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Effectiveness of negative pressure wound therapy on chronic wound healing: A systematic review and meta-analysis

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Abstract

Background: Negative Pressure Wound Therapy (NPWT) is considered an effective treatment in facilitating the healing of chronic wounds. However, its effect remains inconsistent, which allows for further investigation.

Objective: This study aimed to assess the effectiveness of the NPWT program in improving the management of chronic wound healing.

Design: Systematic review and meta-analysis was used.

Data Sources: The search strategy ranged from 2016 to 2021 in PubMed, CINAHL, ProQuest, and ScienceDirect.

Review Methods: Risk of bias was done based on the Risk of Bias 2.0 guideline using RevMan 5.4.1, and meta-analysis was done using Jeffreys's Amazing Statistics Program (JASP) software version 0.16.3. Critical appraisal of the included articles was done according to Joanna Briggs Institute's (JBI) appraisal checklist.

Results: A total of 15 articles were included, with 3,599 patients with chronic wounds. There was no publication bias in this study seen from the results of the Egger's test value of 0.447 (p >0.05), symmetrical funnel plot, and fail-safe N of 137. However, heterogeneity among studies was present, with I^2 value of 66.7%, Q = 41.663 (p <0.001); thus, Random Effect (RE) model was used. The RE model showed a significant positive effect of the NPWT on chronic wound healing, with z = 3.014, p = 0.003, 95% CI 0.085 to 0.400. The observed effects include decreased rate of surgical site infection, controlled inflammation, edema, and exudate, as well as increased tissue with varying forest plot size, as demonstrated by the small effect size (ES = 0.24, 95% CI -0.26 to 0.79, p <0.05).

Conclusion: The analysis results show that the standard low pressure of 80-125 mmHg could improve microcirculation and accelerate the healing process of chronic wounds. Therefore, applying the NPWT program could be an alternative to nursing interventions. However, it should be carried out by competent wound nurses who carry out procedure steps, implement general patient care, and give tips on overcoming device problems and evaluation.

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Keywords

negative pressure wound therapy; chronic wounds; wound healing; patient care; meta-analysis; nursing intervention

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Background

Chronic wounds can cause bacteria to form biofilms as a defense against unknown host cells and become resistant to topical and systemic antimicrobials. Biofilms allow pathogens to develop when microorganisms adhere to cells, colonize and increase their expansion on the wound surface (Kadam et al., 2019). Optimal management of chronic wound healing can be achieved by controlling several complex and dynamic factors (Han & Ceilley, 2017), which will improve the maintenance of anatomical continuity and function (FrykbergRobert, 2015). Furthermore, the ideal wound healing is to restore the structure, function, and normal skin anatomy to a perfect condition (Rodrigues et al., 2019). Unfortunately, it takes a long time when inhibiting factors interfere with the process, including various local and systemic factors (Gonzalez et al., 2016).

Negative Pressure Wound Therapy (NPWT) is a non-invasive procedure that uses negative pressure to control and absorb exudate. It prevents internal and external infection of the wound surface through a dressing combined with foam connected to a negative pressure device and vessel (Apelqvist et al., 2017). NPWT can prevent cross-infection by controlling several factors that complicate wound healing, and increase peripheral microcirculation, thereby stimulating the formation of new blood vessels (Ma et al., 2017). Additionally, it enables faster granulation and re-epithelialization of wounds, reduces bacterial counts, and improves tissue oxygenation (Ahajj & Goyal, 2022).

Previous systematic reviews have been carried out to evaluate the effectiveness of NPWT in improving the chronic wound healing process. However, it is difficult to reach conclusions because the included studies were randomized control trials (RCTs) and non-RCTs (Janssen et al., 2016; Rhee et al., 2015). Combining randomized control trials is expected to help achieve larger sample sizes (Janssen et al., 2016). It has also been proposed to provide high-quality evidence for the long-term use of NPWT in the treatment of chronic wounds (Xie et al., 2010).

In addition, based on previous reports, the NPWT intervention has mixed results on chronic wound healing. In an RCT study (N = 115) in America, the intervention showed a significant effect after 12 weeks of treatment in improving quality of life (Kirsner et al., 2019). Meanwhile, a study in Germany (N = 154) reported that NPWT was not superior to standard wound care in improving healing (Seidel et al., 2014). Another study also reported several gaps in standard methods of determining wound eligibility, outcome measures, and interventions (Webster et al., 2019).

Therefore, to address the gap in previous reports, we aimed to conduct a systematic review and meta-analysis focusing on identifying and including all available RCTs to improve the comparability of studies that investigated the effectiveness of NPWT interventions on wound healing, microcirculation improvement, infection control, and critical components.

Methods

Design

Systematic review and meta-analysis were used.

Search Strategy

This study was conducted in line with the Preferred Items for Systematic Review and Meta-analyses (PRISMA) guideline, based on several element items, including Population, Intervention, Control, and Study design (PICOS), as shown in **Table 1**. The following online databases were included: PubMed/Medline, CINAHL, ProQuest, and Science Direct. The search strategy ranged from 2016 to 2021. Using a combination of several subjects, the search terms were in two categories, namely: (1) Negative Pressure Wound Therapy (NPWT) or Vacuum Assisted Closure, Chronic Wounds or Ulcers, Clinical and Randomized Control Trials, and (2) search combinations according to different characteristics and databases. The search strategy was limited to the form of journals that have DOI and were written in English. The details of the search strategy can be seen in the **supplementary file**.

Inclusion Criteria

The inclusion criteria used in searching the database for articles were as follows: articles published between 2016 and 2021, English-only papers, focused on harmful pressure wound therapy intervention in chronic wounds associated with pressure, t-pressure therapy in the healing process at home or a public health center and hospital. The article must also use a quantitative design in the form of a clinical or randomized controlled trial (RCT), not a protocol and a systematic review.

Table 1 Inclusion and exclusion criteria

Criteria	Inclusion	Exclusion
Types of studies	RCTs, quasi-RCTs, CCTs	Animal studies, case studies, case reports, qualitative correlation studies, and review studies
Participants	Patients who have chronic wounds on the skin with signs of infection, excessive exudate, pain, injuries>2 cm, postoperatively that have not healed after 30 days	Postoperative patients without infection, odor, or pain healed before 30 days, and acutely injured patients
Interventions	Negative Pressure Wound Therapy Management	If the intervention is not carried out for 14 days and the TIN is not applied to humans
Control	Placebo, pads, and treatment	Pre-test post-test using NPWT compared to standard wound care
Outcomes	Wound healing, microvascular repair, infection control, and exudate management	A study in the paper discusses the costs of chronic wound care

Study Selection

AB, NAK, and SMS determined the databases and introduction in the agreed PICOS stage and independently read the title and abstract identification. Afterward, the complete text was read, and analyses were performed based on PICOS. When there were differences in the opinion between the three reviewers, discussion and further consultation were carried out with the fourth reviewer to make a final decision. Data were then explicitly extracted on the author, study type, subject characteristics, participant, country, number of respondents, intervention, instrument, and outcome. In one published study, data were extracted as needed, and only the most recent or comprehensive were included.

Quality Appraisal of the Studies

The study quality was analyzed based on PRISMA guidelines (Page & Moher, 2017; Shamseer et al., 2015) as well as the methodology for a systematic review of quantitative Randomized Control Trials (RCT) and Clinical Trials (CT) from the Joanna Briggs Institute (JBI) (Lockwood et al., 2011). In addition, risk of bias was performed using Rev-Man 5.4.1 and the Critical Appraisal Skills Program RCT with possible scores ranging from 0 to 13 (Joanna Briggs Institute, 2020).

Data Extraction
Data were extracted using a table, including author, study type, subject characteristic, participant, country, number of respondents, intervention, instrument, and outcome.

Risk of Bias
Three authors assessed the bias in a study based on the Risk of Bias 2.0 guideline with five domain items. The data were entered into the software Review Manager version 5.4.1 to view them graphically (Review Manager, 2022). The high risk of bias was observed in the randomized population allocation, blind intervention in data entry and execution, review of the initial and final assessments, the validity of the instruments used, and blind data analysis. Furthermore, the data were homogeneous and low in a large study.

Meta-Analysis
The meta-analysis was conducted using Jeffreys's Amazing Statistics Program (JASP) software version 0.16.3 (JASP, 2021). Subsequently, an effect size analysis in the category data was performed to distinguish between low and high mean results for the combined effect on the measured data. The effect size was presented with a 95% CI value of p <0.05. Next, the heterogeneity was assessed using the Omnibus test value <0.001. When the study showed heterogeneity, it was then followed by the Random Effect (RE) model test to analyze the effect of the p-value <0.001; 95% CI, with value category *r = 0.1 (low); *r = 0.3 (medium); *r = 0.5 (height) (Cohen, 1988). Studies that showed heterogeneity were further tested with the Moreover, Egger's test, Fail-safe N, and Funnel Plot were conducted to investigate publication bias in meta-studies.

Results

Synthesis Results
Search results and analysis of international databases, including CINAHL, PubMed, ProQuest, and ScienceDirect, were limited based on the criteria and exclusions set. Although, initially, a total of 9,060 articles were obtained, after performing duplicate screening and a manager reference system using endnotes, only 427 were left. The following process was the selection through Clinical and Randomized Control Trials, where 15 articles were obtained, as shown in **Figure 1**. The articles to be reviewed were selected based on the topic of the effectiveness of NPWT on chronic wound healing, with a total number of 3,990 respondents, as described in **Table 2**. The risk of bias can be seen in **Figure 2**.

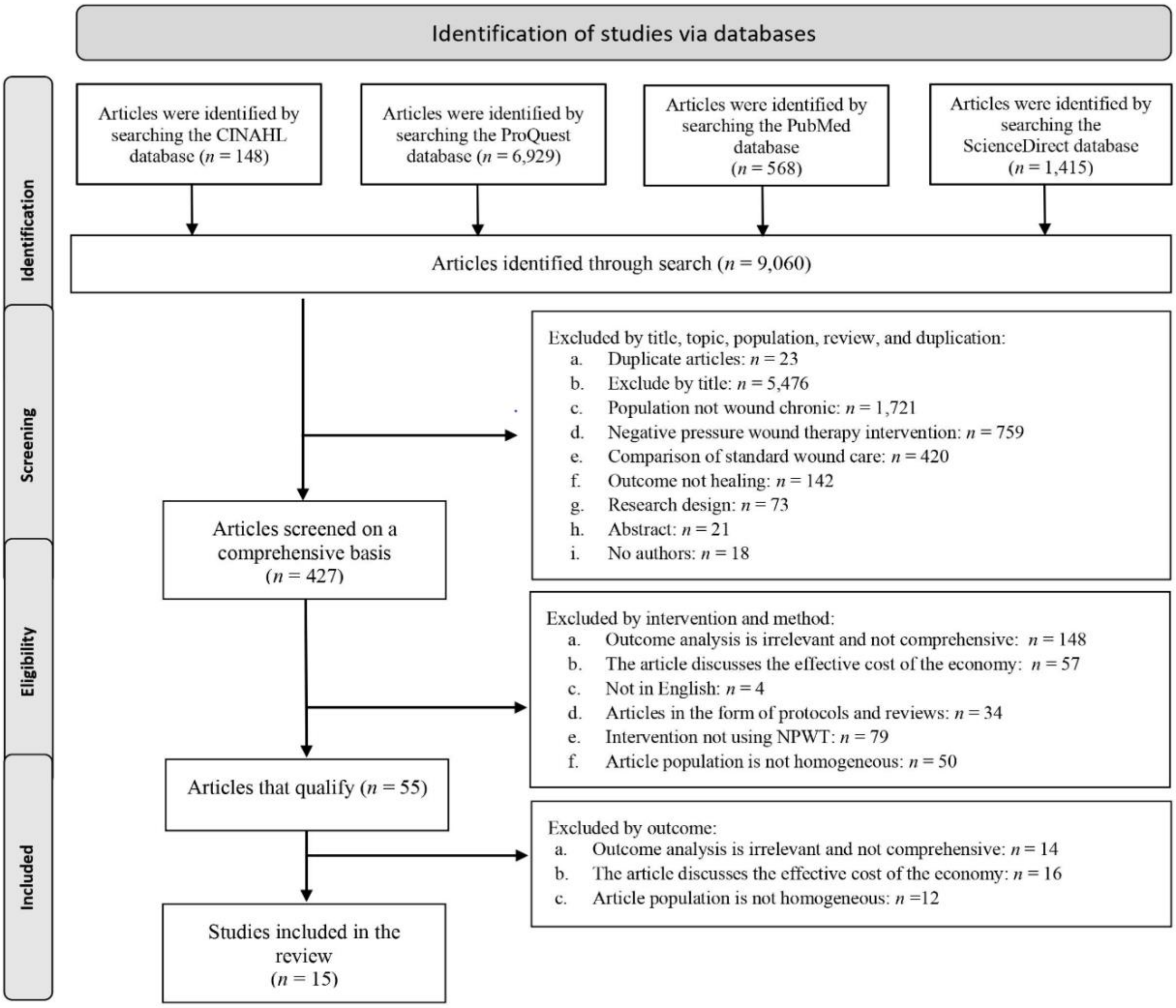

Figure 1 Identification and selection process of the studies

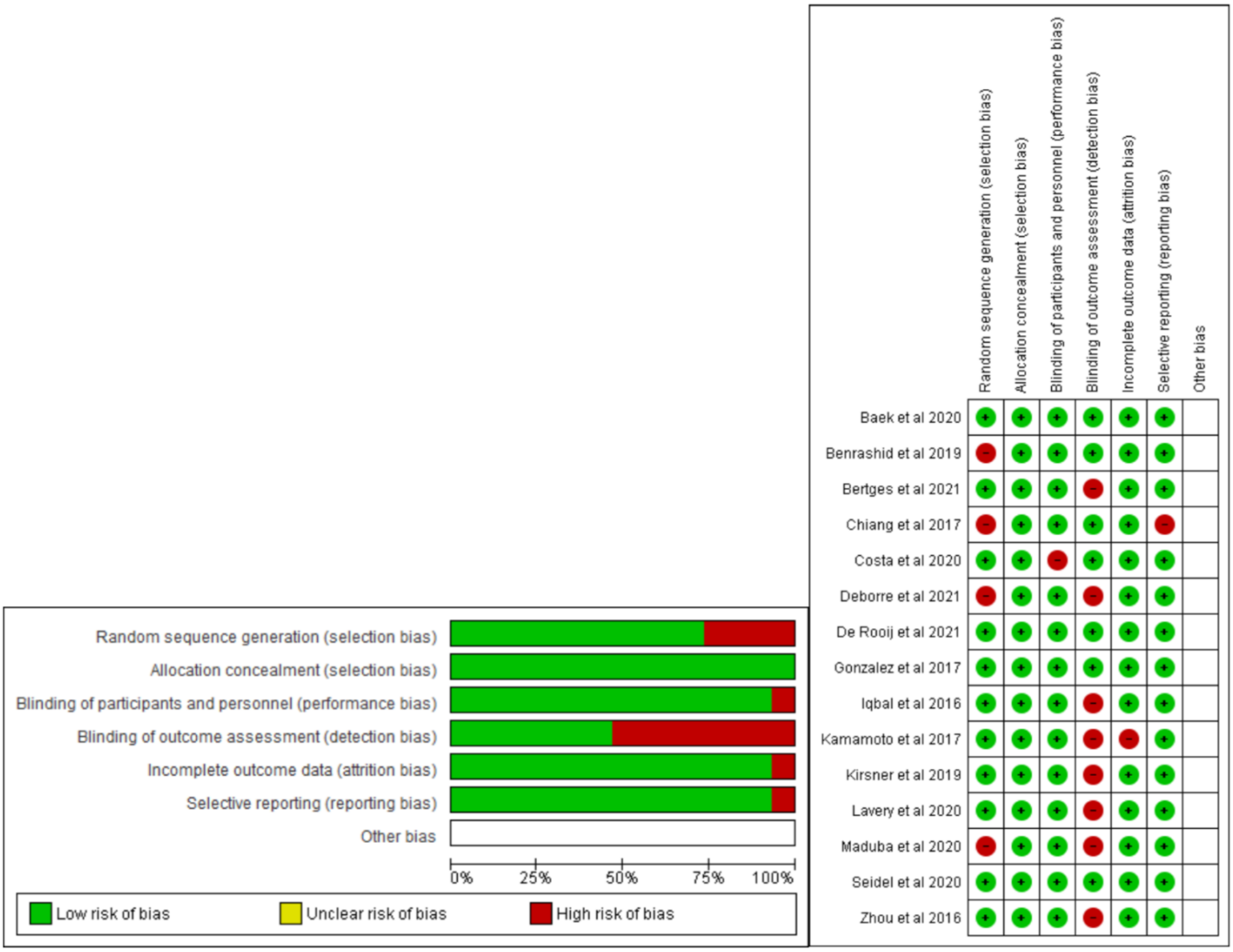

Figure 2 Risk of bias of the included studies using Rev-Man 5.4.1

Furthermore, data on the characteristics of the articles were written in the extract table, including the respondent's age, duration of injury, previous treatment intervention comprising the type, duration, and frequency, sample population, and intervention outcome.

Age

In terms of the age of the respondents in the 15 articles on NPWT in chronic wound patients, nine involved respondents aged 13-35 years (Alghadir et al., 2018; Benrashid et al., 2020; Bertges et al., 2021; Costa et al., 2020; Iqbal et al., 2016; Kamamoto et al., 2017; Kirsner et al., 2019; Lavery et al., 2020; Seidel et al., 2020; Zhou et al., 2016), while one involved those aged between 18-80 years. Meanwhile, the remaining five articles employed those aged >60 years old, namely 60 to 80 years old (Baek et al., 2020; Chiang et al., 2017; De Rooij et al., 2021; Deborre et al., 2021; Maduba et al., 2020).

Negative Pressure Wound Therapy (NPWT)

Based on the results of the literature search, several articles discussed NPWT. The first, second, and third articles focused on postoperative foot patients in the presence of surgical site infection (SSI) (Benrashid et al., 2020; Costa et al., 2020; Deborre et al., 2021), while the fourth, fifth, and sixth discussed NPWT for split skin grafts of diabetic foot ulcers on the wound healing process with a decrease in infection in vivo and in vitro (Gonzalez et al., 2017; Maduba et al., 2020; Seidel et al., 2020). Furthermore, the seventh article examined infection control in postoperative mastectomy patients (De Rooij et al., 2021), while the eighth reported vascular foot wound healing (Chiang et al., 2017). The ninth article discussed traditional methods and NPWT against chronic wounds (Kirsner et al., 2019), while the tenth, eleventh, and twelfth aimed at reducing patient hospitalizations and the development of the wound healing process, including infection, surface area, size, and differences in treatment costs (Kamamoto et al., 2017; Lavery et al., 2020). Moreover, the thirteenth article examined the healing of pressure ulcers against increased granulation and control of infection on the wound surface (Baek et al., 2020). Finally, three articles discussed the effectiveness of NPWT in increasing wound size, controlling infection, speeding up closure, and reducing hospitalization (Bertges et al., 2021; Iqbal et al., 2016; Zhou et al., 2016).

Study design, samples, and measures

Three reviewed articles were randomized control trials (RCT), while three were clinical trial (CT) studies. The first RCT study involved 164 samples with venous leg ulcers for four weeks, divided into the intervention (84 samples) and control group (80 samples) with ABI of 0.7-1.2 mmHg, TBI 30-

40 mmHg, and Bates Jensen Assessment wound Tool (Kirsner et al., 2019). The second article used the CT method comprising a sample size of n=504 with vascular incisions of the lower extremity infranguinal vein and artery with infection. They were divided into the intervention (*n* = 225) and the control group with *n* = 279, while the measuring instrument was surgical site infection (SSI) (Benrashid et al., 2020). Furthermore, the third article used the RCT method, and the samples (*n* = 62) were those that failed in the postoperative wound healing process on the legs divided into an intervention (*n* = 31) and a control group (*n* = 31) (Maduba et al., 2020). The fourth article used the same method on infected post-flaps with a total sample of 161. Moreover, they were divided into the intervention (*n* = 50) and the control group (*n* = 111) using a Surgical Site Infection measuring instrument. The fifth article used the CT design with a total sample (*n* = 36) which was classified into an intervention (*N* = 18) and a control group (*n* = 18) after minor amputation surgery. The measuring instruments were stereographic wound and hyperspectral transcutaneous oxygenation measurements and collagen markers (Chiang et al., 2017). The sixth article used the RCT method with a total sample of *n* = 1,629 that experienced post-foot debridement followed by an infection for 30 days. They were divided into two intervention groups (*n* = 813) and control groups (*n* = 816), while the measuring instruments were SSI, EuroQol, Ed-5D, and Observer scar assessment scale (1-10) (Chiang et al., 2017).

The seventh article used the RCT method on a sample (*n* = 79) with post-arthroplasty infection who experienced infection for eight days. The samples were divided into the intervention (*n* = 40) and the control group (*n* = 39), while the measuring instrument was a wound assessment (Deborre et al., 2021). The eighth article used a similar design with a total sample of *n* = 144 in diabetic ulcer patients with venous and arterial insufficiency for ten days, divided into the intervention (*n* = 72) and the control group (*n* = 72). The measuring instrument was wound assessment (Gonzalez et al., 2017). Furthermore, the ninth article used an RCT design on a total sample of *n* = 72 with post-infected complex injuries and divided into an intervention (*n* = 36) and a control group (*n* = 36). The measuring instrument was the National Institute of Health ImageJ software (Kamamoto et al., 2017).

The tenth article used a similar design with 38 samples categorized into two groups: the intervention (*n* = 19) and the control (*n* = 19) with pressure ulcer stage 3-4 and wound aged nine months. The measuring instrument was VISITRAK for the wound area (Baek et al., 2020). Moreover, the eleventh article was an RCT study on a total sample of 150 with chronic size 5-10 cm, ABI values of 0.5 mmHg, and TBI >30 mmHg. They were divided into the intervention (*n* = 75) and the control group (*n* = 75). The instruments used were Ankle Brachial Index, Skin perfusion pressure measures, and VPTT DPN (Lavery et al., 2020). The twelfth article used a similar method on a total sample of *n* = 345 with diabetic foot ulcers for four weeks, divided into the intervention (*n* = 171) and the control group (*n* = 174). The measuring instruments were the Wagner Scale, PEDIS, Frykberg Anatomical, and Ruther Classification for chronic limb ischemia, as well as CVI (Widmer 1-3) (Seidel et al., 2020).

In the thirteenth article, the study used an RCT method on a sample of *n* = 278 with open wounds of more than 2 cm, divided into the intervention (*n*= 139) and the control group (*n* = 139). The measuring instrument used was the University of Texas Health Science Center San Antonio Image Tool version 3.0 (Iqbal et al., 2016). The fourteenth article also used a similar method on a total sample of *n* = 252, namely patients undergoing surgery for peripheral artery disease who were infected for twelve weeks and were classified into an intervention (*n* = 125) and a control group (*n* = 127). The measuring instruments were surgical site infection (SSI) and EuroQol (EQ-5D-3L) (Bertges et al., 2021). Finally, the fifteenth article used the RCT method on a sample of n=76 with postoperative diabetic foot infections for twelve weeks. They were divided into the intervention (*n* = 22) and the control group (*n* = 54), while the measuring instrument was SSI (Zhou et al., 2016).

Intervention by type, frequency, and effect

Based on the literature search results, four articles were found to be related to NPWT. In the first article, the intervention was carried out in cancer patients with mastectomy for seven days with a pressure of 80 mmHg. Meanwhile, in the fourth article, the intervention in diabetic foot ulcers and infections was conducted for 7 -10 days with wound cleaning every 24 hours and NPWT pressure of 100 mmHg (Gonzalez et al., 2017; Lavery et al., 2020; Maduba et al., 2020; Zhou et al., 2016). The NPWT intervention was also performed in the sixth article for 16 weeks and monitored remotely through CVI Widmer 1-3 with a pressure of 80 mmHg (Seidel et al., 2020). In the seventh article, the intervention was carried out with layer contact on pressure ulcer stages 3-4 for three weeks with a pressure of 100 mmHg (Baek et al., 2020).

Furthermore, the second article discussed NPWT in relation to post-debridement and amputation interventions with an ABI of 0.6 mmHg, TBI >30 mmHg with a dressing change duration of 24 hours for 14 days, and a pressure of 80 mmHg (Bertges et al., 2021; Chiang et al., 2017). The tenth article focused on Venous leg ulcers and used NPWT intervention with a wound size of 0.5-10 cm2, ABI of 0.7-1.2 mmHg, TBI of 30-40 mmHg, and pressure of 80 mmHg with dressing changes every 2-3 days for 12 weeks (Kirsner et al., 2019). The eleventh article examined the lower wound extremity, with a pressure of 10 mmHg, on patients who experienced infection for 30 days with a duration of NPWT of 90 days (Costa et al., 2020). The twelfth article discussed postoperative lower extremity with 80 mmHg pressure NPWT intervention for eight days (Deborre et al., 2021). Moreover, the thirteenth article focused on giving NPWT intervention to post-trauma complex injuries for 12 days with a pressure of 80 mmHg (Kamamoto et al., 2017).

The fourteenth article evaluated the administration of NPWT at a pressure of 10 mmHg by incision of the lower extremity in the inguinal region and the distal femoral artery with infection and administration of NPWT closed surface for 90 days (Benrashid et al., 2020). Finally, the fifteenth article discussed the administration of the intervention on open wounds (>2cm) with 48 hours of dressing change for four weeks (Iqbal et al., 2016).

Table 2 Characteristics of the included studies

No	Author (year)	Study Design	Country	Disease Characteristics	Sample Size	Outcome
1	Zhou et al. (2016)	Randomized controlled clinical trial (RC-CT)	Republic of China	Diabetics foot Wound infection	76 Patients NPWT: 22 SWC: 54	The VAC intervention reduced the postoperative SSI rate in the diabetic ankle by 4.6% compared to the SMWC group of 27.8% with CI *p* = 0.002, and the length of stay in the VAC group was lower with CI *p* = 0.003.
2	Seidel et al. (2020)	RCT	Germany	Diabetic foot ulcers	345 patients NPWT: 171 SMWC: 174	SMWC application is superior to NPWT in diabetic foot ulcer patients in wound practitioners in Germany. Overall, at the stage of chronic wound closure and infection rate reduction with a mean value of 2.5%.
3	Bertges et al. (2021)	RCT	United Kingdom	Peripheral arterial disease wounds	252 patients NPWT: 125 SWC: 127	ciNPT was shown to reduce infection rates, size, and wound healing closure. There was no difference between the ciNPT and sterile gauze groups.
4	Lavery et al. (2020)	RCT	South Korea	Peripheral foot wound infection	150 Patients NPWT-I: 75 SWC: 75	The combination of WPT-I with Polyhexanide Biguanide irrigated 30 ccs per day showed no progress in reducing diabetic foot infections. With a different value for the two groups, *p* = 0.001.
5	Baek et al. (2020)	RCT	United State of America	Pressure ulcer grade 3-4	38 Patients NPWT-L: 19 SWC: 19	The combination of NWPT with the contact layer provides evidence of progress in increasing granulation and infection control and stimulates healing by reducing the size of the PU wound with a different value for the two groups, *p* = 0.001.
6	Kamamoto et al. (2017)	Prospective RCT	Brazil	Trauma complex injury	72 patients VAC: 36 SWC: 36	USP only takes 12 days for chronic wound healing, while in the NPWT group, it only takes nine days for chronic wound healing with a different CI value for the two groups with a mean value of 3.2% *p*-value of 0.379. However, this study did not show any difference in wound expansion, with a mean value of 44.18% NPWT, while SMWC/USP was 53.01% with a *p*-value of 0.934.
7	Gonzalez et al. (2017)	Prospective RCT	Mexico	Diabetics foot ulcers	144 patients NPWT: 72 SWC: 72	Administration of vat-device therapy showed the number of leukocytes, controlled wound inflammation, and a significant reduction in pain with p=0.05, the process of increasing granulation was faster than the control group *p* = 0.05, *p* = 0.003.
8	Iqbal et al. (2016)	Prospective RCT	Pakistan	Wound infection >22cm	278 Patients VAC: 139 SWMC: 139	The NPWT application proved that there was a reduction in wound size that was more effective than standard wound care with a *p*-value of 0.0064.
9	Kirsner et al. (2019)	Prospective RCT	Canada	Venous Leg Ulcers	164 Patients NPWT: 84 SMWC: 80	The application of single-use NPWT proved a significant reduction and an increase in granulation tissue with a difference between the two groups *p* = 0.05. Its wound reduction with a hazard ten scale got *p* = 0.019 with a mean value of 45%.
10	Costa et al. (2020)	Prospective randomized clinical trial	United Kingdom	Lower limb postoperative patients with infection	1629 Patients NPWT: 813 SMWC: 816	NPWT can control and reduce the high risk of infection in chronic wounds for 30 days with a mean of 11.4%, with a different value between groups of *p* = 0.04. Still, at 90 days of NPWT application & standard wound care, there was no significant difference in controlling infection on the mean surface of 5.84%, with a different value of *p* = 0.77.
11	Chiang et al. (2017)	Clinical Trial	New Zealand,	Post-amputation patients with infection	36 Patients NPWT: 18 SMWC: 18	Management of NPWT proved a reduction in wound depth on day 14 with a mean of 36%, with a different value in both groups p=0.03. Average peripheral tissue perfusion circulation will increase granulation tissue oxyhemoglobin saturation by 19.4%. Therefore, NPWT can be used to treat chronic wound healing by reducing wound depth.

Table 2 (Cont.)

12	De Rooij et al. (2021)	RCT	Netherlands	Breast cancer wound patients with infection	161 Patients NPWT: 50 SMWC:111	The application of NPWT showed that the toxic combination of Avelle in chronic post-mastectomy wounds caused fewer complications. In addition, it significantly reduced postoperative seroma, hematoma, and wound care visits with a mean of 18.9% with OR p = 0.199.
13	Maduba et al. (2020)	Clinical trial	Nigeria	Diabetic foot ulcers	62 Patients NPWT: 31 SMWC: 31	This NPWT application proves that there is a decrease in complications by 12.9% in the NPWT group, while 96.8% in the standard wound care group has a score of 7.5 times more complications than the NPWT group with a significant p-value < 0.001.
14	Benrashid et al. (2020)	Clinical trial	United Kingdom	Infraguinal vascular post op infection	504 Patents NPWT:225 SMWC:279	Administration of NPWT therapy showed a significant difference in surgical site infection (SSI) (9.8% vs. 19.0% in standard dressings; p < 0.01). There was an increase in return to the operating room in the conventional dressing group (48.3% vs. 26.2%; p < 0.01).
15	Deborre et al. (2021)	Prospective RCT	Germany	Infectious wound after arthroplasty surgery	79 Patients NPWT: 40 SMWC:39	The administration of NPWT therapy showed a significant decrease in edema, wound secretion, and a reduction in wound dressing change p = 0.017; there were differences in wound length between 14-29 in the study group and 15-34 in the control group and gradually in the process of movement/physiotherapy activities, while conventional ones were often renewed, increasing increased infection and increased hematoma.

Meta-Analysis Results

The JASPtast software was used to perform a meta-analysis on the incidence rate of adverse reactions, and relative risk was taken as the combined effect measure.

Our study results show that the included 15 studies were heterogeneous, with an I^2 value of 66.7%, Q = 41.663 (p <0.001). Therefore, the RE model was more suitable for estimating their mean effect sizes.

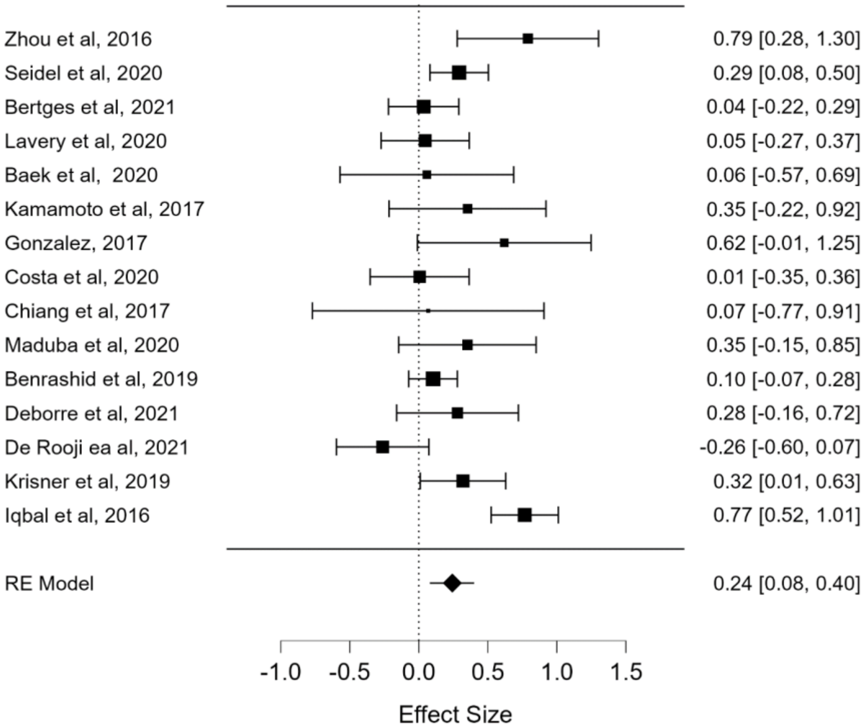

Figure 3 Forest plot

The results also indicated that the moderating variables influencing the effect of NPWT and chronic wound healing could be evaluated. Based on the RE model test, NPWT management had significant positive effects on chronic wound healing with z = 3.014, p = 0.003, CI 0.085 to 0.400 (**Figure 3**). This effect was included in the low category value based on the following classification: *(rxz = 0.822).*r = 0.1 (low); r = 0.3 (medium), r = 0.5 (high) (Hunter & Schmidt, 2000; Selya et al., 2012). In addition, there was no publication bias in this meta-analysis study seen from the results of the Egger's test value of 0.411 (p >0.05), a symmetrical funnel plot (**Figure 4**), and Fail-safe N of 137 (>5K + 10). A reasonable guideline for discounting publication bias is if the fail-safe N exceeds 5K + 10, where K is the number of studies (Rosenthal, 1984).

The forest plot shows an effect size (ES) of 0.24, with 95% CI varied from -0.26 to 0.79, indicating a low significant effect (**Figure 3**).

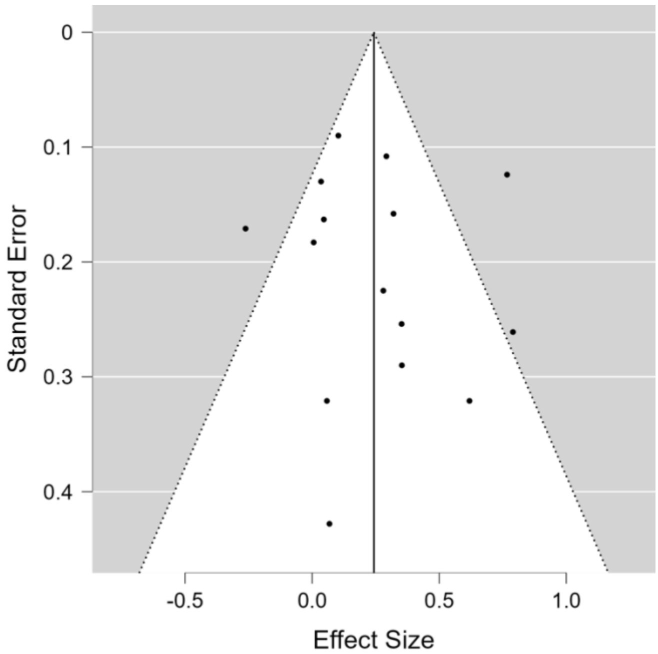

Figure 4 Funnel plot

Discussion

A few well-designed and conducted studies with a wide range of pressure ranging from 80 -125 mmHg and durations of use from 2 weeks to 25 weeks were found to evaluate this technology in a hospital setting. Based on the results, most studies showed low methods and outcome points yields, as indicated in **Figure 2**, while low publication bias was also identified. The studies included are those that identified patients with chronic wound care in hospitals, use of the NPWT intervention pressure, and consistent with guidelines for the RCT method (**Table 2**). Several studies have demonstrated a well-identified comparison group in the randomization and intervention system. Therefore, it can be concluded that proper use will improve the healing process of chronic wounds. A systematic review recommended debridement before the use of NPWT for maximum results (Janssen et al., 2016). Based on the results, this study confirms the effect of the NPWT program in chronic wound care.

The results showed that the intervention program compared to usual care, was very helpful in improving the treatment outcome, such as infection control, reduction of pain, exudate, edema, vascularization, granulation, and healing time. However, a previous systematic review stated that NPWT is not relevant for long-term use in chronic wound care (Rhee et al., 2015). Based on the meta-analysis results, there was an average wound infection control and differences in chronic wound healing between the intervention and control groups. This positive post-discharge outcome might be related to the presence of controlled influencing factors and the characteristics of the wound condition, with the correspondence between various wound care professionals being the segment responsible for the several benefits (Chen et al., 2019).

Using NPWT technology for wound healing complications can solve problems in managing chronic wound care. All studies reported a reduction in postoperative and chronic wound infection scores (Benrashid et al., 2020; Bertges et al., 2021; Costa et al., 2020; Gonzalez et al., 2017; Lavery et al., 2020; Seidel et al., 2020; Zhou et al., 2016). NPWT can also reduce dressing changes, hence, it provides an opportunity for increased granulation, but in all studies, debridement interventions were performed before the use of NPWT (Yoon & Kim, 2021). There is a need to increase the competence of wound nurses with the help of NPWT technology in solving chronic wound care problems.

Moreover, a decrease in pain intensity was found with the application of NPWT, but reduced dressing changes caused pain. Frequent dressing changes can activate the body's stress response and interfere with the typical wound-healing cascade. This is also in line with Sandoz (2015), which stated that the intensity of patient pain when changing dressings could prevent granulation damage, minimize bleeding and limit the dehiscence of surgical incisions with infections that control bacterial metabolism, thereby reducing pain intensity in the wound area. Furthermore, foam in NPWT can reduce wound staging and bioburden, hence controlling significant sources of pain during dressing changes (Yoon & Kim, 2021). The development of technology in wound care is an opportunity for the future, one of which is to control factors that can cause the duration of chronic wound healing.

Liu et al. (2018) confirmed reviews focused on treating infected and post-amputation surgical wounds in hospitals. The results indicate gaps in earlier studies, specifically regarding the stage of assessing wound degree, length and width, use of pressure, duration, and alternation of interventions, which were significantly different from several studies. Wound assessment, protocols, and procedures for appropriate NPWT can support future chronic wound care management. This is achieved through the use of randomization, blinded participants, staff, analysis process, and outcome, systematic use of PICOs starting from population identification, intervention characteristics, and appropriate and precise comparison with valid results to support the consistency of further investigations. In addition, the characteristics of intervention tools need to be considered because they affect the results of the chronic wound healing process.

The average use of pressure ranged from 80-125 mmHg with varying duration of wound healing within two weeks of NPWT. The intervention can control infection, reduce pain intensity when changing dressings, facilitate peripheral vascularization, prevent edema formation, and increase granulation with faster healing time. These results are in line with Agarwal et al. (2019), which reported that a pressure of 50 – 125 mmHg stabilizes the wound environment, reduces wound edema/bacterial load, increases tissue perfusion, and stimulates granulation tissue and angiogenesis in chronic wound patients. This is achieved by maximally channeling oxygen and nutrients to peripheral tissues, thereby accelerating the process of angiogenesis (Matiasek et al., 2018). Furthermore, cell migration activity within cells occurs through the upregulation of proteins. High glucose intervention significantly reduces the negative pressure effect on cells, which can improve chronic wound healing by reducing peripheral blood and wound tissue expression, thereby enhancing the epithelialization process (Liu et al., 2018).

This meta-analysis review was conducted to evaluate the efficacy and safety of NPWT for treating chronic wounds. Based on the results, it can be concluded that the healing of infected wounds and diabetes-associated chronic and limb wounds is accelerated using NPWT. The evidence for its efficacy in various other acute and chronic wounds is promising for reducing stress due to reduced pain during dressing changes. However, it remains of insufficient quality to serve as a basis for general long-term policy decisions considering the patient's condition of use. Evidence of the benefit of NPWT for the treatment of pressure ulcers, pressure ulcers, and postoperative wound infections remains the standard of wound care.

Implications of the Study

The results provide a better understanding of NPWT use in chronic wound management. However, before using this intervention, nurses should enhance their competence in chronic wound care, including wound assessment, debridement management, and evaluation. Nurses also need to review the practical applications of NPWT, including prescribing prescriptions, procedural steps, general patient care, and tips for dealing with device problems. Our study findings confirm that treatment with NPWT focuses more on microcirculation improvement, wound surface infection control, and chronic wound healing.

Limitations of the Study

This study examined the effectiveness of NPWT in an outpatient setting, which could increase difficulties in the chronic wound healing process. Although this review presents strong evidence with targeted test study plans and outcome estimates to suggest future technological developments for chronic wound care, there were several potential limitations. These included the involvement of small studies, keyword searches, limited English articles, and various outcome measures, while heterogeneity was also observed in some studies. Besides, a common criticism of meta-analyses is that several types of studies are combined in similar investigations; hence, the overall impact might overlook significant differences across studies. This bias of this study was assessed using measurements from the results of the meta-analysis.

Conclusion

NPWT is an effective and potential therapeutic modality in facilitating chronic wound healing. However, debridement and wound care need to be carried out before its application to the wound. The study results showed a low significant effect on wound healing factors in the level of infection, pain quality, frequency of exudate, oxygen demand in peripheral tissues, and frequency of dressing changes. Infection, pain, and exudate can be minimized, which are investigation priorities. Several factors can affect the results of NPWT, namely pressures of 80-125 mmHg with foam for two weeks, indicating accelerated exudate control, increased granulation, and development of epithelialization. However, the current investigation base is underdeveloped, and studies into the impact of oxygen on wound peripheral tissues are lacking. Factors for using different medications to reduce pain caused by wounds need to be identified. Furthermore, investigators need to consider the quality of pain and tissue oxygen demand during the various stages of NPWT to enhance their effect on chronic wound healing.

Declaration of Conflicting Interest

The authors declared no conflict of interest.

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Authors' Contributions

All authors contributed equally to the conception and design of the study, databases search, methodology, data extraction, analysis of the risk of bias, data analysis, interpretation, review, and editing. All authors were accountable in each stage of the study and agreed with the final version of the manuscript to be published.

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Data Availability

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

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