nature communications

Article

https://doi.org/10.1038/s41467-025-58120-x

Cost-effectiveness of community-based integrated care model for patients with diabetes and depressive symptoms

Received: 13 August 2024

Accepted: 13 March 2025

Published online: 27 March 2025

Check for updates

Yanshang Wang[1,2], Dan Guo[3], Yiqi Xia[1,2], Mingzheng Hu[1,2], Ming Wang[1,2], Zhenyu Shi[1,2], Xiaolong Guan[1,2], Dawei Zhu[4] & Ping He[2]

The coexistence of type 2 diabetes (T2DM) and depression is a prominent example of multimorbidity. In previous work, we reported the results of a completed cluster-randomized controlled trial that was conducted in eight community health centers in China. We enrolled adults (≥18 years) with type 2 diabetes and depressive symptoms. In the intervention group, a comprehensive care plan was developed based on the Integrated Care Model for Patients with Diabetes and Depression (CIC-PDD). In this study, we explore the cost-effectiveness of the CIC-PDD by conducting a one-year within-trial economic evaluation from the health system, multipayer and societal perspectives. Health outcomes are quality-adjusted life years (QALYs) and depression-free days (DFDs), and we calculate incremental cost-effectiveness ratios (ICERs) and cost-effectiveness probability. Among 630 participants (275 intervention, 355 usual care), the cost per QALY gained is $7,922.82, $7,823.85, and $7,409.46, with cost-effectiveness probabilities of 66.41%- 94.45%. The cost per DFD is $2.63–$2.82, requiring a willingness-to-pay of $9.00–$10.50 for >95% probability of cost-effectiveness. We find that the CIC-PDD model demonstrates cost-effectiveness within primary health care settings, but further studies are needed to assess its long-term sustainability and scalability. Trial registration: 35 ChiCTR2200065608.

Multimorbidity has emerged as one of the greatest challenges facing healthcare systems in the 21st century[1,2]. Moreover, there is not a greater challenge than providing effective and high-quality healthcare for patients with coexisting physical-mental multimorbidity[3,4], marked by increasing prevalence and diverse patterns of healthcare utilization, placing substantial burdens on individuals, families, and society[5].

Among the various patterns of physical-mental multimorbidity, the coexistence of type 2 diabetes (T2DM) and depression is particularly prominent[2], especially in China. Research indicates that individuals with T2DM are twice as likely to suffer from depression compared to those without T2DM[2], a trend particularly evident in primary health care (PHC) settings[6]. T2DM prevalence among adults aged 20–79 years in China is projected to increase from 8.2% in 2020 to 9.7% in 2030[7,8], making it the country with the largest population affected by comorbid T2DM and depression globally. Moreover, the coexistence of T2DM and depression leads to poorer health outcomes compared to either condition alone. Depression is linked to heightened rates of T2DM complications, increased disability[9], and reduced life expectancy[2,10]. Treatment costs for T2DM escalate significantly when depression is present, amounting to 4.5 times higher expenses compared to managing T2DM alone[2]. As the prevalence continues to rise and health outcomes deteriorate, the health system faces dual

[1]School of Public Health, Peking University, Beijing, China. [2]China Center for Health Development Studies, Peking University, Beijing, China. [3]Department of Research and Teaching, China Aerospace Science & Industry Corporation 731 Hospital, Beijing, China. [4]School of Pharmaceutical Sciences, Peking University, Beijing, China. e-mail: phe@pku.edu.cn

challenges: delivering quality care and managing the substantial economic burden[11,12].

While the beneficial effects of integrated care for patients with T2DM and depression are well established, evidence regarding health economics evaluation is scarce. Individuals with both conditions exhibit higher hospitalization rates and costs, more frequent and costly outpatient visits, increased specialist consultations and total healthcare costs compared to those with a single condition[6,13]. However, these challenges are compounded by the increasing specialization and fragmentation within healthcare systems[2]. This underscores the urgent need for integrated and continuous healthcare delivery strategies to address these complexities[5,13–15]. Integrated care has emerged as an effective approach for managing T2DM and depression multimorbidity, by meeting the complex health needs of patients through seamless coordination across primary and secondary care and the integration of healthcare with social support[16]. However, there is a lack of consistent evidence on the economic evaluation of integrated care for this condition, although initial findings indicate potential cost savings and better outcomes[17]. Existing evidence on the cost-effectiveness of integrated care predominantly originates from developed countries and may not fully account for the intricacies of PHC settings[18]. Given the limited mental health resources in low- and middle-income countries (LMICs), conducting economic evaluation is crucial for informing decision-makers about effective implementation strategies to support integrated care delivery[19].

In our previous study, we demonstrated that the Community-based Integrated Care for Patients with Diabetes and Depression (CIC-PDD) program could enhance patient health outcomes by enhancing health perceptions and promoting behaviors[20]. This raises an important health policy question: Can CIC-PDD improve quality of life and prove cost-effective, thereby supporting the development of an evidence-based integrated care model? To address this, our current study evaluates the 12-month cost-effectiveness of community-based integrated care from multiple perspectives as part of the CIC-PDD trial.

Results

Patient characteristics

Out of the 3759 patients invited for the baseline assessment, 275 individuals were eventually assigned to the integrated care group, while 355 were assigned to the control group. Supplementary Fig. 1 delineates the trial profile by study arm. The mean depressive symptoms score is 1.37 (0.67) in the CIC-PDD group and 1.38 (0.69) in the usual care group. Health utility at baseline is also similar across both groups. Cost components are divided into four categories: costs related to screening, intervention costs, costs related to health care utilization, and indirect costs. There are no statistically significant differences in these four categories of costs between the two groups at baseline (Supplementary Table 1).

No evidence is found of a difference in the number of patients lost to follow-up between the intervention and control groups (χ^2 1.58; $p = 0.208$) (Supplementary Table 2).

Cost components

Table 1 presents a descriptive overview of costs and health effects at 12 months for integrated care group and usual care group. From the perspectives of the health system, multipayer, and society, the accumulated mean (SD) total costs for patients in the integrated care group are 1245.35 (1705.26) US dollars, 1276.95 (1769.46) US dollars, and 1407.53 US dollars (1889.26), respectively. In comparison, for the usual care group, the costs are 1043.89 (2066.30) US dollars, 1078.07 (2139.24) US dollars, 1219.39 (2374.66) US dollars, respectively. In terms of cost composition, healthcare utilization costs represent the largest proportion of all costs for both the integrated care and usual care groups, accounting for 71.11% and 87.83%, respectively (Supplementary Fig. 2). Intervention-related costs constitute 16.69% of the total costs for the integrated care group.

Table 1. | Descriptive analysis of costs, utility, and effectiveness outcomes after 12 months

Group	Usual care group	Integrated care group
Costs types and components		
Direct costs related to screening		
Depression screening by PCP, mean	8.68	8.68
Overhead, mean	0.87	0.87
Subtotal, mean	9.54	9.54
Direct costs related to the intervention		
Intervention setup		
Model development cost, mean		31.90
Training cost, mean		3.14
Intervention delivery		
Case manager salaries, mean		92.11
Manuals cost, mean		1.46
Collaborative meetings cost, mean		34.45
Health videos cost, mean		8.61
Health communicators salaries, mean		28.71
Gift cost, mean		13.16
Overhead, mean		21.35
Subtotal, mean		234.88
Direct costs related to health care utilization		
Outpatient cost, mean (SD)	201.43 (397.94)	208.36 (321.93)
Inpatient cost, mean (SD)	689.38 (1793.68)	610.15 (1550.56)
Self-treatment cost, mean (SD)	143.55 (788.26)	182.41 (404.25)
Subtotal, mean (SD)	1034.35 (2066.30)	1000.92 (1705.26)
Indirect costs		
Food costs for outpatient visits, mean (SD)	3.19 (4.09)	3.63 (4.92)
Transportation costs for outpatient visits, mean (SD)	4.15 (8.21)	4.29 (6.78)
Food and transportation cost of escorts for outpatient visits, mean (SD)	3.10 (5.75)	3.19 (4.68)
Food costs for inpatient visits, mean (SD)	15.86 (43.68)	13.80 (37.92)
Transportation costs for inpatient visits, mean (SD)	10.97 (35.42)	9.88 (31.44)
Food and transportation cost of escorts for inpatient visits, mean (SD)	19.94 (51.23)	17.78 (44.28)
Subtotal, mean (SD)	57.21 (133.57)	52.57 (113.43)
Time costs and lost productivity		
Lost productivity due to outpatient care, mean (SD)	37.57 (92.65)	50.33 (95.19)
Lost productivity due to inpatient care, mean (SD)	48.80 (153.80)	32.81 (71.01)
Escort time costs for outpatient visits, mean (SD)	7.51 (18.53)	10.07 (19.04)
Escort time costs for inpatient visits, mean (SD)	24.40 (76.90)	16.41 (35.50)
Subtotal, mean (SD)	118.29 (312.42)	109.62 (191.92)
Total, mean (SD)		
Health System Perspective	1043.89 (2066.30)	1245.35 (1705.26)
Multipayer Perspective	1078.07 (2139.24)	1276.95 (1769.46)

Table 1 (continued) | Descriptive analysis of costs, utility, and effectiveness outcomes after 12 months

Group	Usual care group	Integrated care group
Societal Perspective	1219.39 (2374.66)	1407.53 (1889.26)
Health effects		
DFDs, mean (SD)	147.74 (109.90)	218.63 (98.81)
QALYs, mean (SD)	0.77 (0.13)	0.79 (0.11)

Please see Supplementary Table 1 for the cost calculation details.
SD standard deviation, *DFDs* depression-free days, *QALYs* quality-adjusted life years.

Unadjusted between-group differences in cost details are presented in Table 2.

Formal health sector: screening and intervention

The screening administered by PCPs to identify eligible patients incurred a cost of 9.54 US dollars per patient. On average, the intervention costs for the integrated care group amount to 234.88 US dollars per patient (Table 1). The intervention setup, constituting 14.91% of these costs, is primarily driven by model development expenses, which total 31.90 US dollars per patient. The largest share of the intervention costs is attributed to case manager salaries, at 92.11 US dollars per patient, accounting for 39.21%. Additionally, collaborative meeting expenses represented 14.67% of the intervention costs, amounting to 34.45 US dollars per patient.

Formal health sector: health care utilization

The total mean healthcare utilization costs for the integrated care group (1000.92 (1705.26) US dollars) are lower than those for the usual care group (1034.35 (2066.30) US dollars), though this difference is not statistically significant. Notably, the integrated care group incurs higher costs for outpatient services and self-treatment compared to the usual care group (Tables 1 and 2). Healthcare utilization emerges as the most substantial non-intervention cost component (Table 1).

Indirect costs

Costs related to food, transportation, time, and lost productivity are largely similar between the two groups (Table 1). The integrated care group shows slightly lower food and transportation costs (41.45 (111.69) US dollars) compared to the usual care group (46.76 (128.35) US dollars), as well as lower time costs and lost productivity (integrated care group: 109.62 (191.92) US dollars; usual care group: 118.29 (312.42) US dollars) due to inpatient care in the usual care group. Conversely, indirect costs related to outpatient care are slightly lower in the integrated care group (11.11 (16.07) US dollars) compared to the usual care group (10.44 (16.06) US dollars), though these differences are not statistically significant.

Health effects

As indicated in Table 2, patients in the integrated care group experience greater gains in both QALYs and DFDs over the course of 12 months compared to those in the usual care group (Table 1). Specifically, the unadjusted between-group difference in DFDs is 70.89 (95% CI 61.76 to 80.02) (Table 2). Regarding QALYs, a notable improvement of 0.03 is observed in the integrated care group (0.79 (0.11)) compared to the usual care group (0.77 (0.13)), resulting in a between-group difference in QALYs of 0.03 (95% CI 0.01 to 0.04). We examined the variation in effects of the intervention across sex using interaction term and found no statistically significant differences between male and female participants (Supplementary Table 3).

Cost-effectiveness

Table 3 presents the ICERs based on the differences in cost and effectiveness over the 12-month period. For QALYs assessed from the perspectives of the health system, multipayer, and society, the integrated care intervention incurs costs of 7922.82 US dollars, 7823.85 US dollars, and 7409.46 US dollars per QALY gained, respectively. The likelihood that the intervention proves to be cost-effective ranges from 66.41% to 94.45% across different willingness-to-pay thresholds, spanning from 13,064 US dollars to 39,192 US dollars. Concerning DFDs, the integrated care intervention incurs costs of 2.82, 2.78, and 2.63 US dollars per DFD gained, respectively. To achieve a probability of cost-effectiveness exceeding 95%, the required willingness-to-pay per DFD ranges from 9.00 to 10.50 US dollars. Furthermore, across all perspectives considered, the integrated care intervention demonstrated cost-effectiveness compared to usual care for all outcomes.

Sensitivity analyses

The bootstrapped estimates of net costs and QALYs are presented on a cost-effectiveness plane in Fig. 1. The simulations predominantly reside in the upper-right quadrant, indicating that integrated care incurs net costs but also delivers a net health benefit (QALY gain). The spread of points is more vertical than horizontal, indicating greater uncertainty in the estimated net QALYs compared to the estimated net costs. As illustrated in Fig. 1, the integrated care intervention demonstrates a probability of being cost-effective for QALYs ranging from 75.88% (3794/5000 replications) to 97.88% (4894/5000 replications) from the health system perspective, 74.66% (3733/5000 replications) to 97.80% (4890/5000 replications) from the multipayer perspective, and 72.20% (3610/5000 replications) to 97.72% (4886/5000 replications) from the societal perspective, at willingness-to-pay thresholds of 1 to 3 times the per capita GDP (13,064 to 39,192 US dollars).

The cost-effectiveness acceptability curve (CEAC) depicted in Fig. 2 supports this estimation.

Robustness checks

Our findings remained robust across various sensitivity analyses. Firstly, after adjusting for baseline outcomes, the differences in DFDs and QALYs between the integrated care group and usual care group remained statistically significant, with values of 75.59 (95% CI: 61.98–89.20) and 0.03 (95% CI: 0.00– 0.05), respectively (see Supplementary Table 4). Secondly, considering the inherent characteristics of cluster RCTs, we observed some baseline imbalances between the two groups. To address this, we conducted a reanalysis after adjusting for baseline characteristics (DFDs: 66.95 [95% CI: 56.92–76.98]; QALYs: 0.02 [95% CI: 0.00–0.04]) and found that our results remained robust (see Supplementary Table 5 and Supplementary Table 6). Thirdly, when using different thresholds to define DFDs, the resulting ICER ranged from 2.86 to 4.25, well below the threshold necessary for achieving 95% cost-effectiveness (see Supplementary Table 7). Fourthly, upon calculating DFD-QALYs and re-implementing the analysis, the probability of cost-effectiveness exceeded 95%, significantly higher than the current results (see Supplementary Table 8). Fifthly, the clustered bootstrap method revealed the probability of being cost-effective ranged from 73.98% (3699/5000 replications) to 97.22% (4861/5000 replications) (see Supplementary Fig. 3). Sixthly, our results remained consistent after multiple imputations (see Supplementary Table 9 and Supplementary Table 10). Seventhly, re-estimating the incremental costs using a Tobit model showed that for QALYs, the probability of cost-effectiveness for the integrated care model exceeded 75% at willingness-to-pay values ranging from 1 to 3 times the per capita GDP, with ICERs for DFDs ranging from 1.80 to 2.05 across the three perspectives (see Supplementary Table 11, Supplementary Table 12 and Supplementary Table 13). Finally, we reanalyzed using T2DM-specific costs from three different perspectives and found that the probability of cost-effectiveness ranged from 75.07% to 96.76%, which is higher than the current results (see Supplementary Table 14).

Table 2. | Unadjusted incremental costs, utility, and effectiveness outcomes after 12 months

	Usual care group	Integrated care group	Incremental difference between intervention and control (Unadjusted)	95% CI	*P* value
Cost estimates: direct part					
Costs related to screening	9.54	9.54			
Costs related to intervention setup and delivery		234.88			
Costs related to health care utilization	1034.35 (2066.30)	1000.92 (1705.26)	-33.50	-562.94 to 495.94	0.901
Cost estimates: indirect part					
Food and transportation costs due to outpatient	10.44 (16.06)	11.11 (16.07)	0.67	-4.68 to 6.02	0.806
Food and transportation costs due to inpatient	46.76 (128.35)	41.45 (111.69)	-5.36	-35.40 to 24.67	0.726
Time costs and lost productivity	118.29 (312.42)	109.62 (191.92)	-8.72	-116.62 to 99.18	0.874
Utility and effectiveness estimates					
DFDs	147.74 (109.90)	218.63 (98.81)	70.89	61.76 to 80.02	<0.001
QALYs	0.77 (0.13)	0.79 (0.11)	0.03	0.01 to 0.04	0.012

DFDs depression-free days, measured by SCL-20, *QALYs* quality-adjusted life years, measured by SF-12.

Discussion

To our knowledge, this study represents the first health economic evaluation of a randomized controlled trial examining integrated care for multimorbidity in China. It is also the largest trial of its kind to date. Through a within-trial economic assessment of a culturally tailored, 12-month integrated care intervention for patients with T2DM and depression across eight diverse PHC settings in China, we determine that the community-based integrated care model is a cost-effective strategy.

Our study findings contribute significantly to the existing research on the development of integrated care models for patients with physical and mental multimorbidity. In our review, we identified only one study from LMICs: the Integrating Depression and Diabetes Treatment (INDEPENDENT) study in India[18]. They revealed a probability of cost-effectiveness of 56.4% using a willingness-to-pay threshold of $16,654 per QALY, with a threshold per DFD exceeding $19.9 to achieve a probability of cost-effectiveness >95%[18]. Notably, the INDEPENDENT study differed from ours in its intervention components, prominently featuring a decision-support electronic health record system, and was limited to urban clinics with a smaller sample size.

In contrast, research from developed countries has yielded different results due to varying contexts. For instance, the TEAMcare and Multifaceted Diabetes and Depression Program (MDDP) studies from the United States reported divergent findings. The TEAMcare study indicated that collaborative care reduced costs rather than increasing them[21]. Conversely, the MDDP reported an ICER of $4053 per QALY gained[22]. It's important to note that the TEAMcare study focused on patients with depression and poorly controlled diabetes or coronary heart disease (CHD), which differs from the population in our study. Similarly, the Collaborative Interventions for Circulation and Depression (COINCIDE) study from the UK reported an incremental cost of $16,597.63 per QALY gained, suggesting potential cost-effectiveness in population with mental–physical multimorbidity[23]. Additionally, Canadian research identified incremental cost-effectiveness ratios of $6.57 per DFD or $17,788.64 per QALY for collaborative care under the health system perspective[24]. Our comparative analysis highlights that the cost per QALY gained with CIC-PDD is lower than the majority of previous studies. While the benefits in DFDs are not as pronounced as in other investigations, the observed ICER in our trial is notably lower than reported in other economic evaluations.

The cost-effectiveness analysis contributes to a thorough evaluation of CIC-PDD intervention. Aligned with our protocol's theoretical framework, this health economics evaluation stands as a crucial component. Our original effectiveness analysis indicated enhancements in depressive symptoms and glycemic control in the integrated care group[20]. The current study's findings serve to complement and extend previous evidence by demonstrating not only effectiveness but also cost-effectiveness. Moreover, the analyses from multiple perspectives and sensitivity analyses suggest the cost-effectiveness of CIC-PDD, enhancing the robustness of the results and strengthening the quality of evidence. Nevertheless, it is essential to conduct more in-depth analysis, such as qualitative analysis, to explore the economic impact and health effects of CIC-PDD. This will provide deeper insights into how the intervention influences patient experiences and healthcare delivery within PHC settings[25], especially given the limited mental health resources that require careful allocation by decision-makers. Additionally, when optimizing the components of the CIC-PDD model, it is crucial to balance the costs and effectiveness associated with each element. For instance, integrating health electronic systems could improve decision-making and service efficiency but might also raise intervention costs. Furthermore, our analyses revealed that CIC-PDD was not associated with significant medical cost savings but rather increased outpatient visits and self-treatment healthcare utilization, with a small effect size in QALYs. Therefore, while the CIC-PDD intervention proved highly cost-effective, further research is necessary to determine its clinical relevance and whether integrated care would decrease patients burden and alter health utilization behavior.

The economic evaluation provides crucial evidence supporting CIC-PDD implementation in practice and offers valuable insights for decision-makers shaping integrated healthcare systems. This study strengthens the evidence base for managing patients with T2DM and depression, addressing gaps arising from limitations in comprehensive analyses across various perspectives[17]. Additionally, implementation research underscores the significance of health economics evaluations that consider resource implications and hidden costs to facilitate evidence-based practice[26]. Our study contributes by conducting a detailed cost analysis that spans from model development to mid-term intervention costs and subsequent post-implementation costs. We also comprehensively evaluate health effects using measures such as DFDs, QALYs, and DFD-QALYs, which helps mitigate measurement biases and enables a thorough economic assessment. These comprehensive analyses are both theoretically and practically valuable as they directly address payer budget concerns and align with implementation science contexts where financial considerations impact program adoption and sustainability[19]. While our study focuses on T2DM and depression multimorbidity, the CIC-PDD model serves as a guiding framework for

https://doi.org/10.1038/s41467-025-58120-x

Table 3. | The cost-effectiveness results of CIC-PDD

Cost Perspective	Cost difference- US dollar (95% CI)	Effectiveness difference- QALYs (95% CI)	ICER-US dollar	Probability of cost-effectiveness, %	Effectiveness difference- DFDs (95% CI)	ICER- US dollar	WTP per DFD to achieve probability of cost-effectiveness > 95%
Unadjusted analysis							
Health System	199.58 (−318.99 to 718.15)	0.03 (0.01 to 0.04)	7922.82	66.41 to 94.45	70.89 (61.76 to 80.02)	2.82	9.00
Multipayer	197.08 (−339.76 to 733.93)		7823.85	66.28 to 94.30		2.78	9.50
Societal	186.65 (−452.70 to 825.99)		7409.46	65.31 to 93.37		2.63	10.50
Adjusted analysis[a]							
Health System	262.74 (−300.95 to 826.42)	0.03 (0.00 to 0.05)	10207.39	66.20 to 91.35	75.59 (61.98 to 89.20)	3.48	8.00
Multipayer	266.20 (−326.73 to 859.13)		10341.94	66.13 to 91.25		3.52	9.00
Societal	295.44 (−438.15 to 1029.02)		11477.82	65.22 to 90.50		3.91	9.50

DFDs depression-free days, *QALYs* quality-adjusted life years, *ICER* incremental cost-effectiveness ratio, *WTP* willingness-to-pay.
[a]Adjusted analyses were conducted using a two-sided Generalized Linear Model (GLM) with a Gamma distribution, incorporating baseline outcome adjustments.

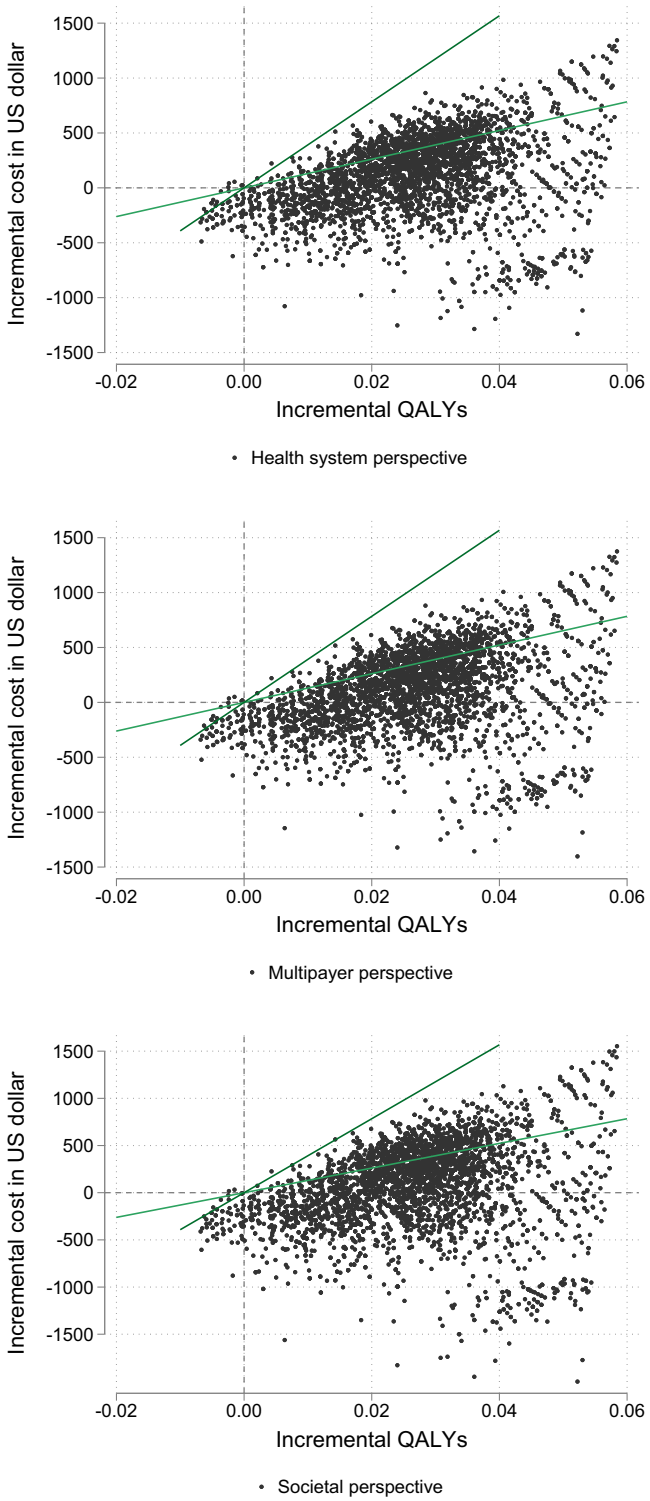

Fig. 1 | Cost-effectiveness plane with bootstrapped incremental costs and QALYs (clustered bootstrap). QALY quality-adjusted life-year. The incremental cost-effectiveness plane shows 5000 bootstrap replications of incremental cost and QALY pairs. The two lines denote the willingness to pay threshold, which is 13,064 US dollar to 39,192 US dollar /QALY gained. The probability of cost-effectiveness is represented by the proportion of simulation points (out of 5000) located below and to the right of the $39,192/QALY threshold line. Source data are provided as a Source Data file.

managing other multimorbidity conditions. Furthermore, future implementations could potentially avoid significant upfront costs associated with model development when extending the CIC-PDD model to other healthcare practices.

https://doi.org/10.1038/s41467-025-58120-x

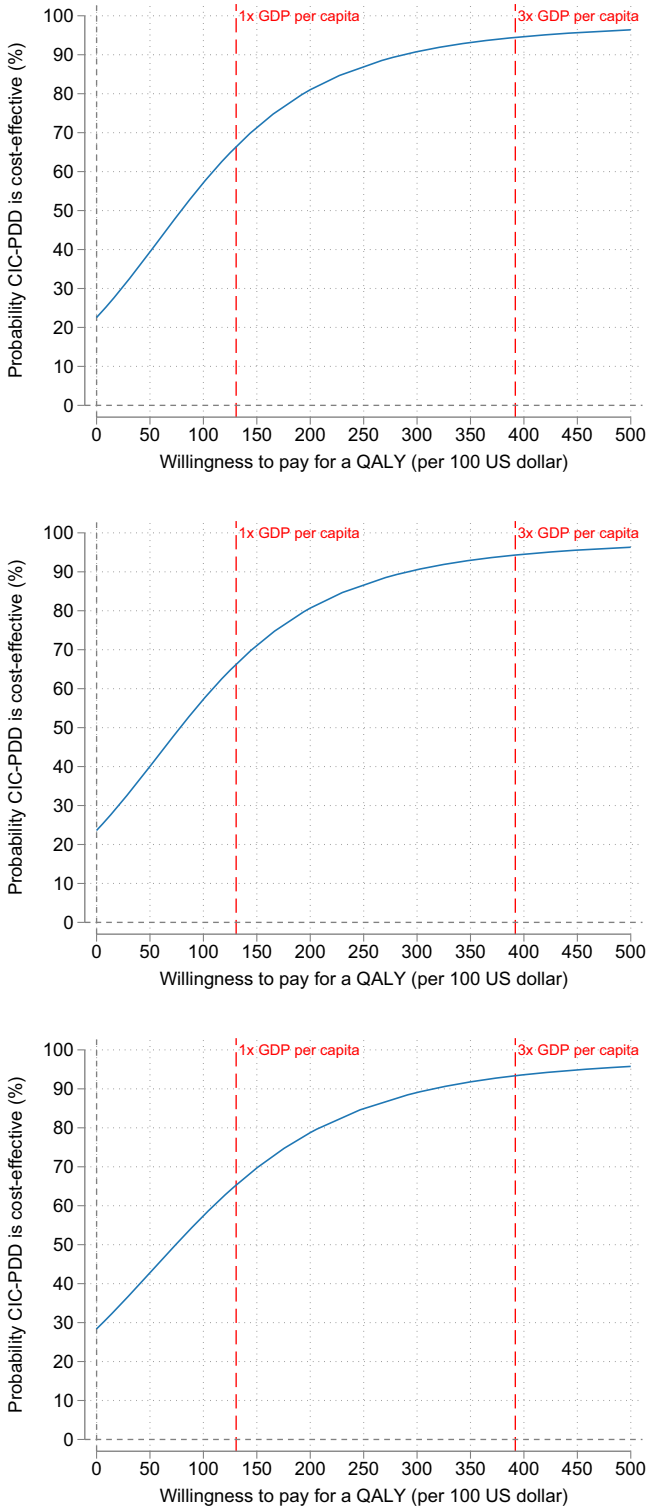

Fig. 2 | The cost-effectiveness acceptability curve. The vertical dotted lines represent the willingness-to-pay thresholds. QALY quality-adjusted life years, GDP gross domestic product. The CEAC illustrate the cost-effectiveness probability of CIC-PDD across different willingness-to-pay thresholds. Source data are provided as a Source Data file.

Our study possesses several notable strengths. Firstly, we utilized health administrative records to meticulously measure health utilization and costs. In contrast to other studies[18,21–24] that primarily rely on self-reported data, which can be susceptible to recall bias and may not always accurately reflect actual usage. By integrating claim data with survey data, our method minimizes these biases and enhances the robustness and precision of our findings. Secondly, our rigorous data collection and calculation procedures enabled comprehensive health economics evaluations from multiple perspectives. To our knowledge, apart from the INDEPENDENT[18], many other research efforts have encountered difficulties conducting such analyses due to limitations in capturing detailed cost data. A systematic review examining health economics evaluations of integrated care models has pointed out that only around one-third of these studies included sensitivity analyses from the societal perspective[17]. This limitation often arises from inadequate cost information. Thirdly, this study represents the largest trial to date, incorporating a wide array of implementation settings. Unlike studies confined to urban clinics, our research spans a broad spectrum of PHC settings, encompassing both rural and urban areas. This diversity significantly enhances the generalizability and scalability of the care model, making it relevant across diverse regions and healthcare environments.

Our study also faces several limitations. Firstly, our current health economics evaluation is limited in its ability to capture long-term and maintenance phase effects. This study is a within-trial economics evaluation conducted over a 12-month intervention period, which means we cannot yet determine whether the CIC-PDD model remains cost-effective in the post-intervention maintenance phase. From an implementation science perspective, ensuring the durability of evidence is essential, emphasizing the need for extended evaluation periods to ascertain long-term impacts and sustainability. Secondly, as a study conducted in China, the findings may not be generalizable to other countries or healthcare systems. Despite encompassing diverse PHC settings, adapting this care model elsewhere will necessitate adaptations to harmonize with local health systems. Moreover, refining cost components to accurately reflect regional conditions will be essential for ensuring the model's effectiveness and cost-effectiveness in new contexts. Thirdly, we are unable to disaggregate healthcare service costs specifically attributable to depression. Nevertheless, this limitation is unlikely to substantially impact our findings because individuals with severe pre-existing depression or other psychiatric conditions were excluded from the trial. Moreover, feedback from PCPs indicated no occurrence of serious adverse events related to depression during the intervention period. Fourthly, the calculation of service team salaries utilizes a fixed-cost approach. In China, village doctors often do not receive standardized salary incomes, and health communicators who are medical students. For salaries, we referenced payment standards from the basic public health service package to ensure consistency and acceptability in our calculations. Lastly, we acknowledge that not all costs from a societal perspective could be fully captured. Despite a thorough analysis of indirect costs, certain elements—such as informal caregiver time, lost household production, and potential accommodation costs—remain unaccounted for.

Integrated care, as implemented in the CIC-PDD trial, represents a promising strategy for managing patients with T2DM and depression multimorbidity. This health economics evaluation underscores the cost-effectiveness of the integrated care model in PHC settings. Further long-term analysis and qualitative studies are essential to assess the sustainability and scalability of the CIC-PDD model.

Methods

The CIC-PDD study was a pragmatic cluster randomized controlled trial (RCT) conducted in two counties in China, approved by Institutional Review Board at Peking University (no. IRB00001052-21104). Randomization took place at community health centers (CHCs), with CHCs in each county randomized on a 1:1 ratio (see Supplementary Fig. 1). This ensured that the ratio of urban to rural CHCs in both the intervention and control groups was maintained at 1:1. The trial protocol was previously published[27].

Participants

Patient recruitment involved initial screening and eligibility testing. Primary healthcare providers (PCPs) identified potential participants with T2DM through electronic health records and provided a brief study overview. Eligible patients were then invited for further assessment and detailed information on the CIC-PDD intervention.

Eligible participants are between 18 and 85 years old and have a confirmed diagnosis of T2DM and a PHQ-9 score of 10 or higher. They must not have serious hearing or vision impairments and must be able to complete telephone interviews. All participants provided written informed consent. Recruitment commenced on December 1, 2022, and was completed on January 20, 2023.

Randomization and masking

We randomized CHCs in each county on a 1:1 ratio, and the ratio of urban to rural CHCs in both the intervention and control groups was maintained at 1:1. The allocation of clusters to each study arm was overseen by a statistician who was not involved in implementing the study.

All outcome assessors remained blinded and worked independently from both the intervention and study teams. Additionally, data were coded and anonymized to ensure that researchers were blinded during the entire analysis and reporting phases.

Intervention

The CIC-PDD intervention is based on an integrated care model, with the goal of merging healthcare and social services, as well as primary and secondary healthcare, along with mental and physical healthcare. Key components of the model include:

(1) Multidisciplinary approach: The team comprises diabetes specialists, psychiatrists, psychotherapists from secondary or tertiary hospitals, case managers (CMs), and health communicators, who are students from medical universities.

(2) Customized patient management plan: Each patient receives an individualized treatment plan, emphasizing patient-centered assessment and engagement. It incorporates Behavioral Activation (BA) strategies and employs self-management plans.

(3) Regular patient follow-ups: Patients benefit from proactive management by CMs, involving up to 18 sessions over one year.

(4) Improved inter-professional communication: All team members participate in collaborative meetings, facilitated by health communicators, to ensure thorough reviews of patients' health status.

(5) Supplementary resources: Intervention manuals and WeChat official accounts complement the intervention.

Comparators

In the control group, PCPs were informed about patients' depressive symptoms, and these patients received usual care. Notably, the health management of patients with T2DM is a key component of the Basic Public Health Service Package (BPHSP), with PCPs providing essential health education and promotion services.

As outlined in our protocol (Supplementary Protocol)[27], we conducted a comprehensive assessment of CIC-PDD using the RE-AIM (reach, efficacy, adoption, implementation, and maintenance) framework. Here, the health economics evaluation serves as a part of the evaluation plan. Our findings are reported in accordance with the current guidelines for cost-effectiveness research, namely the Consolidated Health Economic Evaluation Reporting (CHEERS) guidelines (see Supplementary Note 1)[28].

Economic evaluation

Here, we evaluated the health effects, cost, and cost-effectiveness over the 12-month follow-up evaluation period.

(1) Health Effects

In assessing effectiveness, we employed two measures: health utility and health effects, specifically focusing on quality-adjusted life years (QALYs) and the number of depression-free days (DFDs) during the follow-up period.

QALYs serve as a comprehensive longitudinal measure of treatment effectiveness, combining health-related quality-of-life (HRQoL) associated with an individual's health state and the duration spent in that health state. Health utilities were evaluated using the Short-Form Health Survey (SF-12)[29]. QALYs were then computed from these utility scores, representing the area under the curve and assuming linear changes in scores between baseline, 6, and 12 months[30].

We computed DFDs based on the SCL-20 score, following the method proposed by ref. 31. To calculate DFDs, we used threshold scores to classify depression severity at baseline and follow-up visits. Patients were classified as depression-free (DFD = 1) if their score was below this threshold (SCL-20 score < 0.5) and as experiencing symptomatic depression (DFD = 0) if their score exceeded the upper threshold (SCL-20 score > 1.37), which was derived from the mean SCL-20 score at baseline. Scores falling between these thresholds were linearly interpolated to convert them into proportional DFDs ranging from 0 to 1. The ultimate calculation of DFDs accrued by patients involves multiplying the number of days between assessment time points by the corresponding severity level of depression (ranging from 0 to 1). This calculation represents the area under the depression severity curve over time. Supplementary Note 2 gives the details of calculation.

(2) Cost Components

Direct costs: screening/case finding. To identify T2DM and depression multimorbidity, we initially conducted screening among patients with T2DM. The total screening cost is calculated by multiplying the number of potentially eligible patients (n = 1594 + 2145) by the screening cost per patient. This fee is a fixed payment to the PCP. Per-patient screening costs are determined by dividing the total screening costs by the number of patients randomly assigned to the study.

We add a 10% overhead to account for the training on the PHQ-9, as well as the review and verification of screening results by the research team during this process.

Direct costs: intervention setup and delivery. Costs related to the intervention encompass two main components: intervention setup and delivery. First, the intervention setup costs include the costs of the CIC-PDD model development and the offline training costs. Development costs specifically include fees for expert consultations, as well as accommodation and travel expenses incurred during site visits. Offline training costs encompass the expenses associated with training the integrated care teams, comprising CMs, health communicators, and the specialist team, to ensure proficiency in their roles and requisite skills. These costs involve expenditures for expert lectures conducted both onsite and online, as well as costs of the curriculum and educational materials.

For intervention delivery, the costs include the salaries for CMs conducting visits, labor costs for the care team during collaborative meetings (including time spent by psychiatrists, diabetologists, and psychotherapists), and salaries for health communicators. Additionally, expenses include the instructional costs for the specialist team to maintain ongoing skills, printing costs for educational materials, and the cost of gifts provided to patients.

Lastly, a 10% administrative overhead is added to account for the marginal impact on the primary care work.

Direct costs: health care utilization. Costs associated with healthcare utilization include expenses for outpatient care, inpatient care, and self-treatment. Data on utilization and costs for outpatient and

inpatient care are sourced from medical insurance claims, whereas self-treatment data are collected through semi-annual surveys.

Indirect costs: time, lost productivity, food, and transportation costs. Patient and escort expenses for food and transportation related to outpatient and inpatient care are derived from survey data. For patients, the cost of lost productivity is estimated by combining the number of outpatient visits and inpatient days, multiplied by their average daily wage. Specifically, each outpatient visit is assumed to result in a 0.5-day loss, and the loss for inpatient care equals the total number of hospitalization days. Escort costs for lost time are estimated using self-reported data provided by patients. Please see Supplementary Note 3 for more details.

All costs are measured in US dollar. Given that the analytic horizon is only one year, no discounting of costs and effects is applied.

Supplementary Table 15 provides an overview of costs and cost perspectives.

Statistical analysis

We conducted an intent-to-treat analysis to assess the intervention's effects, utilizing a rich dataset for the economic evaluation of CIC-PDD. We performed within-trial cost-effectiveness analyses comparing integrated care with usual care from healthcare, multipayer, and societal perspective. The multipayer perspective included costs incurred directly within the health sector, intervention costs, as well as, indirect costs related to food and transportation. The societal perspective further included all other indirect costs, such as patient time costs for care and lost productivity due to illness. A societal perspective is the recommended option for public health economic analyses, as it comprehensively considers all costs affecting both beneficiaries and payers, thereby reflecting the broader impact on society as a whole (see Supplementary Note 4 and Supplementary Table 1).

Cost-effectiveness is measured using the incremental cost-effectiveness ratio (ICER), calculated by comparing the incremental cost (the difference in mean cost between integrated care and usual care) to the incremental health effects (the accompanying differences in mean DFDs and QALYs). The ICER represents the additional costs per additional effectiveness gained from the CIC-PDD intervention compared to usual care.

For QALYs, we followed World Health Organization guidelines, which suggest using a threshold ranging from one to three times the country-specific gross domestic product (GDP) per capita[32]. In the context of China's 2023 per capita GDP, this translates to thresholds between 13,064 and 39,192 US dollars per QALY[32]. Since there is no established willingness-to-pay threshold for DFDs, we calculated the theoretical willingness to pay per DFD needed to achieve a predefined probability of cost-effectiveness at 95%.

We then constructed a cost-effectiveness acceptability curve (CEAC) to represent the probability that the ICER would fall below a specified willingness-to-pay threshold for QALYs from various costing perspectives. This CEAC enables decision-makers to evaluate the likelihood that the interventions are cost-effective, considering the uncertainties inherent in decision-making and sampling[32].

To mitigate uncertainty stemming from sampling variation, we employed a nonparametric bootstrap procedure with 5000 replications. This approach involved resampling with replacement to generate an empirical joint distribution of incremental costs and health effects[33,34]. This uncertainty is subsequently illustrated in cost-effectiveness planes.

We allow for within-CHC correlation in patients' costs and health effects by clustering the standard error at the CHC level. To address missing measurements, including those from individuals who either died or withdrew from the study, we employed multiple imputation techniques. Our primary analysis excluded these participants' data. As a sensitivity analysis, we reevaluated our findings using data after multiple imputations (30 imputation datasets).

Patients were surveyed face-to-face at baseline, with outcomes reported at 6 months and 12 months subsequent to enrollment. Trained outcome assessors, blinded to group assignments, conducted the interviews. Additionally, we utilized medical insurance system and work logs to obtain data on some costs and health care utilization (outpatient and inpatient utilization), which were linked with the patient survey data (see Supplementary Table 1).

The study's statistical power was calculated to detect differences between arms in the primary outcome, incorporating an intraclass correlation coefficient (ICC) of 0.03 based on prior literature to account for clustering effects[35]. With 480 patients (240 per group) across 8 CHCs, the study was powered at over 80% to detect a 20% absolute mean difference between groups for the primary outcome ($\alpha = 0.05$). To mitigate the impact of an anticipated 10%–15% loss to follow-up, the sample size was increased to 280 per group. All analyses were conducted using Stata 17, and estimates were reported with 95% confidence intervals (CIs) using two-sided statistical tests, with a significance threshold set at $P < 0.05$. The study was approved by Institutional Review Board at Peking University (no. IRB00001052-21104). This trial was registered with ClinicalTrials.gov, registration number ChiCTR2200065608.

We conducted sensitivity analyses to assess the robustness of our findings. Firstly, to mitigate potential confounding factors inadequately balanced by randomization, we conducted a sensitivity analysis by adjusting for baseline values of outcomes and baseline characteristics. Secondly, we varied the definition of DFDs by using different thresholds, specifically employing an SCL-20 score greater than 1.7 to classify fully symptomatic depression (DFD = 0). Thirdly, we computed depression-specific QALYs (DFD-QALYs) based on the SCL-20 score[21]. Fourthly, given the cluster RCT design of our study, we addressed within-group correlation by employing a clustered bootstrap method to re-simulate uncertainty from three perspectives[36]. Fifthly, we recalculated the cost differences using a Tobit model. Lastly, we reanalyzed the cost-effectiveness using healthcare costs attributed to T2DM. For more details of sensitivity analyses, please see Supplementary Note 5.

Reporting summary

Further information on research design is available in the Nature Portfolio Reporting Summary linked to this article.

Data availability

Access to the data underlying this study is restricted to protect participant privacy and confidentiality in accordance with ethical guidelines and data protection regulations. Researchers with an approved research proposal may request access to the data, which will be provided in as de-identified/anonymized participant data to ensure confidentiality, including participants characteristics, health outcomes, and cost data. The study protocol is provided in the Supplementary Information. Requests for data access should be directed to Ping He at phe@pku.edu.edu. Each request will be assessed, and a response will be issued within 90 days of submission. Source data are provided with this paper.

Code availability

The code used for data analyses in this study can be obtained by contacting the corresponding authors. Requests for access to the code will be considered for academic use and provided within 30 days of submission.

References

1. Pearson-Stuttard, J., Ezzati, M. & Gregg, E. W. Multimorbidity—a defining challenge for health systems. *Lancet Public Health* **4**, e599–e600 (2019).

2. Sartorius, N. Depression and diabetes. *Dialogues Clin. Neurosci.* **20**, 47–52 (2018).
3. Gunn, J. Designing care for people with mixed mental and physical multimorbidity. *BMJ* **350**, h712 (2015).
4. McLean, G. et al. The influence of socioeconomic deprivation on multimorbidity at different ages: a cross-sectional study. *Br. J. Gen. Pract.* **64**, E440–E447 (2014).
5. Zhao, Y. et al. The impact of mental and physical multimorbidity on healthcare utilization and health spending in China: a nationwide longitudinal population-based study. *Int. J. Geriatr. Psychiatry* **36**, 500–510 (2021).
6. Egede, L. E., Zheng, D. & Simpson, K. Comorbid depression is associated with increased health care use and expenditures in individuals with diabetes. *Diab. Care* **25**, 464–470 (2002).
7. Yang, W. Y. et al. Prevalence of diabetes among men and women in China. *N. Engl. J. Med.* **362**, 1090–1101 (2010).
8. Liu, J. et al. Projected rapid growth in diabetes disease burden and economic burden in China: a spatio-temporal study from 2020 to 2030. *Lancet Reg. Health West. Pac.* **33**, 100700 (2023).
9. Egede, L. E. Diabetes, major depression, and functional disability among U.S. adults. *Diab. Care* **27**, 421–428 (2004).
10. Park, M., Katon, W. J. & Wolf, F. M. Depression and risk of mortality in individuals with diabetes: a meta-analysis and systematic review. *Gen. Hosp. Psychiatry* **35**, 217–225 (2013).
11. Tinetti, M. E., Fried, T. R. & Boyd, C. M. Designing health care for the most common chronic condition—multimorbidity. *JAMA* **307**, 2493–2494 (2012).
12. Tran, P. B. et al. Costs of multimorbidity: a systematic review and meta-analyses. *BMC Med.* **20**, 234 (2022).
13. Hutter, N., Schnurr, A. & Baumeister, H. Healthcare costs in patients with diabetes mellitus and comorbid mental disorders-a systematic review. *Diabetologia* **53**, 2470–2479 (2010).
14. Salisbury, C., Johnson, L., Purdy, S., Valderas, J. M. & Montgomery, A. A. Epidemiology and impact of multimorbidity in primary care: a retrospective cohort study. *Br. J. Gen. Pract.* **61**, e12–e21 (2011).
15. Quinaz Romana, G. et al. Healthcare use in patients with multimorbidity. *Eur. J. Public Health* **30**, 16–22 (2020).
16. Wang, Y., Hu, M., Zhu, D., Ding, R. & He, P. Effectiveness of collaborative care for depression and HbA1c in patients with depression and diabetes: a systematic review and meta-analysis. *Int J. Integr. Care* **22**, 12 (2022).
17. Rocks, S. et al. Cost and effects of integrated care: a systematic literature review and meta-analysis. *Eur. J. Health Econ.* **21**, 1211–1221 (2020).
18. Emmert-Fees, K. M. et al. Cost-effectiveness of a collaborative care model among patients with type 2 diabetes and depression in India. *Diab. Care* **46**, 11–19 (2023).
19. Eisman, A. B., Hutton, D. W., Prosser, L. A., Smith, S. N. & Kilbourne, A. M. Cost-effectiveness of the adaptive implementation of effective programs trial (ADEPT): approaches to adopting implementation strategies. *Implement. Sci.* **15**, 109 (2020).
20. Wang, Y. et al. Effect of community-based integrated care for patients with diabetes and depression (CIC-PDD) in China: a pragmatic cluster-randomized trial. *Diabetes Care* dc241593 https://doi.org/10.2337/dc24-1593 (2024).
21. Russo, J. Cost-effectiveness of a multicondition collaborative care intervention: a randomized controlled trial. *Arch. Gen. Psychiatry* **69**, 506 (2012).
22. Hay, J. W., Katon, W. J., Ell, K., Lee, P.-J. & Guterman, J. J. Cost-effectiveness analysis of collaborative care management of major depression among low-income, predominantly hispanics with diabetes. *Value Health* **15**, 249–254 (2012).
23. Camacho, E. M. et al. Long-term clinical and cost-effectiveness of collaborative care (versus usual care) for people with mental–physical multimorbidity: cluster-randomised trial. *Br. J. Psychiatry* **213**, 456–463 (2018).
24. Johnson, J. A. et al. Cost-effectiveness evaluation of collaborative care for diabetes and depression in primary care. *Am. J. Prev. Med.* **51**, e13–e20 (2016).
25. Wildman, J. & Wildman, J. M. Combining health and outcomes beyond health in complex evaluations of complex interventions: suggestions for economic evaluation. *Value Health* **22**, 511–517 (2019).
26. Roberts, S. L. E., Healey, A. & Sevdalis, N. Use of health economic evaluation in the implementation and improvement science fields—a systematic literature review. *Implement. Sci.* **14**, 72 (2019).
27. Wang, Y. et al. Community-based integrated care for patients with diabetes and depression (CIC-PDD): study protocol for a cluster randomized controlled trial. *Trials* **24**, 550 (2023).
28. Husereau, D. et al. Consolidated health economic evaluation reporting standards (CHEERS) statement. *BMJ* **346**, f1049 (2013).
29. Ware, J. E., Kosinski, M. & Keller, S. D. A 12-item short-form health survey - construction of scales and preliminary tests of reliability and validity. *Med. Care* **34**, 220–233 (1996).
30. Manca, A., Hawkins, N. & Sculpher, M. J. Estimating mean QALYs in trial-based cost-effectiveness analysis: the importance of controlling for baseline utility. *Health Econ.* **14**, 487–496 (2005).
31. Vannoy, S. D., Arean, P. & Unützer, J. Advantages of using estimated depression-free days for evaluating treatment efficacy. *PS* **61**, 160–163 (2010).
32. World Health Organization, *Making Choices in Health: WHO Guide to Cost-Effectiveness Analysis*. (World Health Organization, 2003).
33. Briggs, A. H., Wonderling, D. E. & Mooney, C. Z. Pulling cost-effectiveness analysis up by its bootstraps: a non-parametric approach to confidence interval estimation. *Health Econ.* **6**, 327–340 (1997).
34. Anderson, J. P., Bush, J. W., Chen, M. & Dolenc, D. Policy space areas and properties of benefit-cost/utility analysis. *JAMA* **255**, 794–795 (1986).
35. Cummings, D. M. et al. Randomized trial of a tailored cognitive behavioral intervention in type 2 diabetes with comorbid depressive and/or regimen-related distress symptoms: 12-month outcomes from COMRADE. *Diab. Care* **42**, 841–848 (2019).
36. Bachmann, M. O., Fairall, L., Clark, A. & Mugford, M. Methods for analyzing cost effectiveness data from cluster randomized trials. *Cost. Eff. Resour. Alloc.* **5**, 12 (2007).

Acknowledgements

The authors deeply appreciate the contributions of Municipal Health Commission of Weifang, Weifang Mental Health Center, Weifang People Hospital, and all CHCs. We also acknowledge the contributions of experts who have given this project valuable suggestions. This work was supported by the Project of the the Major Project of the National Social Science Fund of China (21&ZD187) and Beijing Municipal Natural Science Foundation (9212009). The funding source was not involved in the design, conduct, or reporting of the knowledge synthesis.

Author contributions

P.H. conceived the study and designed the protocol. Y.W. is responsible for statistical analysis and the reporting of the trials. Y.W. wrote the first draft of the paper. Y.W., D.G., Y.X., M.H., M.W., Z.S., X.G., and D.Z. reviewed, commented on, and revised further drafts. PH is the principal investigator for the trials and supervised all aspects of this study. All authors critically revised successive drafts of the paper and approved the final version. The corresponding author attests that all listed authors meet authorship criteria and that no others meeting the criteria have been omitted.

Competing interests
The authors declare no competing interests.

Additional information
Supplementary information The online version contains supplementary material available at https://doi.org/10.1038/s41467-025-58120-x.

Correspondence and requests for materials should be addressed to Ping He.

Peer review information *Nature Communications* thanks Rimke Vos, who co-reviewed with Jonne ter Braake and the other anonymous reviewer(s) for their contribution to the peer review of this work. A peer review file is available.