Toward the Optimal Use of Negative Pressure Wound Therapy for the Treatment of Complex Wounds

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IN BRIEF

Complex wounds place a great burden on patients, health care professionals, and the entire health care system in Canada. Negative pressure wound therapy (NPWT) is one of the treatment options proposed to help close complex wounds. In recent years, NPWT technology parks have been created in several regions of Quebec to meet a growing demand on the part of clinicians. Given that this technology is expensive compared to standard dressings, that there are no practice guidelines in Quebec, and that the number of individuals likely to develop complex wounds is on the increase, the risks of suboptimal use and increased costs are foreseen. It was in this context that the Direction générale des services de santé et médecine universitaire of the Ministère de la Santé et Services Sociaux (MSSS) appointed the Institut national d'excellence en santé et en services sociaux (INESSS) to develop an optimal use guideline (OUG) on NPWT for the treatment of complex wounds. The objective of this report is to present all the data gathered as part of INESSS’s work and to present the recommendations developed for the judicious use of NPWT in Quebec. This work served as a basis for creating the OUG.

The decision to use NPWT largely depends on the therapeutic intention, which varies according to the nature and complexity of the wound and the characteristics of the patient. Therefore, to benefit from the use of the technology and to ensure its safe application, patient-specific contraindications and risk factors must be taken into consideration as soon as the decision to use NPWT has been made, in the same way that factors that impede healing are taken into consideration. When the clinical objectives are not met within the prescribed time frame, the use of NPWT must be reassessed to determine the relevance of continuing or discontinuing treatment.

The update of the scientific data (SD) following the publication of the report by the Centre hospitalier universitaire (CHU) de Québec’s Health Technology Assessment Unit (HTAU) in 2010 did not result in any changes to the authors’ assessment; namely, that NPWT is not automatically recommended for routine use as first-line treatment in patients with a complex wound. The new published randomized controlled trials (RCTs), like those published prior to 2009, have a high risk of bias and are very heterogeneous, and the clinical efficacy of the observed variations in terms of the different indicators is difficult to determine. The studies often have separate objectives and do not measure the same indicators, which can vary greatly depending on the type of wound. Nonetheless, the efficacy results on two clinical indicators figure more prominently; namely, the time to wound closure and the rate of split-thickness skin graft survival. For the first indicator, the level of evidence is moderate for diabetic foot ulcers but lower for leg ulcers, pressure ulcers, surgical wounds, traumatic wounds, and flaps. The level of evidence for the rate of split-thickness skin graft survival also is moderate, and, for the most part, efficacy was, in the RCTs consulted, assessed in patients who had received or were receiving a split-thickness skin graft for an acute wound. For the other indicators, the levels of evidence are low to very low. The analysis of the safety dimension revealed that NPWT has no major adverse effect on patient safety if good wound care practices are applied. In view of the methodological limitations and the number of studies involved, the SD does not allow the conclusion to be drawn that NPWT has greater advantages or drawbacks than standard treatment regarding patients’ quality of life.
To produce its recommendations, INESSS took into account the data derived from the RCTs on the various types of complex wounds, the data from other types of study designs assessed by the authors of the guidelines consulted, the information presented in the reports from health technology assessment (HTA) agencies, and the experiential knowledge of various Quebec experts and clinicians who collaborated with INESSS.

To conclude, the optimal management of patients — in collaboration with health care professionals with complex wound care expertise — and the use of NPWT could be beneficial for certain patients and effective for the Quebec health care system if they are initiated in a timely manner and for the right patient, and if the criteria for NPWT use and cessation are met.
RÉSUMÉ

Introduction
La thérapie par pression négative est une des options de traitement avancé pour aider à la fermeture des plaies complexes. Au Québec, une augmentation de la prévalence des plaies complexes est anticipée en raison du vieillissement de la population et du nombre croissant de personnes souffrant de maladies chroniques, notamment, le diabète. Ces dernières années, plusieurs régions du Québec se sont dotées de parcs technologiques de thérapie par pression negative (TPN) pour répondre à une demande croissante des cliniciens. En 2010, cette technologie a fait l’objet de deux évaluations indépendantes par des Unité d’évaluation des technologies et des modes d’intervention en santé (UETMIS) québécoises. La première concluait que la TPN était efficace pour l’accélération de la guérison des plaies des membres inférieurs associés au diabète alors que la seconde s’était montrée plus prudente quant aux constats observés suite aux analyses et avait conclu qu’étant donné la faiblesse des preuves scientifiques, des complications possibles, de l’impact sur l’organisation des services et des coûts élevés, les risques d’une utilisation non optimale et d’un accroissement des coûts étaient pressentis et qu’il y avait un besoin d’établir des balises à l’échelle provinciale. C’est dans ce contexte que la direction générale des services de santé et médecine universitaire du MSSS a mandaté l’INESSS afin de réaliser un guide d’usage optimal (GUO) de la TPN pour le traitement des plaies complexes. L’objectif de ce rapport est de présenter l’ensemble des informations recueillies dans le cadre des travaux de l’INESSS et de présenter les recommandations élaborées en vue d’une utilisation judicieuse de la TPN au Québec. Ce travail a servi d’appui à la réalisation du GUO.

Méthodologie
Une revue systématique de la littérature scientifique a été effectuée en vue de documenter et d’actualiser les connaissances depuis la revue systématique de l’UETMIS du CHU de Québec sur l’efficacité, l’innocuité et l’impact de la TPN sur la qualité de vie. À cette fin, les bases de données Medline (PubMed), EMBASE (Ovid), Cochrane et CINAHL ont été consultées. La recherche documentaire s’étend de 2009 à décembre 2013 et seuls les documents en français et en anglais ont été considérés. La méthodologie utilisée pour mener à terme cette revue systématique respecte les normes de production de l’INESSS. Pour les contextes d’utilisation et la recension des bonnes pratiques cliniques, une recherche systématique a été effectuée dans les bases de données scientifiques PubMed (Medline), Embase et Centre for Reviews and Dissemination (CRD) pour répertorer les guides de pratique, les rapports des agences réglementaires, les rapports des agences d’évaluation des technologies de la santé et les lignes directrices concernant le traitement des plaies avec l’utilisation de la TPN publiés entre 2008 et 2013, en français ou en anglais. La recherche de littérature grise a été effectuée en consultant les bases de données du Guidelines International Network (G-I-N) et du National Guideline Clearinghouse (NGC) puis en consultant les sites internet des organismes se spécialisant en soins des plaies, des organismes réglementaires, des agences de la santé et des services sociaux, des associations ou des ordres professionnels. Les monographies officielles des fabricants ont aussi été consultées.

Résultats
L’actualisation des données scientifiques depuis le rapport de l’UETMIS du CHU de Québec publié en 2010, ne permet pas de modifier le jugement porté par les auteurs à savoir que la TPN n’est pas recommandée d’emblée pour une utilisation courante en première intention chez tous les patients souffrant d’une plaie complexe. Les nouveaux essais contrôlés
randomisés (ECR) publiés, tout comme ceux parus avant 2009 ont un risque de biais élevé et l’efficacité clinique des variations observées au regard des différents indicateurs est difficile à cerner. Les principales limites observées lors de l’analyse de la littérature sont dues à la grande hétérogénéité des études. Cette diversité s’est manifestée au sein même des revues systématiques alors que plusieurs auteurs incluaient à la fois des études traitant de plaies aiguës et chroniques qui, d’un point de vue étiologique, sont très différentes. Outre le fait de la diversité des plaies à l’étude, le choix des indicateurs varie beaucoup d’une étude à l’autre, rendant impossibles certaines comparaisons entre les études. Néanmoins, les résultats d’efficacité de deux indicateurs cliniques se démarquent davantage, soit le temps de fermeture de la plaie (se définissant par le recouvrement de celle-ci par un tissu de granulation ou le délai avant une fermeture chirurgicale ou un geste de couverture chirurgicale) et le taux de prise des greffes de peau (chirurgie reconstructive). Pour le premier indicateur, le niveau de preuve est modéré pour les ulcères du pied diabétique alors qu’il est plus faible pour les ulcères de jambe, les ulcères de pression, les plaies chirurgicales, les plaies traumatiques et les lambeaux. Pour le taux de prise de greffe de peau, le niveau de preuve est également modéré et l’efficacité a été majoritairement appréciée dans les ECR consultés chez des patients ayant reçu ou en voie de recevoir une greffe de peau sur une plaie aigüé. Pour les autres indicateurs comme la réduction de la taille/volume, la qualité de vie, la prévention des complications, la durée du traitement et l’utilisation des ressources, les niveaux de preuve en faveur de la TPN sont de faibles à très faibles dus aux limites relatives à l’hétérogénéité de différents paramètres comme le type de plaies, les indicateurs de résultats, les comparateurs et devis d’étude. En ce qui concerne les plaies ouvertes de l’abdomen, le principal indicateur d’intérêt est la capacité de la TPN à constituer un pansement temporaire en vue d’une intervention chirurgicale complémentaire. Or, ce type de plaie se prête moins bien à des ECR et les données disponibles proviennent de devis d’études avec des niveaux de preuves plus faibles mais tout de même un effet en faveur de la TPN. L’évaluation de la dimension « innocuité » suggère que cette technologie est sécuritaire lorsqu’utilisée d’une manière judicieuse, en suivant les bonnes indications et appliquée par des professionnels de la santé adéquatement formés tant sur le plan des traitements des plaies complexes que sur les bonnes pratiques associées à cette technologie. Selon les données rapportées dans la littérature, la TPN apporte des avantages et des inconvénients qui peuvent influencer la qualité de vie du patient. Parmi les inconvénients, notons l’anxiété, le stress, la douleur, un frein à la vie sociale, le sentiment d’être attaché et une baisse de l’estime de soi. Parmi les avantages, on retrouve une diminution dans la fréquence des changements de pansements, une durée d’hospitalisation moins grande et une guérison plus rapide. La qualité de vie est un indicateur relativement subjectif qui dépend du jugement des patients, de leur vécu, de leur valeur et de leur tolérance à la douleur. Les outils de mesures et les critères utilisés sont variés entre les études. Par conséquent, l’analyse des résultats présentés dans les études primaires, puis rapportées dans les revues systématiques, comporte des limites et suggère la prudence dans l’interprétation.

Tous les documents contenant des recommandations de bonnes pratiques cliniques sont réservés, et les auteurs ne recommandent pas l’utilisation de la TPN pour tous les types de plaies. Ils recommandent plutôt son utilisation dans des situations cliniques très circonscrites et pour une catégorie de patients. Certaines informations sur les facteurs à prendre en considération dans la sélection des patients pouvant bénéficier de la TPN, les paramètres de suivi et ceux en lien avec les ressources étaient peu documentées dans les documents retenus.
De façon générale, les différentes parties prenantes ont confirmé l’incertitude relative à l’efficacité de la TPN, mais pour certains patients, la TPN peut procurer un avantage et favoriser la guérison. La sélection judicieuse des patients selon leurs caractéristiques propres et leur type de plaie est un prérequis selon eux à la décision de recourir à l’utilisation de la TPN. Ils ont également souligné l’importance de déterminer des objectifs cliniques clairs et d’arrêter la TPN en absence d’évolution favorable de la plaie ou lors de l’atteinte des objectifs thérapeutiques.

**Conclusions**

Les plaies complexes représentent un défi important pour le patient, les professionnels de la santé et pour l’ensemble du système de santé au Canada et ailleurs. Elles peuvent avoir une incidence importante sur la qualité de vie des patients qui en souffrent et sur les professionnels de la santé qui se sentent souvent impuissants face aux échecs de guérison. Au terme de l’analyse des données de la littérature, triangulée avec les données contextuelles et le savoir expérientiel des parties prenantes consultées, l’INESSS conclut que :

- Des études mieux conçues avec une méthodologie rigoureuse, des participants avec des plaies plus homogènes où il y a peu d’ECR réalisés à ce jour, des comparateurs adéquats, des indicateurs cliniques pour lesquels la TPN pourrait apporter un réel bénéfice et des études échelonnées sur une durée suffisamment longue, seraient utiles pour les évaluations futures et l’appréciation des avantages de la TPN sur différents types de plaies.
- La collaboration interprofessionnelle et l’accessibilité à des équipes dédiées en soins des plaies complexes sont des atouts importants à une prise en charge optimale des patients souffrant de plaies complexes et pour une utilisation judicieuse de la TPN.
- Les bénéfices de la TPN au regard de certains indicateurs cliniques ne dépendent pas toujours de l’étiologie et de la complexité de la plaie, mais aussi des facteurs propres à l’individu. Bien que les données actuelles ne permettent pas de prédire pour quel patient la TPN sera plus efficace\(^1\) que le traitement usuel, il est important de réunir les conditions gagnantes avant l’amorce en stabilisant les facteurs nuisant à la cicatrisation et en appliquant les bons soins de base.
- Une fois la TPN amorcée, l’accent doit être mis sur l’atteinte des objectifs cliniques clairement signifiés en évaluant régulièrement l’évolution de la plaie sous TPN, puis, en absence d’évolution favorable ou de stagnation de la plaie, la thérapie devrait être arrêtée.
- La difficulté à retracer les données pour dresser un portrait de l’utilisation de la TPN au Québec amène l’INESSS à suggérer la création d’un système d’enregistrement des données cliniques des personnes recevant une TPN. L’enregistrement des données sous formes non nominatives permettrait de suivre des indicateurs de performance notamment sur le plan des diagnostics, des durées de traitements, des effets indésirables et des complications pour générer des données d’efficacité, d’efficience et d’innocuité au niveau national. L’enregistrement de données sous formes nominatives serait pertinent pour les professionnels de la santé afin d’assurer le suivi clinique et optimiser la continuité des soins en facilitant la communication interprofessionnelle et inter-établissement à des fins cliniques. Enfin, il pourrait faciliter l’identification des patients « candidats » à la TPN et l’application des bonnes pratiques.

\(^1\) Pour les plaies complexes ayant une indication relative à l'utilisation de la TPN.
SUMMARY

Towards the optimal use of negative pressure therapy for the treatment of complex wounds

Introduction

Negative pressure wound therapy (NPWT) is one of the treatment options proposed to help close complex wounds. In Quebec, an increase in the prevalence of complex wounds is anticipated because of the aging of the population and the growing number of people with chronic diseases, particularly diabetes. In the past few years, NPWT technology parks have been created in several regions of Quebec to meet a growing demand on the part of clinicians. In 2010, this technology was the subject of two independent assessments by Quebec health technology assessment units (HTAU). One concluded that NPWT is effective in accelerating the healing of diabetic wounds of the lower limbs, whereas the other was more cautious given the findings of its analyses and concluded that, given the weakness of the scientific evidence, the potential complications, the impact on services for the organization, and the high costs, a risk of suboptimal use and increased costs was foreseen, and that there was a need to establish provincial guidelines. It was in this context that the Direction générale des services de santé et médecine universitaire of the Ministère de la Santé et Services Sociaux (MSSS) appointed the ministère de la santé et des services sociaux (INESSS) to develop an optimal use guideline (OUG) on NPWT for the treatment of complex wounds. The objective of this report is to present all the data gathered as part of INESSS's work and to present the recommendations developed for the judicious use of NPWT in Quebec. This work served as a basis for creating the OUG.

Methodology

A systematic review (SR) of the scientific literature was conducted to document and update the knowledge since the Centre hospitalier universitaire (CHU) de Quebec's HTAU carried out a SR of the efficacy and safety of NPWT and its impact on quality of life. To this end, we queried the scientific databases (SDs) MEDLINE (PubMed), Embase (Ovid), Cochrane, and CINAHL. The literature search extended from 2009 to December 2013, and only publications in French and English were considered. The methodology used to carry out this SR was in accordance with INESSS's production standards. For the usage contexts and the survey of good clinical practices, we systematically searched the scientific databases MEDLINE (PubMed), Embase, and the Centre for Reviews and Dissemination (CRD) for practice guidelines, reports from regulatory agencies, reports from HTA agencies, and guidelines concerning the treatment of wounds with NPWT published in French or English between 2008 and 2013. The grey literature was searched by querying the databases of the Guidelines International Network (G-I-N) and the National Guideline Clearinghouse (NGC), and by consulting the websites of organizations specializing in wound care, regulatory agencies, health and social services agencies, and professional associations and bodies. Manufacturers' official product monographs were also consulted.

Results

The update of the SD following the publication of the report by the CHU de Québec's HTAU in 2010 did not result in any changes to the authors' assessment; namely, that NPWT is not automatically recommended for routine use as first-line treatment in patients with a complex wound. The new published randomized controlled trials (RCTs), like those published prior to 2009, had a high risk of bias and are very heterogeneous, and the clinical efficacy of the observed variations for the different indicators is difficult to determine. The main limitations observed during the literature analysis are the result of considerable inter-study
heterogeneity. This variability was encountered even within the SRs, with several authors having included studies on both acute wounds and chronic wounds — which are very different from an etiological standpoint.

Apart from the diversity of the wounds in these studies, the choice of indicators varied considerably from study to study, making certain comparisons between these studies impossible. Nonetheless, the efficacy results for two clinical indicators figure more prominently; namely, the time to wound closure (defined as the time required for granulation tissue to cover the wound or the amount of time required prior to surgical closure or surgical coverage) and the split-thickness skin graft survival rate (reconstructive surgery). For the first indicator, the level of evidence is moderate for diabetic foot ulcers but lower for leg ulcers, pressure ulcers, surgical wounds, traumatic wounds, and flaps. For the split-thickness skin graft survival rate, the level of evidence is also moderate, and, for the most part, efficacy was, in the RCTs consulted, assessed in patients who had received or were receiving a split-thickness skin graft for an acute wound. For the other indicators, such as the reduction in size/volume, quality of life, the prevention of complications, the duration of treatment, and resource use, the level of evidence is low to very low because of the limitations regarding the heterogeneity of different parameters (such as wound type, the outcome indicators, the comparators, and the study designs). For open abdominal wounds, the primary indicator of interest is the use of NPWT as a temporary dressing in preparation for an additional surgical procedure. However, this type of wound is less amenable to RCTs, and the available data are from study designs with lower levels of evidence.

The evaluation of the safety aspect suggests that this technology is safe when used judiciously for the right indications by health professionals who are adequately trained in both the treatment of complex wounds and the proper practices associated with this technology. According to the literature data, NPWT has advantages and drawbacks that can affect the patient’s quality of life. Among the drawbacks are anxiety, stress, pain, the patient’s social life being on hold, the feeling of being hooked up, and a decrease in self-esteem. The benefits include a decrease in the frequency of dressing changes, a shorter hospital stay, and faster healing. Quality of life is a very subjective indicator that depends on the patient’s judgment, life experience, values, and pain tolerance. The measurement tools and the criteria used vary from study to study. Consequently, the analysis of the results presented in the primary studies and subsequently reported in the SRs has certain limitations and warrants interpretive caution.

All the publications containing good clinical practice recommendations are guarded, and the authors do not recommend NPWT for all types of wounds. Rather, they recommend its use in very specific clinical situations and for one category of patients. Certain information on the factors to be taken into consideration when selecting patients who might benefit from NPWT and on the follow-up and resource-related parameters is sparse in the publications selected.

In general, the different stakeholders confirmed the uncertainty regarding the efficacy of NPWT, but for some patients, NPWT may confer a benefit and promote healing. In their view, judiciously selecting patients according to their specific characteristics and their wound type is a prerequisite for deciding to use NPWT. They also underscored the importance of establishing clear clinical objectives and of discontinuing NPWT if there is no favourable change in the wound or when the therapeutic objectives have been achieved.
Conclusions

Complex wounds constitute a major challenge for patients, health professionals, and the entire health care system in Canada and elsewhere. They can have a major impact on the patient’s quality of life and on the health professionals, who, faced with treatment failures, often feel powerless. Upon completion of the literature data analysis, which was triangulated with the contextual data and the experiential knowledge of the stakeholders consulted, INESSS concluded that:

- Better-designed and sufficiently long studies with a rigorous methodology, participants with more homogeneous wounds (for which few RCTs have been conducted to date), suitable comparators, and clinical indicators for which NPWT might confer a real benefit would be useful for future assessments and for evaluating the benefits of NPWT for different types of wounds.
- Interprofessional collaboration and access to dedicated complex wound care teams are important for the optimal management of patients with such wounds and for the judicious use of NPWT.
- The benefits of NPWT for certain clinical indicators do not always depend on the wound’s complexity and etiology but also on patient-specific factors. Although the current data do not enable one to predict in which patients NPWT will be more effective than standard treatment, it is important to bring together the winning conditions before initiating NPWT by stabilizing the factors that impede the healing process and providing the proper basic care.
- Once NPWT has been initiated, emphasis should be placed on achieving the clearly stated clinical objectives by regularly evaluating the progression of the wound. If there is no favourable change or if the wound is stagnating, the therapy should be stopped.
- The difficulty in tracking down data to provide an overview of the use of NPWT in Quebec has led INESSS to recommend the creation of a system for recording clinical data from patients treated with NPWT. Recording non-nominal data would make it possible to monitor performance indicators; in particular, for diagnosis, duration of treatment, adverse effects, and complications in order to generate efficacy, efficiency, and safety data throughout Quebec. The recording of non-nominal data would be useful to health professionals for providing the clinical follow-up and optimizing the continuity of care by facilitating interprofessional and inter-facility communication for clinical purposes. Lastly, it could facilitate the identification of patients who are candidates for NPWT, and the use of good practices.
**INITIALISMS AND ABBREVIATIONS**

<table>
<thead>
<tr>
<th>Abbreviation</th>
<th>Description</th>
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<tbody>
<tr>
<td>ASSS</td>
<td>Agence de la santé et des services sociaux</td>
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<td>CHU</td>
<td>Centre hospitalier universitaire</td>
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<tr>
<td>CHUQ</td>
<td>Centre hospitalier universitaire de Québec</td>
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<tr>
<td>CIHI</td>
<td>Canadian Institute for Health Information</td>
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<tr>
<td>CISSS</td>
<td>Centre intégré de santé et de services sociaux</td>
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<tr>
<td>CMQ</td>
<td>Collège des médecins du Québec</td>
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<tr>
<td>CRD</td>
<td>Centre for Reviews and Dissemination</td>
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<tr>
<td>CSSS</td>
<td>Centre de santé et de services sociaux</td>
</tr>
<tr>
<td>CUSM</td>
<td>Centre universitaire de santé McGill</td>
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<tr>
<td>EO</td>
<td>expert opinion</td>
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<tr>
<td>HTA</td>
<td>health technology assessment</td>
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<td>HTAU</td>
<td>health technology assessment unit</td>
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<tr>
<td>INESSS</td>
<td>Institut national d’excellence en santé et en services sociaux</td>
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<tr>
<td>MSSS</td>
<td>Ministère de la Santé et des Services sociaux</td>
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<tr>
<td>NPWT</td>
<td>negative pressure wound therapy</td>
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<tr>
<td>OEQ</td>
<td>Ordre des ergothérapeutes du Québec</td>
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<tr>
<td>OIIQ</td>
<td>Ordre des infirmières et infirmiers du Québec</td>
</tr>
<tr>
<td>OPPQ</td>
<td>Ordre professionnel de la physiothérapie du Québec</td>
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<tr>
<td>OUG</td>
<td>optimal use guide</td>
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<tr>
<td>RCT</td>
<td>randomized controlled trial</td>
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<tr>
<td>ROP</td>
<td>required organizational practice</td>
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<tr>
<td>RSSS</td>
<td>réseau de la santé et des services sociaux</td>
</tr>
<tr>
<td>SD</td>
<td>scientific data</td>
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<tr>
<td>SR</td>
<td>systematic review</td>
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<tr>
<td>TPN</td>
<td>thérapie par pression negative</td>
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<tr>
<td>UETMIS</td>
<td>Unité d’évaluation des technologies et des modes d’intervention en santé</td>
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GLOSSARY

Arterial insufficiency
The impairment of arterial blood flow.

Biofilm
Film formed on the surface of a solid or a liquid by a group of microorganisms that produce a protective and adhesive matrix composed of polymeric substances.\(^2\)

Complex wound
A wound that does not heal according to the normal healing process or that requires advanced medical care (as defined in the current documents produced by the Institut national d’excellence en santé et en services sociaux [INESSS]).

Debridement
The process of cleaning a traumatic or infected wound by excising damaged, necrotic or infected tissue to expose healthy surrounding tissue.\(^2\)

Deep wound
Involvement of noble structures (arteries, nerves, viscera).\(^4\)

Dehiscence
Spontaneous opening of an organ or tissue lysis, which leaves the tissue or organ exposed.\(^2\)

Diabetes
A chronic disease that occurs when the pancreas does not produce enough insulin or when the body cannot effectively use the insulin it produces. This leads to an increased concentration of glucose in the blood (hyperglycemia).\(^3\)

Diabetic foot and diabetic foot ulcer
A result of neuropathy and angiopathy in diabetic patients. As the foot is insensitive to pain and poorly vascularized, there is a high risk of infection; therefore, any minor injury must be treated immediately, as it may lead to complications and, ultimately, amputation of the foot.\(^2\)

The Wagner ulcer classification system [Wagner, 1987] defines the following grades:

- Grade 0: No open lesions, but there may be presence of bone deformity or hyperkeratosis.
- Grade 1: Superficial ulcer without penetration into deep tissues.
- Grade 2: Deep ulcer extending to tendon or bone, and joint capsule without abscess or osteitis.
- Grade 3: Deep ulcer with abscess, osteitis, or septic arthritis.
- Grade 4: Gangrene of the toe or forefoot most often associated with a plantar infection.
- Grade 5: Extensive gangrenous involvement of the foot associated with necrotic lesions and soft tissue infection.


\(^3\) World Health Organization (WHO). Health topics. Available at: http://www.who.int/topics/en/


Enzyme
Enzymes are protein macromolecules characterized by their catalytic activity, which governs specific biochemical reactions in the body.\(^5\)

**Epithelialization**
Regeneration of the epithelium (the tissue lining the outer surface of the mucous membranes and the internal cavities of the body) after an ulceration or, more generally, after a loss of substance. Epithelialization is a form of healing that occurs in two phases: first, the tissue injury is covered by "proud flesh," which ensures connective tissue repair; then, the epithelial cells bordering the wound divide and progressively cover the wound. The healing process is complete only when the epithelial gap is completely closed.\(^6\)

**Exeresis (or ablation)**
A surgical procedure performed to remove, in whole or in part, a natural, pathological, or foreign element from the body.\(^4\)

**Gangrene**
A condition characterized by tissue death that most commonly affects the limbs but occasionally also the viscera such as the liver, lungs, or intestines.\(^5\)

**Granulation tissue**
New connective tissue composed of fibroblasts stimulated to multiply by growth factor released by macrophages, endothelial cells, and fibroblasts. This healthy tissue forms during the normal healing process. It is bright red and shiny, with a granular appearance, and fills and covers the wound cavity (adapted from [St-Cyr, 2012]).

**Hypergranulation**
The formation of excess granulation tissue that exceeds the amount needed to replace the wound’s tissue deficit. It is fragile, friable tissue that bleeds easily and prevents wound healing (adapted from [Stephen-Haynes, 2011] and [St-Cyr, 2012]).

**Hyperkeratosis**
Dermatosis consisting in hyperplasia of the stratum corneum of the epidermis; thickening of the stratum corneum of the Malpighian epithelium or of the non-Malpighian epithelium with epidermoid metaplasia.\(^6\)

**Leg ulcer**
A persistent leg wound caused by impaired circulation. There are four types of leg ulcers: venous, arterial, combined, and arteriolo-capillary.\(^6\)

**Musculocutaneous flap**
A portion of skin, subcutaneous cellular tissue, or muscle transferred from an intact part of the body to cover a wounded part of the body.


**Malnutrition**
A general or specific pathological state caused by undernutrition, overnutrition, nutritional imbalances, micronutrient deficiencies, or nutrient malabsorption.⁷

**Metalloproteinase**
Protease that breaks down proteins into smaller units and that depends on a metal ion such as sulphur, iron, and zinc for its enzymatic activity.⁷

**Non-commercial NPWT**
Vacuum system from hospital facilities applied to a dressing sealed over a wound.

**Original prescriber**
A professional, either a physician or a nurse, authorized to prescribe negative pressure wound therapy (NPWT) in virtue of the regulations established by the Collège des médecins du Québec. The original prescriber makes a decision regarding NPWT, reassesses the relevance of continuing NPWT, and renews the original prescription with the collaboration of a dedicated interprofessional team or a health care professional who specializes in wound care and who is recognized and authorized by the establishment (as defined in current documents produced by INESSS).

**Pressure ulcer (also pressure sore or bedsore)**
Injury to the skin and underlying tissue usually occurring over a bony prominence as a result of pressure, or pressure in combination with shear or friction [Black et al., 2007].

**Protease or peptidase**
An enzyme that ensures the breakdown of proteins by breaking the chemical bonds (peptide bonds) between the amino acids.⁷

**Quality of life**
Quality of life is defined as an individual’s perception of their position in life in the context of the culture and value systems in which they live and in relation to their goals, expectations, standards, and concerns. It is a broad-ranging concept affected in a complex way by the person’s physical health, psychological state, level of independence, social relationships, personal beliefs, and their relationship to salient features of their environment [WHO, 1997].

**Re-epithelialization**
Formation of new epithelium as a result of the healing process.⁸

**Superficial wound**
Affects only the top layer of the skin or the immediate underlying tissue.⁷

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Symbiosis
A mutually beneficial association between two organisms of different species.\(^9\)

Ulcer
Loss of substance of varying depth in surface epithelium. It can be cutaneous or mucosal.\(^9\)

Undernutrition
A form of malnutrition caused by undernourishment or by the inadequate assimilation, use, or metabolism of nutrients.\(^9\)

Wound
A break in the tissue caused by an accident (injury, burn) or a surgical procedure.\(^9\)

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INTRODUCTION

Complex wounds represent a major health problem, with far-reaching consequences for patients, their families, health care professionals, and the health system if not adequately dealt with. For more than 15 years, negative pressure wound therapy (NPWT) has been included in the therapeutic arsenal of clinicians to treat complex wounds that are slow to heal or that require a more specialized approach. The number of clinical indications for the use of NPWT has grown in recent years, despite the limitations of the evidence. This increase, combined with certain advantages inherent to the frequency of dressing changes compared with standard treatment, has led to a significant increase in the use of NPWT. However, the costs associated with NPWT are up to seven times greater than those associated with the use of standard dressings (health technology assessment unit [HTAU] of the Centre hospitalier universitaire de Québec [CHUQ], 2010 and Haute Autorité de Santé/HAS, 2010a). The increased use of this technology also results in a higher risk of incidents. Many complications and adverse effects attributable to NPWT have been reported in Quebec and elsewhere in the world. Inadequate use of the technology, combined with limited knowledge on the part of health care professionals, is suspected in these incidents.

In 2010, the CHUQ’s HTAU published an assessment report on this technology at the request of the Agence de la santé et des services sociaux (ASSS) de la Capitale-Nationale. The report concluded that, despite the lack of solid evidence regarding the efficacy of NPWT, the technology continues to be an asset in the therapeutic arsenal for complex wounds, although for specific and targeted indications. Moreover, the authors emphasized the importance of improving the organization of complex wound care for the optimal use of the therapy. In 2009, there was little consistency in the indications for NPWT use in the literature, and the recommendations for good practice were rather unclear and showed potential bias. It was in this context that the Direction générale des services de santé et médecine universitaire of the Ministère de la Santé et des Services sociaux (MSSS) appointed INESSS, in December 2012, to develop an optimal use guideline (OUG) on NPWT for the treatment of complex wounds to guide and support health care professionals who assess and treat patients with these wounds.

The objectives of this report are to provide an update of the scientific data (SD) on the efficacy and safety of NPWT since 2009, to summarize the effects of NPWT on patients' quality of life, and to identify the recommendations and information derived from best clinical practice guidelines and consensus conferences, and the contextual and experiential data from health care professionals with expertise in the field. This report does not provide a cost-benefit analysis of NPWT, as there is a lack of data on the use of this technology in Quebec. However, it emphasizes that certain efficiency gains could be obtained through the adequate and safe use of the technology.

The information presented in this report served as a basis for the deliberations of the working group assigned to develop the recommendations and key messages included in the OUG.
1 COMPLEX WOUNDS AND NEGATIVE PRESSURE WOUND THERAPY

1.1 Definition and classification of wounds

By definition, a wound is an opening in the skin barrier caused by a physical trauma (e.g., injury, burn, surgery). Depending on the extent of the damage done to the skin, the wound is considered to be either simple or complex. There are various theoretical methods of wound classification in the literature. The classification proposed in 2006 by the Association québécoise d’établissements de santé et de services sociaux [AQESSS, 2006] categorizes wounds according to their acuteness and etiology, and is presented in Table 1.

The complexity of a wound is defined by various factors, including its surface and depth, the nature of the physical trauma, its duration and progression, and its response to a first treatment. An acute wound is a wound for which no factors interfere with the normal healing process. It may or may not be surgical in origin. This type of wound generally closes after a few days or within three to four weeks at most, depending on its extent and depth. The stages of the healing process are discussed in Section 1.3. A wound that does not follow the normal healing process or that is arrested in one of its stages becomes a chronic wound. According to the French National Authority for Health (HAS) in France, a chronic wound is a wound with an extended healing time; that is, it does not heal within four to six weeks with standard treatment [HAS, 2010].

Table 1: Classification of Wounds

<table>
<thead>
<tr>
<th>TYPE OF WOUND</th>
<th>ACUTE</th>
<th>CHRONIC</th>
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<tbody>
<tr>
<td>NON-SURGICAL</td>
<td>Burn Abrasion Tear</td>
<td>Diabetic foot ulcer</td>
</tr>
<tr>
<td></td>
<td>Cut</td>
<td>Pressure Ulcer</td>
</tr>
<tr>
<td></td>
<td>Traumatic wound</td>
<td>Arterial ulcer</td>
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<tr>
<td></td>
<td>Incision</td>
<td>Venous ulcer</td>
</tr>
<tr>
<td></td>
<td>Excision</td>
<td>Neoplastic ulcer</td>
</tr>
<tr>
<td>SURGICAL</td>
<td>Surgical debridement</td>
<td>Dehiscence</td>
</tr>
<tr>
<td></td>
<td>Split-thickness skin graft</td>
<td>Evisceration</td>
</tr>
<tr>
<td></td>
<td>Musculocutaneous skin flap</td>
<td>Wound with complication (e.g., infection)</td>
</tr>
</tbody>
</table>

The panel of experts from the National Pressure Ulcer Advisory Panel (NPUAP) [NPUAP, 2009] proposes a series of six stages to categorize pressure wounds according to the type of tissue affected:
- Stage SDTI (suspected deep-tissue injury): Purple or maroon localized area of discoloured intact skin
- Stage 1: Persistent redness of the skin that does not turn white when pressure is applied to it (approximately half of all pressure wounds). In this case as well, the skin is intact
- Stage 2: Partial loss of the outer layers of the skin (one-third of all pressure wounds)
- Stage 3: A crater produced by the loss of skin and some of the underlying tissue
- Stage 4: A crater produced by damage extending to the muscle or bone
- Stage X or unstageable: Stage of the wound cannot be determined, as there is too much dead tissue.
1.2 Prevalence and risk factors

In 2013, the Canadian Institute for Health Information (CIHI) published the results of a Canadian study on the prevalence of compromised wounds based on 2011-2012 administrative data from hospitals, home care services, hospital-based continuing care, and long-term care facilities [CIHI, 2013]. The results show that the overall prevalence of compromised wounds reported in short-term care is approximately 3.5% for the general Canadian population. In Quebec, this represents slightly more than 4%. However, the authors suspect that the quality of the reports on certain wounds in patients hospitalized in short-term care varies from one province to the next, which is a significant limitation of the study. Quebec was excluded from the analysis of the prevalence in other health care settings as a result of significant differences between the definitions and the data collection standards. Overall, the information available in Canada indicates that compromised wounds were reported in more than 7% of home care clients, nearly 10% of long-term care clients, and nearly 30% of patients in complex continuing care, which represents just over 25,000 cases in Canada.

Several risk factors affecting wound healing and wound chronicity were identified in the literature (e.g., diabetes, peripheral vascular disease, thyroid disease, cerebral vascular accident, other cardiovascular diseases, cognitive impairment, pulmonary disease, neurologic impairment affecting mobility and continence, alcoholism, smoking, malnutrition, inflammatory and immune diseases, and medications) [Sussman and Bates-Jensen, 2011].

CIHI selected several of these that were easily identifiable in administrative data banks to verify their impact on compromised wounds reported in Canada. Results show that diabetes and peripheral vascular diseases are significant risk factors for wound development and delayed wound healing [CIHI, 2013]. Age also is a known risk factor for chronic wounds. Reported rates increase with age and peak between 65 and 74 years of age. However, the Canadian study suggests that the prevalence of wounds does not increase in people over the age of 75. The authors hypothesize that people at greater risk of developing compromised wounds are not likely to live as long.

Compromised wounds are defined by the authors as potentially preventable wounds that are either acquired in health care settings (e.g., surgical site infections and pressure ulcers) or that could be avoided with proper care and management of a patient's underlying chronic conditions (e.g., diabetic foot ulcer).
1.3 The healing process

The wound healing process is a complex physiological mechanism activated to restore the integrity of the skin barrier. It is a dynamic process defined by a series of biochemical and cellular events that can be divided into four phases: inflammatory (debridement), proliferative (formation of granulation tissue), re-epithelialization (wound closure), and remodelling (scarring) [Sussman and Bates-Jensen, 2011].

1.3.1 Inflammatory phase

The inflammatory phase is initiated by coagulation and platelet aggregation as soon as the skin barrier is broken [Roy, 2013; Sussman and Bates-Jensen, 2011]. This phenomenon occurs to stop active bleeding and to ensure the protection of exposed tissue. During this phase, the damaged cells, platelets, and immune cells in the injured tissue release various soluble factors that contribute to the vasodilation of blood vessels, increased permeability, and the recruitment of circulating immune cells such as neutrophils and monocytes [Roy, 2013; Sussman and Bates-Jensen, 2011]. These phenomena give rise to wound edema, redness, and exudate, which contains the soluble factors needed to coordinate the healing process and to control local infections. In addition to preventing and controlling infections, neutrophils and macrophages actively participate in the removal of debris, damaged matrix, necrotic tissue, and fibrillar components of the extracellular matrix (e.g., collagen, elastin, and fibronectin), namely through the action of various matrix metalloproteinases [Gibson D et al., 2010; Trengove et al., 1999]. The inflammatory phase usually lasts three to four days, but it may be prolonged if there is an infection or irritation [Roy, 2013]. The process sometimes remains in the inflammatory phase and leads to wound chronicity. The factors that impede the healing process are discussed in section 1.3.6.

1.3.2 Proliferative phase

During the proliferative phase, the extracellular matrix, commonly referred to as "granulation tissue," is reconstructed. The various soluble factors secreted by the macrophages and platelets cause the endothelial cells and fibroblast, which are located in the dermis, to actively multiply to form new blood vessels (neoangiogenesis) and synthesize the new extracellular matrix [Sussman and Bates-Jensen, 2011]. The clot is gradually replaced with granulation tissue, which contains fibroblasts, fibrillar proteins (e.g., collagen and elastin), and newly synthesized capillaries [Morison et al., 2004; Dowsett, 2002]. Under the action of various soluble factors, some fibroblasts will then differentiate into smooth muscle cells — commonly referred to as "myofibroblasts"— which are responsible for wound contraction (drawing together of wound edges). This phase lasts an average of three to twelve days. The presence of healthy granulation tissue is evidence that the healing process is underway.

1.3.3 Re-epithelialization phase

Re-epithelialization is characterized by the migration and division of skin cells leading to wound closure. The keratinocytes from the basal layer of the epidermis divide and migrate from the wound edges toward the centre, where there is granulation tissue [Sussman and Bates-Jensen, 2011]. Once the wound is covered with a monolayer of keratinocytes, the migration is interrupted and cell proliferation rebuilds the stratified epithelium through mitosis.
1.3.4 Remodelling phase

The remodelling phase can last from one to two years and ends with the formation of a scar. It begins after the wound is completely covered with stratified epithelium. This phase leads to a reorganization of the components and extracellular matrix to optimize the functional capacity of the new tissue [Sussman and Bates-Jensen, 2011].

1.3.5 Types of wound healing

There are three types of wound healing, based on the nature of the wound. Healing by primary intention concerns surgical wounds or surgically sutured traumatic wounds. These are clean wounds; that is, wounds exempt of debris and necrotic tissue, with little or no loss of tissue and edges that can be joined using sutures, staples, or adhesive closure strips. After a few days, the wound closure devices are removed and the healing process continues with the inflammatory, proliferative, re-epithelialization, and remodelling phases.

Healing by secondary intention concerns wounds that cannot be surgically closed as a result of a significant loss of tissue, edema, or infection. They are left open, therefore allowing the natural healing process to cover the wound. A step involving mechanical, chemical, conventional (e.g., with a sharp object), or surgical debridement is often needed to remove debris, biofilms, extracellular matrix, and necrotic tissue to optimize wound healing [Schultz, 2012].

Healing by tertiary intention occurs after the size of the wound has decreased sufficiently through the natural process or after any edema or infection has been managed in preparation for surgical closure or coverage with a skin flap or a split-thickness skin graft.

1.3.6 Factors affecting healing in complex wounds

Various exogenous and endogenous factors can hinder the wound healing process and increase the likelihood of recurrence [Sussman and Bates-Jensen, 2011]. Understanding these factors is crucial for the prevention and early identification of wound recurrence, and the decision-making process for selecting the most suitable therapeutic strategy.

1.3.6.1 Patient-related factors

Aging skin, hyperkeratosis, and certain individual-specific genetic characteristics can affect the normal healing process and cause a delay in wound closure or unsightly scarring without leading to a self-perpetuating, non-healing cycle.

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11 Biofilms bind to the components of the extracellular matrix (e.g., collagen fibres) and to the surface of bones, dressings, and implants. The bacteria that compose them are embedded in a polymeric matrix that protects them against the host's defences.
The majority of exogenous factors responsible for wound chronicity are those that affect immune response, inflammatory response, vascularization, and the synthesis of new cells, blood vessels, and components of the extracellular matrix. These include malnutrition [Bouchard and Lamarche, 2010; Johnston 2007], high blood glucose levels [Collins, 2010]; dehydration [Collins, 2015]; and certain concomitant diseases such as diabetes [Collins, 2010], active neoplasms, chronic inflammatory diseases, immunodeficiency diseases [Baxter, 1994], vascular diseases (e.g., venous diseases, arterial diseases, particularly with a systolic pressure index of less than 0.8 [Sibbald, 2006]), and cardiovascular diseases. The physiological process of these diseases, combined with the medications required to stabilize them, complicate the healing process. Some of the medications that may impede wound healing are corticosteroids, nonsteroidal anti-inflammatory drugs (NSAIDs), immunosuppressants, antineoplastics, beta blockers, and anticoagulants [Sibbald, 2006].

Other patient-related factors may lead to the development of chronic wounds that become increasingly complex over time. These include sensory deficit, reduced mobility, poor health practices, and psychosocial factors such as social isolation and psychological, psychiatric, or cognitive disorders, which can contribute to treatment non-compliance or the inability to understand the extent of the problem (summarized in [EWMA, 2008]).

1.3.6.2 Wound-related factors

Various wound-related characteristics can affect the healing process. Studies conducted by Margolis et al. [Margolis et al., 2002; Margolis et al., 1999] on venous ulcers and diabetic foot ulcers showed that the duration (more than two months), size (greater than 2 cm²), and depth (penetration to the tendons, ligaments, bones, or joints) of ulcers are important clinical indicators that predict the complexity of the wound. The greater the wound surface area, the longer the time to wound closure and the greater the risk of infection if the wound is exposed to the air. Lack of oxygen (ischemia), lack of nutrients, and the presence of debris, foreign bodies, calcium crystals, and necrotic tissue all are powerful local stimuli that support the recruitment of neutrophils in the wound, a phenomenon that confines the healing process to the inflammatory phase [Roy, 2013]. Irritation caused by dressing changes, allergies to the material, an overabundance of exudate, and friction also contribute to maintaining inflammation. A wound stalled in the inflammatory phase can lead to hypergranulation; that is, excessive proliferation leading to an excess of extracellular matrix, a phenomenon caused in part by an imbalance between collagen synthesis and degradation [Stephen-Haynes, 2013].

The presence of a local infection, critical colonization, or biofilm also contributes to wound chronicity by supporting the inflammatory phase. When the skin barrier is breached, bacteria naturally present on the skin (e.g., Staphylococcus sp. and Streptococcus sp.) can penetrate and colonize the wound. Over time, a balance is achieved and the bacteria live in symbiosis with the host, unless local factors encourage their proliferation [Bowler, 2003].
Bacterial colonization is characterized by a bacterial count of less than $10^5$ bacteria/mm$^3$. When the bacterial count exceeds this number, critical colonization takes place, and a local infection may develop.

Unlike critical colonization, which is virtually asymptomatic (no visible signs), infection is characterized by local clinical signs such as abundant, thick, malodorous, and coloured exudate (depending on the bacterial species), perilesional erythema with spontaneous pain, and edema. Recent studies have shown that the majority of chronic wounds are colonized by biofilms mainly composed of bacterial species belonging to the family *Pseudomonas* and *Staphylococcus* (summarized in [Metcalf et al., 2014; James et al., 2008] or by anaerobic bacteria [Stephens et al., 2003]). Biofilms located deep in chronic wounds are particularly resistant to standard antimicrobial agents [Han et al., 2011] and contribute to maintaining wound inflammation. In their article, Metcalf et al. present both a table of clinical indications that suggest the presence of a biofilm and a clinical algorithm [Metcalf et al., 2014]. The acronyms NERDS and STONES may be useful in making decisions concerning antimicrobial therapy [Sibbald et al., 2006].

### 1.3.7 Negative pressure wound therapy

The use of negative pressure to promote wound healing has a long history (summarized in [Fagerdahi, 2013]). However, the first commercial NPWT system was introduced to the market in 1995. The system used polyurethane foam to cover the wound and was indicated for the treatment of acute wounds and compromised wounds. Different types of systems and dressings with a variety of features have since been put on the market to meet the needs of various client groups and health care settings; as a result, clinicians have a wide range of devices and dressings to choose from when they opt for NPWT. The number of clinical indications for the use of NPWT also has increased over the past 20 years; however, the efficacy of NPWT for these indications is still the subject of some debate. NPWT consists in applying a level of pressure below atmospheric ambient pressure to the surface of a wound covered with a special dressing. The treatment is based on two main principles: applying mechanical forces at the site of the wound using suction and creating an occlusive effect [Unité d’évaluation des technologies et des modes d’intervention en santé (UETMIS)-Centre hospitalier universitaire de Québec (CHUQ), 2010].

After more than 15 years of research, the NPWT mechanisms of action are not yet clearly defined. However, experts in the field generally agree that the technology reduces exudate, promotes angiogenesis, and stimulates the formation of granulation tissue (summarized in [Malmstj et al., 2012]). Glass et al. recently published a SR on the molecular mechanisms that can affect the healing process when NPWT is applied to a wound [Glass et al., 2014]. The studies had some limitations and were short-term. Moreover, the storage of samples for the measurement of soluble factors and the quantification methods used did not always seem appropriate.

In summary, human-based studies show that NPWT could, initially, reduce acute inflammation by reducing the expression of certain soluble factors associated with the recruitment and activation of neutrophils (e.g., matrix metalloproteinase) and, subsequently, contribute to increasing the level of vascular endothelial growth factor — a molecule involved in angiogenesis. Animal studies and experimental designs suggest that NPWT increases the concentration of growth factors required for the formation of granulation tissue, and for angiogenesis.
2 METHODOLOGY

The methodology used to prepare this report respects INESSS production standards for systematic reviews (SRs). It was previously developed in an implementation plan, then validated by INESSS’s Comité scientifique permanent en santé et en services sociaux.

2.1 Assessment questions

Question 1
How effective is NPWT in healing complex wounds?\(^{12}\)

Question 2
What are the adverse effects and complications associated with the use of NPWT for the treatment of complex wounds?

Question 3
What are the existing recommendations (modalities of prescription, use, monitoring, and cessation), and the data supporting them, on the context of NPWT use regarding:

- the parameters related to the individual (indications and contraindications)?
- the parameters related to the wound (indications and contraindications)?
- the parameters of the intervention (technical modalities of NPWT, prescription, cessation, and monitoring criteria, including the type of professional responsible for each stage)?
- the parameters related to the resources (type of professional, health care delivery setting). A narrative synthesis of the impact of NPWT on quality of life and pain in patients with complex wounds was also prepared, as was a review of the information concerning the context of wound care practices in Quebec. Consultations with experts from the advisory committee and other stakeholders made it possible to gather experiential knowledge and to contextualize the data from the literature with the use of NPWT.

2.2 Analytical framework

The analytical framework presented in Figure 1 illustrates the relevant factors that were considered in the context of this project. It also includes the assessment questions answered in this report.

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\(^{12}\)It should be noted that complex wounds include acute wounds and chronic wounds. A definition of complex wounds was validated by key informants. The definition is based on the work done by the CHU de Québec's HTAU (2010), which defines complex wounds as chronic wounds (diabetic foot ulcers, venous ulcers, pressure ulcers) or acute wounds (sternal wounds, abdominal wounds, surgical wounds, traumatic wounds, grafts, burns).
2.3 Systematic review — "efficacy" and "safety"

A SR of the literature was conducted to answer questions 1 and 2. It was agreed that the "efficacy" and "safety" dimensions of the SR carried out by the CHU de Québec's HTAU would be updated as part of the development of a health technology assessment (HTA) report published in 2010 at the request of the ASSS de la Capitale-Nationale [UETMIS-CHUQ, 2010]. The scientific literature search was carried using the same criteria as those described by the CHU de Québec [UETMIS-CHUQ, 2010].

An initial search was carried out in the SDs PubMed (MEDLINE), Embase, the Cochrane Library, and the Centre for Reviews and Dissemination (CRD). The CINAHL database was consulted specifically to assess quality of life. This search targeted SRs with or without meta-analyses, RCTs, non-randomized studies, and case studies published between 2009 and 2013 — in French or in English — on the efficacy of NPWT in patients with complex wounds. A search of the grey literature published between 2008 and 2014 was initially carried out by consulting the websites of the HTA agencies consulted during the assessment of the CHU de Québec to verify the new documents published since the publication of their report. The adverse effects, side effects, and complications reported in the studies identified in the grey literature during the literature searches on the efficacy of NPWT were included in the "safety" dimension. The stakeholders also were called upon to inform the project team of any publication they considered to be relevant. In September 2014, a search of new SRs on NPWT published since December 2013 was carried out in PubMed (MEDLINE) and CRD.
The scientific studies and grey literature were independently selected by two reviewers (MJG and JB). An independent assessment of the quality of the studies was conducted by two reviewers (JB and MJG or MT). The AMSTAR assessment tool [Shea et al., 2007a; Shea et al., 2007b] was used to assess the quality of the SRs. The Critical Appraisal Skills Programme (CASP) tool was used to assess the quality of the RCTs. Data extraction was conducted by a reviewer (MJG/JB) using pre-established data extraction forms that were tested beforehand in a few studies to ensure their validity.

The scientific evidence, which was derived from RTCs published since 2009 and other RCTs not included in the systematic review by the CHU de Québec's HTAU but included in some SRs that have since been published, was summarized in the form of an analytical narrative synthesis; the Scottish Intercollegiate Guidelines Network (SIGN) method was used to assess the quality of the evidence based on conclusive data. The complete methodology used to conduct the SR is described in the report on the SR available on the INESSS website entitled Efficacy and safety of negative pressure wound therapy for the treatment of complex wounds.

2.4 Recommendations for good clinical practice for NPWT

In reply to question 3, an initial search was conducted in the SDs PubMed (MEDLINE), Embase, and the CRD to identify clinical practice guidelines, reports by regulatory agencies, HTA reports, consensus conferences, and guidelines for the treatment of wounds using NPWT published between 2008 and 2013, in French or in English. The search was complemented by consulting the bibliography of selected publications and the expert members of the advisory committee. Moreover, the parameters for the resources, the individual, the wound, and the intervention were retrieved, when available, from the studies selected for the preceding questions.

A search of the grey literature was conducted by consulting the databases of the Guidelines International Network (G-I-N) and the National Guideline Clearinghouse (NGC) to identify the clinical practice guidelines that could not be found in standard SDs. The same grey literature search strategy as that focusing on the efficacy of NPWT was used to identify other clinical practice guidelines developed by organizations, agencies, associations, and professional bodies. Manufacturers' official product monographs also were consulted. Document selection was conducted independently by two reviewers (MJG and JB), first based on the title and abstract, then according to the selection criteria presented in Appendix B. Disagreements were resolved by seeking the opinion of a third reviewer (MT).

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13 www.casp-uk.net
14 http://www.sign.ac.uk/guidelines/fulltext/50/annexoldb.html (website viewed March 30, 2015)
15 http://www.g-i-n.net/
16 http://www.guideline.gov/
The Appraisal of Guidelines for Research and Evaluation II (AGREE II)\(^\text{17}\) tool was used to assess the quality of the clinical practice guidelines. The documents determined to be of good methodological quality are those having obtained a mean score arbitrarily set at 50% for the rigour of development of the recommendations domain. Publications of low methodological quality, such as expert consensus without SRs, were consulted only when they provided information that was lacking in good-quality guidelines. The INAHTA\(^\text{18}\) checklist was used for the HTA reports and the reports on the methods of intervention. Disagreements were resolved by consensus and by seeking the opinion of a third reviewer (MT). Data extraction was conducted by a reviewer (MJG/JB) using pre-established data extraction forms that were previously tested in a few studies to ensure their validity. The data were validated by a second reviewer (JB/MT). The results were measured using analytical narrative synthesis.

2.5 Impact of NPWT on quality of life and pain

To determine the impact of NPWT on the quality of life of patients, a search of the scientific literature and grey literature was conducted using the same search strategy as that described in the report Systematic review of the efficacy and safety of negative pressure wound therapy for the treatment of complex wounds, although only the SRs focusing on this aspect were sought. Documents were selected independently by two reviewers (JB and MT) — first, based on the title and abstract; then, according to the selection criteria presented in Appendix B. The AMSTAR tool was used to assess the quality of the SRs, and the same criteria as those previously defined were applied. Data extraction was conducted by a reviewer (JB). Information on the quality of life of patients undergoing NPWT is presented in the form of an analytical narrative synthesis. Any information concerning quality of life and pain identified in the documents selected in previous sections was included in the synthesis.

2.6 Contextual data

A search of the websites of professional bodies (Ordre des infirmières et infirmiers du Québec [OIIQ], Ordre des ergothérapeutes du Québec [OEQ], Ordre professionnel de la physiothérapie du Québec [OPPQ], Collège des médecins du Québec [CMQ]), Accreditation Canada, and teaching hospitals providing telehealth services for complex wound care — as well as the consultation of the HTA report by the CHU de Québec's HTAU helped to identify information on the professional activities reserved for wound care in Quebec, the management of material and cost, accreditation standards, and the organization of wound care. A search of the Régie de l'assurance maladie du Quebec or RAMQ database, namely in the fee-for-service file, was conducted to provide an overview of medical prescriptions for NPWT in Quebec in 2014. The procedure codes for the prescription of NPWT used in the search are 01340, 18121, and 04505. The information obtained from the stakeholders also helped to supplement the contextual data. The information on contextualization is presented in the form of a narrative synthesis.

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\(^\text{17}\) [http://www.agreetrust.org/](http://www.agreetrust.org/)

2.7 Experiential data

Two working groups, the monitoring committee and the advisory committee, were established to assist INESSS in developing the recommendations and the OUG. The objective of these committees was to bring together key stakeholders and have their insight and knowledge of the health and social services network (réseau de la santé et des services sociaux [RSSS]) inform INESSS on the practices and issues specific to Quebec.

The monitoring committee's mandate was to provide opinions on the professional and social relevance and acceptability of the recommendations and the OUG. The members were appointed by their organizations, which were selected by INESSS based on their experience with NPWT and wound care, and their influence and credibility among professionals who use the technology. The composition of the working group is presented in the introductory pages of the document. The members identified some issues and informed INESSS of certain problems associated with suboptimal use and availability issues concerning various technologies based on the different health care settings and their geographic location. They also contributed to the formulation of the final recommendations and presented their views on the knowledge transfer products.

The advisory committee’s mandate is to ensure scientific credibility and clinical relevance by providing information, expertise, opinions, and viewpoints that are essential to the completion of the work. The members were selected based on their specialty, expertise, work setting, and geographic location in order to create a group that is representative of the various settings in which NPWT is used. The composition of this working group is presented in the introductory pages of the document. The members presented their views on the methodology proposed by INESSS and the results of the literature review. They also identified the clinical information clinicians must have to make the decision to use NPWT; to initiate, monitor, and stop treatment; to select and develop recommendations; and to determine which ones should be included in the OUG.

The methods and processes involved in consultations with the stakeholders and experts are presented in the document entitled Context, process, and method of development for the recommendations and development of the optimal use guide.

2.8 Formulation of the recommendations

The factors that affect the strength of a recommendation based on the GRADE (Grading of Recommendations Assessment, Development and Evaluation) approach guided the formulation of the recommendations. Therefore, during advisory committee meetings, the focus of the discussions was on:

- the quality of the evidence presented in the report of the SR combining the data from the RCTs and the SRs consulted, as well as the data presented in the HTA reports, the clinical practice guidelines, and good-quality expert consensus identified, including those from HAS, NHS, and the CHU de Québec's HTAU in this assessment report
- the balance between the benefits and risks associated with the use of NPWT
- the values and preferences of professionals and patients (through the advisory committee and the review of the literature on quality of life) concerning the treatment of complex wounds using NPWT.
More specifically, the quality of the evidence-based data is based on an assessment of the appraisal of the quality of the studies reviewed; that is, those conducted by the authors of the SRs, the clinical practice guidelines, the HTA reports, and the documents derived from the consensus conference selected. The formulation of the recommendations is based on the SD on the efficacy and safety of NPWT, the identified recommendations of good methodological quality for best clinical practice, the impact of NPWT on patients’ the quality of life and the pain, and contextual and experiential data, including that from the experience of clinicians and health care professionals who work in the field.

In order to promote the optimal use of the technology, INESSS provided members with recommendation proposals and key messages for them to disseminate. The first round was conducted via email for an initial selection, and the second was conducted in person to decide on the recommendations and key messages that were unanimously supported. A second meeting was needed to obtain consensus for the new proposals that had to be reformulated. The recommendations were selected if they obtained the approval of at least 80% of the members of the advisory committee. If consensus was not reached regarding the scope of a recommendation or the relevance of including it, the recommendation was either excluded or reformulated. Any recommendation or key message against which an objection was raised was not selected. More information on the methods and processes involved in the consultations with the stakeholders and experts are presented in the document entitled Context, process, and method of development for the recommendations and development of the optimal use guide available on the INESSS website.

2.9 Peer review

The HTA report to support the OUG was sent to four external scientific reviewers. The reviewer’s comments were analyzed by the authors, and the decision of whether or not to include certain comments was left to their discretion.
3 RESULTS OF THE SYSTEMATIC REVIEW OF EFFICACY AND SAFETY

3.1 Document selection
A search of the scientific literature yielded several studies published since 2009 on the efficacy and safety of NPWT for acute and chronic wounds. The meta-analyses and SRs were used to search for the RCTs that were not cited in the SR of the CHU de Québec's HTAU and/or in the aforementioned databases searched. Of the documents identified, 47 were selected:

Efficacy
- Two meta-analyses and five SRs [Azzopardi et al., 2013; Dumville et al., 2013; Dumville and Munson, 2012; Webster et al., 2012; Peinemann and Sauerland, 2011; Suissa et al., 2011; Xie et al., 2010]
- 17 RCTs [Dorafshar et al., 2012; Petkar et al., 2012; Howell et al., 2011; Karatepe et al., 2011; Nain et al., 2011; Petkar et al., 2011; Chio, 2010; Saaiq, 2010; Sepulveda, 2009] [Rasool et al., 2013; Tuncel et al., 2013; Ashby et al., 2012; Pachowsky, 2012; de Laat et al., 2011; Dalla Paola et al., 2010; Perez et al., 2010; Stannard, 2009]]
- Four documents from HTA agencies [HAS, 2010; NHS, 2010; UETMIS-CHUQ, 2010; UETMIS-CUSM, 2010]
- Three SRs derived from a consensus conference [Birke-Sorensen et al., 2011; Krug et al., 2011; Vig et al., 2011]

Safety
- Six RCTs identified for the efficacy dimension [Ashby et al., 2012; de Laat et al., 2011; Howell et al., 2011; Karatepe et al., 2011; Petkar et al., 2011; Sepulveda, 2009]
- Six cohort studies [Carlson et al., 2013; Yang et al., 2013; Vargo, 2012; Blume et al., 2010; Subramonia et al., 2009]
- Two qualitative studies [Dinakar et al., 2013; Kaufman-Rivi et al., 2013]
- Two SRs [Ingargiola et al., 2013; Waldie, 2013]
- Three HTA reports [NHS, 2010; UETMIS-CHUQ, 2010; UETMIS-CUSM, 2010]
- Two documents from the US Food and Drug Administration (FDA) [FDA, 2011; FDA, 2009]
- A clinical practice guideline [HAS, 2010; NHS, 2010]
- In September 2014, a new document on open abdominal wounds derived from the same consensus conference as that previously selected [Bruhin et al., 2014] and an update of the SR by Webster et al. (2012) [Webster et al., 2014] were reviewed.
3.1.1 Characteristics and quality of selected documents

The SR from the CHU de Québec's HTAU of evidence of efficacy was based on 37 primary studies, including 20 RCTs published between 1994 and 2009. The updating process that took place in December 2013 helped to identify 17 published RCTs, including three [Novinscak et al., 2010; Mody et al., 2008; Akbari et al., 2007] that were published between 2007 and 2008 and not cited in the initial SR by the CHU de Québec's HTAU but cited in the SRs published since and identified during the database search. The overall methodological quality of the studies and summary documents is good to moderate. The majority of RCTs have a significant risk of bias.

The SR by the CHU de Québec's HTAU of evidence of efficacy identified 12 SRs published between 1994 and 2009. An update of the search yielded 10 new SRs—including two meta-analyses—that included mostly RCTs. The SRs were judged to be of good to moderate quality. Low-quality reviews and reviews based on observational studies or case series were excluded.

The SR by the CHU de Québec's HTAU of the "safety" dimension was primarily based on one RCT, five case studies, seven observational studies, and one descriptive study—all of which were published between 1994 and 2009. In addition to the documents from the HTA agencies and the regulatory bodies, the update yielded 10 new documents from the systematic literature search. Among the studies selected for the "efficacy" dimension, six reported adverse effects that were also included in the synthesis on safety.

An update of the literature search helped to identify two new SRs that included different study designs. The SRs were deemed of good to moderate quality. A search of the scientific literature identified several documents published in 2008 on good clinical practices for the use of NPWT. The CHU de Québec's HTAU did not include a systematic search to find the clinical practice guidelines for NPWT as part of its assessment. The selection and application of quality criteria allowed INESSS to select a clinical practice guideline on adverse effects and two documents from the FDA. Appendix G provides detailed tables with information found in good-quality documents and documents from the FDA which have not undergone a methodological quality assessment.

Detailed information on the outcome of the SR of the literature is presented in a report entitled *Efficacy and safety of negative pressure wound therapy for the treatment of complex wounds* on the INESSS website.

3.2 Efficacy

The clinical indicators selected are varied and based on the type of wound under consideration. INESSS took the following into account: the healing time or the time needed prior to a surgical procedure for the wound to close by primary intention, the incidence and proportion of closed wounds (re-epithelialization and/or coverage with granulation tissue), split-thickness skin graft survival rate, reduction in wound size, surface area and volume of the wound, quality of life, the total duration of treatment, and the prevention of complications, including infections, amputations, split-thickness skin graft failures, and the accumulation of seroma in wounds. Regarding resource use, data on the number of dressing changes, nursing time, length of hospital stay, and number of hours spent in surgery were reviewed.
Results derived from the RCTs, SRs, and meta-analyses published since 2009 do not show that NPWT offers a greater advantage for targeted indicators related to chronic wounds, such as leg ulcers and stage III or IV pressure ulcers, and complex wounds of various etiologies. However, for diabetic patients with foot ulcers, four new RCTs (251 randomized participants) support earlier findings that NPWT accelerates wound healing time and reduces the time to surgical wound closure (in total, 610 randomized participants in six RCTs). The time for spontaneous healing in the NPWT groups was estimated at approximately three and six weeks compared to five and eight weeks for standard treatments. A meta-analysis [Dumville et al. 2013] that included three RCTs (605 participants) also reported that, compared to moist dressings, NPWT accelerates the healing process in diabetic foot ulcers that have previously undergone debridement. The hazard ratio calculated by Dumville et al. was estimated at 1.82 (95% CI, 1.27 to 2.60), which indicates that at any time during the monitoring period, the probability of healing was 1.8 times higher in the NPWT groups than it was in the control group.

The efficacy data from the scientific literature consulted are not reliable enough to show NPWT’s greater advantage in treating acute wounds such as open fractures or surgical wounds. Furthermore, the data on split-thickness skin grafts (four RCTs, totalling 354 randomized participants) show a favourable trend for NPWT on the rate of split-thickness skin graft survival following surgical coverage. Two studies from the same group show split-thickness skin graft take after nine days in more than 96% of patients with burns, compared with approximately 87% in the control group ($P < 0.001$). An RCT (70 randomized participants) produced data showing that NPWT reduces split-thickness skin graft failure rate in debrided diabetic foot ulcers. Indeed, results show that the split-thickness skin grafts were successful in 80% (28/35) of the patients in the NPWT group compared with 68% (24/35) of the patients in the control group within the three weeks of monitoring ($P < 0.05$). Last, an RCT (100 randomized participants) produced data indicating that NPWT promotes graft survival when it is used prior to reconstructive surgery by preparing the wound bed and therefore accelerating the healing process. The study shows that 90% of the patients who underwent NPWT spent less than three weeks at the hospital, compared with 18% of the patients from the control group ($P < 0.001$).

For other indicators such as reduction in size/volume, quality of life, prevention of complications, duration of treatment, and resource use, the levels of evidence are low to very low as a result of the limitations stemming from the heterogeneity of various parameters such as wound type, outcome indicators, comparators, quality, and the number of RCTs. Table 2 summarizes the available levels of evidence for the efficacy of NPWT for different types of wounds and clinical indicators. Details of the results from the various studies included in the analysis are presented in the SR report entitled Efficacy and safety of negative pressure wound therapy for the treatment of complex wounds, which is available on the INESSS website.
**Table 2: Summary of the Levels of Evidence in Favour of the Use of NPWT for Various Types of Wounds and Clinical Indicators**

<table>
<thead>
<tr>
<th>Clinical Indicators</th>
<th>CLINICAL INDICATIONS</th>
<th>Resource use</th>
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</thead>
<tbody>
<tr>
<td>Formation of healthy granulation tissue and/or time to wound closure</td>
<td>Formation of healthy granulation tissue and/or time to wound closure</td>
<td>Formation of healthy granulation tissue and/or time to wound closure</td>
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<tr>
<td>Reduction in wound size in preparation for surgical closure or coverage</td>
<td>Reduction in wound size in preparation for surgical closure or coverage</td>
<td>Reduction in wound size in preparation for surgical closure or coverage</td>
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<tr>
<td>Incidence of wound closure, proportion of healed wounds or wounds ready for split-thickness skin grafts, graft survival rate</td>
<td>Incidence of wound closure, proportion of healed wounds or wounds ready for split-thickness skin grafts, graft survival rate</td>
<td>Incidence of wound closure, proportion of healed wounds or wounds ready for split-thickness skin grafts, graft survival rate</td>
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<tr>
<td>Prevention of complications</td>
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<td>Prevention of complications</td>
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<td>Resource use</td>
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**CLINICAL INDICATIONS**

**CHRONIC WOUNDS**

Diabetic foot ulcer

- [Karatepe et al., 2011; Nain et al., 2011; Dalla Paola et al., 2010; Sepulveda, 2009; Blume et al., 2008; Armstrong and Lavery, 2005; Etöz et al., 2004]
- [Nain et al., 2011; Akbari et al., 2007]
- [Nain et al., 2011; Novinscak et al., 2010; Blume et al., 2008; Akbari et al., 2007; Armstrong and Lavery, 2005; Etöz et al., 2004]
- [Nain et al., 2011; Dalla Paola et al., 2010]

Stage III or IV pressure ulcer

- [Ashby et al., 2012; Vig et al., 2011; HAS, 2010]
- [Ashby et al., 2012; Vig et al., 2011; HAS, 2010]
- [Nain et al., 2011; Novinscak et al., 2010; Blume et al., 2008; Akbari et al., 2007; Armstrong and Lavery, 2005; Etöz et al., 2004]
- [Nain et al., 2011; Dalla Paola et al., 2010]

**ACUTE WOUNDS**

Surgical wound

- [Rasool et al., 2013; Krug et al., 2011; Stannard, 2009]
- [Rasool et al., 2013; Krug et al., 2011; Stannard, 2009]
- [Pachowsky, 2012]
- [Pachowsky, 2012]

Traumatic wound that cannot be sutured (open fracture)

- [Ashby et al., 2012; Petkar et al., 2012; Vig et al., 2011; Dalla Paola et al., 2010; Llanos et al., 2006]
- [Ashby et al., 2012; Petkar et al., 2012; Vig et al., 2011; Dalla Paola et al., 2010; Llanos et al., 2006]
- [Chio, 2010]
- [Chio, 2010]

Reconstructive surgery

Prior to a split-thickness skin graft

- [Saaiq, 2010]
- [Saaiq, 2010]
- [Saaiq, 2010]

After a split-thickness skin graft

- [Llanos et al., 2006]
- [Llanos et al., 2006]
- [Petkar et al., 2012; Petkar et al., 2011; Dalla Paola et al., 2010; Moisidis et al., 2004]
- [Petkar et al., 2012; Petkar et al., 2011; Dalla Paola et al., 2010; Moisidis et al., 2004]

NPWT = negative pressure wound therapy; NR = not relevant.

No randomized controlled trials (RCTs) reviewed; Moderate level of evidence = more than one Level 1 RCT with moderate risk of bias; Low level of evidence = only one Level 1 RCT with moderate risk of bias or more than one Level 1 RCT with high risk of bias; Very low level of evidence = only one Level 1 RCT with high risk of bias; white square = no advantage of NPWT over comparator.

Level of evidence determined using the SIGN method.
3.3 Safety

The most common harms reported by the CHU de Québec’s HTAU are failure of the wound to heal, or wound deterioration, infections, hematomas, edema, maceration, and necrosis. Some case studies reported deaths among patients with sternal wounds who were treated with NPWT. However, the comparison groups also had a high mortality rate.

An update of the data from 2009 on shows that there is no solid evidence that NPWT has major adverse effects on patient safety if good practices are followed by properly trained health care professionals, or that these effects are more serious than those obtained with standard treatment. No new side effects were reported other than those already identified. Some adverse effects often occur concurrently in control groups, and the application of NPWT sometimes seems to prevent the occurrence of certain adverse effects and complications experienced by participants in the comparison groups. Most of the adverse effects identified in the RCTs are generally manageable and concern quality of life, particularly pain.

In its literature review, the HAS identified serious adverse effects such as septicemia, septic shock, hypovolemic shock, and amputation; however, the authors could not rule out handling errors or directly linking these incidents to the use of NPWT. The authors also noted several disadvantages related to the use of negative pressure devices, such as difficulty of use, permanent dependence on the device, and noise made by the device. The main adverse effects reported in the literature review by the NHS are similar to those previously reported. The FDA published two notifications since 2009, mainly to report complications following the use of NPWT. The 2009 notification stated that six deaths and 77 injuries associated with NPWT were reported in the United States since 2007, most of which occurred in long-term care facilities and were caused by the concurrent use of anticoagulants, which leads to uncontrolled bleeding. The other complications were caused by forgotten dressings and infections following thoracic surgery [FDA, 2009]. In 2011, the FDA issued an update of the death and injury reports, which reported an additional six deaths and 97 injuries [FDA, 2011].

Details of the outcomes of the various studies included in the analysis are presented in the SR report entitled Efficacy and safety of negative pressure wound therapy for the treatment of complex wounds, which is available on the INESSS website.

3.4 Quality of life

3.4.1 Systematic review selection

The scientific information search yielded three SRs on the effect of NPWT on the quality of life of patients with complex wounds. Quality of life, as defined in this section, also includes pain experienced by patients.

3.4.2 Characteristics and quality of the SRs

The quality of the documents was assessed using the AMSTAR checklist. Only one document was judged to be of good methodological quality [Waldie, 2013]; the other two had several limitations [Upton et al., 2013; Ousey et al., 2012]. The quality of the reviews is presented in Appendix E in Table E-1, and the characteristics are given in Appendix F.
3.4.3 Results of the impact of NPWT on quality of life

A SR of the literature on quality of life in patients treated with NPWT was carried out by Upton et al. [Upton et al., 2013]. The review, which was of low quality, included 25 documents on various types of wounds (chronic and acute), with a variety of study designs (SRs, retrospective and prospective monitoring, and case studies). All of the results related to pain and varied from one study to the next. Indeed, one multi-centre study reported that a small number of patients (11%) experienced pain during dressing changes. Another study observed that 22% of patients experienced mild pain when the device was activated, 31% when dressings were changed, and 17% when treatment was stopped. Another three-year observational study of 25 patients reported a high level of pain during dressing changes. The authors of the review suggested that the type of dressing used during treatment might affect the level of pain experienced by patients. The underlying hypothesis is that the granulation tissue adheres to dressings (polyurethane foam) as it forms, causing pain when the dressings are changed. Moreover, some authors measured the patients’ anxiety levels and concluded that the negative pressure device might be a source of anxiety for some of them. Being connected to this type of device can interfere with a patient’s daily care regimen and social life, which can lead to a negative body image and low self-esteem. The authors of the review conclude that a more accurate record should be kept of certain factors associated with the patients’ experiences with NPWT.

A SR of the literature focusing specifically on pain associated with chronic and acute wounds treated with NPWT was conducted by Waldie et al. [Waldie, 2013]. Ten studies were included in this high-quality analysis (five RCTs and five observational studies). The results show that pain intensity was generally higher during dressing changes, and some studies show that a moderate level of pain was experienced during treatment. Most of the studies reviewed reported that pain intensity was lower when measured at the end of treatment than it was when measured at the beginning of treatment, during treatment, or before treatment. The clinical observations reported throughout the literature suggest that the level of pressure applied affects pain intensity in patients during treatment. The authors state that continuous pressure would help to reduce pain, but that given the subjective and cultural dimensions of pain, it is difficult for them to reach a definitive decision and issue recommendations for the use of negative pressure devices. The main limitations of this review lie primarily in the heterogeneity of the measurement scales used, the comparison groups, the lack of information on the analgesics given to the patients, and the types of dressings used during the application of NPWT.

The SR conducted by Ousey et al. [Ousey et al., 2012] on the quality of life of patients with chronic wounds included 28 studies, five of which focused on the primary indicator. The main dimensions under consideration were pain, and mental and physical health, which were measured using validated tools (Short Form Health Survey or SF-36, EQ-5D, EuroQuol, the short-form McGill Pain Questionnaire or SF-MPQ, etc.). Based on the AMSTAR criteria, the review was assessed as being of low methodological quality. The analysis of the results shows significant differences between the studies. First, the study designs (RCTs, observational studies, prospective cohort studies), measurement scales, and types of wounds (venous ulcers, diabetic foot ulcers) differ from one study to the next. Of the two studies that provided data on pain, one (176 patients) reported a significant reduction in pain between the start and end of treatment. A second study involving 30 patients enrolled in a wound care education program suggests that NPWT causes less pain than standard therapy. However, patients reported other undesirable
effects, such as unpleasant odours, itching, and the sensation of being physically constrained. The other studies that used validated tools (e.g., SF-36) to measure NPWT’s effect on quality of life obtained contradictory results.

For example, the randomized study (67 patients) conducted by Karatepe et al. [2011] on diabetic wounds reported high levels of depressed mood at the beginning of treatment. A marked and statistically significant improvement in mental and physical health was observed in the group treated with NPWT at the end of the monitoring period. The exploratory research conducted by Mendonca et al. ([Mendonca et al., 2007] cited in [Ousey et al., 2012]) on 26 patients did not identify any significant changes in quality of life scores at the end of the study. The physical-functioning domain improved in obese patients and worsened in ambulatory/mobile patients. Eleven patients experienced a deterioration in their physical-functioning symptoms, which the authors attribute to limited mobility resulting from the use of NPWT. The RCT conducted by Vuerstaek et al. ([Vuerstaek et al., 2006], cited in [Ousey et al., 2012]) involving 60 patients showed that quality of life improved during treatment (measured weekly), but that the differences observed at the end of treatment were not statistically significant. In conclusion, the authors of the SR report that there is some evidence to suggest that NPWT improves quality of life. However, given the heterogeneity of the studies and the presence of contradictory results, it was impossible for them to conclude that NPWT offers a definitive advantage to a patient’s quality of life.
4 REVIEW OF THE RECOMMENDATIONS FOR GOOD CLINICAL PRACTICE

4.1 Selection of the recommendations for good clinical practice

The scientific information search yielded several documents published since 2008 that focus on good clinical practice for the use of NPWT. Seven of the documents identified were initially selected:

- one clinical practice guideline [HAS, 2010; NHS, 2010];
- three articles from an international expert consensus conference [Birke-Sorensen et al. 2011; Krug et al., 2011; Vig et al., 2011];
- manufacturer’s product monographs (KCI/Kinetic Concepts Inc. and Smith & Nephew)
- two documents from the FDA [FDA, 2011; FDA, 2009];
- four documents that include guidelines derived from expert consensus [Beitz and van Rijswijk, 2012; Desai et al., 2012; Apelqvist et al., 2009; Bovill et al., 2008];
- an HTA report providing a summary of the recommendations for good clinical practice derived from international expert consensus [NHS, 2010].

A flow chart based on the Preferred Reporting Items for Systematic Reviews and Meta-Analyses or PRISMA model illustrating the study selection process, and a detailed list of all excluded documents and the reasons for their exclusion, are presented in Appendices C and D, respectively.

In September 2014, a new document on open abdominal wounds, derived from the same consensus conference as that previously selected [Bruhin et al., 2014], was identified during a search for new scientific documents published since December 2013 in the PubMed (MEDLINE) and CRD databases.

4.2 Characteristics and quality of selected documents

The selection and application of quality criteria helped to identify five documents containing recommendations for good practice, one of which is a clinical practice guideline and four of which are derived from the same expert consensus. The quality of the documents was assessed using the AGREE II/Appraisal of Guidelines for Research and Evaluation checklist [The AGREE Research Trust, 2009]. The HAS guide (2010) is general in nature and includes both chronic and acute wounds. The document by Krug et al. (2011) focuses on traumatic and surgical wounds, whereas the document by Vig et al. (2011) discusses chronic wounds — particularly diabetic foot ulcers, pressure ulcers, and leg ulcers. The document published by Bruhin et al. (2014) examines open abdominal wounds. The methodological quality of the documents is presented in Appendix F. Appendix G contains tables with detailed information derived from high-quality documents such as HTA reports, but also from documents from expert consensus, manufacturers, and the FDA for which methodological quality has not been assessed but which are useful for the deliberations that lead to the development of the recommendations and the OUG. The recommendations for each type of wound are also included.
4.3 Decision-making regarding the use of NPWT

4.3.1 Factors to consider prior to making the decision to initiate NPWT
Following several incidents involving NPWT, the FDA recommended carefully selecting candidates by analyzing risk factors and by identifying contraindications, thus ensuring client safety. A patient’s nutritional and hydration status must be assessed and stabilized; comorbidities must be managed and adequately treated; adequate blood pressure and blood flow, especially in the limb affected by the wound, must be maintained and, if not, actions should be taken to stabilize them; wound infections must be controlled; and the wound bed must be optimized in preparation for the intervention. Included in the recommendations by Vig et al. [Vig et al., 2011] is the importance of stabilizing and treating the patient’s nutritional status, hydration, and comorbidities. The NHS specifies that NPWT is not a substitute for good basic care in the management of complex wounds, particularly pressure wounds.

4.3.2 Indications and clinical objectives
Most of the documents consulted, regardless of their methodological quality, recommend the same indications; that is, those found in the manufacturer's product monographs that were approved by regulatory bodies such as Health Canada. However, given the low level of scientific evidence, the authors are cautious in their conclusions and provide clarifications concerning the elements to take into consideration prior to initiating NPWT. The details are provided in Tables G-1 and G-2. When available, the level of evidence and grade of recommendation are indicated. Table G-4 in Appendix G provides a summary of the clinical objectives from the documents consulted according to indication (type of complex wound).

4.3.2.1 Chronic wounds
4.3.2.1.1 Diabetic foot ulcer
There is some clinical evidence that NPWT would be beneficial in helping to close diabetic foot ulcers and preventing complications (preventing partial amputations or the need for additional surgical procedures). In this respect, on the basis of an RCT and the opinion of expert clinicians, the HAS recommends using NPWT for foot ulcers with extensive loss of substance and/or for deep wounds. The clinical objectives consist in shortening wound healing time and preventing complications. However, the ulcer must be non-ischemic, and the potential for revascularization must have been assessed. Any soft-tissue or bone infection must be managed and the debridement completed. NPWT use should be temporary, following properly administered standard local treatment. Vig et al. state that NPWT should be used only in diabetic patients with recalcitrant foot ulcers, after surgical debridement or partial amputation, and when there is a potential for revascularization (Grade A, levels of evidence 1, 2, and 3). The primary objective is to let the ulcer progress to allow closure by secondary intention, or to reduce its size sufficiently in preparation for surgical coverage. However, NPWT must be stopped as soon as the ulcer has healed sufficiently. There is some clinical evidence that NPWT also prevents complications. For this reason, Vig et al. issued a recommendation that NPWT should be considered for the prevention of amputations or re-amputations (Grade B, levels of evidence 1, 2, 3, and 4).

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20 The panel of international experts [Birke-Sorensen et al., 2011; Krug et al., 2011; Vig et al., 2011] adapted from the Scottish Intercollegiate Guidelines Network or SIGN method of classification to develop their recommendations. For a wound to be classified as Grade A, the required level of evidence was at least 1 (1++, 1+, 1–), Grade B, at least 2 (1+, 1–, 2++), Grade C, at least 2+, and Grade D, 3 (non-analytical study) or 4 (expert opinion).
4.3.2.1.2 Stage III or IV pressure ulcers

The HAS recommendation for pressure ulcers, which is based on two RCTs (non-significant results, i.e. lack of evidence supporting NPWT's significant advantage over standard treatment) and the clinical experience of the experts consulted, is that NPWT should be used for stage III and IV pressure ulcers resistant to properly administered general treatment. The clinical objective is to prepare the ulcer for surgical coverage. In their document, Vig et al. specify that NPWT can be applied until surgical closure is possible (Grade C, levels of evidence 1 and 3) and that it should be considered for closure by secondary intention (Grade B, levels of evidence 1, 2, and 3). Furthermore, based in part on two RCTs and various Level 3 studies reporting that NPWT promotes the formation of granulation tissue on pressure ulcers, Vig et al. issued a recommendation that NPWT should be used to reduce wound dimension and to improve the quality of the wound bed (Grade B, levels of evidence 1, 2, and 3).

4.3.2.1.3 Leg ulcers

HAS has issued only one recommendation — based on one RCT and clinical experience — that NPWT should be used only for leg ulcers resistant to local and sufficiently prolonged treatment of three to six months in preparation for a split-thickness skin graft. The recommendation was motivated by the clinical objective to promote the formation of healthy granulation tissue required for a successful split-thickness skin graft. Vig et al. stated that NPWT should be considered as advanced therapy for leg ulcers caused by chronic vascular insufficiency, but that its use should follow an assessment of the potential for revascularization and should never be considered a substitute for revascularization (Grade C, levels of evidence 1, 3, and 4). The authors confirm that NPWT is not recommended for acute leg ulcers (Grade D). Furthermore, this group of experts recommends having a specialist prescribe NPWT for the treatment of leg ulcers to verify whether other therapeutic options may be of greater benefit in attaining the clinical objectives [Vig et al., 2011]. For venous ulcers, Vig et al. recommend the use of NPWT only to prepare the wound bed for surgical coverage in patients for whom compression therapy — the first-line treatment for this type of wound — did not prove effective (Grade B, level of evidence 1).

4.3.2.2 Acute wounds

The decision to use NPWT to temporarily close a wound during a surgical procedure or following an accident can be made quickly according to the context. For this reason, HAS confirms that NPWT can be implemented immediately (in an emergency) or postponed. In their publication, Krug et al. (2011) suggest that NPWT can be used for an emergency fasciotomy (a surgical procedure in which an incision is made in the fibrous membrane that envelopes muscles to relieve pressure or tension). Once surgical closure is possible, the discontinuation of NPWT is indicated (Grade C, level of evidence 2) [Krug et al., 2011].
4.3.2.2.1 Traumatic wounds (includes surgical wounds with soft tissue incisions and open fractures)

HAS recommends the use of NPWT for non-suturable traumatic wounds with extensive and/or deep loss of substance, with or without infection. This recommendation is based on the SD from two RCTs and the experience of the experts consulted. The primary objective is to promote the formation of healthy granulation tissue to rapidly proceed to surgical closure or to promote healing by secondary intention. However, other objectives such as temporary closure and the removal of exudate may be set for the use of NPWT for these types of wounds. Krug et al. make a distinction between studies focusing on traumatic wounds that affect soft tissues and studies focusing on traumatic wounds from open fractures. Regarding the former, the authors mention that NPWT can be used on a wound that cannot be surgically closed, after or between debridement sessions. In these cases, NPWT can be used to temporarily close the wound in preparation for surgical closure. This recommendation is based on cohort studies and the opinion of experts (Grade C, levels of evidence 2 and 3). The secondary objective is to improve the quality of the granulation tissue to increase the likelihood of successful reconstructive surgery (split-thickness skin graft) (Grade C, levels of evidence 2 and 3). However, it is clearly stated that NPWT should be discontinued as soon as surgical closure is possible. Krug et al. recommend the use of NPWT for open fractures when surgical closure cannot be achieved or between debridement sessions (Grade B, levels of evidence 1, 3, and 4). The objective also is to temporarily close the wound in preparation for surgical closure (Grade B, levels of evidence 1 and 3) and then to reduce the complexity of the wound by promoting the formation of healthy granulation tissue (Grade C, levels of evidence 2 and 3).

4.3.2.2.2 Abdominal surgery wounds

In the case of abdominal wounds, HAS states that NPWT should only be used to temporarily close the abdominal cavity to reduce the risk of intra-abdominal hypertension prior to an additional surgical procedure. However, the evidence is limited to one RCT. Bruhin et al. recommend the use of NPWT as first-line therapy in Grade21 1 and 2 open abdomen wounds to achieve temporary abdominal closure in preparation for additional surgical procedures (Grade B, levels of evidence 2 and 3). To this end, the authors recommend the use of a non-adherent interface layer to protect exposed organs and to prevent wound progression to Grade 3 or 4 (expert opinion [EO]). NPWT can be used for Grade 4 open abdomen wounds to promote granulation tissue formation and to enhance graft take (Grade B, levels of evidence 1, 2, and 3). The clinical objectives, depending on the grade of the wound, are: the protection of the organs and the prevention of complications (e.g., infection, adhesion formation), the management of edema, temporary closure in preparation for additional surgical coverage, and wound bed preparation for split-thickness skin grafting.

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21 The following classification of the open abdomen (OA) is used in the document by Bruhin et al.: Grade 1a — without adherence between the bowel and abdominal wall; Grade 1b — contaminated OA without adherence; Grade 2a — clean OA developing adherence; Grade 2b — contaminated OA developing adherence; Grade 3 — OA complicated by fistula formation; Grade 4 — OA with adherent bowel; unable to close surgically; with or without fistula.
4.3.2.3 Burns

HAS does not take a position on the use of NPWT for burns. Krug et al. mention that the primary clinical objective for the use of NPWT in burns is to prepare the wounds by promoting granulation tissue formation prior to surgical coverage. NPWT should not be used to prevent wound progression.

4.3.2.4 Split-thickness skin grafts and skin flaps

HAS does not take a position on the use of NPWT for split-thickness skin grafts or skin flaps. Krug et al. mention that the clinical objectives for the use of NPWT differ based on the surgical coverage method chosen to close the wound. According to the authors, NPWT should be considered to enhance split-thickness skin graft survival (Grade A, levels of evidence 1 and 2). It should also be considered for patients at a high risk of split-thickness skin graft failure (Grade B, levels of evidence 1, 2, and 3). The primary objective is to promote the formation of healthy granulation tissue on the recipient site. The authors also mention that the dressings should be maintained in place over the graft for three to seven days so as not to destabilize it, and that continuous pressure should be applied (Grade B, level of evidence 1, 2, and 3). The objective is to maintain and secure the split-thickness skin graft. Literature on skin flaps is scarce. This technique requires several debridement sessions to remove necrotic tissue. The recommendations issued by Krug et al. are primarily based on EO. The authors also mention that NPWT can be used on skin flaps following debridement, as the wounds are then considered to be open traumatic wounds (soft tissue). Therefore, the clinical objectives are the same as those previously stated for these types of wounds. Furthermore, NPWT could be used at the donor site to promote wound closure by secondary intention or to allow the wound to progress sufficiently for a split-thickness skin graft.

4.3.3 Contraindications

Of the five documents selected, two make no mention of contraindications for the use of NPWT [Vig et al., 2011; Krug et al., 2011]. The HAS guide, NHS report, and FDA report state the contraindications found in the manufacturers' official product monographs consulted. The list is provided in the table in Appendix G.

4.4 Identification of technical parameters

4.4.1 Choice of device

HAS states that there currently is no scientific evidence supporting any technology’s advantage over another.

4.4.2 Pressure and mode

There are few indications concerning the level of pressure to use for each type of wound in the good-quality documents selected. HAS remains vague and mentions that continuous or intermittent pressure between −50 mm Hg and −200 mm Hg can be applied. Krug et al. (2011) propose continuous levels of pressure when NPWT is used to bolster a split-thickness skin graft (after the graft). Birke-Sorensen et al. mention that low levels of pressure are recommended if patients are experiencing pain, that high levels of pressure should be avoided in individuals with vascular problems or at risk of developing ischemia, and that high levels of pressure should be used when there is a large volume of exudate [Birke-Sorensen et al., 2011]. According to the authors, a pressure level of –
40 mm Hg to –150 mm Hg should generally be used. It should be noted that the recommendations made by the authors concerned split-thickness skin grafts.

4.4.3 Types of dressings
The publication by Birke-Sorensen et al. is the only one to report on the types of dressings to use for split-thickness skin grafts (before or after surgical coverage). The authors mention that gauze should be used to reduce pain during dressing changes. They also suggest the use of gauze for non-contractile wounds and deep cavities. According to the authors, foam dressings should be used when there is a need for granulation tissue to form quickly or when the wounds are deep and uniform. However, it should be noted that they do not specify the sources of information used to arrive at these recommendations, which appear to be based on EO.

4.4 Initiation of NPWT and precautions for use
Regarding resources and care delivery settings, HAS recommends having a medical specialist prescribe NPWT and having the treatment be initiated in a health facility. However, NPWT can be used at home, subject to a weekly assessment by the prescriber [HAS, 2010]. The FDA recommends that patients undergoing NPWT be monitored frequently in an adequate health care setting and by well-trained health care professionals. The regulatory body points out that patients and their caregivers must be informed about how the device operates when it is used at home. They should also be informed about signs of complications and the technical aspects of the intervention, as should the health care personnel. To minimize the risks associated with dressing changes, the FDA recommends recording the number of dressing pieces applied to the wound and avoiding cutting dressings directly over the wound.

4.5 Dressing changes, assessment, monitoring, duration, and renewal
HAS recommends having the original prescriber conduct the monitoring and renewal. Any other health care provider must receive the appropriate training. All the documents consulted suggest changing the dressings every 48 to 72 hours. Only HAS recommends a maximum of 30 days for treatment duration, renewable only once. The FDA suggests reporting any complications and adverse effects by noting patient information (age, medical condition, type of wound), adverse effects and complications (date, type, etc.), details on the technical parameters, the frequency of dressing changes, and the location of the injury.

4.6 Criteria for discontinuing NPWT
HAS issued the following cessation criterion for NPWT: treatment should be discontinued if there is no improvement in the general condition of the wound after two consecutive dressing changes or after one week of use. The NHS recommends discontinuing NPWT if wound size has not decreased by 15% after one to two weeks or if there is periwound inflammation after the first application. The following also are examples of factors that call for the discontinuation of
NPWT: the patient's inability to adhere to treatment, the patient's inability to tolerate the pain caused by the treatment, signs of allergy to the material being used, incontinence, excessive sweating, or the presence of contraindications such as those previously mentioned.
5 CONTEXTUALIZATION AND EXPERIENTIAL KNOWLEDGE

The development of the recommendations for the judicious use of NPWT — intended for the entire province of Quebec and based on SD, best international practices, and the experiential knowledge of clinicians and researchers — also requires a sound knowledge of the legislative, administrative, and organizational context specific to wound care in the province of Quebec.

5.1 Reserved professional activities

An Act to amend the Professional Code and other legislative provisions as regards the health sector, which came into effect in 2003, brought about a revision of the fields of practice of eleven professional orders [National Assembly, 2002]. In particular, it allowed activities reserved for wound care to be added to the field of practice of various types of health care professionals, on an exclusive or shared basis. The reserved activities are delineated by the field of practice of the profession, which defines the scope and limits of the interventions that can be carried out by a particular type of professional. The reserved activities related to wound care are described in Table H-1 in Appendix H.

The CMQ recently submitted a regulatory proposal to the Government of Quebec regarding certain professional activities that can be undertaken by nurses under certain conditions specified by the regulation. The implementation of the regulation is slated for 2016 [CMQ, 2015]. Details of the regulation on activities reserved for nurses are found in Table K-1 in Appendix K.

5.2 Reminder of the ethical requirements for health care professionals

Health care professionals are bound by ethical requirements to act within the limits of their knowledge and skills. As regards wound treatment, the autonomy of health care professionals is dependent on their knowledge and skills in the field, the complexity of the wound, the patient's health status, and the drug products prescribed. Moreover, all health care professionals must take into account the guidelines established by their practice setting and respect the standards of care and internal protocols [OEQ, 2014].

5.3 Required organizational standards and practices

The required organizational practice (ROP) by Accreditation Canada on pressure ulcer prevention for long-term care services came into effect in 2009, and the ROP on skin and wound care for home care services came into effect in 2014.24

The tests for compliance for the ROP for skin and wound care require that organizations providing home care services use an interprofessional and collaborative approach to assess clients who need skin and wound care, and provide evidence-informed care that promotes healing and prevents complications. Table H-2 in Appendix H presents the specific expectations Accreditation Canada surveyors assess to determine whether organizations comply with the ROP for skin and wound care.

5.4 **Interprofessional approach**

The OEQ, OIIQ, and OPPQ recently published a joint document in which they recommended an interprofessional approach for the optimal treatment of chronic and complex wounds [OEQ, 2014]. The main objective of this inter-organization position is to positively influence professional practice and the guidelines applied in health care settings to promote the quality of the care and services delivered to patients.

5.5 **Overview of medical procedures related to NPWT**

It is difficult to track medical prescriptions for NPWT, associated diagnoses, patients who receive the treatment, and the duration of treatment. There are no medical acts associated with the use of NPWT in the RAMQ manual for medical services provided by general practitioners. However, three medical acts are included in the RAMQ manual for certain medical specialities. Consequently, it is difficult to monitor the indicators needed to provide an overview of the use of this technology. A brief search in the file for medical services provided on a fee-for-service basis revealed that the majority of prescribers in 2014 were surgeons who practice in large urban centres (Montreal, Quebec, Estrie, and Saguenay-Lac-Saint-Jean) and that NPWT was prescribed for a variety of diagnoses. The results of the search are not presented in this document, as major limitations were involved and a realistic overview of NPWT use in Quebec could not be provided.

5.6 **Organization of wound care in Quebec's health and social services network**

The results presented in the report by the CHU de Québec's HTAU showed considerable variation in the organization of complex wound care in the RSSS. Some facilities are very well-organized, whereas others are relatively disadvantaged. The disparity can be great depending on the region and type of health care setting (hospital versus the Centre de santé et de services sociaux [CSSS] [intermediate care and home care]). Certain facilities in Quebec have adopted the practice of forming teams dedicated to complex wound care to supervise the practice and promote the optimal management of patients with complex wounds.

Although some health care settings do not have a dedicated team, they may still have a health care professional with complex wound care expertise who often is available for consultations on an ad hoc basis. In addition, Quebec has a few ambulatory care units for wound care in health facilities, private clinics, and one centre of expertise for complex wounds associated with the CSSS Alphonse-Desjardins in Lévis.25

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The centre also offers a wound care tele-assistance service in collaboration with the RUIS de l’Université Laval. The Centre hospitalier Universitaire de Sherbrooke, in collaboration with the RUIS de l’Université de Sherbrooke, also provides the same services (wound care tele-assistance, leg ulcer clinic, multidisciplinary diabetic foot clinic).\(^{26}\)

### 5.7 Acquiring NPWT devices

Health facilities in Quebec can acquire NPWT devices in either of two ways: on an individual basis, for specific needs; or as a group, for common regional, supraregional, or provincial needs. There are currently eleven joint procurement groups (comité d’allocation des ressources et de suivi des ententes de gestion [CAR]).\(^{27}\) Prior to Bill 10 and the establishment of the Centre intégré de santé et de services sociaux (CISSS), requests for NPWT devices, following a medical prescription or nursing care plan, were the responsibility of the ASSS, the fiduciary bodies. Applications for devices are routed via liaison nurses in hospitals, Centre local de services communautaires or CLSCs, or rehabilitation centres and analyzed by the technical aids department of the ASSS before they are sent to the distributors or the organization managing the NPWT park. According to the agreements negotiated with the manufacturers, storage, transport logistics, disinfection, maintenance, and repairs may be the responsibility of the distributor. With the reorganization of the RSSS and the elimination of the ASSS, the management of the NPWT park will likely be redistributed within the CISSS; however, few details are currently available. There are wide disparities among regions in terms of types of devices available in NPWT parks. Some parks supply devices from a single company, while others offer devices from two currently well-established companies in Quebec, including vacuum-assisted closure or V.A.C. devices by KCI and RENASYS devices by Smith & Nephew. Other manufacturers, such as Medela (Invia technology) sell NPWT devices in Quebec. Dressings used for NPWT are not listed in the RAMQ database. However, there is a ministerial circular for authorized dressings paid by the facilities.

### 5.8 Experiential knowledge

Experiential knowledge was drawn from a variety of sources, including members of the monitoring committee, members of the advisory committee, and health care professionals working in the field who were consulted for the OUG. However, the recommendations were developed with the members of the advisory committee, who stated that the results presented in the SR of the literature on efficacy and safety were consistent with their view, that the uncertainty of the data was representative of their clinical experience with the technology, and that the work carried out was useful in supporting the recommendations developed by INESSS. The systematic search of the clinical practice guidelines, consensus conferences, and reports by the HTA and regulatory bodies led to the identification of good quality documents that provided important information for clinical practice and contained recommendations the work team drew on to develop the recommendations for INESSS while taking the Quebec context into account. The committee put forward de novo recommendations when information was missing from the documents consulted. Members of the monitoring committee and future OUG users received the recommendations and were able to comment on them. The following section is subdivided into categories that will be included in the recommendations section and in the OUG.

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\(^{27}\) [https://www.cpacsante.qc.ca](https://www.cpacsante.qc.ca) (viewed February 9, 2015)
5.8.1 General
There are various definitions for complex wounds and chronic wounds. As part of the work done for INESSS, the members of the advisory committee agreed on the following definition: a complex wound is a wound that does not heal according to the normal healing process or that requires advanced medical care.

5.8.2 Decision-making regarding NPWT use
Members of the advisory committee emphasized the importance of selecting patients for whom NPWT will be safe, and of greater clinical benefit than standard treatment. Identifying and stabilizing the causes of delayed healing are key elements in managing patients with complex wounds. For this reason, basic care adapted to the type of wound and based on best practices should always be provided before considering NPWT as a treatment option. According to the experience of the members, it appears that many patients in certain regions of Quebec are currently undergoing NPWT without their underlying conditions having been optimized. To help select individuals who could benefit from NPWT while minimizing the risks, assessment tools, decision trees, and checklists may be useful clinical tools for the identification of risk factors associated with NPWT and those risk factors that may impede healing. Malnutrition screening would also be key to managing patients with complex wounds, as the condition affects the healing process on several levels. Laboratory data on serum albumin, serum prealbumin, and hemoglobin should be interpreted according to the clinical context and the patient's inflammatory status. Albumin is not an absolute or reliable indicator of nutritional status. Moreover, high or very high C-reactive protein levels indicate that there might be a protein synthesis problem and that intake should be increased. Screening for malnutrition should be performed by a dietitian or nutritionist, or at least using validated and standardized tools or criteria.

The advantages and disadvantages of the various therapeutic options available, including NPWT, must be in line with the clinical objectives in order to determine the best approach for the patient. To this end, the original prescriber of NPWT should always discuss and collaborate with a health care professional with complex wound care expertise who is recognized and authorized by the health facility or, better yet, with a dedicated wound care team if one is available within the facility. The health care professionals consulted should be adequately trained and have updated knowledge of the healing process, wound chronicity, the care needed to manage complex wounds, and the various therapeutic options available. The experts specified that the facilities should have an interprofessional team dedicated to wound care that includes at least one physician with complex wound care expertise and a nurse. If possible, core team members should also include a dietitian or a nutritionist. A physiotherapist and an occupational therapist with wound care expertise may also be added on an ad hoc basis and depending on the availability of resources in the facility. The consultation may be held in the facility or externally if a team or professionals dedicated to complex wound care is not available. Forming these teams is important at present to meet the Accreditation Canada ROP requirements for skin and wound care.

28 It was mentioned that the physiotherapist may suggest additional modalities to promote wound healing, such as electrical muscle stimulation, ultrasound, ultraviolet light, pulsed electromagnetic field therapy, laser therapy, or topical oxygen therapy. Some of these methods can sometimes be less costly than NPWT.
Regarding the setting in which NPWT is to be initiated, the majority of the members of the advisory committee agree on the importance of initiating NPWT in a health care facility and consider the home care services offered by the CSSS to be part of "a health facility." With the establishment of the CISSS and CIUSSS, the vast majority of health care settings are in health facilities that include home care.

5.8.3 **Indications, contraindications, and adverse effects**

The clinical experience of the members of the advisory committee helped to identify situations in which NPWT would be of interest. These situations are in agreement with the recommendations from HAS and with the authors of the best practice recommendations derived from the good quality consensus conference selected. On the whole, the clinical situations selected take into account currently available and reliable literature data from RCTs, SRs, HTA reports, the consulted documents on good clinical practice, and the experiential knowledge of the experts from the committee. Table H-3 in Appendix H summarizes the clinical indications selected by the experts of the committee, which must be aligned with the clinical objectives for the use of NPWT, including those found in the literature consulted.

The experts consider it important to convey the message that NPWT must not be used as a substitute for debridement or to completely close the wound. NPWT can delay healing if it is left for too long over a wound covered with granulation tissue. The experts also specified that NPWT is not a viable option for venous ulcers, which require compression therapy to promote venous return, exudate reduction, and re-epithelialization. The members were in agreement with all of the contraindications that were presented in the documents consulted and that complied with the manufacturers' official product monographs. However, they pointed out some adverse effects, and absolute and relative contraindications, and added certain elements based on their experiences.

The working group noted that factors of a social, medical (e.g., cognitive impairment), or psychological nature that prevent treatment adhesion or safety should be considered as contraindications to NPWT. Considering the costs associated with the technology, patients with a history of treatment non-adherence should not receive NPWT.

5.8.4 **Determining clinical objectives**

The experts concurred with the clinical objectives presented by the HAS and the authors of the recommendations for good clinical practice derived from the high-quality consensus conference selected, while specifying that the terms should be adapted to Quebec's context. They emphasized the importance of not using NPWT to debride a wound or to close it (re-epithelialization phase). They also reiterated the importance of discontinuing NPWT before the granulation tissue reaches the wound edges, as that would impede the re-epithelialization process. Some authors of the recommendations for good clinical practice specify percentages of granulation tissue or reductions in volume in the clinical objectives. The concept of percentage was not selected, as it is subjective in nature; that is, the assessment methods are not very objective and the threshold is arbitrary.

5.8.5 **Determining the technical parameters**

The working group holds the view that the choice of device depends on device availability in the facility, on certain parameters related to the patient (e.g., sensitivity to
pain) and, when the patient is being transferred, on cost, ease of use, health care setting, adverse effects, and the differences between the technologies regarding types of dressings, pressure, and mode. They also emphasized that it is the responsibility of clinicians to determine which level of pressure and mode to use, and that they can refer to the product monographs. Following a request by members of the monitoring committee, a recommendation on the type of dressing had to be produced. Most of the literature on this topic is derived from animal studies, or from clinical observations with no control group. INESSS identified a pilot study derived from the systematic search that compared gauzes and foam dressings for the treatment of surgical wounds. The authors did not observe any difference in efficacy. Consequently, the experts from the working group were of the opinion that, given the lack of good quality clinical data showing the differences in efficacy between the two types of interfaces, the choice of dressing should be based on the nature of the wound, the technology available in the facility and, when the patient is being transferred, the experience of the health care professionals with wound care expertise and the patient's sensitivity to pain.

5.8.6 Initiating NPWT
To ensure the optimal use of NPWT and the safety of the intervention, and to facilitate the work of the professionals who will monitor the patient and the wound, the original prescriber's instructions must be clear. Certain documents related to good clinical practice and methods of care outline the elements that should be included in the prescription to foster communication among health care professionals. INESSS drew up a list of these elements and submitted it to the committee. Included in the list were the general objectives and clinical criteria for treatment, the estimated time frame for achieving the clinical objectives, the choice of device, and the technical and monitoring parameters. The members of the advisory committee suggested also adding the treatment plan review date.

5.8.7 Dressing changes and parameters to assess
It is very important to prepare the wound and the patient to optimize the benefits of NPWT and to promote the achievement of the objectives in a safe environment. The working group emphasized the importance of ensuring that the wound is debrided and free of necrotic tissue prior to initiating NPWT. They were also in agreement with the recommendations put forth by the HAS and the FDA concerning precautions for use. The product monographs indicate that to keep the wound moist, the NPWT system must be reinstalled as soon as possible following a patient's transfer to another health care setting or back home. However, the experts stated that to ensure continuity of care, the dressing specifically designed for the device that will be used during the transfer or at home should be applied at the patient care unit prior to the patient's departure from the hospital, and that ideally, the device should accompany the patient, as well. However, some nurses familiar with CSSS procedure stated that this is rarely the case, and that NPWT is often initiated at home, not at the hospital.

5.8.8 Monitoring, duration, and renewal
The experts did not specify the type of health care professional qualified to perform dressing changes, and stated that it should be left to health facilities to make that decision, based on the availability of resources and their standards of care. Dressings should be changed by nurses, but in some cases they can be changed by nursing assistants, and, exceptionally, by physiotherapists or occupational therapists. However, the experts emphasized that it is important for health care professionals to be
adequately trained in the technology, and in complex wounds, by entities independent of manufacturers. The proposed frequency of dressing changes is consistent with the documents consulted, including the manufacturer product monographs. The working group stated the importance of having a nurse or health care professional authorized by the facility assess the wound at least once a week, and having the original prescriber assess the relevance of pursuing NPWT two weeks after the start of treatment. The experts of the committee were in agreement with the recommendations put forward by the HAS that the duration of the original prescription should be 30 days, and that it can be renewed only once. At present, some patients are expected to undergo NPWT for several months and even up to one year. To prevent these non-optimal practices, the experts of the committee specified that the original prescriber should consult with a dedicated team or a health care professional with complex wound care expertise prior to renewing the prescription, and that a renewal should be obtained only once, and only if wound healing progresses favourably.

5.8.9 Cessation criteria
The members agreed to the cessation criteria defined by HAS, although they added a few points. They emphasized the importance of avoiding the long-term use of NPWT if it does not produce results. In cases in which there is no response, it is preferable to discontinue treatment and to review any factors that may be hindering the healing process.
DISCUSSION

The purpose of this report was to gather information on the efficacy and safety of NPWT for the treatment of complex wounds, acquire knowledge on NPWT's impact on patients' quality of life, provide a summary of the best current clinical practices, identify certain aspects of the context specific to Quebec concerning the use of this technology, and develop recommendations for the judicious use of NPWT. To do so, INESSS conducted a SR of the literature on the efficacy and safety of NPWT for the treatment of complex wounds, a review of available SRs on the technology's impact on patients' quality of life, a SR of the recommendations for good clinical practice concerning the use of NPWT, a summary analysis of the context of use for NPWT in Quebec, and several exchanges with various multidisciplinary working groups. The main findings that emerged from the data are subsequently presented.

Summary and analysis of the results

In 2010, the CHU de Québec's HTAU concluded that as a result of the weakness of the data and the limitations of the clinical studies published, a recommendation favouring NPWT over standard treatment could not be made on a large scale for all complex wounds, as the level of evidence was low. However, the authors believe that the use of NPWT could be of greater benefit in certain clinical situations. The recent update of the SD does not alter the conclusions, since the new studies that were published still involve a high risk of bias and are highly heterogeneous. Overall, it is difficult to determine the clinical benefit of the variations observed for the different indicators. The quantitative analysis of the data by indicator was considered impracticable given the lack of data, the heterogeneity of the wounds, the nature of the comparators, the type of NPWT device, the disparities between the methods used to measure the indicators, and the frequency and time at which the measurements were recorded.

Some authors failed to explain the method used to handle the missing data, or they used a method that might introduce biases. Furthermore, it is often difficult to confirm the reliability and validity of the statistical analyses, particularly as the sample size calls into question the type of statistical tests used, or because losses were incurred during the monitoring process that appear not to have been taken into account in the analysis. Last, the authors of the RCTs did not perform any subgroup analyses to emphasize the characteristics of the patients who are the most responsive to NPWT.

The findings of the various SRs included in the analysis are also often difficult to use because of some of the methodological choices made by the authors. The choice of studies included in some of the reviews adds to the confusion and makes it impossible to reach a conclusion on the efficacy of NPWT. Indeed, some authors included chronic wounds of various etiologies, whereas others included both chronic and acute wounds. Furthermore, although some authors focused on acute wounds, they combined studies on traumatic wounds and surgical wounds, often without having performed subgroup analyses.
Nevertheless, two clinical indicators stand out from the analysis and show that there are some benefits in using NPWT for certain types of complex wounds and for a category of individuals. These are the time to wound closure, and split-thickness skin graft survival rate.

The findings for the first indicator apply mainly to a category of diabetic patients with complex wounds for whom basic care specific to the types of wounds was provided beforehand, as specified in the studies. Although the selected RCTs focusing on diabetic patients have a certain risk of bias, the level of evidence is moderate and all the results tend in the same direction. However, the data on the proportion of patients and/or wounds that showed an improvement compared with the entire group are indicators not often given in these RCTs. Only one study, judged to be of low methodological quality, provides data on both proportion and the time it takes for the granulation tissue to cover the wound; in both cases, the authors conclude that some benefit is derived from NPWT. These findings are consistent with those of the meta-analysis carried out by Dumville et al. in 2013, which report the benefits of NPWT in accelerating the healing process in diabetic foot ulcers, following quantitative analyses of the various RCTs available.

The conclusions for the second indicator apply to patients who have received or are receiving a split-thickness skin graft over an acute wound. The three RCTs identified had an adequate sample size, and all the patients had completed the studies. The level of evidence for this indicator is moderate, based on one good-quality RCT that focuses on the preparation of the wound bed prior to the graft and on two moderate-quality RCTs that focus on the application of NPWT following surgery. No SRs on graft survival rate were identified in the literature. The SRs published by Webster et al. in 2012 and 2014 focus on NPWT’s effect on the proportion of healed wounds, mortality, adverse effects, complete wound healing time, pain, and quality of life. NPWT did not show an advantage over standard treatments for all these indicators.

Despite the weakness of the data, various clinical indications and situations going well beyond diabetic foot ulcers and split-thickness skin grafts were approved by regulatory bodies following requests by manufacturers. The role of these bodies is to ensure the safety of the population more than it is to determine the clinical efficacy of the interventions, which is the role of HTA agencies.

Statements concerning the uncertainty of the data and the inability to conclude that NPWT is more effective than standard treatment were common to the various guidelines consulted, including those from the assessment agencies and from expert consensus. These organizations and working groups propose the use of NPWT for very specific clinical situations and for a certain category of patients, including diabetic patients with foot ulcers that are well vascularized or that have a confirmed potential for revascularization, and patients with acute wounds requiring a split-thickness skin graft.
The experts involved in the work for INESSS were also of the opinion that although NPWT does not perform miracles, it can be an interesting and useful alternative for certain wounds, as it can accelerate the healing process or neutralize the self-perpetuating cycle of non-healing. However, to ensure that the benefits of the treatment are obtained, the factors that impede healing must be stabilized, good wound care practices must be applied, and the clinical objectives must be identified to ensure treatment is discontinued once they are attained.

There is no solid evidence that NPWT has major adverse effects that can affect patient safety if good clinical practices are applied, nor that the effects are greater than those obtained after the administration of standard treatment. Adverse effects often occur concurrently in control groups, and the application of NPWT sometimes seems to prevent the occurrence of certain adverse effects and complications experienced by participants in the comparison groups. Indeed, the FDA emphasized that complications related to NPWT rarely occur—usually doing so in long-term care facilities or at home—and are caused by the injudicious use of the technology, which includes not always taking patient-specific characteristics into account. Most adverse effects reported in the RCTs usually are manageable and concern quality of life, particularly as it relates to pain. The data from the documents consulted do not provide conclusive evidence that NPWT has more advantages or disadvantages than standard therapy regarding the patient's quality of life. This stems in part from the fact that quality of life is a very subjective indicator that depends on the patients' own judgment, life experience, values, and tolerance to pain, and the methods used to measure this indicator are not always appropriate. Nevertheless, it is worth noting that one high-quality RCT showed results that were in favour of NPWT for improving the physical and mental health of patients with diabetic foot ulcers who received this treatment. Moreover, another study revealed that positive effects also were observed in patients who received a split-thickness skin graft, as they were discharged sooner from the hospital — a factor the authors believe improved their quality of life. One of the adverse effects attributable to NPWT is its inability to prevent complications.

Although many RCTs attempted to show NPWT's positive impact on the prevention of complications for various types of wounds, the data are too heterogeneous and the sample sizes too small to generalize findings. However, a trend emerges in favour of NPWT for the prevention of infections, the accumulation of seroma in the wound, and split-thickness skin graft rejections. These findings are supported by the data from a 10-year retrospective cohort study conducted by Blume et al. in 2010 [Blume et al., 2010]. In short, the authors showed that for patients who received NPWT after a split-thickness skin graft, the need for a second split-thickness skin graft was not as great as it was in the control group, fewer infections occurred, and less seroma accumulated at the graft site. The prevention of complications and the need for additional surgical procedures have a significant impact on a patient's resource use. Although data on this indicator are scarce, and the studies have risks of bias, the overall perception, for all wound types, is in favour of NPWT if it is used appropriately.
In Quebec, various health care professionals are authorized to assess complex wounds and to prescribe and apply NPWT. Resource availability varies according to health care setting and region; for this reason, it is the responsibility of health facilities to identify professionals who meet their standards of care and who are authorized to assess complex wounds and apply NPWT in their facility. Prescriptions for NPWT from general practitioners and nurses are difficult to trace, whereas prescriptions from specialists, although indexed in the RAMQ’s fee-for-services file, are difficult to interpret on account of the lack of clinical information. It is very difficult to obtain clinical information and information on direct and indirect costs associated with the use of NPWT for a patient and for the population of Quebec as a whole.

Implications of the findings for the practice

The benefits of NPWT for certain clinical indicators do not always depend on the etiology and complexity of the wound, but on factors specific to the individual. Current data cannot be used to predict for which patients NPWT would be more effective than standard treatment. The duration of the healing process varies from one individual to another, mainly according to age, nutritional deficiencies or excesses, medical history, and medications taken. It also appears to be affected by the nature, size, depth, site, and level of contamination of the wound. Moreover, although this technology may be the best option for a particular wound or patient when it is applied in a hospital, it might not be if it were applied at home or in another health facility. Various winning conditions are therefore required to ensure the successful and safe delivery of NPWT, not only in regard to wounds and patients as a whole (e.g., their specific characteristics, medical history, environment, and social network), but also in regard to health care settings and available resources.

The work currently being done by INESSS helps to establish parameters to promote the optimal use of NPWT and harmonize practices throughout Quebec. It is based on the most recent SD derived from RCTs and is enhanced by recommendations from other jurisdictions and the experience of Quebec experts and clinicians from various backgrounds and fields of practice with a good knowledge of the field. This work reveals that the training of health care professionals who make decisions regarding the use and application of NPWT and the assessment of wounds is essential for ensuring the safe use of the technology and obtaining its intended benefits.

Moreover, given the limitations of NPWT and the uncertainty as to which patients will respond best to treatment, a discussion with patients and their families is essential for avoiding unrealistic expectations and for informing them of any adverse effects and possible complications; this would enable them to make informed decisions freely regarding this therapeutically choice. Using this type of approach in the decision-making process is particularly relevant when the level of scientific evidence of a treatment’s efficacy is low and marked by uncertainty [van der Weijden et al., 2013].

Considering the importance of carefully selecting patients, clearly identifying the factors that delay healing, and determining clinically realistic objectives in accordance with the technology’s mechanism of action and the type of complex wound, it seems appropriate, upon completion of the work, to ensure that the treatment is always given in collaboration with health care professionals with complex wound expertise and up-to-date knowledge of wound pathophysiology and the healing process.
Strengths and limitations of the report

The assessment of the scientific findings and their generalization on a larger scale are limited by various parameters inherent to the design of the primary studies selected according to PICO criteria. Although the patients were carefully selected and generally free of any contraindications and factors known to delay the healing process, not all the patients derived a clinical benefit from the use of NPWT. Moreover, most of the studies on patients with diabetes or acute wounds requiring split-thickness skin grafts are from Chile, Pakistan, India, and Eastern Europe, where health habits are likely to be very different from those of Canadians, particularly in terms of nutrition, medical history, and medication — all factors that can affect the healing process. The choice of comparator may also have introduced a bias and given NPWT an advantage, in some RCTs, over other currently available dressings. Moreover, the application of NPWT requires a certain dexterity on the part of health care professionals to derive maximum benefit from the therapy. This is especially the case for maintaining negative pressure, which requires the proper positioning of the dressings over the wound. Improperly applied dressings can delay or prevent the attainment of the clinical objectives for the use of NPWT. In most of the studies, it was specified that the health care professionals who prepared the wound, applied NPWT, and assessed wound progression were medical specialists or specialty nurses. Considering these factors, it is possible that the clinical benefits observed in certain RCTs might not be obtained in the target population under normal conditions of use, particularly as the environment in certain health facilities and home care settings is not as controlled as it is in the RCTs. Moreover, patients in research studies often are not treated for concurrent pathologies that might require medication, which could hinder the healing process or jeopardize the patients’ safety.

The small number of adverse effects and complications reported in the RCTs may be explained not only by the exclusion of patients at the highest risk but also by the small sample size, strict monitoring in health facilities (hospital or specialized clinic), and well-trained health care personnel aware of possible complications. However, some adverse effects that affect the patients' quality of life may not have been taken into account in the RCTs, or the results may not have been published. It is important to emphasize that the "quality of life" dimension was seldom used. Only SRs were used in the analysis, which is based on an assessment of the data from the primary studies conducted by the authors of the SRs consulted, of which only one was judged to be of good quality according to AMSTAR criteria. The data from the surveys or consultations with the patients and caregivers could have improved the conclusions and expanded on the messages conveyed in the report.

Overall, a comprehensive systematic search of the literature was conducted for the "efficacy" and "safety" dimensions; therefore, it is unlikely that major RCTs were overlooked other than those published in languages other than French or English. It should be noted that the observational studies, case series, and case studies were not included in the analysis of the "efficacy" dimension. A search on the Clinical Trials website in February 2015 showed that nearly 80 clinical studies were undertaken since 2008 to assess NPWT's efficacy in various types of wounds.
Many studies are currently in the recruiting phase; others were completed, and some were terminated as a result of recruitment problems. A list of ongoing studies is provided in Appendix I. The outcome of these studies should be published in the coming years, and the results may lead to modifications in the level of evidence for certain indicators and types of wounds.

The work undertaken revealed the weakness of the data for the comparison of the various types of technologies and dressings available in Quebec. Yet, these are major issues, and clinicians and managers would need the data to make informed decisions.

Regarding the parameters associated with clinical practice, some data in the documents containing recommendations for good practice were missing or inadequate. The experts of the advisory committee were invited to improve certain elements by drawing on their clinical experience and their knowledge of the RSSS.
CONCLUSION

Complex wounds constitute a major challenge for patients, health professionals, and the entire health care system in Canada and elsewhere. They can have a major impact on the patient’s quality of life and on the health professionals, who, faced with treatment failures, often feel powerless. The optimal management of patients, in collaboration with health care professionals with complex wound care expertise, would undoubtedly limit the costs attributable to inadequate interventions, lead to a more efficient distribution of human and financial resources for wound care, and help identify the best option for patients by taking their characteristics, environment, preferences, and values into account. Upon completion of the literature data analysis, which was triangulated with the contextual data and the experiential knowledge of the stakeholders consulted, INESSS concluded that:

- Better-designed and sufficiently long studies with a rigorous methodology, participants with more homogeneous wounds (for which few RCTs have been conducted to date), suitable comparators, and clinical indicators for which NPWT might confer a real benefit would be useful for future assessments and for evaluating the benefits of NPWT for different types of wounds.

- Interprofessional collaboration and access to dedicated complex wound care teams are important for the optimal management of patients with such wounds and for the judicious use of NPWT.

- The benefits of NPWT for certain clinical indicators do not always depend on the wound’s complexity and etiology but also on patient-specific factors. Although the current data do not enable one to predict in which patients NPWT will be more effective than standard treatment, it is important to bring together the winning conditions before initiating NPWT by stabilizing the factors that impede the healing process and providing the proper basic care.

- Once NPWT has been initiated, emphasis should be placed on achieving the clearly stated clinical objectives by regularly evaluating the progression of the wound. If there is no favourable change or if the wound is stagnating, the therapy should be stopped.

- The difficulty in tracking down data to provide a portrait of the use of NPWT in Quebec led INESSS to recommend the creation of a system for recording clinical data from patients treated with NPWT. Recording non-nominal data would make it possible to monitor performance indicators — in particular, for diagnosis, duration of treatment, adverse effects, and complications — in order to generate efficacy, efficiency, and safety data at the national level. The recording of non-nominal data would be useful to health professionals for providing the clinical follow-up and optimizing the continuity of care by facilitating interprofessional and inter-facility communication for clinical purposes. Lastly, it could facilitate the identification of patients who are candidates for NPWT and the use of good practices.

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29 For complex wounds with an indication related to the use of NPWT.
RECOMMENDATIONS FOR CLINICAL PRACTICE

The recommendations developed by INESSS are based on current knowledge of wound pathophysiology, the analysis of SD related to NPWT, the best recommendations for clinical practice, the context for the organization of wound care in Quebec, and the experiential knowledge of the various stakeholders who contributed to the work. When there is insufficient scientific evidence, the recommendations are derived from EO, which consists primarily of experiential knowledge. The recommendations are presented in an OUG available on the INESSS website.

Decision-making process for the use of NPWT

- The original prescriber must refer the patient to a dedicated interprofessional team or a health care professional with wound care expertise who is recognized and authorized by the facility in order for the patient and wound to be given a comprehensive assessment prior to the initiation of NPWT.
- A dedicated team or individual with wound care expertise must be clearly identified and readily available for the original prescriber and/or the attending physician, who may have to monitor the use of NPWT when the patient is discharged from the hospital.
- The health care professionals consulted for an EO must be adequately trained and have up-to-date knowledge of the healing process, wound chronicity, the care required to manage complex wounds, and the therapeutic options.
- NPWT must be initiated in a health facility.
- Candidates for NPWT must be carefully selected based on their specific characteristics and on wound-related factors, while taking into account their values and preferences. This step is fundamental in identifying the risk factors that affect wound healing potential.

Indications, contraindications, and adverse effects

- NPWT can be used in carefully selected patients with wounds for which NPWT is indicated and:
  - that do not heal within a predictable amount of time, despite the adequate management of the risk factors that impede healing
  - whose size and depth must be reduced in preparation for surgical closure or coverage, or to promote healing by secondary intention.
- NPWT may be indicated to promote the closure of a chronic wound by secondary intention in the following situations:
  - non-ischemic diabetic foot ulcer associated with significant loss of tissue after any bone or soft tissue infection has been treated and after the debridement of necrotic tissue and off-loading of the ulcer
  - arterial or mixed ulcer after an assessment of the potential for revascularization
  - stage III or stage IV pressure ulcer after the pressure has been off-loaded from the wound and any bone or soft tissue infection has been managed.
- NPWT may be indicated to promote acute wound closure in preparation for healing by secondary intention in the following situations:
  - a traumatic wound that cannot be sutured and that is associated with significant
and/or deep tissue loss without infection, or after treatment, if necessary
  o exeresis associated with significant and/or deep tissue loss without infection, or after treatment, if necessary
  o dehiscence of an extensive surgical wound and/or adverse situation (when surgical closure is impossible).

- NPWT may be indicated to promote the closure of an acute wound in preparation for healing by primary or tertiary intention in the following situations:
  o open wound of the abdomen or thorax
  o surgical wound associated with a high risk of dehiscence.
- NPWT may be indicated to prepare the wound bed for a split-thickness skin graft.
- NPWT may be indicated to secure and maintain a split-thickness skin graft or a skin flap.

Determining the clinical objectives
- NPWT must be initiated in collaboration with a dedicated interprofessional team or a wound care specialist who is recognized and authorized by his or her health facility.
- Clear treatment objectives associated with the wound's progression, its complexity, and the characteristics of the patient to be treated must be determined and specified prior to initiating NPWT.
- The clinical objectives for the use of NPWT are the following:
  o to accelerate the formation of healthy granulation tissue
  o to reduce the time to wound closure
  o to remove exudate and reduce perilesional edema
  o to reduce wound size in preparation for surgical closure (e.g., sutures, staples) or coverage (e.g., split-thickness skin graft, skin flap)
  o to prevent the separation of wound edges in the case of surgical wound dehiscence
  o to serve as a temporary dressing prior to an additional surgical procedure.

Determining the technical parameters
- Consider the following factors when choosing the device: availability, cost, ease of use, health care setting, adverse effects, and the differences between the technologies regarding dressing types, pressure, and mode. Certain parameters related to patients should also be taken into account during the decision-making process.
- A pressure of −80 mm Hg to −125 mm Hg is usually recommended to treat acute or chronic wounds.
- Intermittent pressure should be used for a wound in an area of low sensitivity (e.g., diabetic foot) and continuous pressure, in the following situations:
  o the patient is at an increased risk of bleeding
  o it is a high exudate wound, recent skin flap, or graft
  o for wounds with acute enteric fistulas
  o in unstable body structures
  o for a perianal wound
for a patient with increased sensitivity to pain.

- The choice of dressing is based on the nature of the wound, the technology available in the facility and, when the patient is transferred, the experience of the health care professionals with wound care expertise and the patient's sensitivity to pain.

**Initiating NPWT**

- Ensure that the prescription and treatment plan are clear and comprehensive, and that they provide at least the following information:
  - the general objectives and clinical criteria of the treatment
  - the estimated time to achieve the established clinical objectives
  - the treatment plan revision date
  - the recommended choice of device
  - the technical parameters related to the NPWT system (pressure, intensity, mode, type of dressing)
  - the parameters to assess during the follow-up and the frequency of dressing changes.

**Precautions for use**

- The following precautions should be taken into consideration prior to setting up the device and during dressing changes:
  - Ensure that standard precautions for infection control are observed for all patients and that they adhere to the protocol pre-established by the facility regardless of the diagnosis or presumed infection status.
  - Ensure that the wound bed is free of debris and necrotic tissue.
  - In the case of a laparotomy, avoid contact between the digestive tract and the NPWT system to prevent the creation of a gastrointestinal fistula.
  - Position the tubing so as to prevent the formation of pressure ulcers.
  - Minimize the risks associated with dressing changes by:
    - noting the number of dressing pieces placed in the wound on the cover dressing
    - avoiding cutting sponges, foam dressings, or gauze directly over the wound
    - properly cleaning the wound bed and performing a thorough examination.
    - ensuring that the wound is filled to skin level (that is, place a sufficient number of sponges or compresses in the wound without compacting) once NPWT has begun.
  - Never leave a dressing in place for a prolonged period of time without the active use of the pump. Refer to the manufacturers’ product monographs to adjust the time frames according to the type of dressing and device used.
  - Avoid interrupting NPWT during treatment, insofar as possible, to optimize its effect.
  - To ensure continuity of care, the NPWT device — or at least the dressing used with the device intended for home care — should be set up at the nursing unit prior to the patient's discharge from the hospital.
Dressing changes and parameters to assess

- Dressings should be changed every 48 to 72 hours, depending on the status of the wound and on the volume of exudate. Frequency can vary, especially in the presence of infection or when NPWT is used before or after surgical coverage.
- The wound, the surrounding skin, and the patient should be closely monitored once a week.
- The following parameters should be assessed:
  - the patient's general state of health, complications, adverse effects, and treatment adherence
  - the progression of granulation (wound size, quality, appearance, and percentage of granulation tissue, absence/presence of necrotic tissue), the removal of exudate (quantity and appearance), the presence of infection, the state of the wound edges, and the presence of odour after the wound has been cleaned
  - the appearance of the surrounding tissue (edema, redness, sign of infection, allergic reaction to dressing, maceration).
- The health care professionals who apply NPWT must have the requisite skills to use the technology, recognize any signs of complications, and take appropriate action, if necessary.
- The health care professionals who assess wounds that are undergoing NPWT must have the relevant and up-to-date skills to assess wound progression — including the formation of granulation tissue — recognize any signs of complications, and take appropriate action, if necessary.
- Patients, their caregivers, and the nursing staff must be well-informed to ensure that they recognize the signs that, when present, can pose a risk to patients. They must also be informed of the technical aspects of NPWT.

Monitoring, duration, and renewal of NPWT

- The maximum duration of the original prescription is 30 days.
- A medical reassessment must be carried out by the original prescriber, in collaboration with the team or individual dedicated to wound care, two weeks after the start of treatment.
- The original prescription may be renewed following a reassessment by a team or individual dedicated to wound care.

Criteria for cessation

Cessation of NPWT is recommended in the following situations:

- as soon as healthy granulation tissue covers the wound and before it reaches the edges of the wound
- as soon as the clinical objectives have been met
- if there is evidence of necrotic tissue, hypergranulation, or stagnation; or if the wound is not progressing favourably after two weeks of NPWT
- in the absence of any benefits related to the health care objectives and the pre-established clinical criteria
- when the use of NPWT is not appropriate (e.g., negative pressure is difficult to maintain because of the location of the wound)
• if there is no health care team or professional authorized to change the dressings
• if a complication occurs that threatens the patient's life
• if moderately severe adverse events occur, namely:
  o excessive bleeding
  o severe wound or periwound infection
  o intense pain
  o an allergic reaction following application
• when patients and/or their caregivers do not adhere to the treatment.
APPENDIX A

Information search strategy

Scientific literature

Date of search: July 29 to 31, 2013 Limitations: 2009 to 2013; English and French

MEDLINE (PubMed)

#1 wounds and injuries[mh]) OR wound healing[mh]
#2 wound*[tiab]
#3 negative-pressure wound therapy[mh]
#5 guidelines as topic[mh] OR practice guidelines as topic[mh] OR guideline[pt] OR practice guideline[pt]
#6 guideline*[tiab] OR guidance[tiab] OR health technology assessment[tiab] OR hta[tiab]
#7 (#1 OR #2) AND (#3 OR #4) AND (#5 OR #6)
#8 treatment outcome[majr:noexp]
#9 efficacy[tiab] OR effectiveness[tiab] OR outcome*[tiab]
#10 adverse[tiab] OR safety[tiab] OR side[tiab]
#11 emotions[mh:noexp] OR stress, psychological[mh]
#13 costs and cost analysis[mh:noexp]
#14 expense*[tiab] OR cost*[tiab] OR pricing[tiab] OR expenditure*[tiab]
#15 quality of life[majr]) OR quality-adjusted life years[majr]
#16 quality of life[tiab]
#17 professional practice[majr]) OR health care quality, access, and evaluation[majr]) OR health services administration[majr]
#18 #8 OR #9 OR #10 OR #11 OR #12 OR #13 OR #14 OR #15 OR #16 OR #17
#19 #7 AND #18

EBM Reviews (OvidSP)

Cochrane Database of Systematic Reviews; Database of Abstracts of Review of Effects; Health Technology Review; NHS Economic Evaluation Database)

#1 wound*.ti,ab.
#2 pressure wound therapy.mp.
#3 #1 AND #2
#4 topical negative pressure.ti,ab.
#5 #3 OR #4
**Embase (OvidSP)**

<table>
<thead>
<tr>
<th>#</th>
<th>Term(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>wound/exp OR wound care/ OR wounds.ti,ab.</td>
</tr>
<tr>
<td>#2</td>
<td>negative-pressure wound therapy/ OR topical negative pressure/ OR vacuum/ OR (negative-pressure wound therapy) OR topical negative pressure OR vacuum OR vacuum-assisted OR VAC OR suction dressing OR sub-atmospheric OR subatmospheric).ti,ab.</td>
</tr>
<tr>
<td>#3</td>
<td>#1 AND #2</td>
</tr>
<tr>
<td>#4</td>
<td>emotion/ OR anxiety/ OR nervousness/ OR stress/ OR (emotion OR anxiety OR anguish OR nervousness OR stress).ti,ab.</td>
</tr>
<tr>
<td>#5</td>
<td>(adverse effect* OR safety OR side effects).ti,ab.</td>
</tr>
<tr>
<td>#6</td>
<td>health economics/ OR hospital cost/ OR health care cost/ OR health care expenditure/ OR hospital expenditure/ OR (expense* OR cost* OR pricing OR expenditure).ti,ab.</td>
</tr>
<tr>
<td>#7</td>
<td><em>treatment outcome/ OR (efficacy OR effectiveness OR outcome</em>).ti.</td>
</tr>
<tr>
<td>#8</td>
<td>quality of life/ OR quality of life.ti,ab.</td>
</tr>
<tr>
<td>#9</td>
<td>(organisation OR management OR practice OR administration).ti.</td>
</tr>
<tr>
<td>#10</td>
<td>#4 OR #5 OR #6 OR #7 OR #8 OR #9</td>
</tr>
<tr>
<td>#11</td>
<td>#3 AND #10</td>
</tr>
</tbody>
</table>

**CINAHL (EBSCO)**

<table>
<thead>
<tr>
<th>#</th>
<th>Term(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>#1</td>
<td>wound*</td>
</tr>
<tr>
<td>#2</td>
<td>negative-pressure wound therapy OR topical negative pressure OR vacuum-assisted</td>
</tr>
<tr>
<td>#3</td>
<td>quality of life</td>
</tr>
<tr>
<td>#4</td>
<td>(organization* OR organisation* OR administration) AND (program* OR care)</td>
</tr>
<tr>
<td>#5</td>
<td>(#1 AND #2) AND (#3 OR #4)</td>
</tr>
</tbody>
</table>

A PubMed search on September 15, 2014 yielded two new SRs on NPWT.

**GREY LITERATURE**

Grey literature

Date of search: March 6, 2014 Limitations: 2009 to 2014; English and French

Health technology assessment (HTA)

International

- Guidelines International Network (G-I-N) (www.g-i-n.net)
- NICE/National Institute for Health and Care Excellence
- HAS/Haute Autorité de Santé

United States

- National Guideline Clearinghouse (NGC) (https://guideline.gov)

Theses, dissertations, and institutional repositories

- Open Access Theses and Dissertations (https://oatd.org)
- Papyrus (https://papyrus.bib.umontreal.ca)
- SUDOC (http://www.sudoc.abes.fr/xslt/DB=2.1/SET=3/TTL=1/SHW?FRST=1x3)
• Theses Canada (http://www.bac-lac.gc.ca/eng/services/theses/Pages/theses-canada.aspx)
• theses.fr (http://www.theses.fr/)
• ProQuest index to theses from Great Britain and Ireland (http://www.proquest.com/products-services/pqdt_uk_ireland.html)
• TEL: thèses en ligne (http://www.theses.fr/)

Other
Limitations: 2013-2014; English and French
• Google (http://www.google.ca)
• Google Scholar (https://scholar.google.ca/)
## APPENDIX B

### Inclusion and exclusion criteria

**Table B-1: Inclusion Criteria for the Scientific Studies**

<table>
<thead>
<tr>
<th>Inclusion Criteria — Scientific Studies</th>
<th>&quot;Efficacy&quot; dimension</th>
<th>&quot;Safety&quot; Dimension</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Population</strong></td>
<td>Individuals with a complex wound</td>
<td></td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Negative pressure wound therapy</td>
<td></td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
<td>All types of treatments compared with NPWT</td>
<td></td>
</tr>
<tr>
<td><strong>Indicators</strong></td>
<td>Indicators presented in the SR of the CHU de Québec's HTAU: Primary indicators: time to granulation tissue formation, incidence of complete wound closure, time to wound closure (complete or sufficient to perform controlled closure), wound-related complication, length of hospital stay, quality of life. Secondary indicators: change in the volume, thickness, or surface of the wound, frequency of dressing changes, required treatment time. Indicators selected in collaboration with experts from the advisory committee: Wound closure (healing time or time required prior to a surgical procedure for closure by primary intention); proportion of closed wounds (re-epithelialization and/or granulation tissue coverage); reduction in size, surface, or volume of the wound; prevention of complications (infections, recurrent infections, amputations, split-thickness skin graft failure, accumulation of seroma in the wound or at the graft site), split-thickness skin graft survival rate, quality of life, resource use (duration of hospital stay, dressing changes, visits from nurses, surgery time), duration/time of treatment.</td>
<td></td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>All health care facilities or at home.</td>
<td></td>
</tr>
<tr>
<td><strong>Types of publications</strong></td>
<td>Systematic reviews with or without RCT meta-analysis, randomized controlled trials, assessment reports, practical guideline/guidelines.</td>
<td></td>
</tr>
<tr>
<td><strong>Years of publication</strong></td>
<td>2009 to 2013.</td>
<td></td>
</tr>
<tr>
<td><strong>Methodological quality</strong></td>
<td>Publications judged to be of moderate or good methodological quality according to the selected checklists.</td>
<td></td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Individuals with a complex wound.</td>
<td></td>
</tr>
<tr>
<td><strong>Intervention</strong></td>
<td>Negative pressure wound therapy.</td>
<td></td>
</tr>
<tr>
<td><strong>Comparator</strong></td>
<td>None or all types of treatments compared with NPWT.</td>
<td></td>
</tr>
<tr>
<td><strong>Indicators</strong></td>
<td>Adverse effects (infection, odour, anxiety, stress, quality of life, complications, contraindications), mortality.</td>
<td></td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>All health care facilities or at home.</td>
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</tr>
<tr>
<td><strong>Types of publications</strong></td>
<td>Systematic reviews with or without meta-analysis, randomized controlled trials, observational studies with or without comparators, assessment reports, practical guideline/guidelines, manufacturers' product monographs, reports by regulatory bodies such as the US Food and Drug Administration (FDA) and Health Canada.</td>
<td></td>
</tr>
<tr>
<td>Years of publication</td>
<td>2009 to 2013.</td>
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<td>----------------------</td>
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</tr>
<tr>
<td><strong>Methodological quality</strong></td>
<td>Publications judged to be of moderate or good methodological quality according to the selected checklists (based on the type of document).</td>
<td></td>
</tr>
<tr>
<td><strong>Quality of Life and Pain</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Population</strong></td>
<td>Individuals with a complex wound and undergoing NPWT.</td>
<td></td>
</tr>
<tr>
<td><strong>Indicators</strong></td>
<td>Various parameters associated with quality of life and pain.</td>
<td></td>
</tr>
<tr>
<td><strong>Setting</strong></td>
<td>All health care facilities or at home.</td>
<td></td>
</tr>
<tr>
<td><strong>Types of publications</strong></td>
<td>Systematic reviews.</td>
<td></td>
</tr>
<tr>
<td><strong>Years of publication</strong></td>
<td>2009 to 2013.</td>
<td></td>
</tr>
<tr>
<td><strong>Inclusion Criteria — Other Documents</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Types of publications</strong></td>
<td>Assessment reports, practical guideline/guidelines, and other relevant documents derived from facilities in Quebec, professional bodies, the Collège des médecins du Québec, Accreditation Canada, and teaching hospitals offering complex wound care services, such as telemedicine.</td>
<td></td>
</tr>
<tr>
<td><strong>Years of publication</strong></td>
<td>2008 to 2013.</td>
<td></td>
</tr>
<tr>
<td><strong>Methodological quality</strong></td>
<td>Publications judged to be of moderate or good methodological quality according to the checklists selected, if relevant.</td>
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</tr>
</tbody>
</table>

| **Exclusion Criteria** | |
| **Population** | Non-human subjects. |
| **Intervention** | Publication not specifically focusing on negative pressure wound therapy for the treatment of complex wounds. Studies using multimodal interventions in which it is impossible to identify the outcomes attributable to the use of NPWT. |
| **Types of publications** | Study designs other than randomized controlled trials, with the exception of the "safety" dimension, for which other designs were included during the selection process. |
| **Methodological quality** | Publications judged to be of low methodological quality when other documents of higher quality on the parameters sought were identified. |
| **Language** | Other than French or English. |
| **Research period** | Publications prior to 2009 for the efficacy and safety dimensions, and 2008 for the recommendations for good clinical practice and context of use. |

* Systematic review updates generally meet original PICO criteria. However, consultation with the experts from the advisory committee led to the addition and/or modification of certain indicators originally presented in the report by the CHU de Québec’s HTAU.
APPENDIX C

Flow Charts

Figure C-1: Selection of the Recommendations for Good Clinical Practice, Consensus Conferences, and Guidelines

Documents identified in the databases (n = 30)

Documents from other sources (n = 2)

Documents identified (n = 32)

Documents excluded based on their titles and abstracts (n = 1)

Full-text documents assessed for eligibility (n = 31)

Full-text documents excluded, with reasons (n = 25)

Documents included in the summary (n = 5)

Two documents containing recommendations for good clinical practice

Four systematic reviews derived from one consensus conference

Two documents from the FDA
Figure C-2: "Quality of Life and Pain" Selection

Documents identified in the databases
(n = 19)

Documents from other sources
(n = 1)

Documents identified (n = 20)

Documents excluded based on their titles and abstracts
(n = 0)

Full-text documents assessed for eligibility
(n = 20)

Full-text documents excluded, with reasons
(n = 17)

Documents included in the summary
(n = 3)
Three systematic reviews
APPENDIX D
Reasons for excluding the systematic review

Table D-1: Summary — "Recommendations" Selection, Scientific Literature

<table>
<thead>
<tr>
<th>Included (5)</th>
<th>Excluded (25)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>One consensus conference (four systematic reviews):</strong></td>
<td></td>
</tr>
<tr>
<td>‒ Bruhin (2014)</td>
<td>AHRQ (2009): already included in the systematic review of the CHU de Québec's HTAU,</td>
</tr>
<tr>
<td>‒ Krug (2011)</td>
<td>Back (2013): specific to NPWT with instillation</td>
</tr>
<tr>
<td></td>
<td>Beitz (2012): methodological approach inadequate for assessing quality</td>
</tr>
<tr>
<td><strong>Reports by regulatory bodies and HTAs (4):</strong></td>
<td>Borgquist (2011): a methodological approach inadequate for assessing quality</td>
</tr>
<tr>
<td>‒ NHS (2010)</td>
<td>CADTH (2012): low level of evidence, as no studies were selected from the Rapid</td>
</tr>
<tr>
<td>‒ FDA Alert (2009)</td>
<td>Response Service</td>
</tr>
<tr>
<td></td>
<td>Gupta (2012): a methodological approach inadequate for assessing quality</td>
</tr>
<tr>
<td></td>
<td>ICIS (2012): does not specifically focus on NPWT Kim (2013): specific to NPWT</td>
</tr>
<tr>
<td></td>
<td>Malahias (2012): methodological approach inadequate for assessing quality</td>
</tr>
<tr>
<td></td>
<td>Murphy (2012): not specific to NPWT</td>
</tr>
<tr>
<td></td>
<td>Negosanti (2012): methodological approach inadequate for assessing quality</td>
</tr>
<tr>
<td></td>
<td>NICE (2009): no recommendation was derived from this assessment report</td>
</tr>
<tr>
<td></td>
<td>Salgarello (2012): not specific to NPWT</td>
</tr>
<tr>
<td></td>
<td>Teot (2011): recommendations issued by HAS that are already included in the grey</td>
</tr>
<tr>
<td></td>
<td>literature</td>
</tr>
<tr>
<td></td>
<td>Thompson (2007): methodological approach inadequate for assessing quality</td>
</tr>
<tr>
<td></td>
<td>Desa (2012): a methodological approach inadequate for assessing quality</td>
</tr>
<tr>
<td></td>
<td>Manufacturer product monographs (KCI and Smith &amp; Nephew)</td>
</tr>
</tbody>
</table>

AHRQ = Agency for Healthcare Research and Quality; CHU = Centre hospitalier universitaire de Québec; HAS = Haute Autorité de Santé; HTAU = health technology assessment unit; NPWT = negative pressure wound therapy.

a Relevant documents to be consulted for the optimal use guide.
## Table D-2 Summary: "Quality of Life and Pain" Selection

<table>
<thead>
<tr>
<th>Included (3)</th>
<th>Excluded — Reasons for Exclusion (17)</th>
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<tbody>
<tr>
<td><strong>Systematic reviews:</strong></td>
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</tr>
<tr>
<td></td>
<td>Bolas, N. (2012): study design not selected, n &lt; 20</td>
</tr>
<tr>
<td></td>
<td>Bowers, B. (2009): study design not selected, nurse's role</td>
</tr>
<tr>
<td></td>
<td>Chadwick, P. (2012): study design not selected, other type of NPWT Fagerdahi, A.M. (2013): study design not selected, thesis</td>
</tr>
<tr>
<td></td>
<td>Hurd, T. (2010): study design not selected, use of gauze during NPWT</td>
</tr>
<tr>
<td></td>
<td>Karatepe, O. (2011): study design not selected, diabetic foot ulcer, n &gt; 20, retained for efficacy dimension</td>
</tr>
<tr>
<td></td>
<td>Moffatt, C. J. (2011): study design not selected, n &lt; 20</td>
</tr>
<tr>
<td></td>
<td>Ousey, K. J. (2012): study design not selected, n &lt; 20, comparative</td>
</tr>
<tr>
<td></td>
<td>Upton, D (2013): study design not selected, n &gt; 20, clinicians' perspective</td>
</tr>
<tr>
<td></td>
<td>Upton, D (2013): study design not selected, n &lt; 20, semi-structured interviews, clinicians Upton, D (2013): study design not selected, n &gt; 20, patients' perspective</td>
</tr>
<tr>
<td></td>
<td>Weir, Dot (2011): study design not selected, study on a new disposable NPWT</td>
</tr>
</tbody>
</table>

NPWT = negative pressure wound therapy.
## APPENDIX E

### Document quality assessment

**Table E-1: AMSTAR**

<table>
<thead>
<tr>
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<tbody>
<tr>
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<td>Was an a priori design provided?</td>
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<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>2</td>
<td>Was there duplicate study selection and data extraction?</td>
<td>Yes</td>
<td>NR</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
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<td>Yes</td>
<td>Yes</td>
<td>NR</td>
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</tr>
<tr>
<td>3</td>
<td>Was a comprehensive literature search performed?</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
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<td>Yes</td>
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<td>4</td>
<td>Was the status of publication (i.e., grey literature) used as an inclusion criterion?</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>NR</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>5</td>
<td>Was a list of studies (included and excluded) provided?</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
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<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
</tr>
<tr>
<td>Items</td>
<td>Questions</td>
<td>Author (Year)</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>7</td>
<td>Was the scientific quality of the included studies assessed and reported?</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>NR</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>NR</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
</tr>
<tr>
<td>8</td>
<td>Was the scientific quality of the included studies used appropriately in formulating conclusions?</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
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<td>Yes</td>
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<td>Yes</td>
</tr>
<tr>
<td>9</td>
<td>Were the methods used to combine the findings of studies appropriate?</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
<td>Yes</td>
<td>N/A</td>
<td>N/A</td>
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<td>N/A</td>
<td>Yes</td>
<td>N/A</td>
</tr>
<tr>
<td>10</td>
<td>Was the likelihood of No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
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<td>Questions</td>
<td>Author (year)</td>
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<td></td>
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</tr>
<tr>
<td>11</td>
<td>Was the conflict of interest stated?</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>Yes</td>
<td>No</td>
</tr>
<tr>
<td></td>
<td>Overall quality assessment</td>
<td>Average</td>
<td>Poor</td>
<td>Good</td>
<td>Good</td>
<td>Average</td>
<td>Poor</td>
<td>Good</td>
<td>Good</td>
<td>Average</td>
<td>Poor</td>
<td>Good</td>
<td>Good</td>
<td>Good</td>
<td>Good</td>
<td>Poor</td>
</tr>
</tbody>
</table>

N/A = not applicable; NR = not reported in the systematic review.

\(^1\) Systematic review on quality of life and pain associated with negative pressure wound therapy.
Table E-2: AGREE II

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>MJG</td>
<td>JB</td>
<td>%</td>
<td>MJG</td>
<td>JB</td>
</tr>
<tr>
<td>Scope and purpose</td>
<td>17</td>
<td>17</td>
<td>78</td>
<td>8</td>
<td>15</td>
</tr>
<tr>
<td>Stakeholder involvement</td>
<td>10</td>
<td>12</td>
<td>44</td>
<td>8</td>
<td>7</td>
</tr>
</tbody>
</table>
| Rigour of development of the
  recommendations                    | 38  | 36 | 60 | 39  | 40 | 66 | 39  | 40 | 66 | 39  | 41 | 67 | 32  | 35 | 53 |
| Clarity and presentation           | 14  | 18 | 72 | 15  | 19 | 78 | 15  | 14 | 64 | 14  | 13 | 58 | 16  | 14 | 67 |
| Applicability                      | 14  | 11 | 35 | 10  | 13 | 31 | 9   | 4  | 10 | 9   | 15 | 33 | 7   | 9  | 17 |
| Editorial independence             | 10  | 7  | 54 | 5   | 9  | 42 | 6   | 7  | 38 | 3   | 11 | 42 | 10  | 9  | 63 |
| Overall quality assessment of the
  guideline                          | 6   | 5  | 4  | 4   | 5  | 4  | 4   | 5  |    |     |    |     |     |    |    |
| Recommendation for the
  use of the document               | YES | YES | YES | YES | YES | YES | YES | YES |     |     |     |     |     |     |     |     |
| Total (maximum 168)                | 109 | 106 | 89 | 109 | 90  | 97 | 80  | 105 |     |     |     |     |     |     |     |     |
## APPENDIX F

### Characteristics of the systematic reviews — Quality of life

<table>
<thead>
<tr>
<th><strong>Objective</strong></th>
<th>Document dimensions such as pain and mental and physical health measured with validated tools.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Type of study</strong></td>
<td>Systematic review of the literature</td>
</tr>
<tr>
<td><strong>Number and design of included studies</strong></td>
<td>A total of 48 included studies (RCTs, case studies, and retrospective studies)</td>
</tr>
<tr>
<td></td>
<td>Augustin and Zschocke (2006), n = 176; case study; type of wound not specified.</td>
</tr>
<tr>
<td></td>
<td>Kanogsumthornrat et al. (2006), n = 30; case study; type of wound not specified. Karatapa et al. (2010), n = 67; RCT; foot ulcer (diabetic patients).</td>
</tr>
<tr>
<td></td>
<td>Mendonca et al. (2007), n = 26; prospective cohort study; type of wound not specified.</td>
</tr>
<tr>
<td></td>
<td>Vuerstaek et al. (2006), n = 60; RCT; venous or mixed ulcers.</td>
</tr>
<tr>
<td><strong>Total number of participants</strong></td>
<td>N = 359</td>
</tr>
<tr>
<td><strong>Types of wounds</strong></td>
<td>Foot ulcers (diabetic patients), venous ulcers</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>All types of devices</td>
</tr>
<tr>
<td><strong>Length of follow-up</strong></td>
<td>1950 to 2011</td>
</tr>
<tr>
<td><strong>Outcome measures</strong></td>
<td>Mean scores, n, percentage, P value</td>
</tr>
<tr>
<td><strong>Type of data analysis</strong></td>
<td>Narrative synthesis</td>
</tr>
<tr>
<td><strong>Conflicts of interest</strong></td>
<td>The authors were subsidized by Smith &amp; Nephew</td>
</tr>
<tr>
<td><strong>Authors’ overall conclusion</strong></td>
<td>The authors of this systematic review state that there is some evidence that NPWT improves quality of life. However, given the heterogeneity of the studies and the presence of contradictory results, they were unable to conclude that NPWT offers a definitive advantage for improving patients’ quality of life.</td>
</tr>
<tr>
<td><strong>Objective</strong></td>
<td>Document the physical and psychological factors that can interfere with the quality of life of patients who receive NPWT.</td>
</tr>
<tr>
<td>---------------</td>
<td>---------------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td><strong>Type of study</strong></td>
<td>Systematic review of the literature</td>
</tr>
<tr>
<td><strong>Number of included studies</strong></td>
<td>A total of 25 included studies (two RCTs, clinical studies, case studies, retrospective studies, and literature reviews) (Schimp et al. (2003); Stansby et al. (2010); Apostoli and Caula (2008); Vuolo (2009); Hurd et al. (2010); Panicker (2009); Fracalvieri et al. (2011); Teot et al. (2006); Wolvos (2004); Verbelen et al. (2011); Nease (2009); Keskin et al. (2008); Assenza et al. (2011); Bryan and Dukes (2009); Ozturk et al. (2009); Wondburg et al. (2008); Mendonca et al. (2007); Ousey et al. (2012); Wallin et al. (2001); Karetpe et al. (2011); Ford-Dunn (2006); Vuerstaek et al. (2006); Abbotts (2010); Bolas and Holloway (2012); Moffatt et al. (2011))</td>
</tr>
<tr>
<td><strong>Total number of participants</strong></td>
<td>n = 720</td>
</tr>
<tr>
<td><strong>Types of wounds</strong></td>
<td>All types of wounds</td>
</tr>
<tr>
<td><strong>Interventions</strong></td>
<td>All types of devices</td>
</tr>
<tr>
<td><strong>Length of follow-up</strong></td>
<td>2001 to 2012</td>
</tr>
<tr>
<td><strong>Outcome measures</strong></td>
<td>n, percentage, P value</td>
</tr>
<tr>
<td><strong>Type of data analysis</strong></td>
<td>Narrative review, table describing the studies</td>
</tr>
<tr>
<td><strong>Conflicts of interest</strong></td>
<td>The authors did not identify any conflicts of interest.</td>
</tr>
<tr>
<td><strong>Authors’ overall conclusion</strong></td>
<td>The authors conclude that NPWT improves and accelerates the healing process, which has a positive effect on quality of life. However, dressing changes, the types of dressings, and certain parameters associated with NPWT may cause pain and anxiety and affect body image and self-esteem.</td>
</tr>
</tbody>
</table>
### Waldie et al., 2013 AMSTAR: Good

<table>
<thead>
<tr>
<th>Objective</th>
<th>Describe the management of pain associated with NPWT.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Type of study</td>
<td>Systematic review of the literature</td>
</tr>
<tr>
<td>Number of included studies</td>
<td>A total of 10 included studies (RCTs, cohorts, prospective studies with or without a comparator)</td>
</tr>
<tr>
<td></td>
<td>Fracalvieri et al. 2011: N = 31 patients, acute traumatic wounds, prospective cohort</td>
</tr>
<tr>
<td></td>
<td>Hurd et al. 2010: N = 152, chronic wounds, prospective studies (no comparator)</td>
</tr>
<tr>
<td></td>
<td>Stansby et al. 2010: N = 14, amputation wounds (diabetic patients), prospective cohort</td>
</tr>
<tr>
<td></td>
<td>Ozturk et al. 2009: N = 10, Fournier gangrene, comparative study</td>
</tr>
<tr>
<td></td>
<td>Bondokji et al. 2011: N = 18, acute and chronic wounds, prospective studies (no comparator)</td>
</tr>
<tr>
<td></td>
<td>Vuerstaek et al. 2006: N = 60, chronic leg ulcers, RCT</td>
</tr>
<tr>
<td></td>
<td>Albert et al. 2012: N = 11, surgical wounds, RCT (unblinded)</td>
</tr>
<tr>
<td></td>
<td>Téot et al. 2006: N = 66, acute and chronic wounds, clinical studies (no comparator)</td>
</tr>
<tr>
<td></td>
<td>Franczyk et al. 2009: N = 70, types of wounds not specified, RCT</td>
</tr>
<tr>
<td></td>
<td>Dorafshar et al. 2012: N = 87, traumatic and surgical wounds, RCT (unblinded)</td>
</tr>
<tr>
<td>Total number of participants</td>
<td>N = 519</td>
</tr>
<tr>
<td>Types of wounds</td>
<td>All types of wounds</td>
</tr>
<tr>
<td>Interventions</td>
<td>VAC (KCI)</td>
</tr>
<tr>
<td>Length of follow-up</td>
<td>N/A</td>
</tr>
<tr>
<td>Outcome measures</td>
<td>Level of pain experienced by patients</td>
</tr>
<tr>
<td>Type of data analysis</td>
<td>Narrative synthesis of the literature</td>
</tr>
<tr>
<td>Conflicts of interest</td>
<td>The authors did not identify any conflicts of interest.</td>
</tr>
<tr>
<td>Authors’ overall conclusion</td>
<td>The authors could not reach a definitive conclusion as to whether NPWT should be recommended for pain management.</td>
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</table>
APPENDIX G

Summary of the main recommendations for good clinical practice

Table G-1: General Recommendations

<table>
<thead>
<tr>
<th>Principles of Use</th>
<th>Author (Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ Must be initiated in a health facility by a medical specialist</td>
<td>HAS (2010)</td>
</tr>
<tr>
<td>▪ Monitoring and renewal must be carried out by the original prescriber</td>
<td></td>
</tr>
<tr>
<td>▪ Treatment may be continued on a home care basis, subject to a weekly assessment by the prescriber</td>
<td></td>
</tr>
<tr>
<td>▪ Training required for all health care professionals</td>
<td>Apelqvist et al. (2009)</td>
</tr>
<tr>
<td>▪ Specific training required for all health care professionals</td>
<td></td>
</tr>
<tr>
<td>▪ Referral to a vascular surgeon required for ischemic wounds</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Initiation Criteria (Objectives)</th>
<th>Author (Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>▪ After considering, and, depending on the case, trying conventional treatments</td>
<td>HAS (2010)</td>
</tr>
<tr>
<td>▪ Common objectives:</td>
<td></td>
</tr>
<tr>
<td>o Accelerate the formation of healthy granulation tissue</td>
<td></td>
</tr>
<tr>
<td>o Remove exudate</td>
<td></td>
</tr>
<tr>
<td>▪ Objectives specific to acute wounds:</td>
<td></td>
</tr>
<tr>
<td>o Serve as a temporary dressing prior to an additional surgical procedure</td>
<td></td>
</tr>
<tr>
<td>o Prevent the retraction of wound edges</td>
<td></td>
</tr>
<tr>
<td>▪ Objectives specific to chronic wounds:</td>
<td></td>
</tr>
<tr>
<td>o Prevent complications associated with wound chronicity</td>
<td></td>
</tr>
<tr>
<td>▪ Particulars of laparotomy cases:</td>
<td></td>
</tr>
<tr>
<td>o Limit the retraction of the musculoaponeurotic edges to help achieve early laparotomy closure</td>
<td></td>
</tr>
</tbody>
</table>

30Only the documents from HAS and the Vig/Krug and Birke group have an evidence based methodology
• Requires the medical stabilization of: nutritional status
  o blood pressure
  o blood glucose
  o fluid balance
  o infection

• Characteristics of the patient:
  o presence of few comorbidities, or effectively controlled comorbidities
  o well-being (no pain)
  o adherence and compliance with Tx

• Characteristics of the wound:
  o good blood flow
  o debrided
  o healthy granulation bed
  o ↑ volume of exudate
  o wound ≥ 2 cm deep

• Specific objectives of negative pressure wound therapy:
  o 50% ↓ in wound volume
  o 80% formation of granulation tissue or complete closure

• General objectives:
  o ↓ periwound edema
  o remove exudate
  o ↑ local blood circulation
  o promote the formation of granulation tissue
  o ↓ complexity and size of the wound
  o prepare the wound bed for surgical closure
  o reduce the complexity of surgical wound closure procedures
  o prevent complications and control the symptoms
  o improve time to wound healing

• Objectives:
  o improve blood circulation and microcirculation of the wound bed and periwound
  o stimulate angiogenesis and the integrity of the basement membrane

• assess and optimize the nutritional status and hydration of patients
• characteristics of the wound bed:
  o moist with moderate to abundant exudate
  o contains < 25% necrotic tissue and > 75% granulation tissue

Apelqvist et al. (2009)
Azzopardi et al. (2013)
Negative pressure wound therapy should be considered only as an adjuvant therapy in the presence of wound infection.

• Prior to initiation of negative pressure wound therapy:
  1. Assessment of the wound
  2. Preparation of the wound bed (debridement)
  3. Optimization of the patient's comorbidities

• Winning conditions:
  o treat underlying medical conditions
  o debride the wound to remove any debris and necrotic tissue
  o ensure that the wound has sufficient vascular supply
  o use compression stockings to improve venous insufficiency and venous stasis
  o maintain good glycemic control
  o control the infection
  o optimize the patient's comorbidities and the wound bed

### Indications (Types of Wounds)

<table>
<thead>
<tr>
<th>• Acute wounds: Treatment by primary and secondary intention:</th>
<th>Author (Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>o traumatic wound that cannot be sutured with extensive and/or deep loss of substance; with or without infection</td>
<td>HAS (2010)</td>
</tr>
<tr>
<td>o surgical resection with extensive and/or deep loss of substance; with or without infection</td>
<td></td>
</tr>
<tr>
<td>o opening of extensive surgical wound and/or adverse situation, prepared beforehand, if necessary, with or without infection</td>
<td></td>
</tr>
<tr>
<td>o laparotomy or &quot;open abdomen&quot;</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>• Chronic wounds: Tx by secondary intention:</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>o leg ulcer requiring a split-thickness skin graft</td>
<td>Bovill et al. (2008)</td>
</tr>
<tr>
<td>o stage III or IV pressure ulcer in preparation for surgical coverage</td>
<td></td>
</tr>
<tr>
<td>o diabetic foot ulcer with extensive and/or deep loss of substance</td>
<td></td>
</tr>
<tr>
<td>o non-suturable traumatic wound</td>
<td></td>
</tr>
<tr>
<td>o burn</td>
<td></td>
</tr>
<tr>
<td>o open abdominal wound</td>
<td></td>
</tr>
<tr>
<td>o open thoracic wound</td>
<td></td>
</tr>
<tr>
<td>o split-thickness skin graft</td>
<td></td>
</tr>
<tr>
<td>o fasciotomy</td>
<td></td>
</tr>
<tr>
<td>o soft tissue injury</td>
<td></td>
</tr>
<tr>
<td>o leg ulcer</td>
<td></td>
</tr>
<tr>
<td>o diabetic foot ulcer</td>
<td></td>
</tr>
</tbody>
</table>

Beitz et al. (2012)
Birke-Sorensen et al. (2011)
Desaï et al. (2012)
- burn
- split-thickness skin graft
- stage III or IV pressure ulcers
- traumatic wound that cannot be sutured
- surgical wound dehiscence
- leg ulcer
- diabetic foot wound or ulcer
- open abdominal wound
- split-thickness skin graft
- stage III or IV pressure ulcer
- traumatic wound that cannot be sutured
- surgical resection
- leg ulcer
- diabetic foot ulcer
- burn
- open thoracic wound
- surgical wound or any type of wound requiring surgical closure
- split-thickness skin graft
- traumatic wound that cannot be sutured
- surgical wound dehiscence
- burn (prevent progression)
- split-thickness skin graft
- fasciotomy
- stage III or IV pressure ulcer
- leg ulcer
- diabetic foot ulcer
- lower limb ischemia
  - abdominal open wound
  - Grade 1 to 4

| OHTAC (2010) |
| Apelqvist et al. (2009) |
| Beitz et al. (2012) |
| Birke-Sorensen et al. (2011) |
| Krug et al. (2011) |
| Vig et al. (2011) |
| Bruhin et al. (2014) |
### Cessation Criteria (Contraindications)

| ▪ Obtention of granulation tissue or conditions suitable for a surgical procedure | Author (Year) |
| ▪ No sign of improvement after two consecutive dressing changes or one week of use | HAS (2010) |
| ▪ **Contraindications:** | Apelqvist et al. (2009) |
| ▪ active bleeding | ▪ **Contraindications:** |
| ▪ fistula not excluded | ▪ active bleeding |
| ▪ uncontrolled wound infection | ▪ uncontrolled wound infection |
| ▪ tumoural wound | ▪ tumourous wound |
| ▪ presence of necrotic tissue that has to be removed | ▪ sepsicemia |
| ▪ lack of interface between the digestive tract and the negative pressure system | ▪ untreated osteomyelitis |
| ▪ for the lower limbs: non-revascularized arterial insufficiency | ▪ allergy to any of the material required for the procedure |
| ▪ Stop negative pressure wound therapy if ↑ signs of inflammation | ▪ non-enteric fistula |
| ▪ Stop negative pressure wound therapy if there is no improvement in the appearance of the wound after one to two weeks | ▪ anticoagulant therapy |
| ▪ Stop negative pressure wound therapy if there is any sign of infection or deterioration | ▪ exposed vital organs and structures |
| ▪ **Contraindications:** | ▪ dry wound bed with minimum exudate |
| ▪ uncontrolled wound infection | ▪ **Contraindications:** |
| ▪ non-revascularized arterial insufficiency | ▪ active bleeding |
| ▪ untreated osteomyelitis | ▪ uncontrolled wound infection |
| ▪ Stop negative pressure wound therapy if surgical closure is indicated | ▪ presence of necrotic tissue |
| ▪ **Contraindications:** | ▪ exposed vital organs and structures |
| ▪ tumourous wound | ▪ tumourous wound |
| ▪ sepsicemia | ▪ presence of necrotic tissue |
| ▪ untreated osteomyelitis | ▪ untreated osteomyelitis |
| ▪ allergy to any of the material required for the procedure | ▪ Contraindications: |
| ▪ non-enteric fistula | ▪ tumourous wound |
| ▪ anticoagulant therapy | ▪ presence of necrotic tissue |
| ▪ exposed vital organs and structures | ▪ untreated osteomyelitis |
| ▪ dry wound bed with minimum exudate | ▪ Contraindications: |

**Apelqvist et al. (2009)**

**Beitz et al. (2012)**
- non-enteric fistula
- exposed vital organs and structures

**Contraindication:** presence of necrotic tissue

<table>
<thead>
<tr>
<th>Duration of Treatment</th>
<th>Author (Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Maximum duration of treatment: 30 days (may be renewed once)</td>
<td>HAS (2010)</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Monitoring (Intervention/Frequency of Follow-Ups)</th>
<th>Author (Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Inform the patient of treatment objectives, adverse effects, and constraints associated with negative pressure wound therapy use</td>
<td>HAS (2010)</td>
</tr>
<tr>
<td>• Change the dressing two to three times per week</td>
<td></td>
</tr>
<tr>
<td>• Continuous or intermittent negative pressure may be applied (between 50 mm Hg and 200 mm Hg)</td>
<td></td>
</tr>
<tr>
<td>• Precautions for use:</td>
<td></td>
</tr>
<tr>
<td>o verify the absence of residual tumourous tissue</td>
<td>Apelqvist et al. (2009)</td>
</tr>
<tr>
<td>o if necessary, protect exposed vascular pedicle</td>
<td></td>
</tr>
<tr>
<td>o in the case of a laparotomy, avoid contact between the digestive tract and the negative pressure system to prevent the creation of a gastrointestinal fistula</td>
<td></td>
</tr>
<tr>
<td>o make sure the patient is not lying on tubing (risk of pressure ulcer)</td>
<td></td>
</tr>
<tr>
<td>• Regularly assess the wound (wound edges and bed)</td>
<td></td>
</tr>
<tr>
<td>• Continue negative pressure wound therapy if the volume of the wound ↓ = 15% after one to two weeks</td>
<td></td>
</tr>
<tr>
<td>• Consider the use of gauze to reduce pain during dressing changes</td>
<td></td>
</tr>
<tr>
<td>• Consider the use of polyvinyl alcohol (PVA) foam to reduce pain during dressing changes</td>
<td></td>
</tr>
<tr>
<td>• Use polyurethane foam wound filler when a rapid surface granulation response is sought</td>
<td></td>
</tr>
<tr>
<td>• Use foam for deep, uniform, and contractible wounds</td>
<td></td>
</tr>
</tbody>
</table>

Bovill et al. (2008)
Desaï et al. (2012)
Birke-Sorensen et al. (2011)
- Use gauze for non-contracting wounds or complex deep cavities
- Use a non-adherent wound contact layer when polyurethane foam is required to bolster a split-thickness skin graft
- Use a level of pressure within a therapeutic range of 40 mm Hg to 150 mm Hg
- Use low pressure to reduce pain
- Avoid using high levels of pressure in wounds with reduced or compromised vascularity or at risk of ischemia
- Use higher levels of pressure to manage high levels of wound exudate or wound fluid a/n
- Antimicrobial dressings, silver dressings, antimicrobial wound contact layer, and fluid instillation may contribute to infection control

- Precautions for use:
  - in the presence of active bleeding
  - use of anticoagulants
  - difficulty achieving hemostasis

<table>
<thead>
<tr>
<th>Comments (e.g., Conflicts of Interest, Psychological Factors, Economic Factors, Other)</th>
<th>Author (Year)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Side effects:</strong></td>
<td>HAS (2010)</td>
</tr>
<tr>
<td>- pain</td>
<td></td>
</tr>
<tr>
<td>- maceration of perilesional skin</td>
<td></td>
</tr>
<tr>
<td>- risk of hemorrhage</td>
<td></td>
</tr>
<tr>
<td><strong>Disadvantages:</strong></td>
<td></td>
</tr>
<tr>
<td>- implementation and monitoring difficulties</td>
<td></td>
</tr>
<tr>
<td>- permanent dependence on the device</td>
<td></td>
</tr>
<tr>
<td>- noise</td>
<td></td>
</tr>
<tr>
<td><strong>Winning conditions:</strong></td>
<td></td>
</tr>
<tr>
<td>- treat comorbidities and underlying conditions of the wound</td>
<td></td>
</tr>
<tr>
<td>- optimize the patient's physical, nutritional, and psychosocial status to obtain maximum benefits</td>
<td></td>
</tr>
<tr>
<td>- Under ideal conditions (particularly in the absence of infection), a well-perfused</td>
<td></td>
</tr>
<tr>
<td>wound should respond rapidly (within one week) with the formation of granulation tissue</td>
<td></td>
</tr>
<tr>
<td><strong>Sign of healing:</strong></td>
<td>Apelqvist et al. (2009)</td>
</tr>
<tr>
<td>- the formation of thin, white epithelium at the wound edges after the second and subsequent applications</td>
<td></td>
</tr>
<tr>
<td>- Sign of inadequate perfusion: the wound bed is granular and red in appearance</td>
<td></td>
</tr>
<tr>
<td>- Granulation of tissue should ↑ ≈ 3% to 5% each day.</td>
<td></td>
</tr>
</tbody>
</table>
### Table G-2: Recommendations for Chronic Wounds Presented in the Documents Determined to be of Low Methodological Quality and Not Selected

#### Pressure Ulcers

<table>
<thead>
<tr>
<th>Author/Organization (Year)</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apelqvist et al. (2009)</td>
<td>NPWT is not recommended for stage II ulcers and should not be used when a deep tissue injury is suspected under intact skin. NPWT is recommended as first-line treatment for stages III and IV in certain situations. The effects of NPWT should be continually assessed for up to two weeks. The duration of NPWT should be defined according to the initial size of the wound and the volume of tissue available for reconstruction. NPWT is not a substitute for proper basic care and should be combined with appropriate pressure redistribution and proper skin care. The insertion and removal of dressings is easier in wounds ≥ 2 cm. The application of NPWT requires additional expertise for wounds close to the anus.</td>
</tr>
</tbody>
</table>

#### Diabetic foot ulcers

<table>
<thead>
<tr>
<th>Author/Organization (Year)</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apelqvist et al. (2009)</td>
<td>NPWT is not recommended for superficial wounds. NPWT can be used to ↓ wound size by promoting the formation of granulation tissue. NPWT can be used to prevent the need for a split-thickness skin graft or to downscale the complexity of closure procedures. Use a special dressing for plantar wounds to prevent pressure ulcers. The recommended duration of initial therapy is one to two weeks. Continue NPWT if progress is good (↑ daily formation of healthy granulation tissue, ↓ wound size, good blood flow, no infection), until the objectives are achieved. Stop NPWT if there is any deterioration or limited improvement. Use NPWT only when underlying diseases have been diagnosed and treated and following the appropriate debridement of nonviable tissue. Combine NPWT with effective off-loading and proper wound care. Use NPWT following partial foot amputation and to help secure and maintain a split-thickness skin graft. It is not always appropriate to initiate NPWT immediately following surgery; it may be beneficial to observe the wound for one to two days prior to the application.</td>
</tr>
</tbody>
</table>
Stop NPWT when the clinical objective has been attained (↓ volume of the wound, adequate preparation of the wound bed for a split-thickness skin graft).
Use with caution if TcpO₂ is between 20 mm Hg and 30 mm Hg and sensitivity is low (adjust NPWT pressure to low levels).

<table>
<thead>
<tr>
<th>Author/Organization (Year)</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Apelqvist et al. (2009)</td>
<td>Stop NPWT if there is wound deterioration after the first dressing change.</td>
</tr>
</tbody>
</table>

NPWT = negative pressure wound therapy; TcpO₂ = transcutaneous oxygen.

Table G-3: Recommendations for Acute Wounds Presented in the Documents Determined to be of Low Methodological Quality and Not Selected

<table>
<thead>
<tr>
<th>Traumatic Wounds</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td>Author/Organization (Year)</td>
<td>Requires the involvement of a multidisciplinary team with considerable expertise. NPWT is indicated for the treatment of extensive loss of soft tissue.</td>
</tr>
<tr>
<td>Apelqvist et al. (2009)</td>
<td>Objectives of NPWT:</td>
</tr>
<tr>
<td></td>
<td>o stabilize soft tissue</td>
</tr>
<tr>
<td></td>
<td>o minimize the degree of secondary damage</td>
</tr>
<tr>
<td></td>
<td>o help to preserve compromised tissue</td>
</tr>
<tr>
<td></td>
<td>o stimulate the formation of granulation tissue</td>
</tr>
<tr>
<td></td>
<td>o reduce edema</td>
</tr>
<tr>
<td></td>
<td>o reduce infection rates</td>
</tr>
<tr>
<td></td>
<td>o reduce the complexity and size of the wound</td>
</tr>
<tr>
<td></td>
<td>o reduce the complexity of the reconstruction procedure and scar formation</td>
</tr>
<tr>
<td></td>
<td>o reduce the number and frequency of dressing changes (optimize patient care and well-being)</td>
</tr>
<tr>
<td></td>
<td>o stabilize split-thickness skin grafts and improve healing of donor site</td>
</tr>
<tr>
<td></td>
<td>o promote skin substitute fixation</td>
</tr>
<tr>
<td></td>
<td>o stabilize patient requiring transfer to a tertiary centre</td>
</tr>
<tr>
<td></td>
<td>o treat open fractures</td>
</tr>
</tbody>
</table>
prevent wound progression in partial-thickness burns

Note: p. 11 describes quality of life factors to consider. It may be worthwhile to reconsult to compare the data that will be extracted on quality of life.

<table>
<thead>
<tr>
<th>Split-thickness skin grafts</th>
<th>Recommendations</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Author/Organization (Year)</strong></td>
<td><strong>Use NPWT to prepare a wound bed for grafting, where the wound and its donor site may be potentially downgraded or where infection or poor granulation prevents the immediate application of the graft. NPWT may be safely used for all split-thickness skin grafts but should be considered standard care for grafts at particular risk of low &quot;take&quot; because of excess mobility, exudate, or anatomical configuration. NPWT should be used continuously at -100 mm Hg to 125 mm Hg for three to four days prior to inspection. Sheet perforation/meshing of dermal substitute prior to NPWT does not hinder &quot;take&quot; and may prevent fluid collections. Objectives for the use of NPWT: Preparation of the wound bed</strong></td>
</tr>
</tbody>
</table>
| Bovill et al. (2008) | **↓ wound size or grade**  
| | **improve granulation**  
| | **control infection**  
| | **APPLICATION OF THE GRAFT**  
| | **drain serous fluid or hematoma**  
| | **support the graft**  
| | **↑ rate of angiogenesis**  
| | **support the graft bed in challenging areas**  
| | **facilitate dressing changes**  
| | **NPWT promotes blood circulation and microcirculation of the wound bed and periwound. NPWT stimulates angiogenesis and the integrity of the basement membrane. NPWT can reduce graft loss due to shearing and edema reduction. NPWT applied to split-thickness skin grafts can provide significant improvement compared with standard dressings.** |
| Azzopardi et al. (2013) | **NPWT: preparation of the wound bed**  
| | **↓ wound size or grade**  
| | **improve granulation**  
| | **control infection**  
| | **Application of the graft**  
| | **drain serous fluid or hematoma**  
| | **support the graft**  
| | **↑ rate of angiogenesis**  
| | **support the graft bed in challenging areas**  
| | **facilitate dressing changes**  
<p>| | <strong>NPWT promotes blood circulation and microcirculation of the wound bed and periwound. NPWT stimulates angiogenesis and the integrity of the basement membrane. NPWT can reduce graft loss due to shearing and edema reduction. NPWT applied to split-thickness skin grafts can provide significant improvement compared with standard dressings.</strong> |</p>
<table>
<thead>
<tr>
<th>Author/Organization (Year)</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| Apelqvist et al. (2009)   | NPWT can be used to achieve delayed primary closure with fascia or to accelerate granulation tissue formation prior to split-thickness skin grafting. Benefits of NPWT:  
  o improves survival rate  
  o ↓ number of dressing changes  
  o enables a higher rate of total abdominal wall closure  
  o ↓ the need for secondary surgical reconstruction  
  o ↓ complications (incisional hernia, infection).  
  NPWT should be used only by specialists with appropriate expertise and training.  
  Dressings must be changed every 48 hours to 72 hours in the absence of wound infection.  
  The exact frequency of dressing changes is dependent on the individual patient's circumstances but ideally should not be less than three times a week.  
  Patients with existing fistulas should be referred to a specialist centre, as special techniques are required.  
  Exposed bowel must be adequately protected using a non-adherent interposed layer to prevent fistula formation or other complications. |
| Bovill et al. (2008)      | NPWT should be applied from initial laparotomy to maximize benefits to patient care. Optimum wound results may take 21 days or more to achieve.  
  Continue NPWT in the presence of physiological progress.  
  For Grade 2 abdominal wounds and above, place a fenestrated non-adherent apron over the abdominal viscera and beneath the peritoneum.  
  Use NPWT in specialized units only, and be aware of high-output abdominal fistulas.  
  Objectives for the use of NPWT:  
  o to prevent abdominal compartment syndrome  
  o to protect abdominal contents and facilitate other explorations  
  o to remove intra-abdominal fluid  
  o to ↓ edema in tissues and intestines  
  o to preserve the peritoneal cavity  
  o to reverse tissue expansion |
## Sternal Wounds

<table>
<thead>
<tr>
<th>Author/Organization (Year)</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| **Apelqvist et al. (2009)** | Consider NPWT as a first-line treatment for dehisced sternal wounds following cardiac surgery.  
   Objectives for the use of NPWT:  
   - to promote definitive surgical closure  
   - to stabilize the sternum  
   - to facilitate sternal salvage  
   - to facilitate drainage of the anterior mediastinum  
   - to enable patients to be extubated and mobilized early  
   - ↓ long-term mortality  
   Debridement of bone is essential in deep infected sternal wounds.  
   Initiate NPWT for 48 hours and reassess.  
   Daily levels of serum C-reactive protein may also be used to guide therapy.  
   Involvement of a cardiothoracic surgeon is essential. |
| **Bovill et al. (2008)** | Apply NPWT at a continuous pressure of 125 mm Hg.  
   The early involvement of a plastic surgery team is required in the case of a sternal infection.  
   Perform early aggressive debridement.  
   A perforated protective sheet material with lubricant properties should be used to minimize the risks to underlying structures.  
   A double-layer foam dressing enables optimal thoracic stabilization combined with even distribution of negative pressure over the entire wound surface.  
   Dressing changes should be performed three times a week, unless C-reactive protein levels are rising.  
   Dressing changes under general anesthesia allow the debridement of devitalized tissue to be carried out.  
   The duration of NPWT application may be best guided by stable low C-reactive protein levels (30 g/dL to 70 g/dL) together with a visual assessment of adequate granulation tissue formation.  
   Active bleeding or anticoagulation beyond the therapeutic range precludes the use of NPWT. |
<table>
<thead>
<tr>
<th>Author/Organization (Year)</th>
<th>Recommendations</th>
</tr>
</thead>
</table>
| Bovill et al. (2008)      | Involvement of specialists. Subatmospheric pressure should ideally begin within six hours of the injury and continue for at least 48 hours. Objectives for the use of NPWT:  
  o prevent the progression of the burn  
  o secure the graft and skin substitutes  
  o contain the wound bed  
  o accelerate healing of the donor site  
  o facilitate the administration of topical antimicrobials |

NPWT = negative pressure wound therapy.
<table>
<thead>
<tr>
<th>Goals</th>
<th>Indications</th>
<th>Acute</th>
<th>Reconstructive Surgery (Surgical Coverage)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Chronic</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>DFU</td>
<td>PU</td>
<td>LU</td>
</tr>
<tr>
<td></td>
<td>DFU</td>
<td>(III or IV)</td>
<td>LC</td>
</tr>
<tr>
<td></td>
<td>DFU</td>
<td>PU</td>
<td>LU</td>
</tr>
<tr>
<td>Allow the wound to progress and/or prepare it for closure by primary or secondary intention (acceleration of granulation tissue formation)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>● ● ● ● ●</td>
<td>○</td>
<td>● ● ● ● ● ● ○</td>
</tr>
</tbody>
</table>
### APPENDIX H

**Context and experiential knowledge**

**Table H-1: Reserved Activities for Wound Care Based on the Types of Health Care Professionals Other than Physicians**

<table>
<thead>
<tr>
<th>Care Professionals</th>
<th>Reserved Activities</th>
</tr>
</thead>
</table>
| Nurse              | Determining the treatment plan for wounds and alterations of the skin and teguments, and providing the required care and treatment (Nurses Act, L.R.Q., c. I-18).<sup>a</sup>  
*Field of Practice*
(Nurses Act, sec. 36)  
assessing health;  
determining and carrying out the nursing care and treatment plan;  
providing nursing and medical care and treatment in order to maintain and restore the health of a person in interaction with his environment and prevent illness, and providing palliative care.  

<sup>a</sup>CMQ<sup>b</sup> Draft Regulations  
A nurse may, as part of the activity reserved to nurses to determine the treatment plan for wounds and alterations of the skin and teguments and provide the required care and treatment:  

- prescribe the laboratory analyses specified in the draft regulations;  
- prescribe the products, medications, and dressings associated with the treatment of wounds and alterations of the skin and teguments specified in the draft regulations.  

The nurse must consult a physician or team of professionals dedicated to wound care when the wound has not responded favourably within the normal or expected time for the care given.
| Nursing assistant | Provide the required care and treatment for alterations of the skin and teguments, according to a prescription or a nursing plan (Professional Code, sec. 37.1 par.5 c) \(^c\) [OIIAQ, 2011].

**Field of Practice**
1. participate in the assessment of a person’s state of health and in the carrying out of a care plan;
2. provide nursing and medical care and treatment to maintain or restore health and prevent illness, and provide palliative care.

| Physiotherapists | Provide treatment for wounds (Professional Code, sec. 37.1 par.3 f)

**Field of Practice**
1. Assess physical function limitations and disabilities related to the neurological, musculoskeletal, and cardiopulmonary systems;
2. Determine a treatment plan;
3. Apply treatment in order to obtain optimal functional performance.

**CMQ\(^d\) Draft Regulations**
A physiotherapist or physical rehabilitation therapist may administer topical medications for the purpose of using invasive forms of energy and when providing treatment for wounds.

| Occupational therapist | Provide treatment for wounds (Professional Code, sec. 37.1 par.4 c) \(^{17}\)

**Field of Practice**
1. Assess functional abilities;
2. Determine and implement a treatment and intervention plan;
3. Develop, restore, or maintain a person’s skills;
4. Compensate disabilities;
5. Reduce handicapping situations;
6. Tailor the environment to needs in order to foster optimal autonomy.

**CMQ\(^e\) Draft Regulations**
An occupational therapist may administer topical medications when providing treatment for wounds.

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\(^a\) [http://legisquebec.gouv.qc.ca/fr/ShowDoc/cs/I-8](http://legisquebec.gouv.qc.ca/fr/ShowDoc/cs/I-8)

\(^b\) [http://www2.publicationsduquebec.gouv.qc.ca/dynamicSearch/telecharge.php?type=1&file=3621.PDF](http://www2.publicationsduquebec.gouv.qc.ca/dynamicSearch/telecharge.php?type=1&file=3621.PDF)

\(^c\) [http://legisquebec.gouv.qc.ca/fr/ShowDoc/cs/C-26](http://legisquebec.gouv.qc.ca/fr/ShowDoc/cs/C-26)

\(^d\) [http://legisquebec.gouv.qc.ca/fr/ShowDoc/cc/M-9-%20r.%204](http://legisquebec.gouv.qc.ca/fr/ShowDoc/cc/M-9-%20r.%204)

Table H-2: Accreditation Requirements for the ROP on Skin and Wound Care for Organizations Providing Home Care Services

<table>
<thead>
<tr>
<th>Major</th>
<th>The organization has a documented and coordinated approach to skin and wound care that supports physicians, nurses, and allied health care providers to work collaboratively and provides access to the range of expertise that is appropriate for the client population.</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major</td>
<td>The organization provides access to education on appropriate skin and wound care, including products and technologies, assessment, treatment, and documentation.</td>
</tr>
<tr>
<td>Major</td>
<td>The organization provides information and education to clients (as well as families and caregivers) about skin and wound self-care, in a format that they can understand.</td>
</tr>
<tr>
<td>Major</td>
<td>The organization uses an evidence-informed assessment of new clients to determine or confirm the diagnosis of the wound and develop an individualized care plan that addresses the cause(s) of the wound.</td>
</tr>
<tr>
<td>Major</td>
<td>The organization supports the delivery of standardized skin and wound care that optimizes skin health and promotes healing.</td>
</tr>
<tr>
<td>Major</td>
<td>The organization implements standardized documentation to create a comprehensive record of all aspects of the client’s skin and wound care (including assessment, treatment goals, treatment provided, and outcomes). The organization established a process to share information between providers, especially at care transitions, about the client’s skin and wound care.</td>
</tr>
</tbody>
</table>

ROP = required organizational practices.
# Table H-3: Relationship Between the Clinical Objectives for the Use of NPWT and the Indications (Types of Complex Wounds)

## Objectives of Negative Pressure Wound Therapy Use

<table>
<thead>
<tr>
<th>Objective</th>
<th>Accelerate the formation of healthy granulation tissue</th>
<th>Reduce time to wound closure</th>
<th>Reduce wound size in preparation for surgical closure or coverage</th>
<th>Remove exudate and reduce perilesional edema</th>
<th>Prevent wound edge retrac-tion in the case of surgical wound de-hiscence</th>
<th>Serve as a temporary dressing prior to additional or reconstructive surgery</th>
<th>Prevent complications</th>
<th>Limit resource use</th>
</tr>
</thead>
</table>

## Clinical Indications

### Chronic Wounds

<table>
<thead>
<tr>
<th>Clinical Indication</th>
<th>Reference(s)</th>
<th>Reference(s)</th>
<th>Reference(s)</th>
<th>Reference(s)</th>
<th>Reference(s)</th>
<th>Reference(s)</th>
<th>Reference(s)</th>
<th>Reference(s)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Non-ischemic diabetic foot ulcer associated with significant tissue loss; after the treatment of any bone or soft tissue infection, if necessary; after debridement and off-loading of the ulcer</td>
<td>[Karatepe et al., 2011; Nain et al., 2011; Dalla Paola et al., 2010; Sepulveda, 2009]</td>
<td>[Karatepe et al., 2011; Nain et al., 2011; Dalla Paola et al., 2010; Sepulveda, 2009]</td>
<td>[Nain et al., 2011; Akbari et al., 2007]</td>
<td>[Vig et al., 2011; HAS, 2010]</td>
<td>NR</td>
<td>[Vig et al., 2011; HAS, 2010]</td>
<td>[Nain et al., 2011; Dalla Paola et al., 2010]</td>
<td>[Dalla Paola et al., 2010]</td>
</tr>
<tr>
<td>Arterial or mixed ulcer after an assessment of the potential for revascularization</td>
<td>[Vig et al., 2011; HAS, 2010]</td>
<td>[Vig et al., 2011; HAS, 2010]</td>
<td>[Vig et al., 2011; HAS, 2010]</td>
<td>NR</td>
<td>[Vig et al., 2011; HAS, 2010]</td>
<td>Ø</td>
<td>Ø</td>
<td></td>
</tr>
<tr>
<td>Stage III or stage IV pressure ulcer after the removal of pressure from the wound site and the treatment of any bone or soft tissue infection, if necessary</td>
<td>[Ashby et al., 2012; Vig et al., 2011; HAS, 2010]</td>
<td>[Ashby et al., 2012; Vig et al., 2011; HAS, 2010]</td>
<td>[Vig et al., 2011; HAS, 2010]</td>
<td>NR</td>
<td>[Vig et al., 2011; HAS, 2010]</td>
<td>Ø</td>
<td>[Ashby et al., 2012; Vig et al., 2011]</td>
<td></td>
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<tr>
<td>ACUTE WOUNDS</td>
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<tr>
<td><strong>Surgical procedure</strong></td>
<td></td>
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</tr>
<tr>
<td>Surgical resection associated with significant and/or deep tissue loss without infection or after treatment, if necessary</td>
<td>[Krug et al., 2011; HAS, 2010]</td>
<td>Ø</td>
<td>[HAS, 2010]</td>
<td>[HAS, 2010]</td>
<td>NR</td>
<td>[Krug et al., 2011; HAS, 2010]</td>
<td>Ø</td>
<td>Ø</td>
</tr>
<tr>
<td>Dehiscence of extensive surgical wound and/or adverse situation (surgical closure not possible)</td>
<td>[HAS, 2010]</td>
<td>[HAS, 2010]</td>
<td>[HAS, 2010]</td>
<td>[HAS, 2010]</td>
<td>Ø</td>
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</tr>
<tr>
<td>Surgical wound with a high risk of dehiscence (i.e., any wound requiring a complex approach)</td>
<td></td>
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<td></td>
<td></td>
<td></td>
<td>[Pachow sky, 2012]</td>
<td>Ø</td>
</tr>
<tr>
<td>Open abdominal or thoracic wound</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
<td>[Bruhin et al., 2014]</td>
<td>NR</td>
<td>Bruhin et al., 2014</td>
<td>[Bruhin et al., 2014]</td>
<td>[HAS, 2010]</td>
</tr>
<tr>
<td><strong>Traumatic-open fracture</strong></td>
<td></td>
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<tr>
<td>Traumatic wound that cannot be sutured and that is associated with significant and/or deep tissue loss, without infection or after treatment, if necessary</td>
<td>[Rasool et al., 2013; Krug et al., 2011; Stannard, 2009]</td>
<td>[Rasool et al., 2013; Krug et al., 2011; Stannard, 2009]</td>
<td>[Krug et al., 2011; HAS, 2010]</td>
<td>[Krug et al., 2011; HAS, 2010]</td>
<td>NR</td>
<td>[Krug et al., 2011; HAS, 2010]</td>
<td>[Stannard d, 2009]</td>
<td>Ø</td>
</tr>
<tr>
<td><strong>Reconstructive surgery</strong></td>
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<td></td>
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<td></td>
</tr>
<tr>
<td>Just before a split-thickness skin graft</td>
<td>[Saaqi, 2010]</td>
<td>Ø</td>
<td>*</td>
<td>Ø</td>
<td>NR</td>
<td>NR</td>
<td>[Saaqi, 2010]</td>
<td>[Saaqi, 2010]</td>
</tr>
<tr>
<td>Following a split-thickness skin graft</td>
<td>NR</td>
<td>[Petkar et al., 2012; Krug et al., 2011]</td>
<td>NR</td>
<td>[Krug et al., 2011]</td>
<td>NR</td>
<td>NR</td>
<td>[Chio, 2010]</td>
<td>[Petkar et al., 2012; Llanos et]</td>
</tr>
</tbody>
</table>
Following a skin flap procedure

| Petkar et al., 2011; Dalla Paola et al., 2010; Llanos et al., 2006; Moisidis et al., 2004 | Krug et al., 2011 | [Krug et al., 2011] | NR | [Krug et al., 2011] | NR | Krug et al., 2011 | Ø |

NR = not relevant; Ø = no studies identified; Moderate level of evidence = Level 1 with moderate risk of bias; Low level of evidence = Level 1 with high risk of bias; Assessment of the evidence by the authors of the BPR consulted = Levels of evidence 1 to 3; Expert opinion
APPENDIX I

Ongoing clinical studies

Table I-1: List of Clinical Studies Registered on the Clinical Trials Website

<p>| Start  | Status                        | Sponsor                | Country      | Title                                                                 |
|--------|-------------------------------|                       |              |                                                                     |
| 2014   | Recruiting                    | KCI and University    | Canada       | NPWT for the prevention of surgical site infection following lower limb revascularization |
| 2013   | Open, but not yet recruiting  | KCI                    | Canada       | NPWT use to decrease surgical nosocomial events in colorectal resections |
| 2012   | Recruiting                    | University            | United States| Incisional NPWT                                                      |
| 2014   | Recruiting                    | University and KCI    | United States| NPWT in Caesarean section                                           |
| 2013   | Recruiting                    | Hospital               | Denmark      | Incisional NPWT for prevention of post-operative infection following Caesarean section |
| 2013   | Recruiting                    | Hospital               | Belgium      | NPWT and allogenic human split-thickness skin grafts for wound bed preparation |
| 2009   | Active                        | University            | United States| Comparison of two methods of securing split-thickness skin grafts using NPWT: VAC and GSUC |
| 2013   | Recruiting                    | KCI                    | United States| Surgical site infection rate after intra-abdominal surgery using NPWT at initial closure |
| 2013   | Recruiting                    | KCI                    | United States| NPWT to reduce site infection                                      |</p>
<table>
<thead>
<tr>
<th>Year</th>
<th>Status</th>
<th>Location</th>
<th>Country</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>2011</td>
<td>Active</td>
<td>University, KCI, and Smith &amp; Nephew</td>
<td>Germany</td>
<td>Treatment study of NPWT for diabetic foot wounds</td>
</tr>
<tr>
<td>2013</td>
<td>Recruiting</td>
<td>University</td>
<td>Denmark</td>
<td>Intervention for postpartum infections following Caesarean section</td>
</tr>
<tr>
<td>2015</td>
<td>Open, but not yet recruiting</td>
<td>University and KCI</td>
<td>Canada</td>
<td>A randomized controlled trial exploring the ability of NPWT to reduce colorectal surgical site infections</td>
</tr>
<tr>
<td>2014</td>
<td>Open, but not yet recruiting</td>
<td>Hospital</td>
<td>Israel</td>
<td>NPWT-PREVENA in prevention of infections after total knee arthroplasty</td>
</tr>
<tr>
<td>2015</td>
<td>Open, but not yet recruiting</td>
<td>University</td>
<td>United States</td>
<td>Improvement in wound with NPWT for post-operative total hip arthroplasty</td>
</tr>
<tr>
<td>2014</td>
<td>Open, but not yet recruiting</td>
<td>University</td>
<td>United States</td>
<td>NPWT in obese gynecologic oncology patients</td>
</tr>
<tr>
<td>2013</td>
<td>Recruiting</td>
<td>KCI</td>
<td>United States</td>
<td>A prospective multi-centre trial evaluating the effectiveness of the V.A.C. Ultra NPWT system with V.A.C VeraFlo Dressing system in operatively debrided wounds</td>
</tr>
<tr>
<td>2013</td>
<td>Recruiting</td>
<td>Hospital</td>
<td>United States</td>
<td>Pilonidal disease wound healing study</td>
</tr>
<tr>
<td>2013</td>
<td>Open, but not yet recruiting</td>
<td>University</td>
<td>Switzerland</td>
<td>Incisional negative pressure dressing on clean, closed, groin incisions</td>
</tr>
<tr>
<td>2013</td>
<td>Recruiting</td>
<td>KCI and Mayo Clinic</td>
<td>United States</td>
<td>NPWT for the prevention of poststernotomy infection</td>
</tr>
<tr>
<td>2010</td>
<td>Recruiting</td>
<td>Hospital</td>
<td>Sweden</td>
<td>NPWT: therapy effects and the impact on the patient’s quality of life</td>
</tr>
<tr>
<td>2012</td>
<td>Recruiting</td>
<td>KCI and university</td>
<td>Europe</td>
<td>Treatment study of vacuum-assisted closure for postsurgical subcutaneous abdominal wound healing impairments</td>
</tr>
<tr>
<td>2011</td>
<td>Terminated</td>
<td>KCI</td>
<td>United States</td>
<td>The use of the PREVENA incision management system on post-surgical Caesarean section incision</td>
</tr>
<tr>
<td>2014</td>
<td>Recruiting</td>
<td>Hospital</td>
<td>Ireland</td>
<td>Randomized control study to assess the role of NPWT in the management of wound in surgical patient</td>
</tr>
<tr>
<td>Year</td>
<td>Status</td>
<td>Sponsor</td>
<td>Country</td>
<td>Description</td>
</tr>
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<td>----------</td>
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</tr>
<tr>
<td>2014</td>
<td>Recruiting</td>
<td>Smith &amp; Nephew</td>
<td>United States</td>
<td>Prevention of seroma formation and wound complications using NPWT devices</td>
</tr>
<tr>
<td>2012</td>
<td>Active</td>
<td>Smith &amp; Nephew</td>
<td>Multiple</td>
<td>PICO breast reduction clinical study looking at incision healing complications</td>
</tr>
<tr>
<td>2014</td>
<td>Recruiting</td>
<td>Hospital</td>
<td>United States</td>
<td>Use of NPWT in high-risk, surgical closed incisions</td>
</tr>
<tr>
<td>2013</td>
<td>Active</td>
<td>ProMedica</td>
<td>United States</td>
<td>Evaluating the advantage of PREVENA after hip and knee arthroplasty</td>
</tr>
<tr>
<td>2013</td>
<td>Open, but not yet recruiting</td>
<td>Hospital</td>
<td>Sweden</td>
<td>PICO above incisions after vascular surgery</td>
</tr>
<tr>
<td>2014</td>
<td>Open, but not yet recruiting</td>
<td>KCI</td>
<td>United States</td>
<td>Evaluation of wound management with negative pressure dressing versus standard dressing after revision arthroplasty</td>
</tr>
<tr>
<td>2013</td>
<td>Completed in 2014</td>
<td>University</td>
<td>China</td>
<td>Continuous topical instillation for open abdomen in the septic patients with complicated intra-abdominal infections</td>
</tr>
<tr>
<td>2010</td>
<td>Unknown</td>
<td>Spiracur</td>
<td>United States</td>
<td>Clinical evaluation of the SNaP wound care system</td>
</tr>
<tr>
<td>2012</td>
<td>Unknown</td>
<td>Hospital</td>
<td>Israel</td>
<td>Regulated negative pressure-assisted wound therapy device</td>
</tr>
<tr>
<td>2009</td>
<td>Terminated</td>
<td>KCI</td>
<td>United States</td>
<td>Evaluating the ease of use of a V.A.C. GranuFoam Bridge Dressing on diabetic foot ulcers receiving VAC NPWT</td>
</tr>
<tr>
<td>2012</td>
<td>Recruiting</td>
<td>Spiracur</td>
<td>United States</td>
<td>Clinical evaluation of the combined use of Apligraf and the SNaP wound care system</td>
</tr>
<tr>
<td>2008</td>
<td>Completed in 2014</td>
<td>University</td>
<td>United States</td>
<td>Role of vacuum-assisted closure device in post-operative management of pelvic and acetabular fractures</td>
</tr>
<tr>
<td>2012</td>
<td>Unknown</td>
<td>Smith &amp; Nephew</td>
<td>United Kingdom</td>
<td>Clinical and health economic study of PICO in a community care setting</td>
</tr>
<tr>
<td>2012</td>
<td>Unknown</td>
<td>University</td>
<td>United States</td>
<td>Prospective observation of wound healing with the PREVENA incision management system</td>
</tr>
<tr>
<td>2014</td>
<td>Recruiting</td>
<td>KCI</td>
<td>Europe</td>
<td>The use of the PREVENA incision management system on clean, closed, sternal midline incisions in subjects at high risk for surgical site occurrences</td>
</tr>
<tr>
<td>2008</td>
<td>Unknown</td>
<td>University</td>
<td>United States</td>
<td>Incisional wound VAC in obese patients</td>
</tr>
<tr>
<td>2007</td>
<td>Completed in 2013</td>
<td>KCI</td>
<td>United States</td>
<td>Vacuum-assisted closure as a treatment for draining hematomas</td>
</tr>
<tr>
<td>Year</td>
<td>Status</td>
<td>Location</td>
<td>Country</td>
<td>Description</td>
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<tr>
<td>2013</td>
<td>Terminated</td>
<td>Hospital</td>
<td>China</td>
<td>Preventing seroma formation after stripping saphenous vein in coronary bypass</td>
</tr>
<tr>
<td>2014</td>
<td>Open, but not yet recruiting</td>
<td>Hospital</td>
<td>Korea</td>
<td>Comparative study of antimicrobial effect on silver dressing of negative pressure wound</td>
</tr>
<tr>
<td>2013</td>
<td>Recruiting</td>
<td>Hospital and KCI</td>
<td>United States</td>
<td>V.A.C. VeraFlo instillation therapy versus V.A.C. Ultra therapy on biofilm in chronically infected wounds</td>
</tr>
<tr>
<td>2012</td>
<td>Active</td>
<td>University and KCI</td>
<td>Canada</td>
<td>Negative pressure after saphenous vein harvest</td>
</tr>
<tr>
<td>2009</td>
<td>Active</td>
<td>University</td>
<td>Germany</td>
<td>Randomized pilot study comparing two vacuum wound dressings for open abdomen treatment</td>
</tr>
<tr>
<td>2007</td>
<td>Completed in 2011</td>
<td>KCI</td>
<td>United States</td>
<td>Randomized controlled multi-centre trial of vacuum-assisted closure therapy in diabetic foot ulcers</td>
</tr>
<tr>
<td>2011</td>
<td>Recruiting</td>
<td>KCI</td>
<td>United States</td>
<td>The use of the PREVENA incision management system on closed incisions in renal transplant subjects</td>
</tr>
</tbody>
</table>

GSUC = gauze suction; KCI = Kinetic Concepts Inc.; NPWT = negative pressure wound therapy; VAC = vacuum assisted closure.
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