79 over the 4-month study period.

## BMJ Open

	вмј Ор
Conclusions: Delivering a supplemented medication reconciliation service by a clinical	en: firs
pharmacist for CKD patients is cost beneficial from the healthcare perspective in Jordan, an	t publis
example of a low- and middle-income country (LMIC). This finding further confirms the pivotal	shed as
role of clinical pharmacists in multidisciplinary healthcare teams.	s 10.1136/b
role of clinical pharmacists in multidisciplinary healthcare teams.     Weywords: Medication reconciliation, clinical pharmacist, cost-benefit, chronic kidney disease,     Jordan.	BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26
Jordan.	February 2025. Enseigneme
text and data mining,	wnloaded from http: uperieur (ABES).
Al training, and similar technologies	//bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l
ologies.	une 8, 2025 at Agence
4 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	Bibliographique de l

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

1 2		
3	106	Strengths and limitations of this study
4 5 6	107	• The study was carried out alongside a prospective interventional study, allowing
7 8	108	for a more accurate estimation of the time required to complete the medication
9 10 11	109	reconciliation service and providing a closer examination of potential drug related
12 13	110	problems (DRPs).
14 15 16	111	• Evaluation of the probability scores of DRPs was conducted by an expert panel
17 18	112	composed of five independent evaluators.
19 20	113	• The exact real cost of adverse events resulting from DRPs could not be measured.
21 22 23	114	• The study relied on admission charges, medication prices, and lab prices rather than
24 25	115	actual costs.
26 27	116	
28 29	117	
30 31	118	
32	119	
33 34 35	120	actual costs.
36 37	121	
38	122	
39 40	123	
41 42	124	
43 44	125	
45 46	126	
47 48	127	
49 50	128	
51 52	129	
53	130	
54 55 56	131	
57		
58 59 60		5 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

## **BMJ** Open

#### Introduction

Chronic kidney disease (CKD) is associated with high financial burden globally, exceeding expenditures incurred by other highly burdened patients such as those with stroke and cancer.<sup>1, 2</sup> CKD is a complex medical state accompanied by multiple concurrent illnesses, which inflate the cost of management. Around \$18 billion had been spent by the national US Department of Veterans Affairs for the care of patients with CKD without renal replacement therapy (RRT), with expenditures increased across the advanced stages of CKD.<sup>3, 4</sup> In Jordan, the Ministry of Health expended approximately \$17.7 Million per year for hemodialysis patients management in 2010, with an average of annual cost of \$9,979 per patient.<sup>5</sup> A study conducted in Lebanon reported the median cost for all CKD stages per year of \$4,764.02 (IQR \$2,475.24 - \$23,455.61) in 2019 from a society perspective.<sup>6</sup> Studies highly recommend implementing programs and policies to reduce progression and complications of CKD to mitigate the growing disease burden especially in countries with limited resources. 7,8 

Patients with CKD are very vulnerable to medication discrepancies and other Drug related problems (DRPs).<sup>9, 10</sup> Interestingly, many serious DRPs are preventable in CKD patients.<sup>11</sup> Developing DRPs increased the exposure to re-hospitalization, extended length of hospital stays, and early death, and therefore expanded the cost.<sup>12-14</sup> Clinical pharmacy services targeting DRPs have revealed a positive economic impact on healthcare organizations across the literature.<sup>15</sup> Medication reconciliation and medication review, primarily led by a clinical pharmacist, are vital services focused on preventing and resolving medication discrepancies and other drug-related problems (DRPs). These processes play a key role in enhancing patient outcomes and reducing healthcare costs. <sup>16</sup> Medication reconciliation ensures that the patient's medication list is accurate and up-to-date during transitions of care, while medication review involves a thorough and 

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

structured assessment of the patient's medications to ensure they are receiving the most appropriate treatment regimen. 17 

The economic burden of medication discrepancies and other DRPs is understudied, particularly in developing countries, including Jordan. Moreover, there is a dearth of data regarding the efficiency of clinical pharmacy services implemented in patients with CKD, especially in low-income to middle-income countries. Although medication reconciliation has the potential to be beneficial in this population, it also incurs costs, highlighting the need for a health economic analysis to determine whether this service can deliver clinical benefits at a reasonable cost, providing a solid rationale for its clinical application. Efforts to evaluate the cost-benefit of medication reconciliation provide essential evidence for healthcare providers and policymakers regarding the value of implementing this clinical service particularly in CKD patients. Examining the costs associated with drug-related problems (DRPs) during CKD hospitalizations will further emphasize the burden of the disease and support efforts to reduce the significant healthcare expenses related to CKD. These insights will underscore the crucial role clinical pharmacists play as part of the multidisciplinary hospital team in alleviating the financial impact of CKD on the healthcare system. Therefore, this study aimed to evaluate the cost-benefits of implementing a clinical pharmacist-led service for supplemented medication reconciliation for admitted patients with CKD in Jordan, compared to the absence of this intervention. 

Methods 

Study design 

> The cost-benefit analysis was developed along with a prospective interventional clinical study that involved patients with stages 2-5 CKD, who were admitted to two healthcare hospitals in Jordan: King Abdullah Hospital (KAUH) and Princess Basma Hospital (PBH). A clinical

Page 9 of 37

### **BMJ** Open

pharmacist was responsible for providing supplemented medication reconciliation to CKD-admitted patients over four months (from February to May 2023). The costs and benefits during the study period were assessed in comparison to absence of this intervention. The primary outcome measure was the net benefit generated by the supplemented medication reconciliation service provided to CKD patients during the study period. The net benefit was estimated according to the following equation: [net benefit = total benefits (cost avoidance + cost saving)-service cost]. In addition, the benefit-to-cost ratio was estimated. The health care system perspective was adopted in the current study. Base case calculations were performed using Excel software. The cost-benefit analysis model is depicted in Figure 1. The demographic and clinical characteristics of the study sample are summarized in the Supplemental Material (Table S1). 

188 Descri

## Description of supplemented medication reconciliation

Patients received a supplemented medication reconciliation service across the transitions of care during their admission to the internal medicine ward, in addition to a medication review for possible DRPs. The procedure of supplemented medication reconciliation consisted of medication reconciliation at admission, medication review throughout admission, and medication reconciliation at discharge. At admission, demographic, clinical, and medical data for each enrolled patient were collected from the medical records, followed by interviews with the patients or their caregivers to verify the patients' demographics, medical history, and pre-admission medication list. The pre-admission drug lists were also confirmed using all other available sources, such as bottles, prescriptions, and previous medical records, to obtain the best possible medication history (BPMH). The BPMH was compared with the current hospital medication sheet (admission medication orders) to extract discrepancies at admission. Medication reviews and clinical case analyses were conducted regarding dose adjustments, drug interactions, missing medications,

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES)

and data mining, Al training, and similar technologies

Protected by copyright, including for uses related to text

inappropriate medications, unnecessary medications, and monitoring after admission and during the hospitalization period to identify the DRPs. At discharge, the best possible discharge medication plan (BPMDP) was created from the BPMH, the last medication list during index hospitalization, and new medications planned to be started upon discharge. The BPMDP was compared with discharge prescription and summary. Patient education was provided to willing patients before discharge. All identified discrepancies and other DRPs were discussed with the resident responsible for the resolution as accessible.

208 Estimation of costs

Input costs in the current study include the resources used to provide the supplemented medication reconciliation, that is, the pharmacists' time. The time taken by the pharmacist to deliver the supplemented medication reconciliation per patient (in hours) was recorded for each admission. The cost of the medication reconciliation service was estimated by multiplying the service time by the average hourly wage rate for clinical pharmacists, as obtained from the financial department at KAUH. The average annual wage rate was converted to the hourly wage rate based on 240 working days per year and 8 working hours per day.

**Estimation of benefits** 

The economic benefits associated with the potential prevention of DRPs through interventions recommended by clinical pharmacists were evaluated in terms of "cost savings" and "cost avoidance."

220 Cost saving

In the cost-saving analysis, the decreased medication costs due to interventions and the increased medication costs and costs attributed to requesting labs were estimated. The cost of any medication (increased or decreased) was estimated as the cost of medication per unit multiplied by Page 11 of 37

## BMJ Open

the frequency per day and then by the duration of therapy.<sup>18</sup> Acute therapy duration was estimated based on the clinical scenario, while chronic medication use was calculated over three months' time horizon. Public per-unit prices of drugs were obtained from the Jordan Food and Drug Administration (JFDA).<sup>19</sup> For interventions that included the addition of a laboratory test, the increased cost for each intervention was estimated using the prices of laboratory tests obtained from KAUH laboratory department. Both drug and lab prices were converted to costs by multiplying them by an assumed Ratio of Cost to Charge (RCC). The net cost saving was estimated by subtracting the total increased cost from the decreased cost resulting from the implementation of the supplemented medication reconciliation services. Per-patient averages were calculated for total cost savings, drug cost reductions, drug cost increases, and laboratory costs. 

## *Cost avoidance*

Cost avoidance was estimated for each intervention recommended by the clinical pharmacist in the current study as the cost avoided by potential prevention of DRPs. The probability of DRP in the absence of intervention was determined according to the Nesbit et al scale <sup>20</sup> which has five levels of risk of causing DRPs: 0 (none), 0.01 (very low), 0.1 (low), 0.4 (medium), or 0.6 (high). The DRP probability in the absence of the intervention was estimated for all identified discrepancies and other DRPs by a team of experts, comprising four clinical pharmacists and one physician. Examples of the studied clinical cases with potential probabilities of DRPs are presented in Supplemental Material (Table S2). The cost avoidance attributed to each intervention was calculated by multiplying the corresponding DRP probability by the DRP cost. The cost of a DRP was assumed to be the cost of an additional 2 days of hospital stay.<sup>21</sup> Admission charges were retrieved from the billing system for all admissions included in the study, and the

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

average charge per day was calculated for these CKD patients. The average charge per day was adjusted using the assumed RCC to estimate the RCC cost of DRPs. Cost avoidance was estimated in total and as an average per patient. Cost avoidance was also estimated by the Pharmaceutical Care Network Europe (PCNE) Classification for Drug-Related Problems V9.1 based on the cause,<sup>22</sup> and the Medication Discrepancy Taxonomy (MedTax) system.<sup>23</sup> All financial data were extracted in Jordanian Dinar currency unit (JOD) and converted to United States Dollars (USD) at a rate of (1 JOD = 1.41 USD). All cost data were reported in 2023 values. The RCC value was assumed to be 0.8 throughout the base case analysis and varied in the sensitivity analysis. 

## 255 Sensitivity analysis

One-way sensitivity analysis was conducted to account for the variability in the key model parameters. DRP probabilities were varied using the minimum and maximum probabilities assigned by the expert panel. All costs were varied over a range of  $\pm 20\%$  of the base case cost. The average service time was varied over two SD of the mean, as calculated in this study. RCC was varied in the range (0.7 to 0.9). Probabilistic sensitivity analysis was conducted, in which the input variables were varied simultaneously over 10,000 Monte Carlo simulations. Beta distribution was used for DRP probabilities, uniform distribution for RCC and hourly wage rate, normal distribution for service time in minutes, and gamma distribution for cost.

- **Public and patient involvement**
- 265 Patients and the public were not actively involved in the design, conduct, reporting, or
- 266 dissemination plans of this research.
- 267 Ethics approval and consent to participate

This study was approved by the Institutional Review Board (IRB) Committee at KAUH (Ref number: 123/147/2022) and the Ministry of Health (Ref number: 13902). Written informed

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

consent was obtained from the participants after they were given comprehensive information aboutthe study's purpose and details.

**Results** 

## 273 Cost of supplemented medication reconciliation

The average time required to perform a supplemented medication reconciliation service (medication reconciliation plus medication review during admission) was 43.38 (SD= 6.65) minutes, ranging from 26 to 60.5 minutes. The total time spent by the clinical pharmacist on the supplemented medication reconciliation over the four-month intervention period was 6117.1 minutes (101.95 hours). The average duration to accomplish a primary medication reconciliation service at admission was  $15.79 \pm 1.74$  minutes. Though, the average time for medication review during the admission was  $21.6 \pm 4.30$  minutes (ranged from 11.6 to 35.5 minutes) per patient. Medication reconciliation time at discharge averaged  $3.58 \pm 1.55$  minutes per patient. Based on the reported average monthly salary of the clinical pharmacist at KAUH, the wage per hour was \$7 assuming 8 hours per day. Taking this into account, the total intervention cost over 4-month study period was \$713.7 ( $$7 \times 101.95$  hours). 

## 285 Benefits of supplemented medication reconciliation

286 Estimated cost saving

The total increased medication cost was estimated to be \$7479.26 (average of  $$52.67\pm 66.7$ per patient) and lab needed total cost was estimated at \$4198.42 (average of \$29.57\pm 28.8 per patient). The decrease in medication costs owing to the intervention was \$11,210.28(average of \$78.95\pm 84.6 per patient). Total cost saving (after being adjusted with RCC of 0.8) = \$11,210.28 - \$7,479.26 - \$4,198.42 = -\$467.4 (\$3.29 negative cost saving per patient). Table 2 presents cost saving values in total and at the patient level.

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) .

and

data mining, AI training, and similar technologies

Protected by copyright, including for uses related to text

## 293 Estimated cost avoidance

The average admission charge for patients with CKD enrolled in the study was \$2811 (SD= \$2172), and the average admission charge per day was \$340.20 (SD= \$199.48). The assumed cost of a DRP was the estimated cost of two additional hospitalization days for patients with CKD in the current study [\$680.4 multiplied by 0.8 RCC = \$483.1]. The estimated probabilities of DRPs in the absence of intervention were averaged using a panel of five expert evaluators. The majority of DRPs (73.4%; N=735) were in the low-to medium-risk category (0.1-0.4), while 21.2% (N=212) were in the low-risk category (<0.1), and 5.4% (N=54) were in the moderate-to high-risk category (>0.4). The average cost of a potential DRP, estimated by multiplying the average DRP probability by the estimated RCC cost for two additional hospitalization days was \$82.96 (SD=\$57.7). The total estimated cost of all DRPs in the absence of interventions (cost avoidance) was \$3,052.4, averaging  $\$584.88 \pm \$307.5$  per patient. Patient transfer related DRPs (medications discrepancies) were found to be the third most expensive cause-based domain in the PCNE classification of DRPs (V9.1), contributing to around 25% of the total cost avoidance (\$20,623.19; \$145.2 per patient). The greatest weight of discrepancies' cost avoidance was attributed to "drug omission" category (\$12,693.54) followed by "discrepancy in frequency/strength/dose" (\$4,612.56) and "drug addition" (\$2,399.36), Table 1. A detailed summary of the cost avoidance per PCNE cause-based domains is presented in Table 1. Average cost avoidance per patient across the cause-based domains of DRPs (at the patient level) is detailed in the Supplemental Material (Table S3).

313 Cost benefit analysis

## **BMJ** Open

The net benefit was calculated by subtracting the total cost of intervention from total cost avoidance and saving [cost avoidance (\$83,052.4) + cost saving (- \$467.5) - cost of the intervention (\$713.7) = \$81,871.15]. The benefit-to-cost ratio estimated in this study was (115.7:1). Table 2. Sensitivity analyses The study conclusion was insensitive to uncertainty in any of the input variables including DRP probabilities, DRP cost, RCC, per-unit cost of drugs and labs, hourly wage rate, and average service time. The main driver of the outcome was the DRP probability, followed by the DRP cost, as depicted in Figure 2. However, the net benefit was positive over all plausible ranges of the input variables. The minimum estimated net benefit was \$50,203 based on varying DRP probability. In probabilistic sensitivity analysis, the average expected value of the net benefit was 90,451(SD =\$126,294). Only 866 out of 100,000 iterations (8.7%) showed a negative net benefit (Figure 3). Discussion The major findings of the current study emphasize the substantial economic burden of medication discrepancies and other DRPs in patients with CKD. In addition, the results showed that the estimated economic benefit was remarkable compared to the estimated cost of the medication reconciliation service. Overall, the results indicate that supplemented medication reconciliation services mediated by clinical pharmacists are cost beneficial. The majority of DRPs in the current study were classified as having a medium risk of DRPs. Despite the different scales used to evaluate the clinical significance of DRPs in patients with CKD, most studies have found that the majority of DRPs in this high-risk population were with moderate to significant clinical impact. In a study conducted in Jordan among hospitalized 

## Page 16 of 37

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

#### **BMJ** Open

> patients with CKD, the majority of DRPs (62%) were classified among the significant category, however, the study used a different scale (extremely significant, much significant, significant, and slightly significant).<sup>24</sup> In a study conducted in Canada, approximately half of the observed DRPs were moderate in severity in terms of causing harm to CKD patients.<sup>25</sup> The different scales used in severity assessment across the literature makes the comparison seems challenging. Overall, most recognized DRPs were considered clinically important in the current study and potentially preventable.

> This study revealed the beneficial effect of clinical pharmacist medication reconciliation intervention on CKD patients in terms of the cost-benefits associated with this service. A recent review of 47 studies among CKD patients also supports this finding; 7 studies approved the significant cost savings and 15 studies reported improvement in clinical outcomes due to clinical pharmacy care, including blood pressure, anemia, length of hospital stay, readmissions, kidney function, and other laboratory tests (i.e., PTH, calcium, uric acid, cholesterol, and HbA1c).<sup>15</sup>

The average time needed for full supplemented medication reconciliation services provided for each CKD admission in the current study was  $43.38 \pm 6.65$  minutes. This is comparable to other studies that measured the time needed for medication reconciliation services:  $44.4 \pm 21.8$ ,<sup>26</sup>  $40 \pm 17.2$  minutes,<sup>27</sup> and 48 minutes.<sup>28, 29</sup> In addition, the total time to deliver a primary medication reconciliation service at all transitions of care per patient was estimated with a median of 24 minutes (IQR 20-30 minutes).<sup>30</sup> The specific time for medication reconciliation at admission was roughly similar to our finding (15 minutes (IQR 10–21)) in two previous studies.<sup>31, 32</sup> Moreover, medication reconciliation at discharge after conducting medication reconciliation at admission was previously estimated to need approximately 3.5 minutes,<sup>33</sup> which is also comparable to the estimated time in the current study. However, a recent systematic review reported a wider range

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

of the mean time for medication reconciliation implementation across nine studies with an average of 34.5 ( $\pm$ 39.4) minutes.<sup>34</sup> This variability could be originated from the diverse models and services involved across the pooled studies and variations in study population. 

CKD has been associated with a high economic burden.<sup>3, 35-37</sup> DRPs have been associated with high costs that affect patient safety and healthcare expenditures.<sup>38</sup>. Our study estimated the net benefit attributed to avoiding and resolving DRPs to be \$81,871.15 over 4 months for a cumulative number of 142 CKD patients, averaging \$576.56 per patient. Such remarkable benefit confirms the need of implementing supplemented medication reconciliation in CKD patients. Likewise, a recent retrospective cohort in the US among hemodialysis patients estimated cost saving from preventing DRPs to be \$447,355 over a 6-month period of observation, attributing this benefit to performing medication reconciliation with medication review.<sup>39</sup> A Malaysian study measured the cost saving resulted from only dose adjustment in CKD inpatients to be \$2,250 for 212 dose related recommendations over 4 months, in which the clinical pharmacist worked within a multidisciplinary rounds with the nephrology team to adjust the doses as needed.<sup>40</sup> This saved cost is considered much lower than the avoided cost resulting from renal dose adjustment in our study (\$14,756 for 4 months, 94 dose adjustment interventions). An earlier prospective study conducted medication therapy evaluation by pharmacist found that the ratio of pharmaceutical care cost to healthcare system saving is \$1 to \$3.98 among end-stage renal disease patients in the USA.<sup>41</sup> This is much smaller compared to the benefit to cost ratio estimated in the current study (115:1). This variability might be related in part to the relatively lower wage rates of clinical pharmacists in Jordan than in the USA. However, the estimated cost of a DRP is also expected to be higher in terms of admission-day costs in the USA. Another study found annual direct cost savings of more than \$780,000 after implementing supplemented medication reconciliation with

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

patient education in internal medicine wards in Kansas ascribed to reducing readmissions.<sup>42</sup> A Chinese trial found cost saving attributed to antimicrobial dose adjustment (number of adjusted doses= 183) by a clinical pharmacist of \$3,525 per patient with sepsis undergoing continuous dialysis in the ICU.<sup>43</sup> Wage rates and the cost of health care may differ widely across regions and institutions which make the comparison in cost is not sufficiently clear/straightforward. This also highlights the need to obtain relevant data from local or regional studies to better support the decisions of policy makers based on information from relevant settings.

In Jordan, the role of clinical pharmacists appears to be economically effective for other populations. Among outpatients with chronic diseases, the estimated cost avoidance per month due to pharmacist interventions (number of interventions = 79 among 48 patients) was 6,422.41.44In another study conducted in Jordan, clinical pharmacist intervention in the ICU reduced the total cost of drugs consumption by \$211,574.90 over 10 months.<sup>45</sup> Still, the cost benefit of medication reconciliation among CKD patients has not been well addressed in Jordan and other developing countries. The results of the current study strongly support the need to implement medication reconciliation supplemented with continuous medication review during hospital admission in patients with CKD. 

The current study has some limitations. We did not evaluate the actual adverse events resulting from DRPs or the actual role of interventions in decreasing these events. Furthermore, the exact real cost of adverse events resulting from DRPs could not be measured; however, the method of calculating cost avoidance in the current study has considered uncertainty and was implemented in previous studies.<sup>46</sup> In addition, the evaluation of the probability score of each DRP was conducted by an expert panel composed of five independent evaluators. Besides, the assessment of DRP probability scores was conducted independently by the study panel using a Page 19 of 37

## BMJ Open

validated scale.<sup>20</sup> Another limitation is that we relied on admission charges, medication prices, and lab prices rather than actual costs. However, charges are widely used as a proxy for costs in the literature because of accessibility issues. Furthermore, we used an assumed RCC ratio to approach the actual costs, and this RCC was varied in the sensitivity analysis. Conclusions Pharmacist-led medication reconciliation supplemented with contentious medication review is very cost beneficial in CKD admitted patients, with substantial cost avoidance compared to the cost of implementing this service. The results clearly showed that activating the role of clinical pharmacists in providing medication reconciliation with a comprehensive medication review contributed positively to the safety of admitted patients with CKD and had a remarkable economic impact in clinical settings. The net benefit of this intervention could be enhanced by designing an efficient collaborative approach with physicians in hospital settings, and future studies should be directed toward evaluating the cost-benefit of such approaches. Funding: This work was supported by the Deanship of Scientific Research at the Jordan University of Science and Technology [grant number: 20220257]. The funding agency was not involved in the study design, conduct, writing, or decision to submit this article for publication. Competing Interests: The Authors declare that they have no conflicts of interest to disclose. Author contributions 

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

428	SA contributed to conceptualization, methodology, data curation, formal analysis, supervision,
429	project administration, funding acquisition, and writing original draft. NS contributed to
430	conceptualization, methodology, data curation, formal analysis, and writing original draft. MA
431	and OA contributed to conceptualization, methodology, data curation, and writing- reviewing
432	and editing. MB contributed to data curation and writing- reviewing and editing. SA is the
433	guarantor for the manuscript and accepts full responsibility for the overall content.
434	
435	Data availability statement
436	All data underlying this article are presented in the manuscript.
437	
438	
439	
440	
441	
442	
443	
444	
445	
446	

## **BMJ** Open

Small C, Kramer HJ, Griffin KA, et al. Non-dialysis dependent chronic kidney disease is associated

3	447	References
4		

1.

with high total and out-of-pocket healthcare expenditures. BMC Nephrol 2017; 18: 3. 2017/01/07. DOI: 10.1186/s12882-016-0432-2. Silva Junior GBD, Oliveira JGR, Oliveira MRB, et al. Global costs attributed to chronic kidney 2. disease: a systematic review. Rev Assoc Med Bras (1992) 2018; 64: 1108-1116. 2018/12/21. DOI: 10.1590/1806-9282.64.12.1108. Golestaneh L, Alvarez PJ, Reaven NL, et al. All-cause costs increase exponentially with increased 3. chronic kidney disease stage. Am J Manag Care 2017; 23: S163-S172. 2017/10/06. Saran R, Pearson A, Tilea A, et al. Burden and Cost of Caring for US Veterans With CKD: Initial 4. Findings From the VA Renal Information System (VA-REINS). Am J Kidney Dis 2021; 77: 397-405. 2020/09/06. DOI: 10.1053/j.ajkd.2020.07.013. Al-Shdaifat EA and Manaf MR. The economic burden of hemodialysis in Jordan. Indian J Med Sci 5. 2013; 67: 103-116. 2013/12/12. Aoun M, Helou E, Sleilaty G, et al. Cost of illness of chronic kidney disease in Lebanon: from the 6. societal and third-party payer perspectives. BMC Health Serv Res 2022; 22: 586. 2022/05/04. DOI: 10.1186/s12913-022-07936-0. Alshogran OY, Hajjar MH, Muflih SM, et al. The role of clinical pharmacist in enhancing 7. hemodialysis patients' adherence and clinical outcomes: a randomized-controlled study. Int J Clin Pharm 2022; 44: 1169-1178. 2022/07/14. DOI: 10.1007/s11096-022-01453-0. Rizk R, Hiligsmann M, Karavetian M, et al. A societal cost-of-illness study of hemodialysis in 8. Lebanon. J Med Econ 2016; 19: 1157-1166. 2016/06/29. DOI: 10.1080/13696998.2016.1207653. 9. Chia BY, Cheen MHH, Gwee XY, et al. Outcomes of pharmacist-provided medication review in collaborative care for adult Singaporeans receiving hemodialysis. Int J Clin Pharm 2017; 39: 1031-1038. 20170821. DOI: 10.1007/s11096-017-0528-1. Song YK, Jeong S, Han N, et al. Effectiveness of Clinical Pharmacist Service on Drug-Related 10. Problems and Patient Outcomes for Hospitalized Patients with Chronic Kidney Disease: A Randomized Controlled Trial. J Clin Med 2021; 10 20210420. DOI: 10.3390/jcm10081788. Laville SM, Gras-Champel V, Moragny J, et al. Adverse Drug Reactions in Patients with CKD. Clin J 11. Am Soc Nephrol 2020; 15: 1090-1102. 2020/07/03. DOI: 10.2215/CJN.01030120. Bishop MA, Cohen BA, Billings LK, et al. Reducing errors through discharge medication 12. reconciliation by pharmacy services. Am J Health Syst Pharm 2015; 72: S120-126. 2015/08/15. DOI: 10.2146/sp150021. Ernst FR and Grizzle AJ. Drug-related morbidity and mortality: updating the cost-of-illness model. 13. J Am Pharm Assoc (Wash) 2001; 41: 192-199. 2001/04/12. DOI: 10.1016/s1086-5802(16)31229-3. Alrugayb WS, Price MJ, Paudyal V, et al. Drug-Related Problems in Hospitalised Patients with 14. Chronic Kidney Disease: A Systematic Review. Drug Saf 2021; 44: 1041-1058. 2021/09/13. DOI: 10.1007/s40264-021-01099-3. Al Raiisi F, Stewart D, Fernandez-Llimos F, et al. Clinical pharmacy practice in the care of Chronic 15. Kidney Disease patients: a systematic review. Int J Clin Pharm 2019; 41: 630-666. 2019/04/10. DOI: 10.1007/s11096-019-00816-4. 16. Onatibia-Astibia A, Malet-Larrea A, Mendizabal A, et al. The medication discrepancy detection service: A cost-effective multidisciplinary clinical approach. Aten Primaria 2021; 53: 43-50. 2020/10/01. DOI: 10.1016/j.aprim.2020.04.008. World Health Organization, Medication safety in transitions of care: technical report, 2019. 17. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml 

1 2 3 492 Houso A, Hamdan M and Falana H. Cost benefit analysis of clinical pharmacist interventions in 18. 4 493 medical intensive care unit in Palestine medical complex: Prospective interventional study. Saudi Pharm J 5 494 2022; 30: 1718-1724. 2023/01/06. DOI: 10.1016/j.jsps.2022.09.017. 6 495 19. Jordan Food and Drug Administration (JFDA) http://jfda.jo/Pages/viewpage.aspx?pageID=336 7 496 (accessed July 2023). 8 497 20. Nesbit TW, Shermock KM, Bobek MB, et al. Implementation and pharmacoeconomic analysis of a 9 10 498 clinical staff pharmacist practice model. Am J Health Syst Pharm 2001; 58: 784-790. DOI: 11 499 10.1093/ajhp/58.9.784. 12 500 21. Chen CC, Hsiao FY, Shen LJ, et al. The cost-saving effect and prevention of medication errors by 13 501 clinical pharmacist intervention in a nephrology unit. Medicine (Baltimore) 2017; 96: e7883. DOI: 14 502 10.1097/MD.00000000007883. 15 503 Pharmaceutical Care Network Europe, The PCNE CLassification V 9.1. Pharmaceutical Care 22. 16 504 Network Europe, p Classification for Drug related problems. 2020. 17 23. 505 Almanasreh E, Moles R and Chen TF. The medication discrepancy taxonomy (MedTax): The 18 506 development and validation of a classification system for medication discrepancies identified through 19 20 507 medication reconciliation. Res Social Adm Pharm 2020; 16: 142-148. 20190414. DOI: 21 508 10.1016/j.sapharm.2019.04.005. 22 509 24. AbuRuz SM, Alrashdan Y, Jarab A, et al. Evaluation of the impact of pharmaceutical care service 23 510 on hospitalized patients with chronic kidney disease in Jordan. Int J Clin Pharm 2013; 35: 780-789. 24 20130725. DOI: 10.1007/s11096-013-9806-8. 511 25 512 Quintana-Barcena P, Lord A, Lizotte A, et al. Prevalence and Management of Drug-Related 25. 26 Problems in Chronic Kidney Disease Patients by Severity Level: A Subanalysis of a Cluster Randomized 513

- Problems in Chronic Kidney Disease Patients by Severity Level: A Subanalysis of a Cluster Randomized
  Controlled Trial in Community Pharmacies. *J Manag Care Spec Pharm* 2018; 24: 173-181. DOI:
  10.18553/jmcp.2018.24.2.173.
  Buckley MS Haripstein LM Clark KB et al. Impact of a clinical pharmacy admission medication
- S16
   S17
   S17
   S17
   S17
   S17
   S18
   S18
   S18
   S19-1610. 20131015. DOI: 10.1177/1060028013507428.
- Mendes AE, Lombardi NF, Andrzejevski VS, et al. Medication reconciliation at patient admission:
   a randomized controlled trial. *Pharm Pract (Granada)* 2016; 14: 656. 20160315. DOI:
   10.18549/PharmPract.2016.01.656.
- S22 28. Cadman B, Wright D, Bale A, et al. Pharmacist provided medicines reconciliation within 24 hours
  of admission and on discharge: a randomised controlled pilot study. *BMJ Open* 2017; 7: e013647.
  S24 20170316. DOI: 10.1136/bmjopen-2016-013647.
- S25 29. Neeman M, Dobrinas M, Maurer S, et al. Transition of care: A set of pharmaceutical interventions
  improves hospital discharge prescriptions from an internal medicine ward. *Eur J Intern Med* 2017; 38: 30S27 37. 20161125. DOI: 10.1016/j.ejim.2016.11.004.
- 528 30. Cornu P, Steurbaut S, Leysen T, et al. Effect of medication reconciliation at hospital admission on
   529 medication discrepancies during hospitalization and at discharge for geriatric patients. *The Annals of* 530 *pharmacotherapy* 2012; 46: 484-494. 20120313. DOI: 10.1345/aph.1Q594.
- 47 531 31. Sebaaly J, Parsons LB, Pilch NA, et al. Clinical and Financial Impact of Pharmacist Involvement in
   48 532 Discharge Medication Reconciliation at an Academic Medical Center: A Prospective Pilot Study. *Hospital* 49 533 *pharmacy* 2015; 50: 505-513. DOI: 10.1310/hpj5006-505.
- 50 534 32. Vira T, Colquhoun M and Etchells E. Reconcilable differences: correcting medication errors at 51 535 hospital admission and discharge. Qual Saf Health Care 2006; 15: 122-126. DOI: 52 536 10.1136/qshc.2005.015347. 53
- 53 537 537 537 537 538 Al-Jazairi AS, Al-Suhaibani LK, Al-Mehizia RA, et al. Impact of a medication reconciliation program 55 538 on cardiac surgery patients. *Asian Cardiovasc Thorac Ann* 2017; 25: 579-585. 20171012. DOI: 56 539 10.1177/0218492317738382.
- 57 58

2		
3	540	34. Fernandes BD, Almeida P, Foppa AA, et al. Pharmacist-led medication reconciliation at patient
4	541	discharge: A scoping review. Res Social Adm Pharm 2020; 16: 605-613. 20190801. DOI:
5 6	542	10.1016/j.sapharm.2019.08.001.
7	543	35. Centers for Disease Control and Prevention. Chronic Kidney Disease
8 9	544	in the United States, 2023. Atlanta, GA: US Department of Health and Human
10	545	Services, Centers for Disease Control and Prevention; 2023. Available at:
11 12	546	https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html.
13	547	36. prevention Cfdca. Chronic Kidney Disease in the United States, 2021. 2021.
14	548	37. Nguyen-Thi HY, Le-Phuoc TN, Tri Phat N, et al. The Economic Burden of Chronic Kidney Disease in
15	549	Vietnam. Health Serv Insights 2021; 14: 11786329211036011. 20210728. DOI:
16	550	10.1177/11786329211036011.
17 18	551 552	38. Slawomirski L, Auraaen A and Klazinga NS. The economics of patient safety: strengthening a value- based approach to reducing patient harm at national level. 2017.
19	553	39. Daifi C, Feldpausch B, Roa PA, et al. Implementation of a Clinical Pharmacist in a Hemodialysis
20	554	Facility: A Quality Improvement Report. <i>Kidney Med</i> 2021; 3: 241-247 e241. 20210210. DOI:
21	555	10.1016/j.xkme.2020.11.015.
22	556	40. Hassan Y, Al-Ramahi RJ, Aziz NA, et al. Impact of a renal drug dosing service on dose adjustment
23 24	557	in hospitalized patients with chronic kidney disease. <i>The Annals of pharmacotherapy</i> 2009; 43: 1598-1605.
24	558	20090923. DOI: 10.1345/aph.1M187.
26	559	41. Manley HJ and Carroll CA. The clinical and economic impact of pharmaceutical care in end-stage
27	560	renal disease patients. <i>Semin Dial</i> 2002; 15: 45-49. DOI: 10.1046/j.1525-139x.2002.00014.x.
28	561	42. Anderegg SV, Wilkinson ST, Couldry RJ, et al. Effects of a hospitalwide pharmacy practice model
29	562	change on readmission and return to emergency department rates. Am J Health Syst Pharm 2014; 71:
30 31	563	1469-1479. DOI: 10.2146/ajhp130686.
32	564	43. Jiang SP, Zhu ZY, Ma KF, et al. Impact of pharmacist antimicrobial dosing adjustments in septic
33	565	patients on continuous renal replacement therapy in an intensive care unit. <i>Scand J Infect Dis</i> 2013; 45:
34	566	891-899. 20130912. DOI: 10.3109/00365548.2013.827338.
35 36	567 568	44. Al-Qudah RA, Al-Badriyeh D, Al-Ali FM, et al. Cost-benefit analysis of clinical pharmacist intervention in preventing adverse drug events in the general chronic diseases outpatients. <i>J Eval Clin</i>
37	569	<i>Pract</i> 2020; 26: 115-124. 20190624. DOI: 10.1111/jep.13209.
38	570	45. Aljbouri TM, Alkhawaldeh MS, Abu-Rumman AE, et al. Impact of clinical pharmacist on cost of
39	571	drug therapy in the ICU. Saudi Pharm J 2013; 21: 371-374. DOI: 10.1016/j.jsps.2012.12.004.
40	572	46. Abushanab D, Gulied A, Hamad A, et al. Cost savings and cost avoidance with the inpatient clinical
41 42	573	pharmacist interventions in a tertiary cancer care hospital. J Oncol Pharm Pract 2023:
42	574	10781552231160275. 20230322. DOI: 10.1177/10781552231160275.
44	<b>F 7 F</b>	
45	575	
46	576	
47 48	576	
49	577	
50		
51	578	
52	579	
53 54	5,5	
54 55	580	
56		
57		
58		
59 60		22 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
50		

1 2		
3 4 5 6 7 8 9 10 11 12 13 14 15	581	
	582	
	583	
	584	Figure Legends:
	585	Protein and Anna Anna Anna Anna Anna Anna Anna
	586	
	587	Figure 1: The cost-benefit analysis model.
16 17		pyrig
18 19	588	<b>Figure 2:</b> Tornado diagram illustrating the impact of various parameters on the net benefit of
20 21	589	Figure 1: The cost-benefit analysis model.         Figure 2: Tornado diagram illustrating the impact of various parameters on the net benefit of supplemented medication reconciliation service (one-way sensitivity analysis).         Figure 3: Probabilistic sensitivity analysis evaluating the net benefit of supplemented medication
22 23 24	590	<b>Figure 3:</b> Probabilistic sensitivity analysis evaluating the net benefit of supplemented medication
24 25 26 27 28 29 30 31 32	591	
	592	ated to tex
	593	o text and da
33 34	594	to text and data mining
35 36	595	ning, , , , , , , , , , , , , , , , , , ,
37 38 39	596	
39 40 41	597	I training, and s
42 43 44	598	
44 45 46 47 48 49 50	599	Al training, and similar technologies
	600	
	601	
51 52 53	602	
54 55 56	603	A training, and similar technologies.
57 58		
59 60		23 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

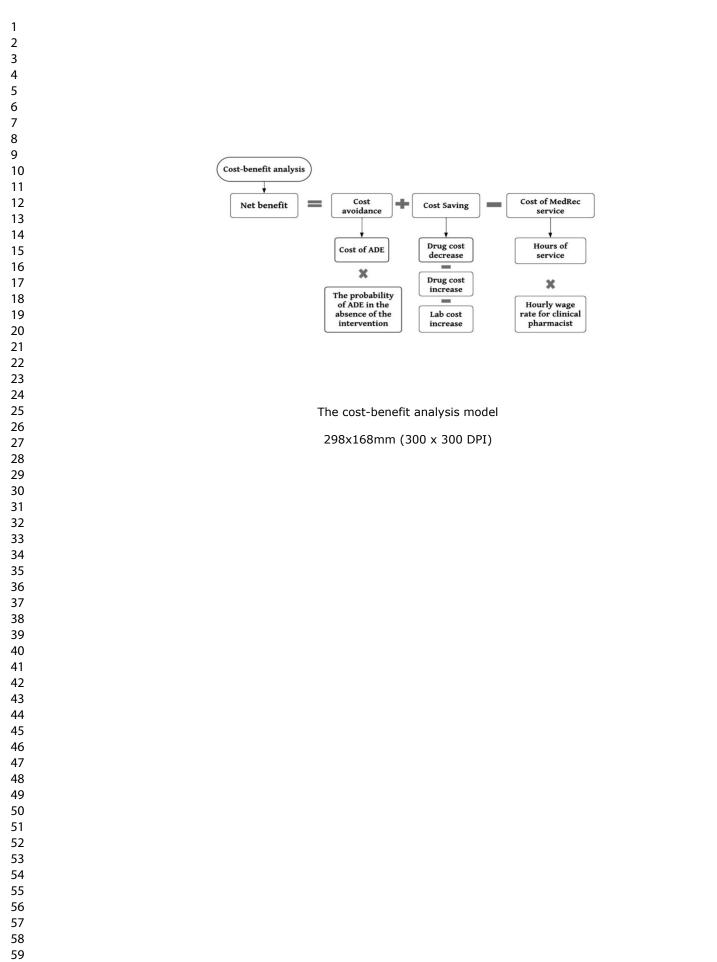
1 2 3 4 5	604 605	<b>Table 1:</b> Cost avoidance per cause-based domains in the PCNE classification of DRPs (V9.1).
6 7 8	606	
9 10	607	
	607	
54 55 56 57 58 59 60		24 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

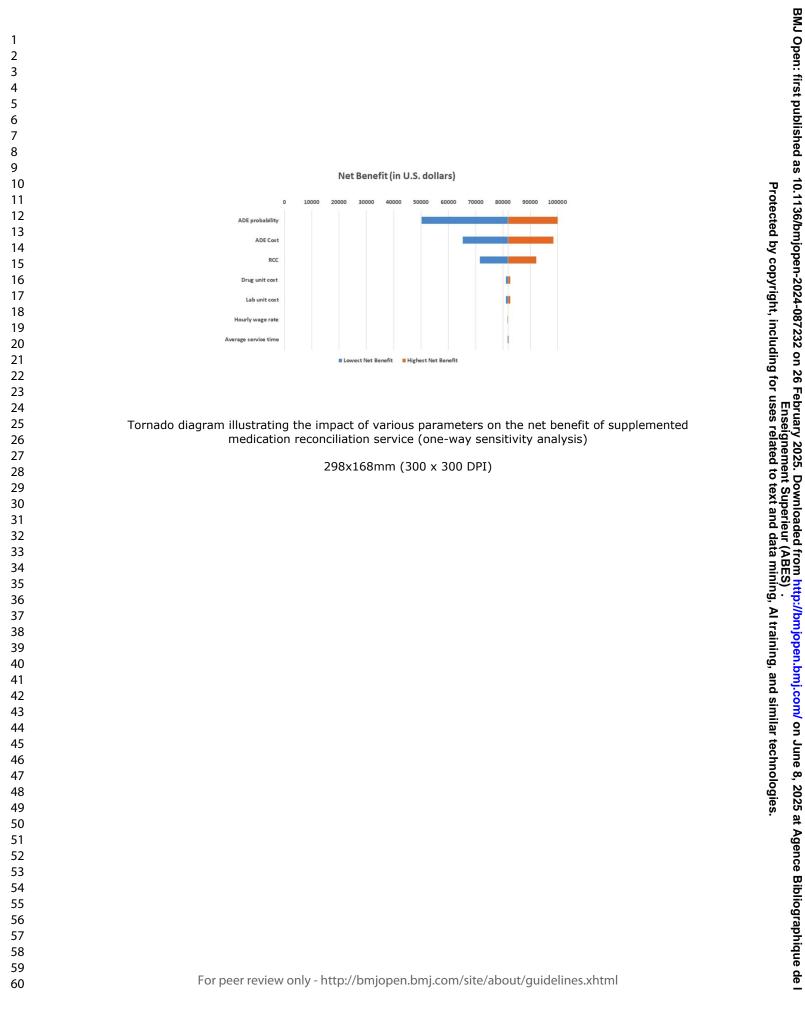
2	
3	
4	
5	
6	
5 6 7 8 9 10	
8	
a	
10	
10	
11 12	
12	
13	
14	
14 15 16 17	
16	
17	
18	
19	
20	
21	
22	
23	
24	
<ol> <li>18</li> <li>19</li> <li>20</li> <li>21</li> <li>22</li> <li>23</li> <li>24</li> <li>25</li> <li>26</li> <li>27</li> <li>28</li> <li>29</li> <li>30</li> <li>31</li> <li>32</li> <li>33</li> </ol>	
25	
20	
27	
28	
29	
30	
31	
32	
34 35	
35	
36	
37	
38	
39	
40	
40 41	
42	
42 43	
44 45	
46	
47	
48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	
50 59	
59	

60

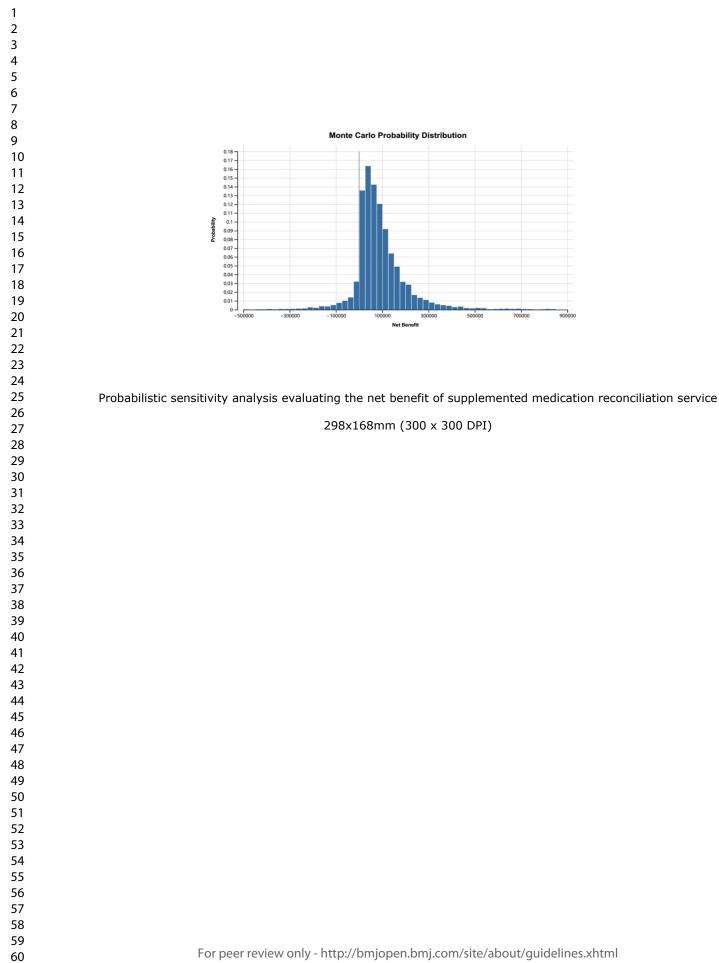
Primary domain	Cause	Cost	Total (\$
		avoidance (\$)	
Drug selection	Inappropriate drug according to	12,480.17	25,588.4
	guidelines/formulary		
	No or incomplete drug treatment despite	8,645.98	
	existing indication		
	No indication for drug	2,295.94	
	Inappropriate combination of drugs or drugs	1,916.01	
	and dietary supplements		_
	Too many different drugs/active ingredients	250.39	-
	prescribed for indication		
	Inappropriate duplication of therapeutic	250.38	-
	group or active ingredient		
Dose selection	Drug dose of a single active ingredient too	13,710.33	21,141.3
	high		
	Dosage regimen too frequent	5,284.26	-
	Drug dose too low	2,146.80	
Patient transfer	Drug omission	12,693.54	20,623.2
related	Discrepancy in the strength and/or	4,612.57	- /
(discrepancies)	frequency and/or number of units of dosage	<b>7</b>	
	form and/or total daily dose		
	Drug addition	2,399.36	-
	Therapeutic class substitution	436.54	
	Drug duplication	337.48	
	Discrepancy in the dosage form/route of	143.70	-
	administration	115.70	
Drug use process	Inappropriate timing of administration or	2,624.71	2,777.12
	dosing intervals by a health professional	_,	_,,,,,,
	Drug administered via wrong route by a	152.41	-
	health professional	102.11	
Treatment	Duration of treatment too long	273.25	469.21
duration	Duration of treatment too short	195.96	
Drug form	Inappropriate drug form/formulation	114.30	114.30
		114.30	114.30
Other	Addition of a lab test	10,531.5	12,088.2
other	No or inappropriate outcome monitoring	1,556.75	12,000.2
Total		1,550.75	<u> </u>
Total			83,052.3

	Outcome	Total (\$)	Average per patient \$ (M± SD)
	Intervention cost over 4 months	713.7	$5.03 \pm 0.77$
	Cost avoidance of all DRPs	83,052.40	584.88± 307.5
	Total cost saving	-467.4 (Negative net saving)	3.29
	Drug cost decrease	11210.28	$78.95 \pm 84.6$
	Drug cost increase	7479.26	52.67±66.
	Lab cost increase	4198.42	29.57±28.
	Net benefit over the study period (4 months)	81,871.25	576.56
	Benefit to cost ratio	115.7:1	
	$M \pm SD$ : Mean $\pm$ Standard deviation	6	
5	The total number of patients is 142.		





BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.



1 2	
3 4	Research Article
5 6	Title: Clinical pharmacist-led medication reconciliation supplemented with medication
7 8 9	review in chronic kidney disease admitted patients: a cost-benefit analysis
10 11 12	Journal: BMJ Open.
13 14	
15 16 17	
18 19	
20 21 22	
23 24	
25 26 27	
28 29	
30 31 32	
33 34 35	
36 37	tor peet terien on
38 39 40	
41 42	
43 44 45	
46 47 48	
49 50	
51 52 53	
54 55 56	
57 58	1
59 60	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

1	
2 3	
5 4	
5	
6	
7	
8	
9	
10	
11	
12	
13	
14	
15	
16	
17	
18 19	
20	
20 21	
22	
23	
24	
25	
26	
27	
28	
29	
30	
31	
32 33	
33 34	
35	
36	
37	
38	
39	
40	
41	
42	
43	
44 45	
45 46	
46 47	
47 48	
49	
50	
51	
52	
53	
54	
55	
56	
57	
58	
59	
60	

1

## Table S1: Patient demographics and clinical characteristics of the study sample.

X7 · 11	Study sample
Variable	N(%) N = 142
Gender n (%)	N = 142
Female	52 (27 22)
Male	53 (37.32)
	89 (62.68) 57.16 ±15.96
Age, years (M $\pm$ SD)	<i>37.</i> 10 ±13.90
BMI n (%) <18.5	6 (1 22)
18.5 -24.9	6 (4.23)
25-29.9	41 (28.87)
> 29.9	42 (29.58)
Marital status	53 (37.32)
Married	109 (76.76)
Not married	33 (23.24)
Smoking status	55 (25.24)
Yes	43 (30.28)
No	75 (52.82)
Ex-smoker	24 (16.90)
Educational level	
Not educated	20 (14.08)
School	93 (65.49)
University/higher education	29 (20.42)
Employment status	
Employed	26 (18.31)
Retired	32 (22.54)
Unemployed	84 (59.15)
Occupation	
Medical	3 (2.11)
Non-medical	64 (45.07)
No	75 (52.82)
Monthly income (JOD)	
<500	110 (77.46)
500 -1000	29 (20.42)
>1000	3 (2.11)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

AKI on Top of CKD related problems	42 (29.58)
CKD/dialysis related problems	71 (50.0)
Others	29 (20.42)
CKD stage	
Stage 2	2 (1.41)
Stage 3a	3 (2.11)
Stage 3b	12 (8.45)
Stage 4	32 (22.54)
Stage 5	93 (65.5)
Years of dialysis (M± SD)	$2.33 \pm 3.66$
Years of CKD (M± SD)	$5.02 \pm 6.80$
Number of comorbidities (M± SD)	$6.36 \pm 2.18$
$CCI (M \pm SD)$	$6.08 \pm 2.93$
Number of medications at admission (M± SD)	$9.58 \pm 3.07$
Number of medications at discharge ( $M \pm SD$ )	$9.24 \pm 4.34$
Death at discharge	5 (3.52)
Length of stay	$8.94 \pm 8.59$

Abbreviation: BMI: Body Mass Index, M± SD: Mean ± Standard deviation, JOD: Jordanian Dinar, CKD: Chronic Kidney Disease, AKI: Acute Kidney Disease, CCI: Charlson Comorbidity Index. SD).

One JOD is equivalent to 1.41 US Dollars (USD).

**Table S2:** Examples of the studied clinical cases with the probability score to cause ADEs.

A patient had a recent myocardial infarction (MI) and had previously	High
undergone stent placement for the main coronary artery. She was taking	(0.6)
febuxostat for gout. The clinical pharmacist recommended switching from	
febuxostat to allopurinol. (Black box warning)	
A female patient on hemodialysis, has a hemoglobin (Hb) level of 12 and a	High
history of stroke. She was on alpha epoetin 4000 units prescribed every	(0.6)
other day (EOD). (Black box warning)	
A 91-year-old female patient with CKD stage 5 (baseline serum creatinine	Medium
is 500 mmol/l). Dialysis was delayed due to her age. The patient is	(0.4)
experiencing uremia, including vomiting symptoms. She was prescribed	
metoclopramide 10 mg intravenously every 8 hours, which is a high dose	
considering her condition. Additionally, she is taking trimetazidine, which	
has a serious interaction with metoclopramide (category X). It is important	
to note that trimetazidine is contraindicated in patients with a GFR <30.	
A patient has osteoporosis and is undergoing hemodialysis. Initially, she	Medium
was prescribed alendronate, but the clinical pharmacist recommended	(0.4),
switching to denosumab. The physician stopped the alendronate as advised	Low
but could not provide denosumab due to economic issues. Subsequently,	(0.1)
the patient visited the outpatient clinic (OPC) due to bone pain, and there	
she received denosumab treatment.	
A patient has a CrCl (Creatinine Clearance) of 13, and he is currently taking	Medium
fenofibrate. Additionally, the triglyceride level is less than 250 mg/dL.	(0.4)
A patient underwent upper endoscopy, which revealed mild gastritis. There	Medium
were no available tests for H. pylori, and the patient's serum creatinine level	(0.4)
was 500 mmol/l (CrCl <15). Nevertheless, upon discharge, the patient was	
	1

prescribed amoxicillin 1g twice daily and clarithromycin 500mg twice	
daily without renal adjustment and without confirming the diagnosis.	
A patient has AKI on top of CKD and has been experiencing severe	Medium
vomiting for over a week. Upon admission, the patient's home medication	(0.4)
included metoclopramide 10 mg three times daily taken orally. However,	
after admission, the route was changed to intravenous 10 mg TID (not renal	
dose) without improvement, the dose was changed to metoclopramide	
intravenously at 20 mg three times daily, which is considered too high. The	
clinical pharmacist recommended discontinuing metoclopramide and	
administering ondansetron as an alternative.	
A patient is undergoing hemodialysis and was diagnosed with deep vein	Medium
thrombosis (DVT). Upon discharge, she was prescribed a therapeutic dose	(0.4)
of Enoxaparin. The clinical pharmacist recommended switching to	
apixaban.	
A patient was admitted for liver cirrhosis, baseline CrCl 32, AKI, diabetes	Medium
mellitus (DM), and recently diagnosed depression. He was initially	(0.4)
admitted while taking metformin 500mg once daily. However, upon	
discharge, his medication regimen included metformin 850mg three times	
daily, mirtazapine, spironolactone, and hydrochlorothiazide. The clinical	
pharmacist was unable to reach the responsible physician to discuss the	
changes. Consequently, the patient was readmitted after 5 days due to	
diarrhea and hyponatremia.	
A patient has a UTI and is currently taking ciprofloxacin, calcium	Low
carbonate, and ferrous gluconate twice daily, both at 6 pm and 6 am, all by	(0.1)
oral route.	
A patient admitted with severe hypophosphatemia; the physician initially	Low
recorded that the patient was on calcium carbonate 500mg BID. With	(0.1)
medication reconciliation we found that the actual home dose was calcium	
carbonate 1g TID, along with sevelamer TID, which was obtained from	
outside the hospital (and was not known by the physician). Resolving these	
discrepancies with the physician led to a change in the diagnosis.	

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES)

Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies

A patient has been taking Combivent® every 8 hours for over than 2 weeks	Low
without any valid indication.	(0.1)
A 32-year-old patient has type 1 diabetes mellitus (DM1), end-stage renal	Low
disease (ESRD), partial retinopathy, and uncontrolled DM with recurrent	(0.1)
hypoglycemia. Upon admission, she was using pre-mixed insulin. The	
clinical pharmacist suggested switching to a basal-bolus insulin regimen.	
A patient was discharged without some of his hypoglycemic and	Low
antihypertensive agents unintentionally.	(0.1)
A patient on HD, was on famotidine 40mg once daily at home. Was not	Very
documented.	low
	(0.01)

# **Table S3:** Average cost avoidance per patient across cause-based domains in the PCNE classification of DRPs (Version 9.1).

Primary domain	Cause	Cost avoidance (\$) Average per patient	Numl of patier
	Inappropriate drug according to guidelines/formulary	195.0	64
	No or incomplete drug treatment despite existing indication	139.5	62
	No indication for drug	71.7	32
Drug selection	Inappropriate combination of drugs or drugs and dietary supplements	174.2	11
	Too many different drugs/active ingredients prescribed for indication	83.5	3
	Inappropriate duplication of therapeutic group or active ingredient	83.5	3
	Drug dose of a single active ingredient too high	207.7	66
Dose selection	Dosage regimen too frequent	83.9	63
	Drug dose too low	89.4	24
	Drug omission	133.6	95
Patient transfer related (discrepancies)	Discrepancy in the strength and/or frequency and/or number of units of dosage form and/or total daily dose	118.3	39
	Drug addition	150.0	16
	Therapeutic class substitution	24.3	18

2 3 4 5 6	
7 8 9 10 11	
12 13 14 15 16	
17 18 19 20 21	
22 23 24 25 26	
20 27 28 29 30 31	
32 33 34 35 36	
37 38 39 40 41	
42 43 44 45	
46 47 48 49 50	
51 52 53 54 55	
56 57 58 59 60	

	Drug duplication	84.4	4
	Discrepancy in the dosage form/route of administration	71.9	2
Drug use process	Inappropriate timing of administration or dosing intervals by a health professional	77.2	34
	Drug administered via wrong route by a health professional	152.4	1
Treatment duration	Duration of treatment too long	91.1	3
Treatment duration	Duration of treatment too short	65.3	3
Drug form	Inappropriate drug form/formulation	38.1	3
	Addition of a lab test	118.3	89
Others	No or inappropriate outcome monitoring	91.6	17

# **BMJ Open**

#### Clinical pharmacist-led medication reconciliation supplemented with medication review in chronic kidney disease admitted patients: a cost-benefit analysis

Journal:	BMJ Open
Manuscript ID	bmjopen-2024-087232.R3
Article Type:	Original research
Date Submitted by the Author:	22-Dec-2024
Complete List of Authors:	Altawalbeh, Shoroq ; Jordan University of Science and Technology, Department of Clinical Pharmacy Sallam, Nahlah M.; Jordan University of Science and Technology, Department of Clinical Pharmacy Al-Khatib, Minas; Jordan University of Science and Technology, Department of Clinical Pharmacy Alshogran, Osama Y.; Jordan University of Science and Technology, Department of Clinical Pharmacy Bani Amer, Mohammad S.; Jordan University of Science and Technology, Department of Internal Medicine
<b>Primary Subject Heading</b> :	Epidemiology
Secondary Subject Heading:	Medical management, Health services research, Health economics
Keywords:	Medication Reconciliation, Health Services, Health economics < HEALTH SERVICES ADMINISTRATION & MANAGEMENT, Health & safety < HEALTH SERVICES ADMINISTRATION & MANAGEMENT

SCHOLARONE<sup>™</sup> Manuscripts



I, the Submitting Author has the right to grant and does grant on behalf of all authors of the Work (as defined in the below author licence), an exclusive licence and/or a non-exclusive licence for contributions from authors who are: i) UK Crown employees; ii) where BMJ has agreed a CC-BY licence shall apply, and/or iii) in accordance with the terms applicable for US Federal Government officers or employees acting as part of their official duties; on a worldwide, perpetual, irrevocable, royalty-free basis to BMJ Publishing Group Ltd ("BMJ") its licensees and where the relevant Journal is co-owned by BMJ to the co-owners of the Journal, to publish the Work in this journal and any other BMJ products and to exploit all rights, as set out in our <u>licence</u>.

The Submitting Author accepts and understands that any supply made under these terms is made by BMJ to the Submitting Author unless you are acting as an employee on behalf of your employer or a postgraduate student of an affiliated institution which is paying any applicable article publishing charge ("APC") for Open Access articles. Where the Submitting Author wishes to make the Work available on an Open Access basis (and intends to pay the relevant APC), the terms of reuse of such Open Access shall be governed by a Creative Commons licence – details of these licences and which <u>Creative Commons</u> licence will apply to this Work are set out in our licence referred to above.

Other than as permitted in any relevant BMJ Author's Self Archiving Policies, I confirm this Work has not been accepted for publication elsewhere, is not being considered for publication elsewhere and does not duplicate material already published. I confirm all authors consent to publication of this Work and authorise the granting of this licence.

terez oni

Enseignement Superieur (ABES) Protected by copyright, including for uses related to text and data mining, AI training, and similar technologies

1		
2		
3 4	1	Research Article
5		
6	2	
7	-	
8	3	Clinical pharmacist-led medication reconciliation supplemented with
9		
10	4	medication review in chronic kidney disease admitted patients: a cost-benefit
11 12		
13	5	analysis
14	0	
15		
16	6	Shoroq M. Altawalbeh, PharmD, PhD, <sup>1</sup> Nahlah M. Sallam, M.S <sup>1</sup> , Minas Al-Khatib, PharmD, <sup>1</sup> Osama Y.
17	-	
18 19	7	Alshogran, M.S, PhD, <sup>1</sup> Mohammad S. Bani Amer, MD <sup>2</sup>
20		
21	8	<sup>1</sup> Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan University of Science and Technology, Irbid,
22	9	Jordan. <sup>2</sup> Department of Internal Medicine, Faculty of Medicine, Jordan University of Science and Technology,
23	10	Irbid, Jordan.
24		
25 26	11	
27		
28	12	Shoroq M. Altawalbeh, PharmD, PhD, Department of Clinical Pharmacy, Faculty of Pharmacy,
29	13	Jordan University of Science and Technology, Irbid 22110, Jordan. Email address:
30	14	smaltawalbeh@just.edu.jo
31 32	1 5	OB CID: 0000 0001 0245 4040
33	15	ORCID: 0000-0001-8345-4048
34	16	
35		
36	17	Nahlah M. Sallam, Msc, Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan
37	18	University of Science and Technology, Irbid 22110, Jordan. Email address:
38 39	19	nmsallam20@ph.just.edu.jo
40	20	ORCID: 0000-0001-9311-600X
41	20	
42	21	Minas Al-Khatib PharmD, Department of Clinical Pharmacy, Faculty of Pharmacy, Jordan
43	22	University of Science and Technology, Irbid 22110, Jordan. Email address:
44 45	23	makhatib@just.edu.jo
45 46	24	ORCID::0000-0003-0209-1578
47		
48	25	
49	26	Osama Y. Alshogran, Msc, PhD, Department of Clinical Pharmacy, Faculty of Pharmacy,
50	20 27	Jordan University of Science and Technology, Irbid 22110, Jordan. Email address:
51 52		
52	28	<u>oyalshogran@just.edu.jo</u>
54	29	ORCID: 0000-0002-2466-4763
55		
56		
57 58		
58 59		1
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

1 2		
3 4	30	Mohammad S. Bani Amer, MD, Department of Internal Medicine, Faculty of Medicine, Jordan
5 6	31 32	University of Science and Technology, Irbid 22110, Jordan. Email address: m.baniamer1997@gmail.com
7	33	
8 9	34	*Corresponding Author:
10 11	35	Shoroq M. Altawalbeh, PharmD, PhD
12	36	Associate Professor
13 14	37	Department of Clinical Pharmacy
15 16 17	38 39	Jordan University of Science and Technology; Faculty of Pharmacy
18 19	40	P.O.Box 3030, Irbid 22110, Jordan
20 21 22	41 42	Tel.:+962(0)27201000 Fax : + 962 (0) 2 7095123
23	43	E-mail: <u>smaltawalbeh@just.edu.jo</u>
24 25	44	ORCID: 0000-0001-8345-4048
26 27	45	
28 29	46	Running Title: Cost-benefit of medication reconciliation in CKD
30 31	47	Number of Tables: 2
32 33 34	48	Number of Figures: 3
35 36	49	Keywords: Medication reconciliation, clinical pharmacist, cost-benefit, chronic kidney disease,
37 38 39	50	Jordan.
40 41 42	51	
43	52	
44 45	53	
46 47	55	
48 49	54	
50	55	
51 52		
53 54	56	
55 56 57	57	
58		
59 60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

#### Page 4 of 37

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) .

data mining, Al training, and similar technologies

Protected by copyright, including for uses related to text

#### **BMJ** Open

Abstract **Objective:** Chronic kidney disease (CKD) is associated with a high economic burden, which is exacerbated by the high susceptibility to drug-related problems (DRPs) in this patient population. This study aimed to evaluate the cost-benefit ratio of medication reconciliation supplemented with medication review for inpatients with CKD, compared to the absence of this intervention. Design: This was a cost-benefit analysis conducted along with a prospective interventional study. Setting: The study was conducted at two hospitals in Jordan between February and May 2023. Participants: The prospective interventional study included 142 admitted patients with CKD. Interventions: Patients received medication reconciliation at admission and discharge as well as medication review throughout admission. Primary and secondary outcome measures: The primary outcome measures were the net benefit and the benefit-to-cost ratio of the intervention. A cost-benefit analysis was conducted from the healthcare system perspective by assessing the cost of the service (the pharmacist time required to complete the service per patient) and the economic benefit, including total and per-patient cost savings and cost avoidance. **Results:** The total estimated cost of all DRPs in the absence of interventions (cost avoidance) was \$3,052 (average of  $\$585\pm 308$  per patient); among which \$20,623 was attributed to medication discrepancies. The cost savings were estimated at -\$467. The supplemented medication reconciliation service was estimated to cost \$714. As a result, the estimated net benefit totaled \$81,871, averaging \$577 per patient, with a benefit-to-cost ratio of 115.7:1 over

79 the 4-month study period.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

#### BMJ Open

	вмј Ор
Conclusions: Delivering a supplemented medication reconciliation service by a clinical	en: firs
pharmacist for CKD patients is cost beneficial from the healthcare perspective in Jordan, an	t publis
example of a low- and middle-income country (LMIC). This finding further confirms the pivotal	shed as
role of clinical pharmacists in multidisciplinary healthcare teams.	s 10.1136/b
role of clinical pharmacists in multidisciplinary healthcare teams.     Weywords: Medication reconciliation, clinical pharmacist, cost-benefit, chronic kidney disease,     Jordan.	BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26
Jordan.	February 2025. Enseigneme
text and data mining,	wnloaded from http: uperieur (ABES).
Al training, and similar technologies	//bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l
ologies.	une 8, 2025 at Agence
4 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml	Bibliographique de l

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de I Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

1 2		
3	106	Strengths and limitations of this study
4 5 6	107	• The study was carried out alongside a prospective interventional study, allowing
7 8	108	for a more accurate estimation of the time required to complete the medication
9 10 11	109	reconciliation service and providing a closer examination of potential drug related
12 13	110	problems (DRPs).
14 15 16	111	• Evaluation of the probability scores of DRPs was conducted by an expert panel
17 18	112	composed of five independent evaluators.
19 20	113	• The exact real cost of adverse events resulting from DRPs could not be measured.
21 22 23	114	• The study relied on admission charges, medication prices, and lab prices rather than
24 25	115	actual costs.
26 27	116	
28 29	117	
30 31	118	
32	119	
33 34 35	120	actual costs.
36 37	121	
38	122	
39 40	123	
41 42	124	
43 44	125	
45 46	126	
47 48	127	
49 50	128	
51 52	129	
53	130	
54 55 56	131	
57		
58 59 60		5 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

#### **BMJ** Open

#### Introduction

Chronic kidney disease (CKD) is associated with high financial burden globally, exceeding expenditures incurred by other highly burdened patients such as those with stroke and cancer.<sup>1, 2</sup> CKD is a complex medical state accompanied by multiple concurrent illnesses, which inflate the cost of management. Around \$18 billion had been spent by the national US Department of Veterans Affairs for the care of patients with CKD without renal replacement therapy (RRT), with expenditures increased across the advanced stages of CKD.<sup>3, 4</sup> In Jordan, the Ministry of Health expended approximately \$17.7 Million per year for hemodialysis patients management in 2010, with an average of annual cost of \$9,979 per patient.<sup>5</sup> A study conducted in Lebanon reported the median cost for all CKD stages per year of \$4,764.02 (IQR \$2,475.24 - \$23,455.61) in 2019 from a society perspective.<sup>6</sup> Studies highly recommend implementing programs and policies to reduce progression and complications of CKD to mitigate the growing disease burden especially in countries with limited resources. 7,8 

Patients with CKD are very vulnerable to medication discrepancies and other Drug related problems (DRPs).<sup>9, 10</sup> Interestingly, many serious DRPs are preventable in CKD patients.<sup>11</sup> Developing DRPs increased the exposure to re-hospitalization, extended length of hospital stays, and early death, and therefore expanded the cost.<sup>12-14</sup> Clinical pharmacy services targeting DRPs have revealed a positive economic impact on healthcare organizations across the literature.<sup>15</sup> Medication reconciliation and medication review, primarily led by a clinical pharmacist, are vital services focused on preventing and resolving medication discrepancies and other drug-related problems (DRPs). These processes play a key role in enhancing patient outcomes and reducing healthcare costs. <sup>16</sup> Medication reconciliation ensures that the patient's medication list is accurate and up-to-date during transitions of care, while medication review involves a thorough and 

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

structured assessment of the patient's medications to ensure they are receiving the most appropriate treatment regimen. 17 

The economic burden of medication discrepancies and other DRPs is understudied, particularly in developing countries, including Jordan. Moreover, there is a dearth of data regarding the efficiency of clinical pharmacy services implemented in patients with CKD, especially in low-income to middle-income countries. Although medication reconciliation has the potential to be beneficial in this population, it also incurs costs, highlighting the need for a health economic analysis to determine whether this service can deliver clinical benefits at a reasonable cost, providing a solid rationale for its clinical application. Efforts to evaluate the cost-benefit of medication reconciliation provide essential evidence for healthcare providers and policymakers regarding the value of implementing this clinical service particularly in CKD patients. Examining the costs associated with drug-related problems (DRPs) during CKD hospitalizations will further emphasize the burden of the disease and support efforts to reduce the significant healthcare expenses related to CKD. These insights will underscore the crucial role clinical pharmacists play as part of the multidisciplinary hospital team in alleviating the financial impact of CKD on the healthcare system. Therefore, this study aimed to evaluate the cost-benefits of implementing a clinical pharmacist-led service for supplemented medication reconciliation for admitted patients with CKD in Jordan, compared to the absence of this intervention. 

Methods 

Study design 

> The cost-benefit analysis was developed along with a prospective interventional clinical study that involved patients with stages 2-5 CKD, who were admitted to two healthcare hospitals in Jordan: King Abdullah Hospital (KAUH) and Princess Basma Hospital (PBH). A clinical

Page 9 of 37

#### **BMJ** Open

pharmacist was responsible for providing supplemented medication reconciliation to CKD-admitted patients over four months (from February to May 2023). The costs and benefits during the study period were assessed in comparison to absence of this intervention. The primary outcome measure was the net benefit generated by the supplemented medication reconciliation service provided to CKD patients during the study period. The net benefit was estimated according to the following equation: [net benefit = total benefits (cost avoidance + cost saving)-service cost]. In addition, the benefit-to-cost ratio was estimated. The health care system perspective was adopted in the current study. Base case calculations were performed using Excel software. The cost-benefit analysis model is depicted in Figure 1. The demographic and clinical characteristics of the study sample are summarized in the Supplemental Material (Table S1). 

188 Descri

#### Description of supplemented medication reconciliation

Patients received a supplemented medication reconciliation service across the transitions of care during their admission to the internal medicine ward, in addition to a medication review for possible DRPs. The procedure of supplemented medication reconciliation consisted of medication reconciliation at admission, medication review throughout admission, and medication reconciliation at discharge. At admission, demographic, clinical, and medical data for each enrolled patient were collected from the medical records, followed by interviews with the patients or their caregivers to verify the patients' demographics, medical history, and pre-admission medication list. The pre-admission drug lists were also confirmed using all other available sources, such as bottles, prescriptions, and previous medical records, to obtain the best possible medication history (BPMH). The BPMH was compared with the current hospital medication sheet (admission medication orders) to extract discrepancies at admission. Medication reviews and clinical case analyses were conducted regarding dose adjustments, drug interactions, missing medications,

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

inappropriate medications, unnecessary medications, and monitoring after admission and during the hospitalization period to identify the DRPs. At discharge, the best possible discharge medication plan (BPMDP) was created from the BPMH, the last medication list during index hospitalization, and new medications planned to be started upon discharge. The BPMDP was compared with discharge prescription and summary. Patient education was provided to willing patients before discharge. All identified discrepancies and other DRPs were discussed with the resident responsible for the resolution as accessible.

208 Estimation of costs

Input costs in the current study include the resources used to provide the supplemented medication reconciliation, that is, the pharmacists' time. The time taken by the pharmacist to deliver the supplemented medication reconciliation per patient (in hours) was recorded for each admission. The cost of the medication reconciliation service was estimated by multiplying the service time by the average hourly wage rate for clinical pharmacists, as obtained from the financial department at KAUH. The average annual wage rate was converted to the hourly wage rate based on 240 working days per year and 8 working hours per day.

216 Estimation of benefits

The economic benefits associated with the potential prevention of DRPs through interventions recommended by clinical pharmacists were evaluated in terms of "cost savings" and "cost avoidance."

220 Cost saving

The cost-saving analysis estimated the reduction in medication costs resulting from interventions,
 along with the additional medication costs and expenses associated with laboratory requests (cost
 savings = reduced drug costs – (increased drug costs + increased lab costs)).

#### BMJ Open

The cost of any medication (increased or decreased) was estimated as the cost of medication per unit multiplied by the frequency per day and then by the duration of therapy.<sup>18</sup> Acute therapy duration was estimated based on the clinical scenario, while chronic medication use was calculated over three months' time horizon. Public per-unit prices of drugs were obtained from the Jordan Food and Drug Administration (JFDA).<sup>19</sup> For interventions that included the addition of a laboratory test, the increased cost for each intervention was estimated using the prices of laboratory tests obtained from KAUH laboratory department. Both drug and lab prices were converted to costs by multiplying them by an assumed Ratio of Cost to Charge (RCC). The net cost saving was estimated by subtracting the total increased cost from the decreased cost resulting from the implementation of the supplemented medication reconciliation services. Per-patient averages were calculated for total cost savings, drug cost reductions, drug cost increases, and laboratory costs.

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

*Cost avoidance* 

Cost avoidance was estimated for each intervention recommended by the clinical pharmacist in the current study as the cost avoided by potential prevention of DRPs. The probability of DRP in the absence of intervention was determined according to the Nesbit et al scale <sup>20</sup> which has five levels of risk of causing DRPs: 0 (none), 0.01 (very low), 0.1 (low), 0.4 (medium), or 0.6 (high). The DRP probability in the absence of the intervention was estimated for all identified discrepancies and other DRPs by a team of experts, comprising four clinical pharmacists and one physician. Examples of the studied clinical cases with potential probabilities

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

of DRPs are presented in Supplemental Material (Table S2). The cost avoidance attributed to each intervention was calculated by multiplying the corresponding DRP probability by the DRP cost. The cost of a DRP was assumed to be the cost of an additional 2 days of hospital stay.<sup>21</sup> Admission charges were retrieved from the billing system for all admissions included in the study, and the average charge per day was calculated for these CKD patients. The average charge per day was adjusted using the assumed RCC to estimate the RCC cost of DRPs. Cost avoidance was estimated in total and as an average per patient. Cost avoidance was also estimated by the Pharmaceutical Care Network Europe (PCNE) Classification for Drug-Related Problems V9.1 based on the cause,<sup>22</sup> and the Medication Discrepancy Taxonomy (MedTax) system.<sup>23</sup> All financial data were extracted in Jordanian Dinar currency unit (JOD) and converted to United States Dollars (USD) at a rate of (1 JOD = 1.41 USD). All cost data were reported in 2023 values. The RCC value was assumed to be 0.8 throughout the base case analysis and varied in the sensitivity analysis. 

#### 259 Sensitivity analysis

One-way sensitivity analysis was conducted to account for the variability in the key model parameters. DRP probabilities were varied using the minimum and maximum probabilities assigned by the expert panel. All costs were varied over a range of  $\pm 20\%$  of the base case cost. The average service time was varied over two SD of the mean, as calculated in this study. RCC was varied in the range (0.7 to 0.9). Probabilistic sensitivity analysis was conducted, in which the input variables were varied simultaneously over 10,000 Monte Carlo simulations. Beta distribution was used for DRP probabilities, uniform distribution for RCC and hourly wage rate, normal distribution for service time in minutes, and gamma distribution for cost. 

**Public and patient involvement** 

#### **BMJ** Open

Patients and the public were not actively involved in the design, conduct, reporting, or dissemination plans of this research. Ethics approval and consent to participate This study was approved by the Institutional Review Board (IRB) Committee at KAUH (Ref number: 123/147/2022) and the Ministry of Health (Ref number: 13902). Written informed consent was obtained from the participants after they were given comprehensive information about the study's purpose and details. **Results** Cost of supplemented medication reconciliation The average time required to perform a supplemented medication reconciliation service (medication reconciliation plus medication review during admission) was 43.38 (SD= 6.65) minutes, ranging from 26 to 60.5 minutes. The total time spent by the clinical pharmacist on the supplemented medication reconciliation over the four-month intervention period was 6117.1 minutes (101.95 hours). The average duration to accomplish a primary medication reconciliation service at admission was  $15.79 \pm 1.74$  minutes. Though, the average time for medication review during the admission was  $21.6 \pm 4.30$  minutes (ranged from 11.6 to 35.5 minutes) per patient. Medication reconciliation time at discharge averaged  $3.58 \pm 1.55$  minutes per patient. Based on the reported average monthly salary of the clinical pharmacist at KAUH, the wage per hour was \$7 assuming 8 hours per day. Taking this into account, the total intervention cost over 4-month study period was \$713.7 ( $$7 \times 101.95$  hours). Benefits of supplemented medication reconciliation *Estimated cost saving* 

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

The average increase in medication costs was \$53 ± 67 per patient, while the total cost of
required lab work averaged \$30 ± 29 per patient. Conversely, the intervention led to an average
reduction in medication costs of \$79 ± 85 per patient.
The total increased medication cost was estimated to be \$7479 and lab needed total cost was

Total cost saving = \$11,210 - \$7,479 - \$4,198 = -\$467 (\$3 negative cost saving per patient).

estimated at \$4198. The decrease in medication costs owing to the intervention was \$11,210.

Table 2 presents cost saving values in total and at the patient level.

#### *Estimated cost avoidance*

The average admission charge for patients with CKD enrolled in the study was \$2811 (SD= \$2172), and the average admission charge per day was \$340 (SD= \$199). The assumed cost of a DRP was the estimated cost of two additional hospitalization days for patients with CKD in the current study [680 multiplied by 0.8 RCC = 483]. The estimated probabilities of DRPs in the absence of intervention were averaged using a panel of five expert evaluators. The majority of DRPs (73.4%; N=735) were in the low-to medium-risk category (0.1-0.4), while 21.2% (N=212) were in the low-risk category (<0.1), and 5.4% (N=54) were in the moderate-to high-risk category (>0.4). The average cost of a potential DRP, estimated by multiplying the average DRP probability by the estimated RCC cost for two additional hospitalization days was \$83 (SD=\$58). The total estimated cost of all DRPs in the absence of interventions (cost avoidance) was \$83,052, averaging  $$585 \pm $308$  per patient. Patient transfer related DRPs (medications discrepancies) were found to be the third most expensive cause-based domain in the PCNE classification of DRPs (V9.1), contributing to around 25% of the total cost avoidance (\$20,623; \$145 per patient). The greatest

weight of discrepancies' cost avoidance was attributed to "drug omission" category (\$12,694) followed by "discrepancy in frequency/strength/dose" (\$4,613) and "drug addition" (\$2,399), Table 1. A detailed summary of the cost avoidance per PCNE cause-based domains is presented in Table 1. Average cost avoidance per patient across the cause-based domains of DRPs (at the patient level) is detailed in the Supplemental Material (Table S3).

318 Cost benefit analysis

The net benefit was calculated by subtracting the total cost of intervention from total cost avoidance and saving [cost avoidance (\$83,052) + cost saving (- \$467) - cost of the intervention (\$714) = \$81,871]. The net benefit was estimated as \$577 per patient. The benefit-to-cost ratio estimated in this study was (115.7:1). Table 2.

323 Sensitivity analyses

The study conclusion was insensitive to uncertainty in any of the input variables including DRP probabilities, DRP cost, RCC, per-unit cost of drugs and labs, hourly wage rate, and average service time. The main driver of the outcome was the DRP probability, followed by the DRP cost, as depicted in Figure 2. However, the net benefit was positive over all plausible ranges of the input variables. The minimum estimated net benefit was \$50,203 based on varying DRP probability. In probabilistic sensitivity analysis, the average expected value of the net benefit was \$90,451(SD = \$126,294). Only 866 out of 100,000 iterations (8.7%) showed a negative net benefit (Figure 3).

333 Discussion

The major findings of the current study emphasize the substantial economic burden of medication discrepancies and other DRPs in patients with CKD. In addition, the results showed

> For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

#### Page 16 of 37

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

#### **BMJ** Open

> that the estimated economic benefit was remarkable compared to the estimated cost of the medication reconciliation service. Overall, the results indicate that supplemented medication reconciliation services mediated by clinical pharmacists are cost beneficial.

The majority of DRPs in the current study were classified as having a medium risk of DRPs. Despite the different scales used to evaluate the clinical significance of DRPs in patients with CKD, most studies have found that the majority of DRPs in this high-risk population were with moderate to significant clinical impact. In a study conducted in Jordan among hospitalized patients with CKD, the majority of DRPs (62%) were classified among the significant category, however, the study used a different scale (extremely significant, much significant, significant, and slightly significant).<sup>24</sup> In a study conducted in Canada, approximately half of the observed DRPs were moderate in severity in terms of causing harm to CKD patients.<sup>25</sup> The different scales used in severity assessment across the literature makes the comparison seems challenging. Overall, most recognized DRPs were considered clinically important in the current study and potentially preventable.

This study revealed the beneficial effect of clinical pharmacist medication reconciliation intervention on CKD patients in terms of the cost-benefits associated with this service. A recent review of 47 studies among CKD patients also supports this finding; 7 studies approved the significant cost savings and 15 studies reported improvement in clinical outcomes due to clinical pharmacy care, including blood pressure, anemia, length of hospital stay, readmissions, kidney function, and other laboratory tests (i.e., PTH, calcium, uric acid, cholesterol, and HbA1c).<sup>15</sup>

The average time needed for full supplemented medication reconciliation services provided for each CKD admission in the current study was  $43.38 \pm 6.65$  minutes. This is comparable to other studies that measured the time needed for medication reconciliation services:  $44.4 \pm 21.8$ ,<sup>26</sup> Page 17 of 37

#### **BMJ** Open

 $40 \pm 17.2$  minutes,<sup>27</sup> and 48 minutes.<sup>28, 29</sup> In addition, the total time to deliver a primary medication reconciliation service at all transitions of care per patient was estimated with a median of 24 minutes (IOR 20-30 minutes).<sup>30</sup> The specific time for medication reconciliation at admission was roughly similar to our finding (15 minutes (IOR 10–21)) in two previous studies.<sup>31, 32</sup> Moreover, medication reconciliation at discharge after conducting medication reconciliation at admission was previously estimated to need approximately 3.5 minutes,<sup>33</sup> which is also comparable to the estimated time in the current study. However, a recent systematic review reported a wider range of the mean time for medication reconciliation implementation across nine studies with an average of 34.5 ( $\pm$ 39.4) minutes.<sup>34</sup> This variability could be originated from the diverse models and services involved across the pooled studies and variations in study population. 

CKD has been associated with a high economic burden.<sup>3, 35-37</sup> DRPs have been associated with high costs that affect patient safety and healthcare expenditures.<sup>38</sup>. Our study estimated the net benefit attributed to avoiding and resolving DRPs to be \$81,871.15 over 4 months for a cumulative number of 142 CKD patients, averaging \$576.56 per patient. Such remarkable benefit confirms the need of implementing supplemented medication reconciliation in CKD patients. Likewise, a recent retrospective cohort in the US among hemodialysis patients estimated cost saving from preventing DRPs to be \$447,355 over a 6-month period of observation, attributing this benefit to performing medication reconciliation with medication review.<sup>39</sup> A Malavsian study measured the cost saving resulted from only dose adjustment in CKD inpatients to be \$2,250 for 212 dose related recommendations over 4 months, in which the clinical pharmacist worked within a multidisciplinary rounds with the nephrology team to adjust the doses as needed.<sup>40</sup> This saved cost is considered much lower than the avoided cost resulting from renal dose adjustment in our study (\$14,756 for 4 months, 94 dose adjustment interventions). An earlier prospective study

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

conducted medication therapy evaluation by pharmacist found that the ratio of pharmaceutical care cost to healthcare system saving is \$1 to \$3.98 among end-stage renal disease patients in the USA.<sup>41</sup> This is much smaller compared to the benefit to cost ratio estimated in the current study (115:1). This variability might be related in part to the relatively lower wage rates of clinical pharmacists in Jordan than in the USA. However, the estimated cost of a DRP is also expected to be higher in terms of admission-day costs in the USA. Another study found annual direct cost savings of more than \$780,000 after implementing supplemented medication reconciliation with patient education in internal medicine wards in Kansas ascribed to reducing readmissions.<sup>42</sup> A Chinese trial found cost saving attributed to antimicrobial dose adjustment (number of adjusted doses= 183) by a clinical pharmacist of \$3,525 per patient with sepsis undergoing continuous dialysis in the ICU.<sup>43</sup> Wage rates and the cost of health care may differ widely across regions and institutions which make the comparison in cost is not sufficiently clear/straightforward. This also highlights the need to obtain relevant data from local or regional studies to better support the decisions of policy makers based on information from relevant settings. 

In Jordan, the role of clinical pharmacists appears to be economically effective for other populations. Among outpatients with chronic diseases, the estimated cost avoidance per month due to pharmacist interventions (number of interventions = 79 among 48 patients) was 6,422.41.44In another study conducted in Jordan, clinical pharmacist intervention in the ICU reduced the total cost of drugs consumption by \$211,574.90 over 10 months.<sup>45</sup> Still, the cost benefit of medication reconciliation among CKD patients has not been well addressed in Jordan and other developing countries. The results of the current study strongly support the need to implement medication reconciliation supplemented with continuous medication review during hospital admission in patients with CKD.

Page 19 of 37

#### **BMJ** Open

The current study has some limitations. We did not evaluate the actual adverse events resulting from DRPs or the actual role of interventions in decreasing these events. Furthermore, the exact real cost of adverse events resulting from DRPs could not be measured; however, the method of calculating cost avoidance in the current study has considered uncertainty and was implemented in previous studies.<sup>46</sup> In addition, the evaluation of the probability score of each DRP was conducted by an expert panel composed of five independent evaluators. Besides, the assessment of DRP probability scores was conducted independently by the study panel using a validated scale.<sup>20</sup> Another limitation is that we relied on admission charges, medication prices, and lab prices rather than actual costs. However, charges are widely used as a proxy for costs in the literature because of accessibility issues. Furthermore, we used an assumed RCC ratio to approach the actual costs, and this RCC was varied in the sensitivity analysis. 

#### Conclusions

Pharmacist-led medication reconciliation supplemented with contentious medication review is very cost beneficial in CKD admitted patients, with substantial cost avoidance compared to the cost of implementing this service. The results clearly showed that activating the role of clinical pharmacists in providing medication reconciliation with a comprehensive medication review contributed positively to the safety of admitted patients with CKD and had a remarkable economic impact in clinical settings. The net benefit of this intervention could be enhanced by designing an efficient collaborative approach with physicians in hospital settings, and future studies should be directed toward evaluating the cost-benefit of such approaches.

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

1 2		
2 3 4	428	Funding:
5 6	429	This work was supported by the Deanship of Scientific Research at the Jordan University of
7 8 9	430	Science and Technology [grant number: 20220257]. The funding agency was not involved in the
10 11	431	study design, conduct, writing, or decision to submit this article for publication.
12 13 14	432	Competing Interests:
15 16	433	The Authors declare that they have no conflicts of interest to disclose.
17 18 19	434	
20 21 22 23	435	Author contributions
24 25	436	SA contributed to conceptualization, methodology, data curation, formal analysis, supervision,
26 27	437	project administration, funding acquisition, and writing original draft. NS contributed to
28 29 30	438	conceptualization, methodology, data curation, formal analysis, and writing original draft. MA
31 32	439	and OA contributed to conceptualization, methodology, data curation, and writing- reviewing
33 34	440	and editing. MB contributed to data curation and writing-reviewing and editing. SA is the
35 36 37	441	guarantor for the manuscript and accepts full responsibility for the overall content.
38 39 40	442	
40 41 42 43	443	Data availability statement
44 45 46	444	All data underlying this article are presented in the manuscript.
47 48 49	445	
50 51 52	446	
53 54 55 56	447	
57 58		
59		19 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml
60		For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

#### **BMJ** Open

Small C, Kramer HJ, Griffin KA, et al. Non-dialysis dependent chronic kidney disease is associated

3	448	References
4	_	

1.

with high total and out-of-pocket healthcare expenditures. BMC Nephrol 2017; 18: 3. 2017/01/07. DOI: 10.1186/s12882-016-0432-2. Silva Junior GBD, Oliveira JGR, Oliveira MRB, et al. Global costs attributed to chronic kidney 2. disease: a systematic review. Rev Assoc Med Bras (1992) 2018; 64: 1108-1116. 2018/12/21. DOI: 10.1590/1806-9282.64.12.1108. Golestaneh L, Alvarez PJ, Reaven NL, et al. All-cause costs increase exponentially with increased 3. chronic kidney disease stage. Am J Manag Care 2017; 23: S163-S172. 2017/10/06. Saran R, Pearson A, Tilea A, et al. Burden and Cost of Caring for US Veterans With CKD: Initial 4. Findings From the VA Renal Information System (VA-REINS). Am J Kidney Dis 2021; 77: 397-405. 2020/09/06. DOI: 10.1053/j.ajkd.2020.07.013. Al-Shdaifat EA and Manaf MR. The economic burden of hemodialysis in Jordan. Indian J Med Sci 5. 2013; 67: 103-116. 2013/12/12. Aoun M, Helou E, Sleilaty G, et al. Cost of illness of chronic kidney disease in Lebanon: from the 6. societal and third-party payer perspectives. BMC Health Serv Res 2022; 22: 586. 2022/05/04. DOI: 10.1186/s12913-022-07936-0. Alshogran OY, Hajjar MH, Muflih SM, et al. The role of clinical pharmacist in enhancing 7. hemodialysis patients' adherence and clinical outcomes: a randomized-controlled study. Int J Clin Pharm 2022; 44: 1169-1178. 2022/07/14. DOI: 10.1007/s11096-022-01453-0. Rizk R, Hiligsmann M, Karavetian M, et al. A societal cost-of-illness study of hemodialysis in 8. Lebanon. J Med Econ 2016; 19: 1157-1166. 2016/06/29. DOI: 10.1080/13696998.2016.1207653. 9. Chia BY, Cheen MHH, Gwee XY, et al. Outcomes of pharmacist-provided medication review in collaborative care for adult Singaporeans receiving hemodialysis. Int J Clin Pharm 2017; 39: 1031-1038. 20170821. DOI: 10.1007/s11096-017-0528-1. Song YK, Jeong S, Han N, et al. Effectiveness of Clinical Pharmacist Service on Drug-Related 10. Problems and Patient Outcomes for Hospitalized Patients with Chronic Kidney Disease: A Randomized Controlled Trial. J Clin Med 2021; 10 20210420. DOI: 10.3390/jcm10081788. Laville SM, Gras-Champel V, Moragny J, et al. Adverse Drug Reactions in Patients with CKD. Clin J 11. Am Soc Nephrol 2020; 15: 1090-1102. 2020/07/03. DOI: 10.2215/CJN.01030120. Bishop MA, Cohen BA, Billings LK, et al. Reducing errors through discharge medication 12. reconciliation by pharmacy services. Am J Health Syst Pharm 2015; 72: S120-126. 2015/08/15. DOI: 10.2146/sp150021. Ernst FR and Grizzle AJ. Drug-related morbidity and mortality: updating the cost-of-illness model. 13. J Am Pharm Assoc (Wash) 2001; 41: 192-199. 2001/04/12. DOI: 10.1016/s1086-5802(16)31229-3. Alrugayb WS, Price MJ, Paudyal V, et al. Drug-Related Problems in Hospitalised Patients with 14. Chronic Kidney Disease: A Systematic Review. Drug Saf 2021; 44: 1041-1058. 2021/09/13. DOI: 10.1007/s40264-021-01099-3. Al Raiisi F, Stewart D, Fernandez-Llimos F, et al. Clinical pharmacy practice in the care of Chronic 15. Kidney Disease patients: a systematic review. Int J Clin Pharm 2019; 41: 630-666. 2019/04/10. DOI: 10.1007/s11096-019-00816-4. 16. Onatibia-Astibia A, Malet-Larrea A, Mendizabal A, et al. The medication discrepancy detection service: A cost-effective multidisciplinary clinical approach. Aten Primaria 2021; 53: 43-50. 2020/10/01. DOI: 10.1016/j.aprim.2020.04.008. World Health Organization, Medication safety in transitions of care: technical report, 2019. 17. For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml 

2 3 493 Houso A, Hamdan M and Falana H. Cost benefit analysis of clinical pharmacist interventions in 18. 4 494 medical intensive care unit in Palestine medical complex: Prospective interventional study. Saudi Pharm J 5 495 2022; 30: 1718-1724. 2023/01/06. DOI: 10.1016/j.jsps.2022.09.017. 6 496 19. Jordan Food and Drug Administration (JFDA) http://jfda.jo/Pages/viewpage.aspx?pageID=336 7 497 (accessed July 2023). 8 498 20. Nesbit TW, Shermock KM, Bobek MB, et al. Implementation and pharmacoeconomic analysis of a 9 10 499 clinical staff pharmacist practice model. Am J Health Syst Pharm 2001; 58: 784-790. DOI: 11 500 10.1093/ajhp/58.9.784. 12 501 21. Chen CC, Hsiao FY, Shen LJ, et al. The cost-saving effect and prevention of medication errors by 13 502 clinical pharmacist intervention in a nephrology unit. Medicine (Baltimore) 2017; 96: e7883. DOI: 14 503 10.1097/MD.00000000007883. 15 504 Pharmaceutical Care Network Europe, The PCNE CLassification V 9.1. Pharmaceutical Care 22. 16 505 Network Europe, p Classification for Drug related problems. 2020. 17 506 23. Almanasreh E, Moles R and Chen TF. The medication discrepancy taxonomy (MedTax): The 18 507 development and validation of a classification system for medication discrepancies identified through 19 20 508 medication reconciliation. Res Social Adm Pharm 2020; 16: 142-148. 20190414. DOI:

509 10.1016/j.sapharm.2019.04.005.
510 24. AbuRuz SM, Alrashdan Y, Jarab A, et al. Evaluation of the impact of pharmaceutical care service on hospitalized patients with chronic kidney disease in Jordan. Int J Clin Pharm 2013; 35: 780-789.

25 512 20130725. DOI: 10.1007/s11096-013-9806-8.

- 513 25. Quintana-Barcena P, Lord A, Lizotte A, et al. Prevalence and Management of Drug-Related
  514 Problems in Chronic Kidney Disease Patients by Severity Level: A Subanalysis of a Cluster Randomized
  515 Controlled Trial in Community Pharmacies. J Manag Care Spec Pharm 2018; 24: 173-181. DOI:
  516 10.18553/jmcp.2018.24.2.173.
- S17 26. Buckley MS, Harinstein LM, Clark KB, et al. Impact of a clinical pharmacy admission medication
   S18 reconciliation program on medication errors in "high-risk" patients. *The Annals of pharmacotherapy* 2013;
   S19 47: 1599-1610. 20131015. DOI: 10.1177/1060028013507428.
- Sing and Sing and
- S23 28. Cadman B, Wright D, Bale A, et al. Pharmacist provided medicines reconciliation within 24 hours
  S24 of admission and on discharge: a randomised controlled pilot study. *BMJ Open* 2017; 7: e013647.
  S25 20170316. DOI: 10.1136/bmjopen-2016-013647.
- S26
  S26
  S27
  S28
  S28
  S29. Neeman M, Dobrinas M, Maurer S, et al. Transition of care: A set of pharmaceutical interventions improves hospital discharge prescriptions from an internal medicine ward. *Eur J Intern Med* 2017; 38: 30-37. 20161125. DOI: 10.1016/j.ejim.2016.11.004.
- 529 30. Cornu P, Steurbaut S, Leysen T, et al. Effect of medication reconciliation at hospital admission on
   530 medication discrepancies during hospitalization and at discharge for geriatric patients. *The Annals of* 531 *pharmacotherapy* 2012; 46: 484-494. 20120313. DOI: 10.1345/aph.1Q594.
- 4753231.Sebaaly J, Parsons LB, Pilch NA, et al. Clinical and Financial Impact of Pharmacist Involvement in48533Discharge Medication Reconciliation at an Academic Medical Center: A Prospective Pilot Study. Hospital49534pharmacy 2015; 50: 505-513. DOI: 10.1310/hpj5006-505.
- 50 535 32. Vira T, Colquhoun M and Etchells E. Reconcilable differences: correcting medication errors at 51 536 hospital admission and discharge. Qual Saf Health Care 2006; 15: 122-126. DOI: 52 537 10.1136/qshc.2005.015347. 53
- 54 538 33. Al-Jazairi AS, Al-Suhaibani LK, Al-Mehizia RA, et al. Impact of a medication reconciliation program 55 539 on cardiac surgery patients. *Asian Cardiovasc Thorac Ann* 2017; 25: 579-585. 20171012. DOI: 56 540 10.1177/0218492317738382.
- 58 59 60

57

2		
3	541	34. Fernandes BD, Almeida P, Foppa AA, et al. Pharmacist-led medication reconciliation at patient
4	542	discharge: A scoping review. Res Social Adm Pharm 2020; 16: 605-613. 20190801. DOI:
5 6	543	10.1016/j.sapharm.2019.08.001.
7	544	35. Centers for Disease Control and Prevention. Chronic Kidney Disease
8 9	545	in the United States, 2023. Atlanta, GA: US Department of Health and Human
10	546	Services, Centers for Disease Control and Prevention; 2023. Available at:
11 12	547	https://www.cdc.gov/kidneydisease/publications-resources/ckd-national-facts.html.
12	548	36. prevention Cfdca. Chronic Kidney Disease in the United States, 2021. 2021.
14	549	37. Nguyen-Thi HY, Le-Phuoc TN, Tri Phat N, et al. The Economic Burden of Chronic Kidney Disease in
15	550	Vietnam. Health Serv Insights 2021; 14: 11786329211036011. 20210728. DOI:
16	551	10.1177/11786329211036011.
17 18	552 553	38. Slawomirski L, Auraaen A and Klazinga NS. The economics of patient safety: strengthening a value-
19	555 554	based approach to reducing patient harm at national level. 2017. 39. Daifi C, Feldpausch B, Roa PA, et al. Implementation of a Clinical Pharmacist in a Hemodialysis
20	555	Facility: A Quality Improvement Report. <i>Kidney Med</i> 2021; 3: 241-247 e241. 20210210. DOI:
21	556	10.1016/j.xkme.2020.11.015.
22	557	40. Hassan Y, Al-Ramahi RJ, Aziz NA, et al. Impact of a renal drug dosing service on dose adjustment
23 24	558	in hospitalized patients with chronic kidney disease. <i>The Annals of pharmacotherapy</i> 2009; 43: 1598-1605.
24 25	559	20090923. DOI: 10.1345/aph.1M187.
26	560	41. Manley HJ and Carroll CA. The clinical and economic impact of pharmaceutical care in end-stage
27	561	renal disease patients. Semin Dial 2002; 15: 45-49. DOI: 10.1046/j.1525-139x.2002.00014.x.
28	562	42. Anderegg SV, Wilkinson ST, Couldry RJ, et al. Effects of a hospitalwide pharmacy practice model
29	563	change on readmission and return to emergency department rates. Am J Health Syst Pharm 2014; 71:
30 31	564	1469-1479. DOI: 10.2146/ajhp130686.
32	565	43. Jiang SP, Zhu ZY, Ma KF, et al. Impact of pharmacist antimicrobial dosing adjustments in septic
33	566	patients on continuous renal replacement therapy in an intensive care unit. Scand J Infect Dis 2013; 45:
34	567	891-899. 20130912. DOI: 10.3109/00365548.2013.827338.
35	568	44. Al-Qudah RA, Al-Badriyeh D, Al-Ali FM, et al. Cost-benefit analysis of clinical pharmacist
36	569	intervention in preventing adverse drug events in the general chronic diseases outpatients. J Eval Clin
37 38	570	Pract 2020; 26: 115-124. 20190624. DOI: 10.1111/jep.13209.
39	571	45. Aljbouri TM, Alkhawaldeh MS, Abu-Rumman AE, et al. Impact of clinical pharmacist on cost of
40	572 573	drug therapy in the ICU. <i>Saudi Pharm J</i> 2013; 21: 371-374. DOI: 10.1016/j.jsps.2012.12.004. 46. Abushanab D, Gulied A, Hamad A, et al. Cost savings and cost avoidance with the inpatient clinical
41	575 574	pharmacist interventions in a tertiary cancer care hospital. J Oncol Pharm Pract 2023:
42	575	10781552231160275. 20230322. DOI: 10.1177/10781552231160275.
43 44	575	10/013522511002/5. 20250522. DOI: 10.11/7/10/015522511002/5.
44 45	576	
46		
47	577	
48	F 7 0	
49 50	578	
50 51	579	
52		
53	580	
54	581	
55	201	
56 57		
57 58		
59		22
60		22 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

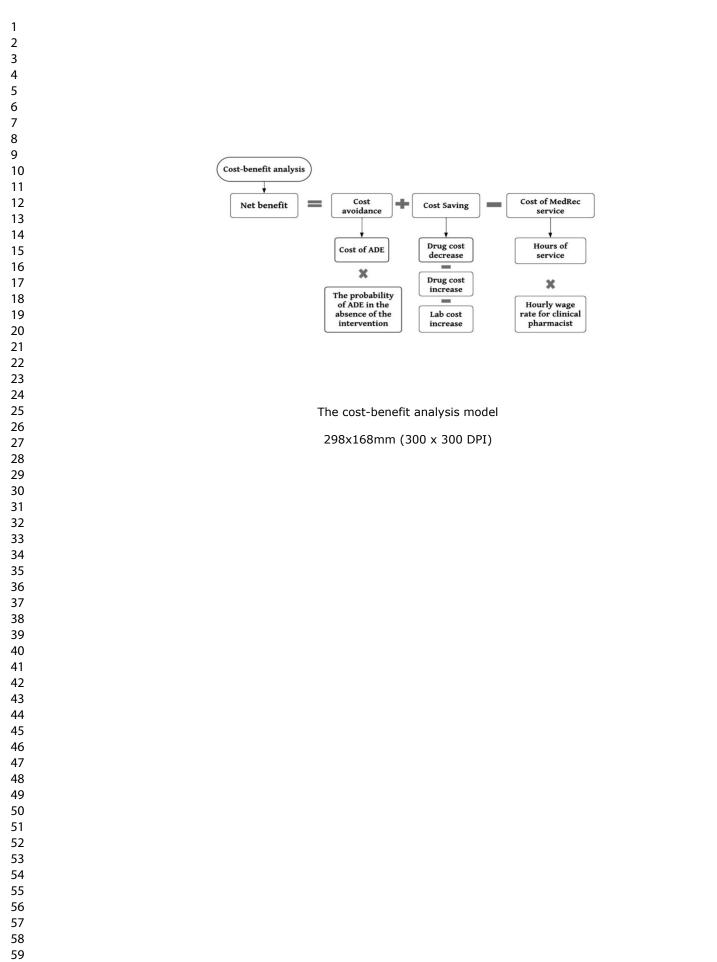
1 2		
3	582	
4 5	583	
6 7	584	
8 9	585	Figure Legends:
10 11	586	
12 13	587	
14		<b>Figure 1.</b> The cost honofit analysis model
15 16	588	Figure 1: The cost-benefit analysis model.
17 18 19	589	<b>Figure 2:</b> Tornado diagram illustrating the impact of various parameters on the net benefit of
19 20 21	590	supplemented medication reconciliation service (one-way sensitivity analysis).
22 23 24	591	Figure Legends:       Figure 1: The cost-benefit analysis model.         Figure 2: Tornado diagram illustrating the impact of various parameters on the net benefit of supplemented medication reconciliation service (one-way sensitivity analysis).         Figure 3: Probabilistic sensitivity analysis evaluating the net benefit of supplemented medication reconciliation service.
25 26	592	reconciliation service.
27 28 29	593	greenent S ated to te
30 31	594	to text and data mining.
32 33 34	595	
35 36	596	ning.
37 38 39	597	Al training, and similar technologies
40 41	598	I training, and s
42 43 44	599	
45 46	600	
47 48	601	
49 50 51	602	
52 53	603	
54 55 56	604	Training, and similar rechnologies.
57 58		
59 60		23 For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

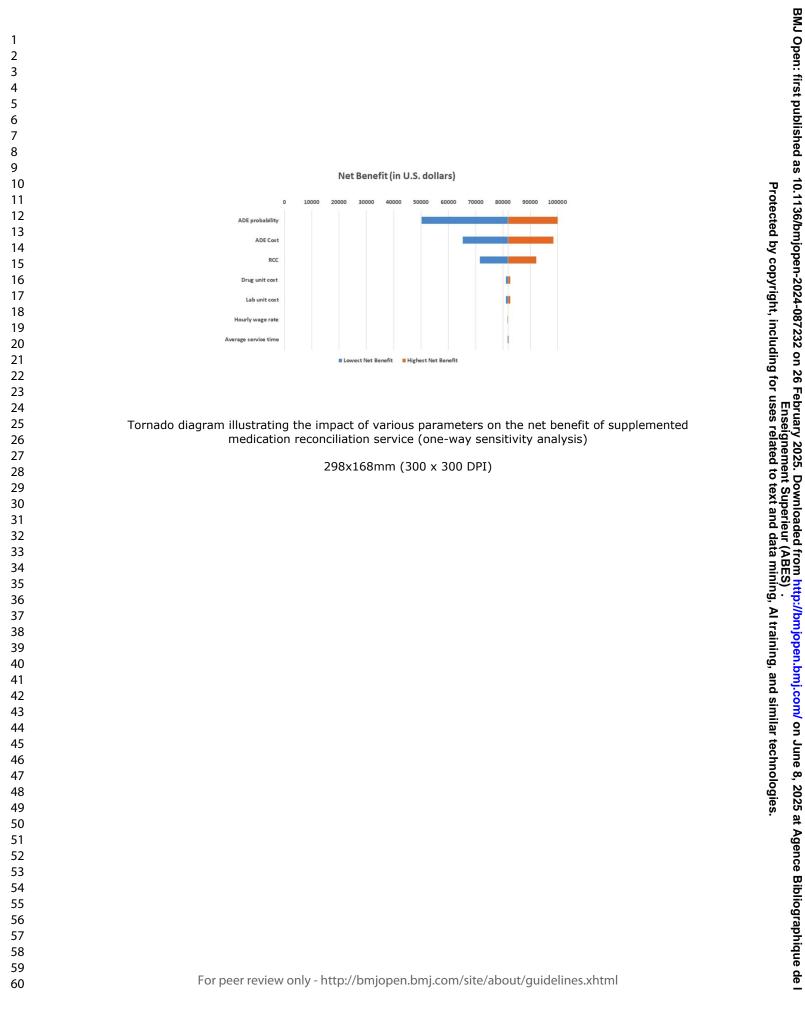
1 2 3 4 5	605 606	<b>Table 1:</b> Cost avoidance per cause-based domains in the PCNE classification of DRPs (V9.1).
6 7 8	607	
9 10	608	
$\begin{array}{c} 10\\ 11\\ 12\\ 13\\ 14\\ 15\\ 16\\ 17\\ 18\\ 9\\ 20\\ 22\\ 23\\ 24\\ 25\\ 26\\ 27\\ 28\\ 29\\ 30\\ 13\\ 23\\ 34\\ 35\\ 36\\ 37\\ 38\\ 9\\ 40\\ 14\\ 23\\ 44\\ 45\\ 46\\ 47\\ 48\\ 9\\ 50\\ 15\\ 23\\ 54\\ 55\\ 56\\ 57\\ \end{array}$	609	
58 59 60		$\begin{array}{c} 24 \\ \mbox{For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml} \end{array}$

1 2	
2	
4	
5	
6	
/ 8	
9	
10	
11	
12	
13 14	
15	
16	
17	
18 19	
19 20	
21	
22	
23	
24 25	
26	
27	
28	
29	
30 31	
32	
33	
34	
35 36	
30 37	
38	
39	
40	
41 42	
43	
44	
45	
46 47	
47 48	
49	
50	
51	
52 53	
55 54	
55	
56	
57 58	
58 59	
60	

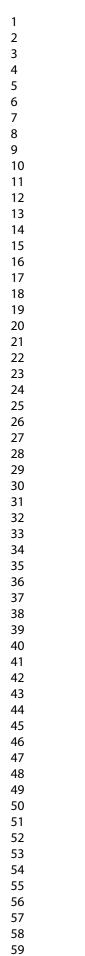
Primary domain	Cause	Cost	Total (\$
		avoidance (\$)	
Drug selection	Inappropriate drug according to guidelines/formulary	12,480	25,588
	No or incomplete drug treatment despite existing indication	8,646	
	No indication for drug	2,296	
	Inappropriate combination of drugs or drugs and dietary supplements	1,916	
	Too many different drugs/active ingredients prescribed for indication	250	
	Inappropriate duplication of therapeutic group or active ingredient	250	
Dose selection	Drug dose of a single active ingredient too high	13,710	21,141
	Dosage regimen too frequent	5,284	
	Drug dose too low	2,147	
Patient transfer	Drug omission	12,694	20,623
related	Discrepancy in the strength and/or	4,613	
(discrepancies)	frequency and/or number of units of dosage		
	form and/or total daily dose		
	Drug addition	2,399	
	Therapeutic class substitution	437	
	Drug duplication	337	
	Discrepancy in the dosage form/route of administration	144	
Drug use process	Inappropriate timing of administration or dosing intervals by a health professional	2,625	2,777
	Drug administered via wrong route by a health professional	152	
Treatment	Duration of treatment too long	273	469
duration	Duration of treatment too short	196	
Drug form	Inappropriate drug form/formulation	114	114
Other	Addition of a lab test	10,532	12,088
	No or inappropriate outcome monitoring	1,557	
Total			83,052

Outcome	Total (\$)	Average per pa (M± SD)
Intervention cost over 4 months	714	5± 1
Impact on the cost of DRPs		
	-83,052	-585± 30
Innest on medication costs		
Impact on medication costs		
Reduced drug costs	-11210	-79± 85
Increased drug costs	7479	53± 67
Increased lab costs	4198	30±29
Net benefit over the study period (4 months) <sup>a</sup>	81,871	577
Benefit to cost ratio <sup>b</sup>	115.7:1	
<ul> <li>a: The benefits of the intervention include (reduced drug costs – (increased drug cost the intervention – Intervention cost over 4 b: Benefit to cost ratio = The benefits of the</li> </ul>	ts + increased lab costs). months.	cost of DRPs) + cost Net benefit = The ben
a: The benefits of the intervention include (reduced drug costs – (increased drug cost the intervention – Intervention cost over 4	cost avoidance (reduced ts + increased lab costs). months.	cost of DRPs) + cost Net benefit = The ben tion cost over 4 month

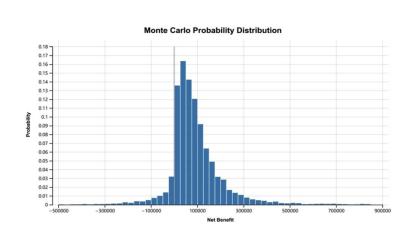




BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.



60



Probabilistic sensitivity analysis evaluating the net benefit of supplemented medication reconciliation service

298x168mm (300 x 300 DPI)

1 2	
3 4	Research Article
5 6	Title: Clinical pharmacist-led medication reconciliation supplemented with medication
7 8 9	review in chronic kidney disease admitted patients: a cost-benefit analysis
8 9 10 11 12 13 14 15 16 17 18 19 20 21 22 23 24 25 26 27 28 29 30 31 32 33 34 35 36 37 38 39 40 41 42 43 44 45 46 47 48	review in chronic kidney disease admitted patients: a cost-benefit analysis Journal: BMJ Open.
49 50 51 52 53	
54 55 56	
57 58 59	1
59 60	For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES) . Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies.

1 2
2
4
5
6
7
8
9 10
10
12
13
14
15
16
17 18
19
20
21
22
23
24 25
25 26
27
28
29
30
31 32
32 33
34
35
36
37
38 39
39 40
41
42
43
44
45 46
46 47
48
49
50
51
52 53
53 54
54 55
56
57
58
59
60

1

## Table S1: Patient demographics and clinical characteristics of the study sample.

X7 · 11	Study sample
Variable	N(%) N = 142
Gender n (%)	N = 142
Female	52 (27 22)
Male	53 (37.32)
Age, years $(M \pm SD)$	89 (62.68) 57.16 ±15.96
$\frac{\text{Age, years (M+SD)}}{\text{BMI n (\%)}}$	57.10 ±15.90
<18.5	6 (4.23)
18.5 -24.9	41 (28.87)
25-29.9	42 (29.58)
> 29.9	53 (37.32)
Marital status	55 (57.52)
Married	109 (76.76)
Not married	33 (23.24)
Smoking status	
Yes	43 (30.28)
No	75 (52.82)
Ex-smoker	24 (16.90)
Educational level	$\sim$
Not educated	20 (14.08)
School	93 (65.49)
University/higher education	29 (20.42)
Employment status	5
Employed	26 (18.31)
Retired	32 (22.54)
Unemployed	84 (59.15)
Occupation	
Medical	3 (2.11)
Non-medical	64 (45.07)
No	75 (52.82)
Monthly income (JOD)	
<500	110 (77.46)
500 -1000	29 (20.42)
>1000	3 (2.11)

For peer review only - http://bmjopen.bmj.com/site/about/guidelines.xhtml

AKI on Top of CKD related problems	42 (29.58)
CKD/dialysis related problems	71 (50.0)
Others	29 (20.42)
CKD stage	
Stage 2	2 (1.41)
Stage 3a	3 (2.11)
Stage 3b	12 (8.45)
Stage 4	32 (22.54)
Stage 5	93 (65.5)
Years of dialysis (M± SD)	$2.33 \pm 3.66$
Years of CKD (M± SD)	$5.02 \pm 6.80$
Number of comorbidities (M± SD)	$6.36 \pm 2.18$
$CCI (M \pm SD)$	$6.08 \pm 2.93$
Number of medications at admission (M± SD)	$9.58 \pm 3.07$
Number of medications at discharge (M± SD)	$9.24 \pm 4.34$
Death at discharge	5 (3.52)
Length of stay	$8.94 \pm 8.59$

Abbreviation: BMI: Body Mass Index, M± SD: Mean ± Standard deviation, JOD: Jordanian Dinar, CKD: Chronic Kidney Disease, AKI: Acute Kidney Disease, CCI: Charlson Comorbidity Index. SD).

One JOD is equivalent to 1.41 US Dollars (USD).

**Table S2:** Examples of the studied clinical cases with the probability score to cause ADEs.

A patient had a recent myocardial infarction (MI) and had previously	High
undergone stent placement for the main coronary artery. She was taking	(0.6)
febuxostat for gout. The clinical pharmacist recommended switching from	
febuxostat to allopurinol. (Black box warning)	
A female patient on hemodialysis, has a hemoglobin (Hb) level of 12 and a	High
history of stroke. She was on alpha epoetin 4000 units prescribed every	(0.6)
other day (EOD). (Black box warning)	
A 91-year-old female patient with CKD stage 5 (baseline serum creatinine	Medium
is 500 mmol/l). Dialysis was delayed due to her age. The patient is	(0.4)
experiencing uremia, including vomiting symptoms. She was prescribed	
metoclopramide 10 mg intravenously every 8 hours, which is a high dose	
considering her condition. Additionally, she is taking trimetazidine, which	
has a serious interaction with metoclopramide (category X). It is important	
to note that trimetazidine is contraindicated in patients with a GFR <30.	
A patient has osteoporosis and is undergoing hemodialysis. Initially, she	Medium
was prescribed alendronate, but the clinical pharmacist recommended	(0.4),
switching to denosumab. The physician stopped the alendronate as advised	Low
but could not provide denosumab due to economic issues. Subsequently,	(0.1)
the patient visited the outpatient clinic (OPC) due to bone pain, and there	
she received denosumab treatment.	
A patient has a CrCl (Creatinine Clearance) of 13, and he is currently taking	Medium
fenofibrate. Additionally, the triglyceride level is less than 250 mg/dL.	(0.4)
A patient underwent upper endoscopy, which revealed mild gastritis. There	Medium
were no available tests for H. pylori, and the patient's serum creatinine level	(0.4)
was 500 mmol/l (CrCl <15). Nevertheless, upon discharge, the patient was	
	I

prescribed amoxicillin 1g twice daily and clarithromycin 500mg twice	
daily without renal adjustment and without confirming the diagnosis.	
A patient has AKI on top of CKD and has been experiencing severe	Medium
vomiting for over a week. Upon admission, the patient's home medication	(0.4)
included metoclopramide 10 mg three times daily taken orally. However,	
after admission, the route was changed to intravenous 10 mg TID (not renal	
dose) without improvement, the dose was changed to metoclopramide	
intravenously at 20 mg three times daily, which is considered too high. The	
clinical pharmacist recommended discontinuing metoclopramide and	
administering ondansetron as an alternative.	
A patient is undergoing hemodialysis and was diagnosed with deep vein	Medium
thrombosis (DVT). Upon discharge, she was prescribed a therapeutic dose	(0.4)
of Enoxaparin. The clinical pharmacist recommended switching to	
apixaban.	
A patient was admitted for liver cirrhosis, baseline CrCl 32, AKI, diabetes	Medium
mellitus (DM), and recently diagnosed depression. He was initially	(0.4)
admitted while taking metformin 500mg once daily. However, upon	
discharge, his medication regimen included metformin 850mg three times	
daily, mirtazapine, spironolactone, and hydrochlorothiazide. The clinical	
pharmacist was unable to reach the responsible physician to discuss the	
changes. Consequently, the patient was readmitted after 5 days due to	
diarrhea and hyponatremia.	
A patient has a UTI and is currently taking ciprofloxacin, calcium	Low
carbonate, and ferrous gluconate twice daily, both at 6 pm and 6 am, all by	(0.1)
oral route.	
A patient admitted with severe hypophosphatemia; the physician initially	Low
recorded that the patient was on calcium carbonate 500mg BID. With	(0.1)
medication reconciliation we found that the actual home dose was calcium	
carbonate 1g TID, along with sevelamer TID, which was obtained from	
outside the hospital (and was not known by the physician). Resolving these	
discrepancies with the physician led to a change in the diagnosis.	

BMJ Open: first published as 10.1136/bmjopen-2024-087232 on 26 February 2025. Downloaded from http://bmjopen.bmj.com/ on June 8, 2025 at Agence Bibliographique de l Enseignement Superieur (ABES)

Protected by copyright, including for uses related to text and data mining, Al training, and similar technologies

A patient has been taking Combivent® every 8 hours for over than 2 weeks	Low
without any valid indication.	(0.1)
A 32-year-old patient has type 1 diabetes mellitus (DM1), end-stage renal	Low
disease (ESRD), partial retinopathy, and uncontrolled DM with recurrent	(0.1)
hypoglycemia. Upon admission, she was using pre-mixed insulin. The	
clinical pharmacist suggested switching to a basal-bolus insulin regimen.	
A patient was discharged without some of his hypoglycemic and	Low
antihypertensive agents unintentionally.	(0.1)
A patient on HD, was on famotidine 40mg once daily at home. Was not	Very
documented.	low
	(0.01)

# **Table S3:** Average cost avoidance per patient across cause-based domains in the PCNE classification of DRPs (Version 9.1).

Primary domain	Cause	Cost avoidance (\$) Average per patient	Num of patie
	Inappropriate drug according to guidelines/formulary	195.0	64
	No or incomplete drug treatment despite existing indication	139.5	62
	No indication for drug	71.7	32
Drug selection	Inappropriate combination of drugs or drugs and dietary supplements	174.2	11
	Too many different drugs/active ingredients prescribed for indication	83.5	3
	Inappropriate duplication of therapeutic group or active ingredient	83.5	3
Dose selection	Drug dose of a single active ingredient too high	207.7	66
	Dosage regimen too frequent	83.9	63
	Drug dose too low	89.4	24
Patient transfer related (discrepancies)	Drug omission	133.6	95
	Discrepancy in the strength and/or frequency and/or number of units of dosage form and/or total daily dose	118.3	39
	Drug addition	150.0	16
	Therapeutic class substitution	24.3	18

2 3 4 5 6	
7 8 9 10 11	
12 13 14 15 16	
17 18 19 20 21	
22 23 24 25 26	
20 27 28 29 30 31	
32 33 34 35 36	
37 38 39 40 41	
42 43 44 45	
46 47 48 49 50	
51 52 53 54 55	
56 57 58 59 60	

	Drug duplication	84.4	4
	Discrepancy in the dosage form/route of administration	71.9	2
Drug use process	Inappropriate timing of administration or dosing intervals by a health professional	77.2	34
	Drug administered via wrong route by a health professional	152.4	1
Treatment duration	Duration of treatment too long	91.1	3
	Duration of treatment too short	65.3	3
Drug form	Inappropriate drug form/formulation	38.1	3
	Addition of a lab test	118.3	89
Others	No or inappropriate outcome monitoring	91.6	17