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Complete List of Authors:	Greenall, Richard; King's College Hospital NHS Foundation Trust, Executive Offices, Princess Royal University Hospital, Farnborough, BR6 8ND Davis, Rachel; King's College London, Centre for Implementation Science , Health Services and Population Research Department, Institute of Psychiatry, Psychology and Neuroscience
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Intermittent pneumatic compression for venous thromboembolism prevention: a systematic review on factors affecting adherence

Authors

Richard Greenall, BSc, MSc[1]
Rachel Davis, BSc, MSc, PhD[2]

[1]King's College Hospital NHS Foundation Trust
Executive Offices
Princess Royal University Hospital
Farnborough
BR6 8ND
Email: writetorichg@gmail.com

Centre for Implementation Science
[2]Health Services and Population Research Department,
Institute of Psychiatry, Psychology and Neuroscience
King's College London
2nd Floor, Room E2.19
16 De Crespigny Park
Denmark Hill
LONDON
SE5 8AF
Email: rachel.davis@kcl.ac.uk

Corresponding author: Richard Greenall

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None declared

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RG and RD designed the paper and were responsible for its conceptualisation. RG drafted the paper and RD edited it. Both authors were involved in the screening of the articles included in the review and have read and approved the final version of the manuscript.

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Abstract

Objective Venous thromboembolism (VTE) is a potentially fatal complication of hospitalisation. Intermittent pneumatic compression (IPC) is one approach to reducing the likelihood of a VTE. Adherence to IPC is known to be inadequate though the reasons for this remain unclear. This systematic review explores factors that affect adherence to IPC in the inpatient context.

Methods EMBASE, MEDLINE and PsycINFO were searched for literature between 1960-2019. Studies were included if they focused on inpatient care and examined factors affecting adherence to IPC devices.

Results A total of 20 out of 1476 studies were included. Eight factors were identified that affected adherence: patient discomfort (n=8), healthcare professionals' knowledge and behaviours (n=6), mobilisation (n=6), equipment supply and demand (n=3), the use of guidelines (n=3), intensive care context (n=2), computer-assisted prescribing (n=2) and patients' knowledge of IPC (n=1).

Conclusion Overall while the evidence base is quite limited, a number of factors were shown to affect adherence to IPC. These findings could be used to inform future research and quality improvement efforts to increase adherence in this very important, but currently under-researched area.

Keywords; Intermittent pneumatic compression, adherence, compliance, thromboprophylaxis, venous thromboembolism, VTE, deep vein thrombosis, pulmonary embolism

Strengths and limitations

- First known review of the evidence affecting adherence to IPC
- Eight factors were identified that resulted in measurable changes to adherence to IPC
- Results largely based on direct observation rather than self-report
- Studies generally had low sample sizes
- Studies with different aims and methodologies were included.

Background

Venous thromboembolism (VTE) is a term that most commonly refers to deep vein thrombosis (DVT) and pulmonary embolism (PE). VTE affects 1 in 1000 people annually[1] and in England in 2018 VTE was recorded as a cause of death in 12,000 cases[2]. Compared to baseline risk, hospitalisation has been correlated with an 8-fold increased risk of VTE in medical admissions and a 21-fold increased risk in surgical admissions[3] with one study estimating that up to 50% of 625 cases of VTE in the community were related to hospitalisation[4]. Secondary to adverse drug events, VTE is the leading complication of hospitalisation worldwide[5].

The financial cost of hospital associated VTE is high. In 2017, a UK survey revealed the average cost of treating VTE was £938,357 for each local NHS region[6]. At a patient level, a review[7] identified an increase in cost of $14,000 for initial diagnosis and the first year of treatment for those with VTE compared with non-VTE affected patients. VTE can have a significant impact on a person's psychosocial well-being with research to suggest that it can be a traumatic, life-changing event which can lead to post traumatic stress disorder[8,9].

Since hospitalisation increases the risk of VTE, it is important to consider if anything can be done to reduce the risk within this context. In England, the national VTE prevention programme combined a mandate for assessment of patient's risk on admission to hospital with best practice prevention guidelines. Early results indicate that its efforts have led to reduced morbidity and mortality[10]. Similar efforts have been made in the USA [11] and throughout Europe, recent evidence indicates that better management of the risk of VTE has reduced VTE related mortality from 12.8 to 6.5 deaths per hundred thousand[12].

Risk assessing all patients on admission to hospital leads to identification of patients at high risk who need thromboprophylaxis (i.e. treatments to prevent VTE). In the UK, national guidelines[13] advise using the chemical thromboprophylaxis low molecular weight heparin for most groups of at-risk hospitalised patients. Mechanical thromboprophylaxis is advised for most surgical patients and other

high-risk groups, such as patients with stroke. Graduated compression stockings (GCS) are one type of mechanical intervention. GCS exerts graded pressure around the legs, increasing the speed of blood flow and reducing the opportunity for VTE to form.

Intermittent pneumatic compression (IPC) is another type of mechanical device. Fabric sleeves that wrap around a patient's legs are attached to a pump using a tube and are periodically inflated and deflated. IPC is thought to reduce VTE by increasing the speed of blood flow and reducing hypercoagulability through the IPC action stimulating the vessel walls fibrinolytic activity[14,15]. Combining IPC and GCS decreases the incidence of VTE to a greater effect than either individually[16] and a systematic review found that that IPC can reduce the incidence of VTE in surgical patients (risk ratio 1.39, CI 0.73-2.64)[17]. However, despite these benefits, research has shown considerable variability in adherence to IPC device use, with a systematic review of 7 studies in acute hospitals reporting a median adherence rate of 78% (range 40%-89%)[18]. The authors concluded that strategies to improve adherence are needed but the question remains as to why non-adherence occurs.

To the best of our knowledge, no attempt has been made to comprehensively investigate the factors that could facilitate or impede adherence to IPC. This paper aims to address this important gap in the evidence base by systematically reviewing the factors that influence adherence to IPC for VTE prevention in acute care. Gaining this understanding is critical in order to develop interventions, strategies and policies that are accurately targeted at meeting the challenges of improving adherence[19].

Methods

Patient and public involvement

No patient invovled

Search strategy

EMBASE, MEDLINE and PsycINFO were searched for relevant literature published between 1960 - 2019. The search strategy comprised terms relating to: 1) population (e.g. 'IPC'); 2) Intervention (e.g. 'strategies') and; 3) outcomes (e.g. 'adherence'). The search was customized to each database and restricted to titles and abstracts to tighten its specificity. A sensitivity analysis was performed to ensure the search results included key articles identified through an initial scoping review. Forward

and backward citation searching and hand searching of key journals were performed to minimize the likelihood of missing relevant papers. The final search was conducted on 30th May 2019 (for the full search strategy please refer to Supplementary file 1).

Inclusion criteria

Based on UK national guidelines that were current at the time of this review's development (January 2018) [13], the definition of IPC in this review includes only devices that are applied to the legs and excludes foot compression devices. The first stage of screening (title and abstract) was intentionally inclusive and retained any empirical articles that mentioned adherence to IPC in any context. In the second stage (full text), tighter restrictions applied. Articles were included if they reported barriers or facilitators to adherence to IPC in the inpatient context and included a measure of the effect (percentage change in adherence to IPC) of such factors on adherence (either as a primary or secondary aim or an indirect finding in the results). Dissertations and doctoral theses, books, book reviews, conference posters and presentations, editorials and commentaries were excluded, as were articles not published in English or those focused on patients under 18 years of age. Review/commentary papers that addressed adherence to IPC[18] were examined for relevant empirical papers but the reviews themselves were excluded.

Study selection and data extraction

Articles were screened for relevance by the lead author (RG). The second author (RD) screened 20% of the articles at abstract stage and 100% at full-text stage. Discrepancies were resolved through joint discussion between the authors. Dual data extraction of the included articles was conducted independently by both authors and then checked for consistency.

Quality Assessment

While numerous scales are available to assess the methodological quality of studies, these are often restricted to specific study designs, including randomised controlled trials[20]; case-control and cohort studies[21]; and qualitative studies[22]. Given our review included articles that employed heterogeneous study designs and differing aims, we did not use a quality assessment scale, nor did we deem this meaningful. We did however consider differences in the methodologies that could potentially bias the findings to enable greater understanding of the relative strengths and weaknesses of the research. To gain a comprehensive understanding of the full body of evidence, we did not exclude articles based on their methodological quality.

Results

Study selection

Of 1476 articles retrieved, 1324 were excluded at the first stage of screening (title/abstract) and 132 (out of the remaining 152) were excluded after full-text screening, resulting in 20 articles. Two of the included articles were added through handsearching[23,24] (see Figure 1). Upon examination, these studies were missed in the initial search due to the use of the word 'external' instead of 'intermittent' to describe pneumatic compression. Further scoping the literature (using the term 'external') revealed there were no other additional articles that needed to be included.

Insert Figure 1 here

Characteristics of included studies

Articles were published between 1992 and 2018 across 6 countries, including the USA (n= 15[23-37]), Spain (n= 1[38]), Japan (n=1[39]), Canada (n=1[40]), France (n=1[16]) and Brazil (n=1[41]). Characteristics of patients and care locations included critical care[16,24,27,38,39], general surgical wards[26,31-33,36,40,41] and gynaecology[23,34,35,37] specialties. Factors affecting adherence to IPC was the primary focus of 13 studies[23,25-32,34,35,37,38]. A further 7 studies[16,24,33,36,39-41] focused on IPC device safety and effectiveness in preventing VTE but also reported barriers or facilitators to IPC adherence. Seventeen of the studies were observational[24-39,41], using surveys and clinical observations as investigation tools. The remaining three studies were RCTs[16,23,40]. Due to wide heterogeneity in study methodologies, meta-analysis was not possible. Table 1 details the characteristics of the included studies.

Insert table 1 here

Factors affecting adherence to IPC

Articles varied considerably in the level of content and detail provided regarding study designs and adherence to IPC. We report the main findings here and provide a more detailed analysis of findings for studies where this was possible. Table 2 outlines the 8 factors that were identified that affected adherence to IPC.

Insert table 2 here

1. *Patient discomfort*

Patient discomfort associated with wearing the IPC device was identified in 8 studies[16,25,26,28,29,33,37,40]. Vignon[16] identified poor adherence in 7% (14/204) of patients due to discomfort, noise and restlessness. Brady[28] observed the effect of the length of the IPC sleeve on comfort and subsequent non-adherence. Overall adherence was 29% (40/137) based on a one-off observation. Eighty-five percent of non-adherent users had been wearing thigh length (53%) or knee length (32%) sleeves. Discomfort was reported as a reason for non-adherence by 39% (58/149) of patients who were non-adherent. Those wearing thigh length sleeves reported double the number of complaints compared to those wearing knee length sleeves (39 vs 15).

Brady[37] examined adherence over several days post-operatively. Taking multiple observations of the same patients, adherence was 75% (43/57) on day zero, 53% (148/278) on day 2, and 44% (11/25) on day 4. Patients who were non-adherent were asked why at the time of observation and 15% (53/362 responses) stated discomfort as a reason. Kim[25] compared two groups of 100 patients in a multifaceted improvement strategy to increase adherence to IPC. Post intervention a slight improvement was achieved (24% versus 26%). Ninety-two percent of nurses (58/63) and 29% (4/14) of non-adherent patients reported discomfort as a reason for the lack of adherence.

Ritsema[26] found that patients were non-adherent 21% of the time (98/457 observations) with patient interviews indicating that discomfort was a reason in 19% (19/100) of responses. Sobieraj-Teague[40] trialled the efficacy of a newly developed IPC machine which allowed the patient to mobilise independently of a power cable through the utilisation of batteries and small product design. Poor adherence was found in 49% of users (35/72), in particular at night, with patients reported they discontinued therapy due to insomnia. Similar findings, but to a much lesser extent were reported by Cindolo(29) when evaluating the comfort and tolerability of a specific IPC device. While non-adherence was only 3% (6/184), patients who requested discontinuation of IPC therapy did so due to noise and insomnia.

A final study by Obi[33] was designed as a retrospective review examining whether a different design of IPC device would reduce non-adherence. Comparing a standard machine to a new machine, adherence to the standard machine was 47% versus 85% for the newer machine. Of responses from those patients wearing the standard compared to the new machine (21 and 24 respectively), problems with discomfort as reported less (33% vs. 13%).

2. Healthcare professional knowledge and behaviours

Failure of healthcare professionals to apply or provide IPC when prescribed was identified in 6 studies[23,28,30,31,36,37]. Brady[28] found that 16% (12/73) of survey respondents reported that the nurse

had never initiated IPC therapy or had not replaced the sleeves after transfer of the patient from another location. Brady[37] found that 23% (82/356) of non-adherent patients stated the nurse had informed them that they did not require IPC anymore.

Cornwell[36] observed adherence of 53% (out of 712/1343 observations of 233 patients). The authors reported that this was because the device was 'not in place'. The time of day that non-adherence was most frequently noted was in the early afternoon and the authors concluded that it is both HCPs and patients who need to be educated about the importance of wearing IPC as the patient may have been the one who removed it.

Elphern[30] reported that errors in the application of IPC therapy were identified in 49% (477/966) of observations of a cohort of 123 patients. In 244 observations the sleeves were incorrectly applied to the patient and in 116 observations the pump was not turned on. Similar findings by Maxwell[23] in 104 patients identified that the reason for non-adherence in 3% (20/736) of observations was that the IPC was not turned on. Gardiner[31] reported that only 26% (89/339) of patients were adherent to IPC on initial audit. A survey of nursing beliefs, practice and knowledge determined that part of the problem was deficiencies in nursing knowledge. Education interventions as well as placing IPC machines in individual rooms of patients improved adherence from 26% to 44%.

3. Mobilisation

Issues relating to mobilisation were identified as factors affecting adherence in 6 studies[26,28,33,34,37,38]. Brady[28], found that of 149 responses from non-adherent patients, 46% (68/149) of patients reported that they had just mobilised. Similarly, Brady[37] found that 16% (59/362) of patients reported that they had just been walking around, 17% (62/362) stated they had just returned to bed and 7% (24/362) were just about to walk around. In a study by Ritsema[26] previously discussed in relation to patient discomfort, patient's identified that not replacing the IPC sleeves after mobilisation was a cause of non-adherence in 50% of 98 non-adherent episodes observed.

Palmerola[34] found adherence to IPC after caesarean delivery was 79.5% (233/293). Of the 60 non-adherent patients, 62% (37/60) had the IPC machine and sleeves in the room but they were not applied and 38% (23/60) had it discontinued due to "*liberal standards for mobilisation*". A study by Obi[33] previously discussed in relation to 'patient discomfort' found that problems with mobilising were reported less using a new machine compared to a standard one (71% vs. 29%). Garcia Olivares[38] found that complete bed rest for >2 days resulted in improved appropriateness of prophylaxis (OR 0.6) with similar findings reported for mechanical ventilation (OR 0.7).

4. Equipment supply and demand

Three studies[26,31,37] highlighted that equipment supply and demand could affect adherence. Brady[37] identified that part of the IPC device was not present in the room in 13% (49/362) of non-adherent episodes although reasons why were not explored. Similar findings by Ritsema[26] found that the second most commonly report reason for non-adherence was no machine or sleeves being available to the patient (22/100 questionnaire responses). As previously discussed within 'healthcare professionals knowledge and behaviours', a study by Gardiner[31] revealed that of 250 patients who were non-adherent, 39% (97/250) did not have part of the equipment in the room. This same study found that adherence increased from 26% to 44% through an educational intervention and making IPC machines widely available instead of difficult to obtain for use.

5. Guidelines

The use of guidelines for VTE prevention was identified as a factor that could affect adherence in 3 studies[38,39,41]. Garcia Olivares[38] used an electronic questionnaire to investigate inappropriateness of VTE prophylaxis (all types) on a single day across multiple ICUs. A total of 777 patients across 73 ICUs were included: the use of a protocol reduced inappropriate VTE prevention prescribing (OR 0.6) as well as a VTE risk scoring system (OR 0.4). Yammamoto[39] obtained data from 99 ICUs and included 470 patients in their analysis. Hospitals using protocols had higher rates of prophylaxis provision than those who did not (89% vs. 80%) and this difference was mainly due to the increase in the combined use of anti-embolic stockings and IPC (26% vs. 15%). A similar effect was demonstrated by Maffei[41] who retrospectively analysed the accuracy of prescribing of VTE prophylaxis after the implementation of guidelines. Compared to before the implementation of guidelines, prescribing of IPC therapy increased from 26% to 32% after.

6. Intensive care context

Care provision in the intensive care unit (ICU) context was identified by two studies as having an impact on adherence[24,27]. Comerota[24] examined 138 patients and found that adherence in the intensive care unit (ICU) setting was higher than elsewhere in the hospital (78% vs. 48%) but did not investigate reasons for this. A study by Bockheim[27] found adherence in the ICU context was 69% (52/75) compared to 40% (30/75) outside of the ICU. The authors concluded the reasons for this were likely to be multifactorial they did not empirically determine what these factors might be.

7. Computer-assisted prescribing

Computer-assisted prescribing was reported as a factor affecting adherence in 2 studies[32,35]. Chen[35] examined the long-term impact of automatic pre-orders for IPC on an electronic prescription system.

Prior to the intervention, prescribing of IPC was carried out on 46% (denominator not reported) of patients. One year later, this had increased to 78% (59/76). IPC was only present in 71% (42/59) of patients who had been prescribed IPC and was only being used by 45% (19/42) of those patients. The authors concluded that the intervention had successfully increased prescribing of IPC but not overall adherence.

Novis[32] utilised a similar approach but did not assess the impact of adherence to IPC at a patient level. Computer generated suggestions of pre-operative prophylaxis were provided to the clinician as a result of information entered about the risk of VTE to the patient. The result was a 40% increase in prescribing of IPC from 215 to 301 patients with an active prescription.

8. Patient knowledge

A study by Kim[25] concluded that the information needs of patients were a factor affecting adherence. An initial survey found that 59% (32/54) of patients did not have IPC applied when prescribed. Several clinician-focused interventions were conducted, and a survey of patients a year later found that 62% (41/66) of patients requiring IPC therapy did not have it applied. From this, thirty percent (11/37) of patients reported that they did not know what a DVT is and 62% (23/37) reported that they had not been educated about IPC. The authors conclude that a lack of education is an important barrier to adherence however evidence to demonstrate that increasing education results in improved adherence was not presented.

Quality Assessment

Seventeen[24-39,41] (out of the 20) articles included in the review were observational in nature. All of these studies (n=17) measured adherence to IPC by direct observation of researchers rather than based on self-report, which could have been subject to recall bias. Eight of these studies measured adherence twice daily[23,24,26,27,31,35,37,40], 3 had a single observation point (the first day post operatively[29,34] and not reported[28]), 1[33] had hourly monitoring across a 24 hour period, and 1[16] did not report when they observed adherence, only that they did this. In addition to direct observations, data on factors affecting adherence using patient surveys was performed in 8 studies[16,23,25,26,28,29,37,40] and indirect indicators such as the effect of a change in device type or the result of a guideline implementation was used in 7 studies[24,27,32,33,35,41]. The 3 RCTs[16,23,40] collected data on adherence using researcher observations and patient surveys

Over half of the articles[23,25-32,34,35,37,38] (n=13) focused on factors affecting adherence to IPC as a primary outcome. The remaining studies[16,24,33,36,39-41] (n=7) investigated as the safety and

effectiveness of IPC as their main outcome. As a result of these investigations, these studies also provided data on factors affecting adherence (though this was not their aim). It is difficult to determine whether additional factors may have been uncovered from these studies (i.e. that are not reported in our findings) if the authors had specifically set out to examine how adherence to IPC could be affected. Taken collectively, the patient sample sizes for each study ranged from between 67[33] to 800[32] with the majority of studies being based on over 100 patients. Articles we included were published across a 27-year period.

Discussion

This paper presents the findings of a systematic review on factors affecting adherence to IPC in the inpatient setting. In total eight factors were identified that affected adherence, with patient discomfort related to wearing the IPC device being most commonly reported and issues related to computer assisted prescribing and patients' knowledge of IPC being the least frequently reported. The majority of factors delineated (such as patient discomfort, mobilising, healthcare professional knowledge and behaviours, patient knowledge, equipment supply and demand) acted as a barrier to adherence to IPC. However, some evidence points to specific facilitators of adherence (for example the use of guidelines and protocols and computer-assisted prescribing).

There are several strengths of this review. To the best of our knowledge, this is the only paper of its kind to systematically review the evidence on factors affecting adherence to IPC. Wider research within the field that has reviewed the literature relating to IPC adherence found a median adherence rate of 78% [18]. The review concluded that strategies to improve adherence are required. Our review helps to address this important gap in the evidence, shedding light on potential indicators of issue.
The evidence in our review was derived from articles that provided an actual measure of adherence in clinical settings and the subsequent factors that could help to explain these adherence rates. Many of the factors relating to adherence were based on direct observation rather than self-report.

A caveat to mention when interpreting our findings is that while data were based on quite a large body of evidence, there were differing (and sometimes low) sample sizes as well as different aims and methodologies and countries and settings of focus. Included studies were also spread over a long period of time (twenty-seven years), in which policies and procedures around IPC may have changed. Equally most of the factors affecting adherence were only reported a few times. While, admittedly this was not the primary aim of the studies included in our review, but rather was reported as

secondary finding in relation to explaining adherence rates, further work is required to understand the relative strength of the evidence. Nonetheless, this review provides a useful first step to delineating important (and perhaps otherwise empirically unknown) factors affecting adherence to IPC. These findings could be used to help inform, implement and evaluate the use of specific strategies to overcome factors causing adherence-related issues.

There are several important implications of this work. First, discomfort with the IPC device was a considerable cause for non-adherence. The development and/or use of new or alternative IPC devices should be considered when addressing adherence issues. Research more widely in the field, that examined the use of a modern IPC device lends support for this view[42] with 86% (26/30) of patients reporting it was comfortable and that they would use it again if required. Two studies[33,40] within this review reported adherence levels when studying different machine designs and one study focused on the length of IPC sleeve[28] and its effect on adherence. There is therefore scope for further research using a randomised control study design to assess widely used IPC machines, the length of sleeves and the effect both factors have on adherence, particularly in relation to comfort.

Second, and related to the above point, mobility was often reported as a barrier to adherence. One likely explanation for this could be that it was uncomfortable for patient to mobilise while wearing the device, so for this reason it was removed. Evidence[24,27] from our review revealed that adherence was less of an issue for those patients that were unable to move around. However, IPC is designed to promote blood flow during immobility and if a patient is mobile, it could be concluded that IPC is no longer required and thus would not meet the criteria for data being collected as adherent or not. While this is a point that warrants further investigation, our findings suggest this could be why mobilisation (perhaps wrongly so) was identified as an adherence-related issue. Within the wider literature, a systematic review[43] on the definition used for immobility within thromboprophylaxis studies concluded that a lack of consistency in the definition of immobility may contribute to the underutilisation of thromboprophylaxis in clinical practice. In our review, the definition of mobility to the extent that IPC was no longer required was not stated by any of our included studies. In place of a widely agreed consensus, an institution-wide definition of mobility could assist individual hospitals to ensure that best practice is promoted in relation to IPC adherence.

Third, we found that HCP knowledge and beliefs could contribute to non-adherence. It is not clear from our studies whether on those occasions when an IPC device was not fitted, the reasons related more to the HCP not knowing they needed to do this, whether they simply forget, or whether there

has been some other unknown issue. While this warrants further investigations, there are some relatively straightforward strategies that could be put in place, based on our preliminary findings. For example, prompts and educational leaflets could be distributed on the hospital wards to remind HCPs when the use of IPC is required and why this is important. Training is essential if optimal adherence levels are to be achieved and maintained. Equally, ensuring the layout of the ward allows easy accessibility of equipment (such as IPC) is also important, particularly, given our review revealed this to be a determinant of adherence.

Finally, our review revealed that the use of guidelines and how they are incorporated into electronic prescribing systems could act as a facilitator to adherence. Similar findings (which examined, in part the use of pre-printed orders) have been reported in a review of the barriers and facilitators to adherence to chemical thromboprophylaxis[44] within the ICU setting. Additional research that examined how electronic prescribing can lead to a reduction in errors, identified an absolute risk reduction of up to 30%[45]. Together with the evidence in this review, it could be concluded that if IPC prescribing is included in electronic prescribing systems, improvements in adherence to guidelines may be achieved.

Conclusion

This systematic review set out to uncover the factors that affect adherence to IPC for VTE prevention in acute care. Gaining this understanding is critical in order to develop interventions, strategies and policies which are accurately targeted at meeting the challenges of improving adherence[19]. While our review has addressed an important gap in the evidence base and taken the first steps to understanding reasons why non-adherence to IPC may occur, it is clear more research is required in this area to further understand the relative strength of the evidence, so that effective strategies to overcome barriers to adherence can be sought.

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Table 1: Characteristics of included studies

Author	Study design	Setting	Studies main objective	Focus was adherence barriers / facilitators?	Sample size	Participants (mean age)	Country
Bockheim 2009 (27)	Prospective observational	Critical care & Ward care	Comparison of IPC compliance between ICU and non ICU areas	Yes	150	Female 73, Male 77 (62)	USA
Brady 2007 (28)	Prospective observational	Acute nursing care wards	To assess comfort and fit and compliance of knee vs thigh length IPC	Yes	137	Female 72, Male 65 (55)	USA
Brady 2015 (37)	Prospective observational	Caesarean or gynaecological surgery	To assess impact of education on compliance to IPC	Yes	228	Female 59 (38)	USA
Chen 2019 (35)	Prospective observational	Obstetrics	Assess the effectiveness of an intervention in improving compliance to IPC	Yes	76	Female 76 (28)	USA
Cindolo 2009 (29)	Prospective observational	Radical retropubic prostatectomy surgery	To assess acceptability and satisfaction to IPC	Yes	184	Male 184 (69)	USA
Comerota 1992 (24)	Prospective observational	Critical care & Ward care	Comparison of IPC compliance between ICU and non ICU areas	No	138	Not reported	USA
Cornwell 2002 (36)	Prospective observational	Surgical trauma	To assess compliance of IPC in trauma patients	No	227	Female 39, Male 188 (37)	USA
Elphern 2013 (30)	Prospective observational	Critical care	Identifying reasons for errors in the application of IPC	Yes	123	Female 42, Male 54	USA
García-Olivares 2016 (38)	Prospective observational	Critical care	Factors associated with inadequate thromboprophylaxis in critically ill patients	Yes	777	Female 270, Male 507 (61)	Spain
Gardiner 2013 (31)	Prospective observational	Surgical wards	Quality improvement to increase IPC compliance	Yes	339	Not reported	USA
Kim 2018 (25)	Cohort Study	Surgical, medical & critical care	Accuracy of VTE assessment, compliance to IPC and effect of education on compliance	Yes	200	Female 97, Male 103 (62)	USA
Maffei 2009 (41)	Retrospective observational	Surgical wards	Before and after study of implementation of thromboprophylaxis guidelines	No	150	Female 77, Male 73 (64)	Brazil
Maxwell 2002 (23)	Randomised controlled trial	Surgical gynaecology	To assess preference and compliance in patients receiving heparin and IPC	Yes	104	Female 104 (61)	USA
Novis 2009 (32)	Prospective observational	Surgical wards	Utilisation of DVT prophylaxis after implementation of electronic risk assessment	Yes	800	Female 15, Male 785 (64)	USA
Obi 2015 (33)	Prospective observational	Surgical wards	Comparison of compliance with a standard vs battery powered IPC device	No	67	Female 32, Male 35 (51)	USA

Palmerola 2015 (34)	Prospective observational	Obstetrics	Compliance with IPC after caesarean delivery	Yes	293	Female 293 (32)	USA
Ritsema 2013 (26)	Observational	Surgical wards	Study of the influence of hospital and patient factors on compliance	Yes	100	Female 24, Male 76	USA
Sobierag-Teague 2012 (40)	Randomised controlled trial	Neurosurgery	Trialling the efficacy and tolerability of an IPC device	No	75	Female 31, Male 44 (62)	Canada
Vignon 2013 (16)	Randomised controlled trial	Critical care	Effectiveness of compression stockings with and without IPC	No	205	Female 72, Male 132 (55	France
Yamamoto 2013 (39)	Prospective observational	Critical care	Exploring the current practice of VTE prevention in Japanese ICUs	No	470	Female 168, Male 302 (65)	Japan

Table 2: Factors affecting adherence

Author	Factors	Findings
Bockheim 2009 (27)	Intensive care context	ICU has greater compliance than non-ICU
Brady 2007 (28)	Patient discomfort	Cause of non-adherence was; 39% discomfort
	Mobilisation	46% had just ambulated
	Healthcare professional knowledge and behaviours	13% the nurse had not reapplied the IPC after transfer from another unit
Brady 2015 (37)	Healthcare professional knowledge and behaviours	When asked, 23% of patients said nurses instruction to not wear
	Equipment supply and demand	13% did not have part of the device in the room
	Mobilisation	17% said they had just returned to bed, 16% walking around, 7% just about to walk around
	Patient discomfort	15% of patients said the IPC was uncomfortable
Chen 2019 (35)	Computer assisted prescribing	A pre-checked electronic order increased prescribing adherence from 46% to 77%
Cindolo 2009 (29)	Patient discomfort	Noise and insomnia were reported as being a negative experience in 23% and 44% of cases respectively. Authors state these issues were reasons why 3% had IPC removed early
Comerota 1992 (24)	Intensive care context	ICU has greater compliance than non-ICU
Cornwell 2002 (36)	Healthcare professional knowledge and behaviours	Compliance rate of 53%. Information reported about non-compliance was that the device was not in place (95%)
Elphern 2013 (30)	Healthcare professional knowledge and behaviours	In 51% of non-adherence observed, IPC sleeves were not correctly applied and 24% the machine was not switched on
García-Olivares 2016 (38)	Mobilisation	Patients with invasive mechanical ventilation and complete bedrest had greater compliance
	Guidelines	use of a protocol and risk scoring system led to decreased risk of inappropriate VTE prophylaxis
Gardiner 2013 (31)	Equipment supply and demand	In 38% of non-adherent cases the IPC machine was not in the room, locating IPC machines in rooms resulted in adherence from 26% to 44%
	Healthcare professional knowledge and behaviours	A nursing knowledge and beliefs survey yields information about barriers that nurses bring to the use of IPC
Kim 2018 (25)	Knowledge	40% overall non-adherence to IPC. Of these, 40% said that no one informed them they needed to keep IPC on
	Patient discomfort	40% overall non-adherence to IPC, 33% said this was due to discomfort
Maffei 2009 (41)	Guidelines	After guidelines were introduced, IPC prescription increased from 26% to 32%
Maxwell 2002 (23)	Healthcare professional knowledge and behaviours	Of 736 observations, non-compliance was noted in 2.7% of cases and this was related to the machine not being switched on
Novis 2009 (32)	Computer assisted prescribing	Electronic suggestion of thromboprophylaxis increased the use of IPC from 50% to 63%
Obi 2015 (33)	Device related	A battery powered device facilitated adherence through enabling mobilisation
	Patient discomfort	A new machine design led to fewer reports of patient discomfort (33% vs 13%)
	Mobilisation	Problems with mobilisation were less using a new machine (71% vs 29%)
Palmerola 2015 (34)	Mobilisation	38% of patients classed as non-adherent to IPC therapy had it discontinued due to liberal standards for ambulation
Ritsema 2013 (26)	Mobilisation	Not replaced after mobilising accounted for 50% of non-compliant observations
	Equipment supply and demand	Lack of machine or cuffs accounted for 22% of non-adherence
	Patient discomfort	Patient discomfort accounted for 19% of non-adherence
Sobierag-Teague 2012 (40)	Patient discomfort	48% of users discontinued the device at night. Comfort related issues discussed but not explicitly linked to non-adherence

Vignon 2013 (16)	Patient discomfort	7% non-compliance in the AES + IPC group. IPC was discontinued due to discomfort, noise and restlessness
Yamamoto 2013 (39)	Guidelines	Combined AES and IPC mechanical prophylaxis was higher in units with a protocol than without (88% vs 80%)

Figure 1: PRISMA flow chart of search results retrieved 30th May 2019

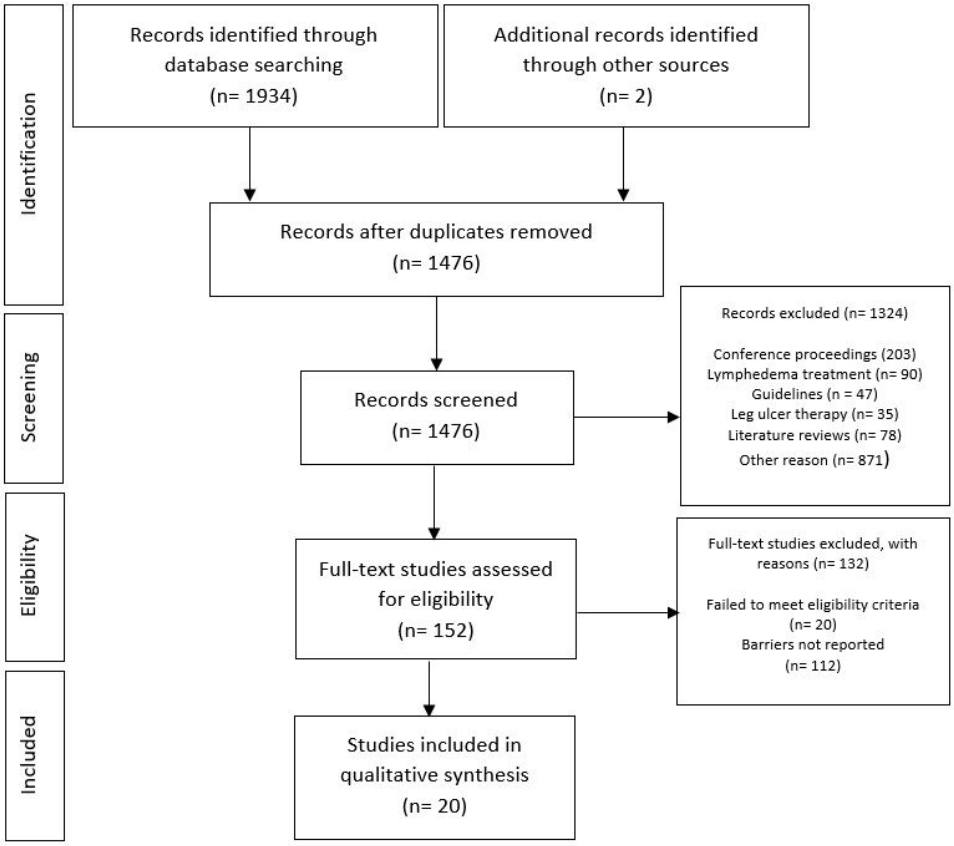

Figure 1

169x156mm (120 x 120 DPI)

Search strategy

Population	Intervention	Comparison	Outcomes
Intermittent pneumatic compression OR Sequential compression	Interven$ OR Strateg$ OR Guideline$ OR Educat$ OR Inform$ OR PDSA OR Plan do study act OR Improv$ OR Implement$ OR Toleran$ OR Aware$ OR Present$ OR Program$ OR Plan$ OR Approach$ OR Project$ OR Procedure$ OR Polic$ OR Method$ OR Design$ OR Action$ OR Part$ OR Involv$ OR Practice$ OR Process$ OR System$ OR Technique$ OR Scheme$	N/A	Complian$ OR Adhere$ OR Efficacy OR Effective$ OR Outcome$ OR Success$ OR Fail$ OR Fidelity

Reporting checklist for systematic review and meta-analysis.

Based on the PRISMA guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMAreporting guidelines, and cite them as:

Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement

		Reporting Item	Page Number
Title			
	#1	Identify the report as a systematic review, meta-analysis, or both.	1
Abstract			

Structured summary	#2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	2
Introduction			
Rationale	#3	Describe the rationale for the review in the context of what is already known.	3
Objectives	#4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
Methods			
Protocol and registration	#5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address) and, if available, provide registration information including the registration number.	4
Eligibility criteria	#6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rational	4
Information sources	#7	Describe all information sources in the search (e.g., databases with dates of coverage, contact with study authors to identify additional studies) and date last searched.	4

Search	#8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	#9	State the process for selecting studies (i.e., for screening, for determining eligibility, for inclusion in the systematic review, and, if applicable, for inclusion in the meta-analysis).	5
Data collection process	#10	Describe the method of data extraction from reports (e.g., piloted forms, independently by two reviewers) and any processes for obtaining and confirming data from investigators.	5
Data items	#11	List and define all variables for which data were sought (e.g., PICOS, funding sources), and any assumptions and simplifications made.	Supp. file
Risk of bias in individual studies	#12	Describe methods used for assessing risk of bias in individual studies (including specification of whether this was done at the study or outcome level, or both), and how this information is to be used in any data synthesis.	5
Summary measures	#13	State the principal summary measures (e.g., risk ratio, difference in means).	n/a
Planned methods of analyis	#14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.	n/a

Risk of bias across studies	#15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	n/a
Additional analyses	#16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
Results			
Study selection	#17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	#18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citation.	6
Risk of bias within studies	#19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	n/a
Results of individual studies	#20	For all outcomes considered (benefits and harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	n/a
Synthesis of results	#21	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency.	7

Risk of bias across studies	#22	Present results of any assessment of risk of bias across studies (see Item 15).	n/a
Additional analysis	#23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
Discussion			
Summary of Evidence	#24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers	10
Limitations	#25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	10
Conclusions	#26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10
Funding			
Funding	#27	Describe sources of funding or other support (e.g., supply of data) for the systematic review; role of funders for the systematic review.	1

BMJ Open

Intermittent pneumatic compression for venous thromboembolism prevention: a systematic review on factors affecting adherence

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Intermittent pneumatic compression for venous thromboembolism prevention: a systematic review on factors affecting adherence

Authors

Richard Greenall, BSc, MSc[1]
Rachel Davis, BSc, MSc, PhD[2]

[1]King's College Hospital NHS Foundation Trust
Executive Offices
Princess Royal University Hospital
Farnborough
BR6 8ND
Email: writetorichg@gmail.com

Centre for Implementation Science
[2]Health Services and Population Research Department,
Institute of Psychiatry, Psychology and Neuroscience
King's College London
2nd Floor, Room E2.19
16 De Crespigny Park
Denmark Hill
LONDON
SE5 8AF
Email: rachel.davis@kcl.ac.uk

Corresponding author: Richard Greenall

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RG and RD designed the paper and were responsible for its conceptualisation. RG drafted the paper and RD edited it. Both authors were involved in the screening of the articles included in the review and have read and approved the final version of the manuscript.

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Abstract

Objective Venous thromboembolism (VTE) is a potentially fatal complication of hospitalisation. Intermittent pneumatic compression (IPC) is one approach to reducing the likelihood of a VTE. Adherence to IPC is known to be inadequate though the reasons for this remain unclear. This systematic review explores factors that affect adherence to IPC in the inpatient context.

Methods – information sources -EMBASE, MEDLINE and PsycINFO were searched for literature between January 1960 to May 2019. Eligibility criteria - studies were included if they focused on inpatient care and examined factors affecting adherence to IPC devices.

Results – included studies - a total of 20 out of 1476 studies were included. Synthesis of results - Eight factors were identified that affected adherence: patient discomfort (n=8), healthcare professionals' knowledge and behaviours (n=6), mobilisation (n=6), equipment supply and demand (n=3), the use of guidelines (n=3), intensive care context (n=2), computer-assisted prescribing (n=2) and patients' knowledge of IPC (n=1).

Conclusion Overall while the evidence base is quite limited, a number of factors were shown to affect adherence to IPC. These findings could be used to inform future research and quality improvement efforts to increase adherence in this very important, but currently under-researched area.

Keywords; Intermittent pneumatic compression, adherence, compliance, thromboprophylaxis, venous thromboembolism, VTE, deep vein thrombosis, pulmonary embolism

Strengths

- First known review of the evidence affecting adherence to IPC
- Eight factors were identified that resulted in measurable changes to adherence to IPC

Limitations

- Results largely based on direct observation rather than self-report
- Studies generally had low sample sizes
- Studies with different aims and methodologies were included.

Background

Venous thromboembolism (VTE) is a term that most commonly refers to deep vein thrombosis (DVT) and pulmonary embolism (PE). VTE affects one in 1000 people annually[1] and in England in 2018 VTE was recorded as a cause of death in 12,000 cases[2]. Compared to baseline risk, hospitalisation has been correlated with an 8-fold increased risk of VTE in medical admissions and a 21-fold increased risk in surgical admissions[3] with one study estimating that up to 50% of 625 cases of VTE in the community were related to hospitalisation[4]. Secondary to adverse drug events, VTE is the leading complication of hospitalisation worldwide[5].

The financial cost of hospital associated VTE is high. In 2017, a UK survey revealed the average cost of treating VTE was £938,357 for each local NHS region[6]. At a patient level, a review[7] identified an increase in cost of $14,000 for initial diagnosis and the first year of treatment for those with VTE compared with non-VTE affected patients. VTE can have a significant impact on a person's psychosocial well-being with research to suggest that it can be a traumatic, life-changing event which can lead to post traumatic stress disorder[8,9].

Since hospitalisation increases the risk of VTE, it is important to consider if anything can be done to reduce the risk within this context. In England, the national VTE prevention programme combined a mandate for assessment of patient's risk on admission to hospital with best practice prevention guidelines. Early results indicate that its efforts have led to reduced morbidity and mortality[10]. Similar efforts have been made in the USA [11] and throughout Europe, recent evidence indicates that better management of the risk of VTE has reduced VTE related mortality from 12.8 to 6.5 deaths per hundred thousand[12].

Risk assessing all patients on admission to hospital leads to identification of patients at high risk who need thromboprophylaxis (i.e. treatments to prevent VTE). In the UK, national guidelines[13] advise using the chemical thromboprophylaxis low molecular weight heparin for most groups of at-risk hospitalised patients. Mechanical thromboprophylaxis is advised for most surgical patients and other high-risk groups, such as patients with stroke. Graduated compression stockings (GCS) are one type of mechanical intervention. GCS exerts graded pressure around the legs, increasing the speed of blood flow and reducing the opportunity for VTE to form[14].

Intermittent pneumatic compression (IPC) is another type of mechanical device. Fabric sleeves that wrap around a patient's legs are attached to a pump using a tube and are periodically inflated and deflated. IPC is thought to reduce VTE by increasing the speed of blood flow and reducing hypercoagulability through the IPC action stimulating the vessel walls fibrinolytic activity[15,16]. Evidence demonstrates that combining IPC and GCS decreases the incidence of VTE to a greater effect than either separately[17]. Systematic reviews found the same increased effect when combining IPC and pharmacological prophylaxis[18] and that IPC can reduce the incidence of VTE in surgical patients[19]. However, despite these benefits, research has shown considerable variability in adherence to IPC device use, with a systematic review of seven studies in acute hospitals reporting a median adherence rate of 78% (range 40%-89%)[20]. The authors concluded that strategies to improve adherence are needed but the question remains as to why non-adherence occurs.

While factors affecting adherence have been reviewed within surgical specialities[19], to the best of our knowledge, no attempt has been made to comprehensively investigate the factors that could facilitate or impede adherence to IPC across all specialities. This paper aims to address this important gap in the evidence base by systematically reviewing the factors that influence adherence to IPC for VTE prevention in acute care. Gaining this understanding is critical in order to develop interventions, strategies and policies that are accurately targeted at meeting the challenges of improving adherence[21].

Methods

Patient and public involvement

No patient was involved.

Search strategy

EMBASE, MEDLINE and PsycINFO were searched for relevant literature published between January 1960 to May 2019. The search strategy comprised terms relating to: 1) population (e.g. 'IPC'); 2) Intervention (e.g. 'strategies') and; 3) outcomes (e.g. 'adherence'). The search was customized to each database and restricted to titles and abstracts to tighten its specificity. A sensitivity analysis was performed to ensure the search results included key articles identified through an initial scoping review. Forward and backward citation searching and hand searching of key journals were performed to minimize the likelihood of missing relevant papers. The final search was conducted on 30th May 2019 (for the full search strategy please refer to Supplementary file 1).

Inclusion criteria

Based on UK national guidelines that were current at the time of this review's development (January 2018) [13], the definition of IPC in this review includes only devices that are applied to the legs and excludes foot compression devices. The first stage of screening (title and abstract) was intentionally inclusive and retained any empirical articles that mentioned adherence to IPC in any context. In the second stage (full text), tighter restrictions applied. Articles were included if they reported barriers or facilitators to adherence to IPC in the inpatient context and included a measure of the effect (percentage change in adherence to IPC) of such factors on adherence (either as a primary or secondary aim or an indirect finding in the results). Dissertations and doctoral theses, books, book reviews, conference posters and presentations, editorials and commentaries were excluded, as were articles not published in English or those focused on patients under 18 years of age. Review/commentary papers that addressed adherence to IPC[20] were examined for relevant empirical papers but the reviews themselves were excluded.

Study selection and data extraction

Articles were screened for relevance by the lead author (RG). The second author (RD) screened 20% of the articles at abstract stage and 100% at full-text stage. Discrepancies were resolved through joint discussion between the authors. Dual data extraction of the included articles was conducted independently by both authors and then checked for consistency. We did not predetermine the factors that could affect adherence to IPC. Rather, we reviewed the data in each article and then grouped these into categories of factors that could affect adherence to IPC. These factors were decided initially by the first author (RG) and then checked by the second author (RD). Disagreements were resolved by joint discussion until consensus was reached.

Quality Assessment

While numerous scales are available to assess the methodological quality of studies, these are often restricted to specific study designs, including randomised controlled trials[22]; case-control and cohort studies[23]; and qualitative studies[24]. Given our review included articles that employed heterogeneous study designs and differing aims, we did not use a quality assessment scale, nor did we deem this meaningful. We did however consider differences in the methodologies that could potentially bias the findings to enable greater understanding of the relative strengths and weaknesses of the research. To gain a comprehensive understanding of the full body of evidence, we did not exclude articles based on their methodological quality.

Results

Study selection

Of 1476 articles retrieved, 1324 were excluded at the first stage of screening (title/abstract) and 132 (out of the remaining 152) were excluded after full-text screening, resulting in 20 articles. Two of the included articles were added through handsearching[25,26] (see Figure 1). Upon examination, these studies were missed in the initial search due to the use of the word 'external' instead of 'intermittent' to describe pneumatic compression. Further scoping the literature (using the term 'external') revealed there were no other additional articles that needed to be included.

Insert Figure 1 here

Characteristics of included studies

Articles were published between 1992 and 2018 across six countries, including the USA (n= 15[25-39]), Spain (n= 1[40]), Japan (n=1[41]), Canada (n=1[42]), France (n=1[17]) and Brazil (n=1[43]). Characteristics of patients and care locations included critical care[17,26,29,40,41], general surgical wards[28,33-35,38,42,43] and gynaecology[25,36,37,39] specialties. Factors affecting adherence to IPC was the primary focus of 13 studies[25,27-34,36,37,39,40]. A further seven studies[17,26,35,38,41-43] focused on IPC device safety and effectiveness in preventing VTE but also reported barriers or facilitators to IPC adherence. Seventeen of the studies were observational[26-41,43], using surveys and clinical observations as investigation tools. The remaining three studies were RCTs[17,25,42]. Due to wide heterogeneity in study methodologies, meta-analysis was not possible. Table 1 details the characteristics of the included studies.

Insert table 1 here

Factors affecting adherence to IPC

Articles varied considerably in the level of content and detail provided regarding study designs and adherence to IPC. We report the main findings here and provide a more detailed analysis of findings for studies where this was possible. Table 2 outlines the eight factors that were identified that affected adherence to IPC.

Insert table 2 here

1. *Patient discomfort*

Patient discomfort associated with wearing the IPC device was identified in eight studies[17,27,28,30,31,35,39,42]. Vignon[17] identified poor adherence in 7% (14/204) of patients due to discomfort, noise and restlessness. Brady[30] observed the effect of the length of the IPC sleeve on comfort and subsequent non-adherence. Overall adherence was 29% (40/137) based on a one-off observation. Eighty-five percent of non-adherent users had been wearing thigh length (53%) or knee length (32%) sleeves. Discomfort was reported as a reason for non-adherence by 39% (58/149) of patients who were non-adherent. Those wearing thigh length sleeves reported double the number of complaints compared to those wearing knee length sleeves (39 vs 15).

Brady[39] examined adherence over several days post-operatively. Taking multiple observations of the same patients, adherence was 75% (43/57) on day zero, 53% (148/278) on day 2, and 44% (11/25) on day 4. Patients who were non-adherent were asked why at the time of observation and 15% (53/362 responses) stated discomfort as a reason. Kim[27] compared two groups of 100 patients in a multifaceted improvement strategy to increase adherence to IPC. Post intervention a slight improvement was achieved (24% versus 26%). Ninety-two percent of nurses (58/63) and 29% (4/14) of non-adherent patients reported discomfort as a reason for the lack of adherence.

Ritsema[28] found that patients were non-adherent 21% of the time (98/457 observations) with patient interviews indicating that discomfort was a reason in 19% (19/100) of responses. Sobieraj-Teague[42] trialled the efficacy of a newly developed IPC machine which allowed the patient to mobilise independently of a power cable through the utilisation of batteries and small product design. Poor adherence was found in 49% of users (35/72), in particular at night, with patients reported they discontinued therapy due to insomnia. Similar findings, but to a much lesser extent were reported by Cindolo[31] when evaluating the comfort and tolerability of a specific IPC device. While non-adherence was only 3% (6/184), patients who requested discontinuation of IPC therapy did so due to noise and insomnia.

A final study by Obi[35] was designed as a retrospective review examining whether a different design of IPC device would reduce non-adherence. Comparing a standard machine to a new machine, adherence to the standard machine was 47% versus 85% for the newer machine. Of responses from those patients wearing the standard compared to the new machine (21 and 24 respectively), problems with discomfort as reported less (33% vs. 13%).

2. Healthcare professional knowledge and behaviours

Failure of healthcare professionals to apply or provide IPC when prescribed was identified in six studies[25,30,32,33,38,39]. Brady[30] found that 16% (12/73) of survey respondents reported that the nurse

had never initiated IPC therapy or had not replaced the sleeves after transfer of the patient from another location. Brady[39] found that 23% (82/356) of non-adherent patients stated the nurse had informed them that they did not require IPC anymore.

Cornwell[38] observed adherence of 53% (out of 712/1343 observations of 233 patients). The authors reported that this was because the device was 'not in place'. The time of day that non-adherence was most frequently noted was in the early afternoon and the authors concluded that it is both HCPs and patients who need to be educated about the importance of wearing IPC as the patient may have been the one who removed it.

Elphern[32] reported that errors in the application of IPC therapy were identified in 49% (477/966) of observations of a cohort of 123 patients. In 244 observations the sleeves were incorrectly applied to the patient and in 116 observations the pump was not turned on. Similar findings by Maxwell[25] in 104 patients identified that the reason for non-adherence in 3% (20/736) of observations was that the IPC was not turned on. Gardiner[33] reported that only 26% (89/339) of patients were adherent to IPC on initial audit. A survey of nursing beliefs, practice and knowledge determined that part of the problem was deficiencies in nursing knowledge. Education interventions as well as placing IPC machines in individual rooms of patients improved adherence from 26% to 44%.

3. Mobilisation

Issues relating to mobilisation were identified as factors affecting adherence in six studies[28,30,35,36,39,40]. Brady[30], found that of 149 responses from non-adherent patients, 46% (68/149) of patients reported that they had just mobilised. Similarly, Brady[39] found that 16% (59/362) of patients reported that they had just been walking around, 17% (62/362) stated they had just returned to bed and 7% (24/362) were just about to walk around. In a study by Ritsema[28] previously discussed in relation to patient discomfort, patient's identified that not replacing the IPC sleeves after mobilisation was a cause of non-adherence in 50% of 98 non-adherent episodes observed.

Palmerola[36] found adherence to IPC after caesarean delivery was 79.5% (233/293). Of the 60 non-adherent patients, 62% (37/60) had the IPC machine and sleeves in the room but they were not applied and 38% (23/60) had it discontinued due to "*liberal standards for mobilisation*". A study by Obi[35] previously discussed in relation to 'patient discomfort' found that problems with mobilising were reported less using a new machine compared to a standard one (71% vs. 29%). Garcia Olivares[40] found that complete bed rest for >2 days resulted in improved appropriateness of prophylaxis (OR 0.6) with similar findings reported for mechanical ventilation (OR 0.7).

4. Equipment supply and demand

Three studies[28,33,39] highlighted that equipment supply and demand could affect adherence. Brady[39] identified that part of the IPC device was not present in the room in 13% (49/362) of non-adherent episodes although reasons why were not explored. Similar findings by Ritsema[28] found that the second most commonly report reason for non-adherence was no machine or sleeves being available to the patient (22/100 questionnaire responses). As previously discussed within 'healthcare professionals knowledge and behaviours', a study by Gardiner[33] revealed that of 250 patients who were non-adherent, 39% (97/250) did not have part of the equipment in the room. This same study found that adherence increased from 26% to 44% through an educational intervention and making IPC machines widely available instead of difficult to obtain for use.

5. Guidelines

The use of guidelines for VTE prevention was identified as a factor that could affect adherence in three studies[40,41,43]. Garcia Olivares[40] used an electronic questionnaire to investigate inappropriateness of VTE prophylaxis (all types) on a single day across multiple intensive care units (ICUs). A total of 777 patients across 73 ICUs were included: the use of a protocol reduced inappropriate VTE prevention prescribing (OR 0.6) as well as a VTE risk scoring system (OR 0.4). Yammamoto[41] obtained data from 99 ICUs and included 470 patients in their analysis. Hospitals using protocols had higher rates of prophylaxis provision than those who did not (89% vs. 80%) and this difference was mainly due to the increase in the combined use of anti-embolic stockings and IPC (26% vs. 15%). A similar effect was demonstrated by Maffei[43] who retrospectively analysed the accuracy of prescribing of VTE prophylaxis after the implementation of guidelines. Compared to before the implementation of guidelines, prescribing of IPC therapy increased from 26% to 32% after.

6. Intensive care context

Care provision in the ICU context was identified by two studies as having an impact on adherence[26,29]. Comerota[26] examined 138 patients and found that adherence in the ICU setting was higher than elsewhere in the hospital (78% vs. 48%) but did not investigate reasons for this. A study by Bockheim[29] found adherence in the ICU context was 69% (52/75) compared to 40% (30/75) outside of the ICU. The authors concluded the reasons for this were likely to be multifactorial they did not empirically determine what these factors might be.

7. Computer-assisted prescribing

Computer-assisted prescribing was reported as a factor affecting adherence in two studies[34,37]. Chen[37] examined the long-term impact of automatic pre-orders for IPC on an electronic prescription

system. Prior to the intervention, prescribing of IPC was carried out on 46% (denominator not reported) of patients. One year later, this had increased to 78% (59/76). IPC was only present in 71% (42/59) of patients who had been prescribed IPC and was only being used by 45% (19/42) of those patients. The authors concluded that the intervention had successfully increased prescribing of IPC but not overall adherence.

Novis[34] utilised a similar approach but did not assess the impact of adherence to IPC at a patient level. Computer generated suggestions of pre-operative prophylaxis were provided to the clinician as a result of information entered about the risk of VTE to the patient. The result was a 40% increase in prescribing of IPC from 215 to 301 patients with an active prescription.

8. Patient knowledge

A study by Kim[27] concluded that the information needs of patients were a factor affecting adherence. An initial survey found that 59% (32/54) of patients did not have IPC applied when prescribed. Several clinician-focused interventions were conducted, and a survey of patients a year later found that 62% (41/66) of patients requiring IPC therapy did not have it applied. From this, thirty percent (11/37) of patients reported that they did not know what a DVT is and 62% (23/37) reported that they had not been educated about IPC. The authors conclude that a lack of education is an important barrier to adherence however evidence to demonstrate that increasing education results in improved adherence was not presented.

Quality Assessment

Seventeen[26-41,43] (out of the 20) articles included in the review were observational in nature. All of these studies (n=17) measured adherence to IPC by direct observation of researchers rather than based on self-report, which could have been subject to recall bias. Eight of these studies measured adherence twice daily[25,26,28,29,33,37,39,42], three had a single observation point (the first day post operatively[31,36] and not reported[30]), one[35] had hourly monitoring across a 24 hour period, and one[17] did not report when they observed adherence, only that they did this. In addition to direct observations, data on factors affecting adherence using patient surveys was performed in eight studies[17,25,27,28,30,31,39,42] and indirect indicators such as the effect of a change in device type or the result of a guideline implementation was used in seven studies[26,29,34,35,37,43]. The three RCTs[17,25,42] collected data on adherence using researcher observations and patient surveys

Over half of the articles[25,27-34,36,37,39,40] (n=13) focused on factors affecting adherence to IPC as a primary outcome. The remaining studies[17,26,35,38,41-43] (n=7) investigated as the safety and

effectiveness of IPC as their main outcome. As a result of these investigations, these studies also provided data on factors affecting adherence (though this was not their aim). It is difficult to determine whether additional factors may have been uncovered from these studies (i.e. that are not reported in our findings) if the authors had specifically set out to examine how adherence to IPC could be affected. Taken collectively, the patient sample sizes for each study ranged from between 67(35) to 800(34) with the majority of studies being based on over 100 patients. Articles we included were published across a 27-year period.

Discussion

This paper presents the findings of a systematic review on factors affecting adherence to IPC in the inpatient setting. In total eight factors were identified that affected adherence, with patient discomfort related to wearing the IPC device being most commonly reported and issues related to computer assisted prescribing and patients' knowledge of IPC being the least frequently reported. The majority of factors delineated (such as patient discomfort, mobilising, healthcare professional knowledge and behaviours, patient knowledge, equipment supply and demand) acted as a barrier to adherence to IPC. However, some evidence points to specific facilitators of adherence (for example the use of guidelines and protocols and computer-assisted prescribing).

There are several important implications of this work. First, discomfort with the IPC device was a considerable cause for non-adherence. The development and/or use of new or alternative IPC devices should be considered when addressing adherence issues. Research has demonstrated that using methods to systematically incorporate the user perspective early in the design process can result in the development of a device which is safe, effective and used by the patient[44]. Research more widely in the field that examined the use of a modern IPC device demonstrates that it is possible to develop comfortable devices[45] with 86% (26/30) of patients reporting it was comfortable and that they would use it again if required. Two studies[35,42] within this review reported adherence levels when studying different machine designs and one study focused on the length of IPC sleeve[30] and its effect on adherence with knee length sleeves being adhered to to a greater degree. The same study found similar results with the length of AES and this was also found in a review of adherence in surgical specialities[46]. There is therefore scope for further research using a randomised control study design to assess widely used IPC machines, the length of sleeves and the effect both factors have on adherence, particularly in relation to comfort.

Second, and related to the above point, mobility was often reported as a barrier to adherence. One likely explanation for this could be that it was uncomfortable for patient to mobilise while wearing the device, so for this reason it was removed. Evidence[26,29] from our review revealed that adherence was less of an issue for those patients that were unable to move around. However, IPC is designed to promote blood flow during immobility and if a patient is mobile, it could be concluded that IPC is no longer required and thus would not meet the criteria for data being collected as adherent or not. While this is a point that warrants further investigation, our findings suggest this could be why mobilisation (perhaps wrongly so) was identified as an adherence-related issue. Within the wider literature, a systematic review[47] on the definition used for immobility within thromboprophylaxis studies concluded that a lack of consistency in the definition of immobility may contribute to the underutilisation of thromboprophylaxis in clinical practice. In our review, the definition of mobility to the extent that IPC was no longer required was not stated by any of our included studies. In place of a widely agreed consensus, an institution-wide definition of mobility could assist individual hospitals to ensure that best practice is promoted in relation to IPC adherence.

Third, we found that HCP knowledge and beliefs could contribute to non-adherence. It is not clear from our studies whether on those occasions when an IPC device was not fitted, the reasons related more to the HCP not knowing they needed to do this, whether they simply forget, or whether there has been some other unknown issue. While this warrants further investigations, there are some relatively straightforward strategies that could be put in place, based on our preliminary findings. For example, prompts and educational leaflets could be distributed on the hospital wards to remind HCPs when the use of IPC is required and why this is important. Training is essential if optimal adherence levels are to be achieved and maintained. Equally, ensuring the layout of the ward allows easy accessibility of equipment (such as IPC) is also important, particularly, given our review revealed this to be a determinant of adherence.

Finally, our review revealed that the use of guidelines and how they are incorporated into electronic prescribing systems could act as a facilitator to adherence. Similar findings (which examined, in part the use of pre-printed orders) have been reported in a review of the barriers and facilitators to adherence to chemical thromboprophylaxis[48] within the ICU setting. Additional research that examined how electronic prescribing can lead to a reduction in errors, identified an absolute risk reduction of up to 30%[49]. Together with the evidence in this review, it could be concluded that if IPC prescribing is included in electronic prescribing systems, improvements in adherence to guidelines may be achieved.

Strengths and limitations

There are several strengths of this review. To the best of our knowledge, this is the only paper of its kind to systematically review the evidence on factors affecting adherence to IPC across medical and surgical specialities. Wider research within the field that has reviewed the literature relating to IPC adherence found a median adherence rate of 78%[20]. The review concluded that strategies to improve adherence are required. Our review helps to address this important gap in the evidence, shedding light on potential indicators of issue.

The evidence in our review was derived from articles that provided an actual measure of adherence in clinical settings and the subsequent factors that could help to explain these adherence rates. Many of the factors relating to adherence were based on direct observation rather than self-report.

A caveat to mention when interpreting our findings is that while data were based on quite a large body of evidence, there were differing (and sometimes low) sample sizes as well as different aims and methodologies and countries and settings of focus. Included studies were also spread over a long period of time (twenty-seven years), in which policies and procedures around IPC may have changed. Equally most of the factors affecting adherence were only reported a few times. While, admittedly this was not the primary aim of the studies included in our review, but rather was reported as secondary finding in relation to explaining adherence rates, further work is required to understand the relative strength of the evidence. Nonetheless, this review provides a useful first step to delineating important (and perhaps otherwise empirically unknown) factors affecting adherence to IPC. These findings could be used to help inform, implement and evaluate the use of specific strategies to overcome factors causing adherence-related issues.

Conclusion

This systematic review set out to uncover the factors that affect adherence to IPC for VTE prevention in acute care. Gaining this understanding is critical in order to develop interventions, strategies and policies which are accurately targeted at meeting the challenges of improving adherence[21]. While our review has addressed an important gap in the evidence base and taken the first steps to understanding reasons why non-adherence to IPC may occur, it is clear more research is required in this area to further understand the relative strength of the evidence, so that effective strategies to overcome barriers to adherence can be sought.

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Figure 1: Prisma flow chart of search results retrieved 30th May 2019

Table 1: Characteristics of included studies

Author	Study design	Setting	Studies main objective	Focus was adherence barriers / facilitators?	Sample size	Participants (mean age)	Country
Bockheim 2009 (29)	Prospective observational	Critical care & Ward care	Comparison of IPC compliance between ICU and non ICU areas	Yes	150	Female 73, Male 77 (62)	USA
Brady 2007 (30)	Prospective observational	Acute nursing care wards	To assess comfort and fit and compliance of knee vs thigh length IPC	Yes	137	Female 72, Male 65 (55)	USA
Brady 2015 (39)	Prospective observational	Caesarean or gynaecological surgery	To assess impact of education on compliance to IPC	Yes	228	Female 59 (38)	USA
Chen 2019 (37)	Prospective observational	Obstetrics	Assess the effectiveness of an intervention in improving compliance to IPC	Yes	76	Female 76 (28)	USA
Cindolo 2009 (31)	Prospective observational	Radical retropubic prostatectomy surgery	To assess acceptability and satisfaction to IPC	Yes	184	Male 184 (69)	USA
Comerota 1992 (26)	Prospective observational	Critical care & Ward care	Comparison of IPC compliance between ICU and non ICU areas	No	138	Not reported	USA
Cornwell 2002 (38)	Prospective observational	Surgical trauma	To assess compliance of IPC in trauma patients	No	227	Female 39, Male 188 (37)	USA
Elphern 2013 (32)	Prospective observational	Critical care	Identifying reasons for errors in the application of IPC	Yes	123	Female 42, Male 54	USA
García-Olivares 2016 (40)	Prospective observational	Critical care	Factors associated with inadequate thromboprophylaxis in critically ill patients	Yes	777	Female 270, Male 507 (61)	Spain
Gardiner 2013 (33)	Prospective observational	Surgical wards	Quality improvement to increase IPC compliance	Yes	339	Not reported	USA
Kim 2018 (27)	Cohort Study	Surgical, medical & critical care	Accuracy of VTE assessment, compliance to IPC and effect of education on compliance	Yes	200	Female 97, Male 103 (62)	USA
Maffei 2009 (43)	Retrospective observational	Surgical wards	Before and after study of implementation of thromboprophylaxis guidelines	No	150	Female 77, Male 73 (64)	Brazil
Maxwell 2002 (25)	Randomised controlled trial	Surgical gynaecology	To assess preference and compliance in patients receiving heparin and IPC	Yes	104	Female 104 (61)	USA
Novis 2009 (34)	Prospective observational	Surgical wards	Utilisation of DVT prophylaxis after implementation of electronic risk assessment	Yes	800	Female 15, Male 785 (64)	USA
Obi 2015 (35)	Prospective observational	Surgical wards	Comparison of compliance with a standard vs battery powered IPC device	No	67	Female 32, Male 35 (51)	USA

Palmerola 2015 (36)	Prospective observational	Obstetrics	Compliance with IPC after caesarean delivery	Yes	293	Female 293 (32)	USA
Ritsema 2013 (28)	Observational	Surgical wards	Study of the influence of hospital and patient factors on compliance	Yes	100	Female 24, Male 76	USA
Sobierag-Teague 2012 (42)	Randomised controlled trial	Neurosurgery	Trialling the efficacy and tolerability of an IPC device	No	75	Female 31, Male 44 (62)	Canada
Vignon 2013 (17)	Randomised controlled trial	Critical care	Effectiveness of compression stockings with and without IPC	No	205	Female 72, Male 132 (55	France
Yamamoto 2013 (41)	Prospective observational	Critical care	Exploring the current practice of VTE prevention in Japanese ICUs	No	470	Female 168, Male 302 (65)	Japan

Table 2: Factors affecting adherence

Author	Factors	Findings
Bockheim 2009 (29)	Intensive care context	ICU has greater compliance than non-ICU
Brady 2007 (30)	Patient discomfort	Cause of non-adherence was; 39% discomfort
	Mobilisation	46% had just ambulated
	Healthcare professional knowledge and behaviours	13% the nurse had not reapplied the IPC after transfer from another unit
Brady 2015 (39)	Healthcare professional knowledge and behaviours	When asked, 23% of patients said nurses instruction to not wear
	Equipment supply and demand	13% did not have part of the device in the room
	Mobilisation	17% said they had just returned to bed, 16% walking around, 7% just about to walk around
	Patient discomfort	15% of patients said the IPC was uncomfortable
Chen 2019 (37)	Computer assisted prescribing	A pre-checked electronic order increased prescribing adherence from 46% to 77%
Cindolo 2009 (31)	Patient discomfort	Noise and insomnia were reported as being a negative experience in 23% and 44% of cases respectively. Authors state these issues were reasons why 3% had IPC removed early
Comerota 1992 (26)	Intensive care context	ICU has greater compliance than non-ICU
Cornwell 2002 (38)	Healthcare professional knowledge and behaviours	Compliance rate of 53%. Information reported about non-compliance was that the device was not in place (95%)
Elphern 2013 (32)	Healthcare professional knowledge and behaviours	In 51% of non-adherence observed, IPC sleeves were not correctly applied and 24% the machine was not switched on
García-Olivares 2016 (40)	Mobilisation	Patients with invasive mechanical ventilation and complete bedrest had greater compliance
	Guidelines	use of a protocol and risk scoring system led to decreased risk of inappropriate VTE prophylaxis
Gardiner 2013 (33)	Equipment supply and demand	In 38% of non-adherent cases the IPC machine was not in the room, locating IPC machines in rooms resulted in adherence from 26% to 44%
	Healthcare professional knowledge and behaviours	A nursing knowledge and beliefs survey yields information about barriers that nurses bring to the use of IPC
Kim 2018 (27)	Knowledge	40% overall non-adherence to IPC. Of these, 40% said that no one informed them they needed to keep IPC on
	Patient discomfort	40% overall non-adherence to IPC, 33% said this was due to discomfort
Maffei 2009 (43)	Guidelines	After guidelines were introduced, IPC prescription increased from 26% to 32%
Maxwell 2002 (25)	Healthcare professional knowledge and behaviours	Of 736 observations, non-compliance was noted in 2.7% of cases and this was related to the machine not being switched on
Novis 2009 (34)	Computer assisted prescribing	Electronic suggestion of thromboprophylaxis increased the use of IPC from 50% to 63%
Obi 2015 (35)	Device related	A battery powered device facilitated adherence through enabling mobilisation
	Patient discomfort	A new machine design led to fewer reports of patient discomfort (33% vs 13%)
	Mobilisation	Problems with mobilisation were less using a new machine (71% vs 29%)
Palmerola 2015 (36)	Mobilisation	38% of patients classed as non-adherent to IPC therapy had it discontinued due to liberal standards for ambulation
Ritsema 2013 (28)	Mobilisation	Not replaced after mobilising accounted for 50% of non-compliant observations
	Equipment supply and demand	Lack of machine or cuffs accounted for 22% of non-adherence
	Patient discomfort	Patient discomfort accounted for 19% of non-adherence
Sobierag-Teague 2012 (42)	Patient discomfort	48% of users discontinued the device at night. Comfort related issues discussed but not explicitly linked to non-adherence

Vignon 2013 (17)	Patient discomfort	7% non-compliance in the AES + IPC group. IPC was discontinued due to discomfort, noise and restlessness
Yamamoto 2013 (41)	Guidelines	Combined AES and IPC mechanical prophylaxis was higher in units with a protocol than without (88% vs 80%)

Figure 1: PRISMA flow chart of search results retrieved 30th May 2019

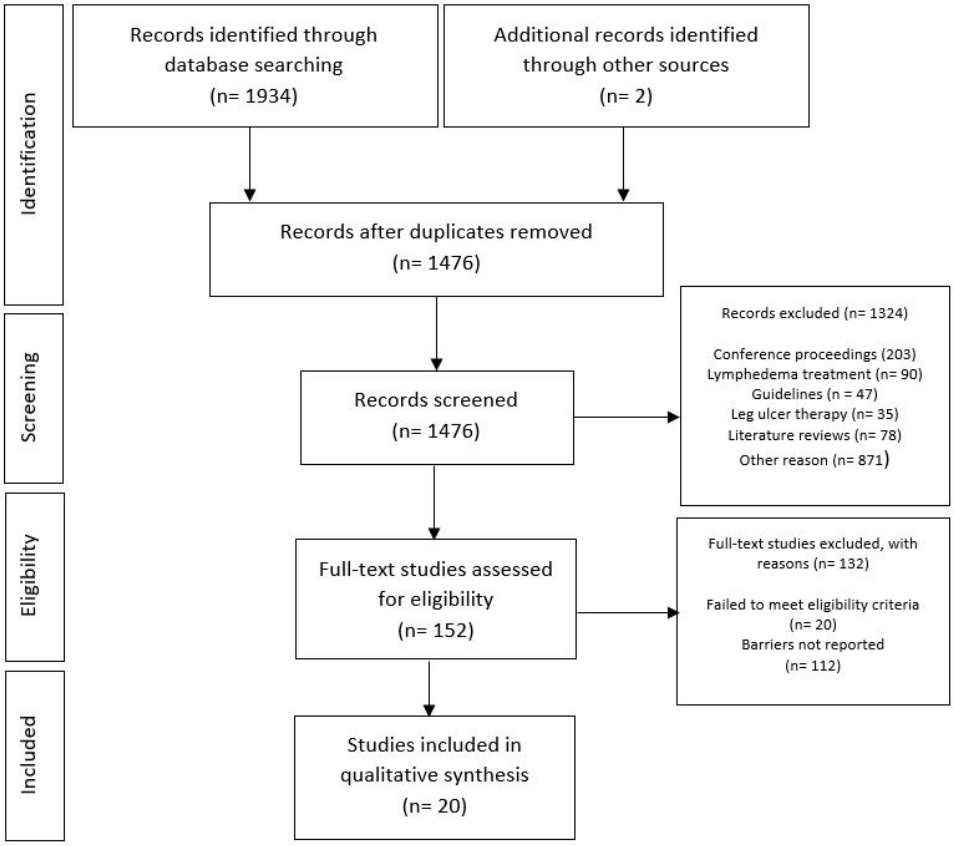

Figure 1

169x156mm (120 x 120 DPI)

Supplementary file

Intermittent pneumatic compression for venous thromboembolism prevention: a systematic review on factors affecting adherence

Search strategy

Population	Intervention	Comparison	Outcomes
Intermittent pneumatic compression OR Sequential compression	Interven$ OR Strateg$ OR Guideline$ OR Educat$ OR Inform$ OR PDSA OR Plan do study act OR Improv$ OR Implement$ OR Toleran$ OR Aware$ OR Present$ OR Program$ OR Plan$ OR Approach$ OR Project$ OR Procedure$ OR Polic$ OR Method$ OR Design$ OR Action$ OR Part$ OR Involv$ OR Practice$ OR Process$ OR System$ OR Technique$ OR Scheme$	N/A	Complian$ OR Adhere$ OR Efficacy OR Effective$ OR Outcome$ OR Success$ OR Fail$ OR Fidelity

Medline Search

1. (Complian$ or Adhere$ or Efficacy or Effective$ or Outcome$ or Success$ or Fail$ or Fidelity).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

2. (Interven$ or Strateg$ or Guideline$ or Educat$ or Inform$ or PDSA or Plan do study act or Improv$ or Implement$ or Toleran$ or Aware$ or Present$ or Program$ or Plan$ or Approach$ or Project$ or Procedure$ or Polic$ or Method$ or Design$ or Action$ or Part$ or Involv$ or Practice$ or Process$ or System$ or Technique$ or Scheme$).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

3. (Intermittent pneumatic compression or Sequential compression).mp. [mp=title, abstract, original title, name of substance word, subject heading word, keyword heading word, protocol supplementary concept word, rare disease supplementary concept word, unique identifier, synonyms]

4. 1 and 2 and 3

Filters

English language
Dates - January 1960 – May 2019

Reporting checklist for systematic review and meta-analysis.

Based on the PRISMA guidelines.

Instructions to authors

Complete this checklist by entering the page numbers from your manuscript where readers will find each of the items listed below.

Your article may not currently address all the items on the checklist. Please modify your text to include the missing information. If you are certain that an item does not apply, please write "n/a" and provide a short explanation.

Upload your completed checklist as an extra file when you submit to a journal.

In your methods section, say that you used the PRISMAreporting guidelines, and cite them as:

Moher D, Liberati A, Tetzlaff J, Altman DG, The PRISMA Group. Preferred Reporting Items for Systematic Reviews and Meta-Analyses: The PRISMA Statement

		Reporting Item	Page Number
Title			
	#1	Identify the report as a systematic review, meta-analysis, or both.	1
Abstract			

Structured summary	#2	Provide a structured summary including, as applicable: background; objectives; data sources; study eligibility criteria, participants, and interventions; study appraisal and synthesis methods; results; limitations; conclusions and implications of key findings; systematic review registration number	2
Introduction			
Rationale	#3	Describe the rationale for the review in the context of what is already known.	3
Objectives	#4	Provide an explicit statement of questions being addressed with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
Methods			
Protocol and registration	#5	Indicate if a review protocol exists, if and where it can be accessed (e.g., Web address) and, if available, provide registration information including the registration number.	4
Eligibility criteria	#6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rational	4
Information sources	#7	Describe all information sources in the search (e.g., databases with dates of coverage, contact with study authors to identify additional studies) and date last searched.	4

Search	#8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	5
Study selection	#9	State the process for selecting studies (i.e., for screening, for determining eligibility, for inclusion in the systematic review, and, if applicable, for inclusion in the meta-analysis).	5
Data collection process	#10	Describe the method of data extraction from reports (e.g., piloted forms, independently by two reviewers) and any processes for obtaining and confirming data from investigators.	5
Data items	#11	List and define all variables for which data were sought (e.g., PICOS, funding sources), and any assumptions and simplifications made.	Supp. file
Risk of bias in individual studies	#12	Describe methods used for assessing risk of bias in individual studies (including specification of whether this was done at the study or outcome level, or both), and how this information is to be used in any data synthesis.	5
Summary measures	#13	State the principal summary measures (e.g., risk ratio, difference in means).	n/a
Planned methods of analyis	#14	Describe the methods of handling data and combining results of studies, if done, including measures of consistency (e.g., I2) for each meta-analysis.	n/a

Risk of bias across studies	#15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	n/a
Additional analyses	#16	Describe methods of additional analyses (e.g., sensitivity or subgroup analyses, meta-regression), if done, indicating which were pre-specified.	n/a
Results			
Study selection	#17	Give numbers of studies screened, assessed for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	5
Study characteristics	#18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citation.	6
Risk of bias within studies	#19	Present data on risk of bias of each study and, if available, any outcome-level assessment (see Item 12).	n/a
Results of individual studies	#20	For all outcomes considered (benefits and harms), present, for each study: (a) simple summary data for each intervention group and (b) effect estimates and confidence intervals, ideally with a forest plot.	n/a
Synthesis of results	#21	Present the main results of the review. If meta-analyses are done, include for each, confidence intervals and measures of consistency.	7

Risk of bias across studies	#22	Present results of any assessment of risk of bias across studies (see Item 15).	n/a
Additional analysis	#23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression [see Item 16]).	n/a
Discussion			
Summary of Evidence	#24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., health care providers, users, and policy makers	10
Limitations	#25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias).	10
Conclusions	#26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	10
Funding			
Funding	#27	Describe sources of funding or other support (e.g., supply of data) for the systematic review; role of funders for the systematic review.	1