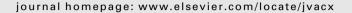


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## Vaccine: X





## Pharmacists-physicians collaborative intervention to reduce vaccine hesitancy and resistance: A randomized controlled trial



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#### ABSTRACT

*Purpose:* Given their negative influence on community health, vaccine hesitancy and resistance are emerging challenges that require healthcare intervention. Therefore, this study aimed to assess the impact of physician-pharmacist collaborative health coaching on rates of hesitancy and resistance for a COVID-19 vaccine

Methods: After an initial assessment of rates of hesitancy and resistance for a COVID-19 vaccine was conducted, hesitant and resistant participants were approached, recruited, and randomized into an active and control group. Pharmacists-physicians collaborative coaching intervention was delivered to active group subjects over two months through Facebook live sessions. The outcome measures were assessed in both groups before coaching, directly after coaching, and a month after coaching.

Results: The proportions of hesitancy and resistance for a COVID-19 vaccine among subjects in the active group were significantly reduced from 64.3% and 35.7% before coaching to 20.1% and 7.8% directly after coaching, respectively. These proportions were further reduced to 11.1% and 3.3% a month after coaching, respectively. Furthermore, the mean scores for knowledge on, and attitude towards COVID-19 vaccine were significantly increased from  $4.6 \pm 1.8$  and  $4.1 \pm 1.7$  before coaching to  $7.5 \pm 3.1$  and  $8.9 \pm 3.8$  directly after coaching, respectively. However, the change in mean score of beliefs about COVID-19 vaccines among active group subjects was not significant.

Conclusion: High rates of hesitancy and resistance for a COVID-19 vaccine were found in Jordan. These rates can be significantly reduced through online pharmacists-physicians collaborative coaching, which can also improve knowledge of and attitude towards COVID-19 vaccines.

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## Introduction

Coronavirus disease 2019 (COVID-19), caused by severe acute respiratory syndrome coronavirus 2 (SARS-CoV-2), has cost the world enormous losses in lives and caused a global economic crisis. Because there were no effective pharmacological treatments or

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*Abbreviations:* COVID-19, coronavirus disease 2019; SARS-Cov-2, Severe acute respiratory syndrome coronavirus 2;  $\chi^2$ , chi-square.

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vaccines to prevent the infection and flatten the curve of cases, governments had enforced extreme precautionary measures including but not limited to mandatory face masks, social distancing, and virtual schooling.

The first hope for humans appeared on March 3d, 2020 when a COVID-19 vaccine was tested on human subjects for the first time. As of June 2021, 18 vaccines were approved by at least one country and approximately a quarter of the world's population received at least one dose of a COVID-19 vaccine [1]. However, vaccination hesitancy has been a major worry to key stakeholders and is seen by WHO as one of the most critical health warnings today [2,3]. Vaccine hesitancy is the withholding, delaying, or agreeing with uncertainty about vaccine usefulness and safety, and is usually impelled by anxiety about side effects [3]. In addition to the obstacles of routine vaccination, misleading information raised through social media platforms regarding the benefits and adverse effects of vaccination has limited patient acceptance [4]. Thus, effectively relieving vaccine concerns and encouraging vaccine confidence through evidence-based health communication methods are required [5]. In a previous study that included 7664 participants from different European countries, roughly a quarter of the participants were either "unsure" or "totally against" COVID-19 vaccines [6]. Several reports indicated that the hesitancy rate in the UK ranges from 11.7% to 31% [7,8]. Similar findings were found in the US [9] and France [10]. In developing countries where public beliefs about COVID-19 conspiracies are outspread, a higher hesitancy rate for COVID-19 vaccine was reported [11]. In addition to socio-demographic factors, the mistrust in sources of information about COVID-19 and misconception about vaccination were significant predictors for COVID-19 vaccine hesitancy [8,11,12]. Nonetheless, some of these studies had small sample size or adopted non-representative sampling technique.

Given that misinformation about COVID-19 is highly prevalent and the lack of trust in governmental decisions in many places worldwide [13,14], correcting the public misconceptions about COVID-19 vaccine through traditional awareness- raising campaigns is not feasible and the aims of the campaigns may not be fulfilled. Given that health coaching substantially altered public health behaviors and led to improved clinical outcomes [15,16], it could be an alternative strategy to reduce hesitancy for COVID-19 vaccines. Nevertheless, face-to-face coaching is a time and money-consuming intervention and may increase the COVID-19 transmission. Additionally, it may suffer from poor public involvement. A health coach provides patients with updated information, continuous advice, and assistance while preserving patientcentred care [17]. Thus, patients will be able to adopt behavioural changes for better self-care and manage both acute or chronic ailments and their complications, to reach full control of their health [18]. As a result, patients will develop a broader vision to deal with emotions and hesitancy, plan for change, take actions to commit a sustainable healthy lifestyle, minimizing health risks, and reducing medical bills [17,18].

Therefore, we developed a health coaching model led by pharmacists and physicians, and delivered by social media applications, the same tools used by those spreading false news about vaccines. Physician-pharmacist collaboration was the main theme of this intervention for several reasons. First, because both pharmacists and physicians are frontline healthcare workers and their efforts saved millions of lives, they have gained the public trust [19]. Second, physicians can utilize their rich experiences to educate the public about the seriousness of COVID-19 complications and long-term effects. Third, pharmacists can utilize their substantial knowledge on vaccines and their communication skills to improve vaccine confidence and reduce hesitancy [20]. Fourth, in several reports, physicians supported collaborative agreement with pharmacists [21–23]. To investigate the vaccine hesitancy in Jordan

and test the effectiveness of physician-pharmacist collaborative intervention in improving hesitancy for a COVID-19 vaccine, we developed three study objectives.

First, we aimed to document the prevalence of vaccine acceptance, hesitancy, and resistance among the general population of lordan.

Second, we aimed to measure the impact of physicianpharmacist collaborative health coaching on adult populations who were reluctant or resistant to COVID-19 vaccine.

Third, we aimed to test the feasibility of using a Facebook private group as a vehicle to deliver the online intervention.

#### Method

Summary of study design, sample size calculation, and eligibility criteria

On January 6th, 2021, we started an initial screening for the adult population in Jordan using stratified random sampling to determine the rates of hesitancy and resistance of a COVID-19 vaccine. Then, we recruited 320 Individuals who were reluctant about or resistant to a COVID-19 vaccine, randomly, and equally divided them into intervention and control groups (Fig. 1). The intervention group participants were added into a private Facebook group. in which they were coached through 16 live coaching sessions delivered on Friday and Tuesday of every week for two months by three physicians and two pharmacists. Participants assigned to the intervention and control groups were surveyed at three points; before coaching (February 2, 2021), directly after coaching (April 6, 2021), and a month after coaching (May 7, 2021). The Ethics committees of the University of Petra and the Jordanian Ministry of Health (MOH/REC/202189) checked and approved the ethical aspects of the study. In order to determine the sample size, it was assumed that pharmacists-physicians collaborative intervention will improve hesitancy for COVID-19 vaccine by 19% [17]. Furthermore, based on the equations used by the G\* Power software [24], and considering the power = 0.8, alpha  $\leq$  0.05, and the effect size = 0.8, the number of participants needed to be included from each group was 160. To ensure proper trial standards for the methodology, we considered the Consolidated Standards of Reporting Trials (Appendix 1) as a reference.

Initial assessment and participants' recruitment and randomization

The inclusion criteria for participants were as follows: being adult, resident in Jordan, and hesitant (being unsure about taking a COVID-19 vaccine) or resistant (complete refusal of a COVID-19 vaccine) for COVID-19 vaccine. The exclusion criteria were: not having a Facebook account, willing to take the vaccine, have taken at least one dose of a COVID-19 vaccine, or were currently or already recovered from COVID-19. To recruit 320 participants matching the above criteria and to determine the rates of hesitancy and resistance for COVID-19 vaccines in Jordan, we used stratified random sampling and screened 1866 individuals through random face-to-face interviews in the streets, pharmacies, restaurants, cafes, hotels, markets, and salons. First, we divided the study population into four groups based on geographic location: Central, Northern, Capital, and Southern districts. Second, the number screened people in each district was proportional to the district's proportion when compared to the total population. In the initial assessment, we only asked participants about their position from the vaccine; accepting the vaccine, hesitant, or resistant. Those hesitant or resistant were approached and screened for other eligibility criteria. A verbal consent was taken from each participant who was willing to join the trial and met the inclusion criteria.

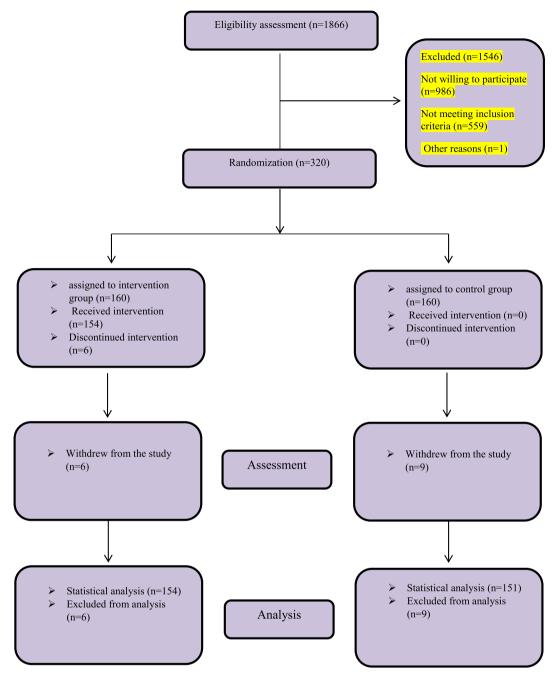


Fig. 1. The assessment, allocation, assessment, and analysis steps of the study.

The names of all participants were coded into an Excel sheet and then entered to SPSS, whereby we used random number creator to randomize participants into the active and control groups. Participants were informed about our confidentially and privacy policy. Additionally, they were informed about their rights to withdraw from the trial anytime without providing justifications.

Pharmacists and physicians' recruitment and training

Exactly, 16 coaching sessions were carried out, of which 8 were delivered by 7 physicians and 8 by 8 pharmacists. To select 7 physicians who were infectious disease specialists or respiratory medicine specialists and have been directly engaged in management of COVID-19 patients or the Jordanian vaccination programme, we delivered a short online questionnaire to 105

physicians working in public and private hospitals across Jordan. Physicians who were appointed after the outbreak of COVID-19 were excluded. Physicians who met the study criteria were asked to sign a consent form and join the training period. To select 8 pharmacists having at least 5 years of experience as a licensed pharmacist and working in major pharmacies of the four major cities in Jordan; Amman, Irbid, Al Zarqa, and Al Karak, we surveyed 84 pharmacists. Those who were already involved in an ongoing trial, busy, or not willing to participate were excluded.

The main author of this study (a senior clinical coach, invited by many hospitals to coach healthcare professionals during the COVID-19 outbreak) conducted an intensive training through five online meetings for physicians and pharmacists. The training focused on coaching tools and behavior change mechanisms that utilize three key elements; capability, opportunity, and motivation

(COM-model). Additionally, the self-determination and concordance theories were considered during the training [25–27].

## Pharmacists-physicians collaborative intervention

Participants allocated to the active group were added to a Facebook group, in which 16 live sessions were scheduled. The first 8 sessions were delivered by physicians who delivered their own experience with COVID-19 severity and complications. Physicians focused on how COVID-19 can infect any age group and how precautionary measures would protect the most vulnerable groups, such as elderly, immunocompromised patients, pregnant women, and those with chronic conditions. Whereas the coaching discussions of pharmacists focused on presenting facts about vaccination importance, efficacy, and safety. More details about the COVID-19 vaccines currently approved in Jordan (Pfizer, AstraZeneca, and Sinopharm) were given to participants. In addition to listening to participants' stories and suffering, physicians and pharmacists offered spiritual support and psychological counselling for those who suffered from losing a job or a loved one.

## Assessment of the study outcomes

After randomization and before coaching, the research team reached participants from both group via phone calls and asked them to answer a series of close-ended questions. The questions were divided into three parts; 1) questions to assess baseline characteristics of the study participants included their age, gender, educational level, annual income, smoking habits, religiosity, current medical conditions, concurrent medications, and past medical history, 2) a question to ensure their position from vaccination (vaccine hesitant, resistant, or accepting), and 3) questions to assess their knowledge, attitude, and beliefs about vaccines using a pre-validated scale [28]. Directly after coaching, we approached participants via phone calls and asked them questions of part 2 and 3. A month after coaching, in addition to part 2 and 3 questions, we asked participants if they got COVID-19 infection.

## Statistical analysis of data

All responses were gathered into one Excel sheet, double checked, and then entered into SPSS version 26 for statistical analysis. To test differences in the proportions of vaccine hesitant, resistant, and accepting participants between the study groups,  $\chi^2$  test was used. For within group comparison and between two groups comparison, Mann-Whitney U was used. Categorical variables are presented as count (n) with proportions (%), whereas, continuous variables are presented as mean  $\pm$  standard deviation.

## Results

## Findings of initial assessment

Of the 1866 adults screened in the initial assessment, 48.9% were hesitant and 24.6% were resistant for a COVID-19 vaccine. The highest rates of vaccine hesitancy and resistance were found in the Central and Northern districts with 53.9% and 33.1%, respectively (Fig. 2).

## Trial participants

Of the 320 subjects who agreed to participate in the trial, 6 withdrew from the active group without completing the coaching online sessions due to COVID-19 infection and 9 withdrew from the control group due to busyness and COVID-19 infection. Addi-

tionally, we were not able to follow up after a month of the coaching with 4 participants (1 from the active and 3 from control groups). Of the 305 subjects who completed the trial (154 in the active and 151 in the control groups), 56.1% were females, of which 10.5% were pregnant. Although 74.1% of the subjects had strong religious beliefs, 37.7% were smokers. Regarding the average social media usage, 71.5% of the subjects reported high usage (Table 1). There were no variations in the baseline characteristics across the study groups.

The impact of Physicians-Pharmacists collaborative coaching on hesitancy and resistance for a COVID-19 vaccine.

Within the active group, the proportions of hesitancy and resistance for a COVID-19 vaccine were significantly reduced from 64.3% and 35.7% before coaching to 20.1% and 7.8% directly after coaching, respectively. These proportions were further reduced to 11.1% and 3.3% a month after coaching, respectively (Table 2). Furthermore, the proportion of subjects vaccinated against COVID-19 was considerably increased from 0.0% before coaching to 51.6% a month after coaching. Before coaching, the active and control groups had similar rates for hesitancy and resistance. However, directly after coaching and a month after coaching, there were clear differences in rates of hesitancy and resistance for a COVID-19 vaccine across the study groups. In contrast to the active group, the proportions of hesitancy, resistance, and vaccination within the control group were similar throughout the study stages.

The impact on knowledge of, attitude towards, and beliefs about COVID-19 vaccine.

Within the active group, the mean scores for knowledge on, and attitude towards COVID-19 vaccine were significantly increased from 4.6  $\pm$  1.8 and 4.1  $\pm$  1.7 before coaching to 7.5  $\pm$  3.1 and 8.9  $\pm$  3.8directly after coaching, respectively. Nonetheless, these scores were dropped to 5.33  $\pm$  2.67 and 7.8  $\pm$  4.5 a month after coaching, respectively. Additionally, the change in mean score of beliefs about COVID-19 vaccines was not significant (Table 3). There was no significant difference in knowledge of COVID-19 vaccine between the active and control groups a month after coaching.

Analysis of change in sources of information about COVID-19 vaccines within the active group

The proportion of subjects who considered social media websites a trusted source of information about COVID-19 vaccines was decreased from 49.4% before coaching to 20.1% directly after coaching to 18.9% a month after coaching (Fig. 3). On the other hand, the trust in healthcare professionals, doctors, and government agencies was variously increased.

## Discussion

## Discussion and implications

Before we started the trial, an initial assessment to the public was conducted and showed higher rates of hesitancy (48.9%) and resistance (24.6%) for a COVID-19 vaccine in Jordan than that reported in the United Kingdom (25% hesitancy and 9% resistance) and the United States (33% of the population hesitant or resistant) [8,29]. These variations could be attributed to the cultural, social, and economic differences across nations. Additionally, lack of knowledge about safety, efficacy, and adverse effects of vaccines might have led to these outcomes. In this regard, a very recent

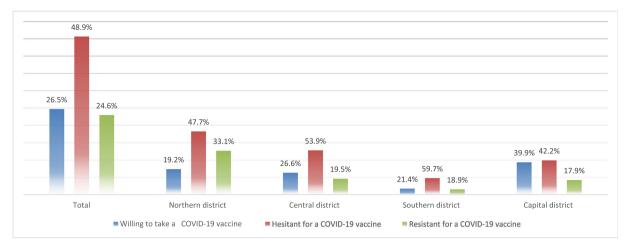


Fig. 2. Findings of initial screening.

**Table 1**Baseline characteristics of the study groups\*.

Items	Total $(n = 305)$	Active group $(n = 154)$	Control arm $(n = 151)$	P values	
Age (years)				0.513	
18-24	56 (21.31)	27 (17.53)	29 (19.20)		
25-34	98 (32.13)	41 (26.62)	57 (37.74)		
35-44	72 (23.60)	39 (25.32)	33 (21.85)		
45-54	61 (20.00)	36 (23.37)	25 (16.55)		
55-64	18 (5.90)	11 (7.14)	7 (4.63)		
Gender, female	171 (56.06)	87 (56.49)	84 (55.62)	0.318	
Pregnant, yes	18 (10.52)	10 (11.49)	8 (9.52)	0.156	
Marital status, married	142 (46.55)	73 (47.40)	69 (45.69)	0.113	
Resident in rural areas	96 (31.47)	45 (29.22)	51 (33.77)	0.192	
Birthplace, outside Jordan	32 (10.49)	16 (10.38)	16 (10.59)	0.236	
Employment status, Unemployed	138 (45.24)	71 (46.10)	67 (44.37)	0.552	
Education, college degree	114 (37.37)	54 (35.06)	60 (39.73)	0.098	
Income (annually)				0.211	
<6,000\$	155 (50.81)	79 (51.29)	76 (50.33)		
6,000-12,000\$	97 (31.80)	47 (30.51)	50 (33.11)		
>12,000\$	53 (17.37)	26 (16.88)	27 (17.88)		
Smoker, yes	115 (37.70)	57 (37.01)	58 (38.41)	0.255	
Underlying health condition, yes	74 (24.26)	38 (24.67)	36 (23.84)	0.144	
Religiosity, yes	226 (74.09)	108 (70.12)	118 (78.14)	0.092	
Mental health history, yes	33 (21.42)	19 (12.33)	14 (9.27)	0.102	
Usage of social media, high	218 (71.47)	110 (71.42)	108 (71.52)	0.582	

Parameters are described as n (%), \$: American dollar, \*: differences in baseline parameters are not significant between the study groups.

 Table 2

 Comparison of changes in proportions of "vaccine hesitant", "vaccine resistant", "willing to take the vaccine", and "vaccinated" across the active and control groups over three time points.

Parameters	Active group			¥P value	Control group				
	Before coaching (n = 160)	Directly after coaching (n = 154)	A month after coaching (n = 153)	*P value	Before coaching (n = 160)	Directly after coaching (n = 151)	A month after coaching (149)	*P value	¥p value
Vaccine hesitant	99 (64.29)	31 (20.12)	17 (11.11)	0.003	97 (60.62)	92 (60.92)	87 (58.38)	0.39	.587 <sup>a</sup> .001 <sup>b</sup> .008 <sup>c</sup>
Vaccine resistant	55 (35.71)	12 (7.79)	5 (3.26)	0.008	63 (39.37)	46 (30.46)	44 (29.53)	0.28	.347 <sup>a</sup> .001 <sup>b</sup> .032 <sup>c</sup>
Willing to take the vaccine	0 (0)	98 (63.63)	52 (33.98)	0.001	0 (0)	8 (5.29)	10 (6.71)	0.11	.427 <sup>a</sup> .006 <sup>b</sup> .003 <sup>c</sup>
Vaccinated	0 (0)	13 (8.44)	79 (51.63)	0.002	0 (0)	5 (3.31)	8 (5.36)	0.14	.317 <sup>a</sup> .03 <sup>b</sup>

Parameters are described as n (%), \*P value is calculated for within group comparison at three points (before coaching, directly after coaching, and a month after coaching). \*P value is calculated for between groups comparison (a: before coaching, directly after coaching, ca month after coaching).

**Table 3**The change in knowledge of, attitude towards, and beliefs about COVID-19 vaccines across the study groups.

Parameters	Active group			Control group					
	Before coaching (n = 160)	Directly after coaching (n = 154)	A month after coaching (n = 153)	*P value	Before coaching (n = 160)	Directly after coaching (n = 151)	A month after coaching (149)	*P value	¥P value
Knowledge	4.68 ± 1.88	7.53 ± 3.14	5.33 ± 2.67	0.003	4.169 ± 1.53	4.48 ± 2.34	4.92 ± 1.87	0.190	.324 <sup>a</sup> .03 <sup>b</sup> .08 <sup>c</sup>
Attitude	4.18 ± 1.77	8.96 ± 3.81	7.84 ± 4.54	0.008	4.58 ± 1.57	4.82 ± 2.31	5.1 ± 2.94	0.187	.174 <sup>a</sup> .002 <sup>b</sup> .006 <sup>c</sup>
Beliefs	5.36 ± 2.80	7.69 ± 3.14	6.93 ± 3.14	0.098	4.98 ± 3.10	5.13 ± 3.34	5.21 ± 3.72	0.133	.317 <sup>a</sup> .009 <sup>b</sup> .04 <sup>c</sup>

Parameters are described as mean ± standard deviation, \*P value is calculated for within group comparison at three points (before coaching, directly after coaching, and a month after coaching). YP value is calculated for between groups comparison (a: before coaching, directly after coaching).

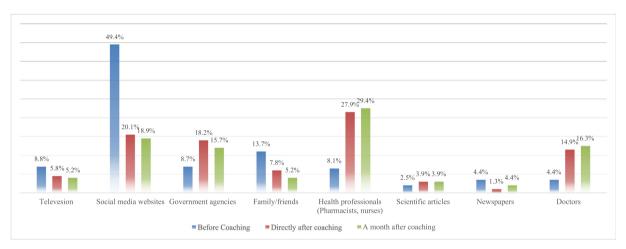


Fig. 3. Findings presented show the change in sources of information about COVID-19 vaccine across participants in the active group.

survey-based study demonstrated a potential role for social media in reducing vaccine hesitancy [30].

Therefore, we created a new model comprising physicians and pharmacists to coach those hesitant for or resistant to vaccination using Facebook live sessions. This study may provide health authorities with a promising approach that can be further developed, optimized, and then generalized to ensure proper vaccination for the public.

The findings of this study showed that vaccine hesitancy and resistance were significantly minimized. Additionally, compared with the control group subjects, of which about 5% were vaccinated against COVID-19 a month after coaching, more than half of active group subjects were immunized after the same period. These findings could be explained by several ways. First, the coaching delivered was not only about negative clinical outcomes of COVID-19 or health outcomes of vaccination, but also more importantly bringing their attention to the fact the vaccination is the shortest road to economic recovery [31]. Second, using Facebook as a bridge between coaches and learners eased communication and enabled learners to review the coaching material offline, which cannot be applicable in face-to-face coaching. Third, physicians-pharmacists collaborative coaching practice might have been seen as a positive motivation for learners, who consider these two health professionals trusted and cannot provide misleading information [22,32]. Our findings were in line with a previous study found that pharmacists have a key role in combating misinformation [33].

The findings of this study demonstrated a significant impact for physicians-pharmacists collaborative coaching on knowledge of and attitude towards COVID-19 vaccine. This may impact not only

the study participants, but also their loved ones such as parents, children, and friends. As evidence-based knowledge is a key driving factor to change behavior and beliefs, our approach did not significantly improve the beliefs about COVID-19 vaccine. This aligns with a previous study that found knowledge itself is not adequate to drive behaviors [34]. It is possible that subject's exposure to coaching was significantly less than that of misinformation spread in the social media. Thus, more improvements on the coaching model could help in changing beliefs of the subjects. Additionally, because most of the subjects in our study had strong religious beliefs, we believe that adding religious texts that encourage people to save their lives from dangers such as natural disasters could change subjects' beliefs about vaccination.

In this study, we found a drop in the proportion of the active group subjects who considered social media websites as their main source of information about COVID-19 vaccines. Because previous studies linked between social media websites and vaccine hesitancy and resistance [35,36], our coaching method focused on taking information about vaccines only from health professionals and relevant government agencies. Additionally, coaches explained how some people misuse social media websites to post misleading information about vaccines to earn a side income.

## Study limitations

As all studies, this has several limitations. First, although we tried to minimize biased findings, the vaccine decision is a multifactorial and it was not feasible to control all confounding factors. For example, the study did not address the impact of governmental

policies and regulations on vaccine acceptance. Second, we only assessed the outcomes directly after coaching and a month after coaching. It has been noted that a more reliable findings would have been reached if the outcome measures were assessed session by session. Third, while recruiting subjects using a nationally representative sample frame is a major strength, subjects included in the study were only from general population, and thus our findings cannot be generalized to community members in hospitals, prisons, refugee camps, and manufactures. Fourth, the number of participants enrolled in this trial is relatively small to fulfil the study objectives. Nonetheless, we believe that this study may draw the attention of research facilities to provide the necessary resources to conduct a pragmatic trial that can present definitive conclusions about the study idea. Fifth, assessment of cost-effectiveness, which is crucial for this intervention to be adopted for a general population, was beyond our scope of investigation. However, this can be the basis for our future research. Additionally, the degree of hesitancy, which can provide a more specific findings, was not addressed. Nonetheless, we adhered to this methodology in order to avoid any confusion regarding the aims of the study.

#### Conclusion

Pharmacists-physicians collaborative coaching could be effective in reducing rates of COVID-19 vaccine hesitancy and resistance. The proportion of subjects vaccinated against COVID-19 was considerably increased from 0.0% before coaching to 51.6% a month after coaching. the mean scores for knowledge on, and attitude towards COVID-19 vaccine were significantly increased.

## CRediT authorship contribution statement

Derar H. Abdel-Qader: Project administration, Methodology. Wail Hayajneh: Conceptualization, Methodology. Abdullah Albassam: . Nathir M. Obeudat: Conceptualization, Methodology. Adel M. Belbeisi: Conceptualization, Methodology. Nadia Al Mazrouei: Methodology, Supervision. Ala'a F. Al-Shaikh: Methodology, Supervision. Khaldoon E. Nusair: Methodology, Supervision. Ahmad Z. Al Meslamani: Supervision. Asma A. El-Shara: Supervision. Husam El Sharu: Supervision. Samah Bahy Mohammed Ebaed: Supervision. Osama Mohamed Ibrahim: Supervision.

## **Declaration of Competing Interest**

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

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## Appendix A. Supplementary material

Supplementary data to this article can be found online at https://doi.org/10.1016/j.jvacx.2021.100135.

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