Not all wounds have the potential to heal. For patients with such wounds, the focus moves from healing and wound closure to promoting comfort and dignity, relieving suffering and improving quality of life. This article summarises information on the management on non-healing wounds from the literature and advocates a focus on quality of life and inter-professional management based on an individualised plan of care to optimise outcomes for patients.

Some wounds persist for months or years (Krasner et al, 2014). Non-healing wounds may be a result of host factors, such as inadequate vasculature, medications that interfere with the healing process, immunocompromised status or critically-ill status with non-modifiable risk factors (terminal disease, end-stage organ failure and other life-threatening health conditions). Among patients who are dying, receiving hospice or palliative care, non-healing or palliative wounds can be associated with complications (Alvarez et al, 2016) [Box 1]. An inter-professional approach is required to meet whole-person care needs, especially for those with terminal illness, chronic debilitating diseases, advanced diseases associated with major organ failure (renal, hepatic, pulmonary or cardiac), profound dementia, complex psychosocial issues, diminished self-care abilities and challenging wound-related symptoms (Krasner and Stewart, 2015).

With the increased prevalence of chronic diseases, chronic non-healing wounds place a significant burden on the health system, individuals living with wounds, and their circle of care. The circle of care is a social term that includes all stakeholders in the patient’s health and wellbeing (Krasner and Stewart, 2015). The term includes, but is not limited to, the patient, a legal guardian or responsible party, a spouse or significant other, interested friends or family members, caregivers, and any other individual(s) who may have an interest in the patient’s care and wellbeing (Krasner and Stewart, 2015).

When caring for wounds that do not have the potential for healing, the focus shifts from traditional wound care, where healing and wound closure are the goals, to promoting comfort and dignity, relieving suffering and improving quality of life (QoL) (Woo et al, 2015a). The care of individuals with chronic, non-healing wounds is complex and time-consuming, and is often complicated by the fragmentation of communication and services between acute, chronic and home care. A comprehensive framework for non-healing wound care necessitates inter-professional team involvement and multilevel interventions [Box 2] and [Figure 1]. When patient concerns are addressed by an inter-professional team, their QoL can be significantly improved (Woo et al, 2015b).

QoL and patient-oriented outcomes

While the usual outcome measure for wound care is time-to-healing (Moore et al, 2015), QoL is often more relevant for people with non-healable wounds. Generally, QoL is defined as a general perception of wellbeing, happiness and satisfaction by an individual. It is a subjective, but dynamic, concept influenced by functional capacity, past experiences, personality, self-esteem and interpersonal relationships (Woo et al, 2015a; Jørgensen et al, 2016). Health-related quality of life (HRQoL) refers to the sense of wellbeing that is specifically associated with health and illness, along with other related efforts to promote health, manage disease and prevent recurrence (Price, 2001). For example, one quality measure (goal) for the palliative patient with a sacral pressure injury would be to prevent wound infection. A HRQoL goal for the same patient would be to reduce pain and
Box 1. Complications associated with end-of-life conditions.
- Gangrene due to severe ischaemia or occlusive vasculopathy
- Malignant fungating wounds
- Kennedy terminal ulcers
- Skin failure
- Skin changes at life’s end (SCALE) (Sibbald et al, 2009; Woo et al, 2014a).

Box 2. Multilevel interventions.
- Biopsychosocial assessment to identify patient-oriented outcomes
- Strategies to communicate and empower the patient in self-management
- Health policy revision to enhance accessibility to appropriate resources
- Healthcare organisation remodelling to focus on issues pertinent to the patient’s quality of life.

Interventions. Box 2. Multilevel interventions. prevent suffering. Striving for quality and HRQoL outcomes in patients with non-healing or palliative wounds is particularly significant when wound healing is not a realistic outcome.

The complexity of QoL is often understood and compartmentalised in terms of its multiple overlapping dimensions (e.g. biological and physiological factors, symptoms, functioning, general health perceptions and overall QoL). The different components may carry more importance at a given time based on the context of health and illness. There are a number of validated instruments to measure QoL in the general population [Box 3].

To examine the impact of chronic wounds on patients’ HRQoL and their key concerns, disease-specific tools have been developed. Instruments designed for people with leg ulcers include: Hyland Leg and Foot Ulcer Questionnaire; Charing Cross Venous Leg Ulcer Questionnaire; and Sheffield Preference-based Venous Leg Ulcer SD. For people with diabetic foot ulcers (DFUs) and related neuropathy, the Norfolk Quality of Life in Diabetes Peripheral Neuropathy Questionnaire, Neuro-QoL, the Manchester–Oxford Foot Questionnaire, DFU Scale and Cardiff Wound Impact Schedule (González-Consuegra and Verdu, 2011) have adequate validity and reliability. The Cardiff Wound Impact Schedule has also been validated in measuring QoL in patients with pressure injuries and leg ulcers (Hogg et al, 2012; Hitzig et al, 2013; Ousey et al, 2014). The Ferrans and Powers Quality of Life Index — Wound Version was developed to evaluate QoL among patients with different acute and chronic wounds in Brazil (González-Consuegra and Verdu, 2011).

**Chronic wound-related QoL framework**

Common themes were identified from a literature review to create a framework for the concept of QoL in patients with chronic wounds [Figure 2]. To improve patients’ QoL, this paradigm places greater emphasis on the need to foster a climate that elicits patient engagement accompanied by mindful scanning of the environment and health resource mapping (Yamada and Stantos, 2009). As each wound patient and his/her wound is unique, individualised wound care plans that address specific concerns, preferences and choices are most likely to succeed and promote the best outcomes; patients may be labelled ‘non-compliant’ when the real problem is that the care plan has not been properly individualised to their specific needs and perspectives on QoL. Assessment of patient needs and wound attributes will drive the identification of patient goals and desired outcomes through self-management support (education and interventions to increase patients’ skills)(Barr et al, 2003). The overall goal of patient engagement and self-management is to foster self-efficacy and help patients master self-care skills and experience the best possible QoL (Barr et al, 2003; Diabetes Canada, 2015). There is no clinical practice guideline for the management of non-healing and palliative wounds, therefore, key concepts derived from the recent palliative literature and expert opinion (National Coalition for Hospice and Palliative Care, 2009; European Oncology Nursing Society, 2015) have been integrated in the following discussion.

**Wound status and treatment**

Even when best practice is implemented, some treatment options are not feasible and do not always serve the best interests of patients. For example, a construction worker with a foot ulcer who cannot use a total contact cast because he needs to wear protective footwear at work; someone with a venous leg ulcer who prefers to shower every day during the hot and humid season, but cannot do so because she needs to wear non-removable compression bandages; or an older person with a pressure ulcer who refuses an air fluidised mattress because she cannot get out of bed independently.
While turning patients every 2 hours has been recommended, repositioning can be uncomfortable, especially if patients also suffer from significant contractures, increased muscle spasticity and spasms. Among critically-ill individuals, repositioning may actually precipitate vascular instability or exacerbate shortness of breath, making this intervention intolerable (Langemo, 2012).

Adherence to compression among people with venous ulcers can be challenging if QoL issues have not been addressed properly. Miller and colleagues (2011) identified pain as a significant predictor of non-concordance with compression bandaging. Another example is negative pressure wound therapy, which may promote healing, but can lead to poor QoL during initial treatment periods due to anxiety (Janssen et al, 2016). Other concerns, such as excessive warmth, pruritus and difficulty with putting on footwear, should also be discussed (Stansal et al, 2013).

Patients are entitled to a variety of treatment options and should be empowered to be active participants in care. This involves taking part in selecting the most appropriate treatment, monitoring responses and communicating concerns to healthcare providers. Patients and family need to understand that chronic wounds are largely preventable but not always avoidable (Sibbald et al, 2009). When circulation is diverted from the skin to maintain haemodynamic stability and normal functioning of vital organs, for instance, skin damage is inevitable and unavoidable.

**Symptoms**

Chronic wound patients experience poor QoL, compromising their ability to work, carry out housework, perform personal hygiene activities and participate in social/recreational activities (Herber et al, 2007; Gorecki et al, 2009, 2010; González-Consuegra and Verdú, 2011). Pain is consistently identified as the most common and disabling symptom, leading to problems with mobility, sleep disorders and loss of employment. Other symptoms, including pruritus, swelling, discharge and odour, are equally distressing, but are often overlooked by caregivers. Patients feel depressed, powerless, controlled by the ulcer and ashamed of their body.

**HOPPES: symptom management**

Clinical assessment of key symptoms should include HOPPES (Box 4).

**Haemorrhage**

Patients with malignant wounds are at risk of haemorrhage that can be very distressing. Granulation tissue within a malignant wound is often friable and bleeds easily because of local stimulation of vascular endothelial growth factor, resulting in the excess formation of abundant, but fragile blood vessels (Woo et al, 2008). Reduced fibroblast activity and ongoing thrombosis of larger vessels in infected and malignant wounds may compromise the strength of collagen matrix formation, rendering the granulation less resilient to trauma (Charlesworth et al, 2014; Woo et al, 2009). Even minor trauma from the removal of wound dressings that adhere to the wound surface can provoke bleeding.

Light bleeding can be addressed with calcium alginate dressings; the calcium component triggers the coagulation cascade to facilitate haemostasis (Woo et al, 2014a). Alginates are derived from brown seaweed or kelp. Depending on the species and the origin of the calcium alginate (leaf or stem), they may have more gelling (high manuronic acid concentration) or higher fibre strength (high galuronic acid concentration). Alternative topical haemostatic agents are oxidised cellulose, topical thrombin and purified porcine skin gelatin (Wasilko et al, 2015). These agents can activate platelets, serve as a scaffold for clot formation or expand to promote haemostasis through local pressure.

Catastrophic bleeding is rare, but may occur when the tumour infiltrates into a major blood vessel. Other systemic factors that may precipitate haemorrhage are advanced hepatic
diseases, thrombocytopenia, myelosuppressive effects of chemotherapy and radiotherapy, abnormal platelet function and clotting factors, coagurolpathy and local infection.

To control profuse bleeding, suturing or cautery may be necessary. Adrenaline nasal sprays or soaked gauze (1 mg in 1 ml) can be applied topically as a compress with pressure for 10 minutes. Antifibrinolytic agents, such as tranexamic acid or etamsylate, which promote plated adhesions, have also been recommended to prevent future bleeding (Alvarez et al, 2007; European Oncology Nursing Society, 2015).

**Odour control**

Odour was one of the most distressing symptoms for people with fungating breast wounds (Probst et al, 2013). Unpleasant odour and putrid discharge is associated with increased bacterial burden, particularly anaerobic and certain Gram-negative (e.g. *Pseudomonas*) organisms. Metabolic by-products that produce this odour include volatile fatty acids (propionic, butyric, valeric, isobutyric and isovaleric acids), volatile sulphur compounds, putrescine and cadaverine (Woo and Sibbald, 2009).

Topical treatments that have demonstrated efficacy in odour control (da Costa Santos et al, 2010; Lund-Nielsen et al, 2011; Kalemikerakis et al, 2012; de Castro and Santos, 2015) are listed in [Box 5]. Topical metronidazole manages odour by reducing anaerobic colonisation in wounds (da Costa Santos et al, 2010; de Castro and Santos, 2015). Although some studies had demonstrated promising findings for topical treatments, substantiating evidence is generally poor. In a survey of 1,444 people from 36 countries, although charcoal and silver dressings were the most frequently used agents to control odour, less than half of respondents considered them to be effective (Gethin et al, 2014).

Following judicious deliberation, conservative debriedment or desloughing may be appropriate. The goal of conservative debriedment is to enhance QoL and decrease the risk of infection, not to facilitate healing.

**Pain**

Wound-associated pain is a common yet devastating symptom, often described as one of the worst aspects of living with chronic wounds (Park et al, 2008). Sleep disturbance, immobility, poor appetite and depression are some of the consequences of unremitting pain (Woo, 2012). In an international survey of 2018 people with chronic wounds, over 60% of respondents reported the experience of pain ‘quite often’ or ‘all the time’ (Price et al, 2008). It should also be noted that pain can persist for 3 months or longer after wound closure (Memeth et al, 2004).

In a prospective study about HRQoL predictors in patients with chronic wounds attending specialised wound, ostomy and continence centres, pain reduction was a predictor of clinical important change for overall QoL and almost all Ferrans and Powers Quality of Life Index — Wound Version domains (Oliveira et al, 2014).

Quirino and colleagues (2003) reported that 80% of pressure ulcer patients experienced moderate wound-related pain that was constant thorough the day, even at rest. The majority of people with venous leg ulcers also experienced moderate to severe levels of pain, described as aching, stabbing, sharp, tender and tiring (Nemeth et al, 2004). Severe pain is typically common among patients who are female, have a low income and have sustained leg ulcers for a prolonged duration of time (Gonçalves et al, 2004; Yamada and Santos, 2005).

Contrary to the commonly-held belief that most patients with DFUs do not experience pain due to neuropathy, up to 50% experience painful symptoms at rest and approximately 40% have moderate to extreme pain when climbing stairs or walking on uneven surfaces (Evans and Pizzur, 2005). Patients with diabetes who reported pain most or all of the time had statistically and clinically significantly poorer HRQoL than those who did not report pain (Goodridge et al, 2006). Pain in diabetes is often underestimated and undertreated.

Wound-related pain can be precipitated by repeated application and removal of adhesive tapes and dressings pulling the skin surface from the epithelial cells and stripping away the stratum corneum (Gorecki et al, 2010).

Dressings with silicone adhesive are the least likely to cause maceration and skin damage with repeated application.

While moisture is essential to promote wound healing, wound fluid contains endogenous protein-degrading enzymes that are caustic and damaging to the intact skin. Periwound skin is particularly vulnerable to moisture-associated skin damage when the drainage volume exceeds the fluid-handling capacity of a dressing. A plethora of preparations can be used to protect the periwound skin [Box 6]. These are available in a number of delivery systems, such as squeezable tubes, sprays, wipes and vials.

Pharmacotherapy continues to be the mainstay for pain management. Appropriate...
agents are selected based on severity and specific types of pain.

Pruritus
Pruritus is frequent complaint among people with chronic wounds; of 199 patients surveyed, 28.1% complained of itching (Paul et al, 2011). Peripheral pruritus is often triggered by pruritogens (e.g. histamine, serotonin, cytokines and opioids) giving rise to signals that are transmitted via pain-related neuronal pathways and terminate in the somatosensory cortex, where the sensation of itch is perceived (Woo and Sibbald, 201). In patients with wounds, itching is commonly caused by peripheral stimulation of itch receptors due to irritation of the skin and related dermatitis (Woo and Sibbald, 2009).

People with chronic wounds are exposed to a plethora of potential contact irritants, accounting for approximately 80% of all cases of contact dermatitis. Excessive washing and bathing strips away surface lipid and induces dryness that can exacerbate pruritus. To replenish skin moisture, humectants or lubricants should be used on a regular basis. Drug treatment with paroxetine, a selective serotonin-reuptake inhibitor, and gabapentin has been shown to be beneficial in palliative care patients (Kelley and Morrison, 2015; Lilley and Sibbald, 2016).

Exudate management
Wound exudate contains endogenous protein-degrading enzymes, known as proteases or proteinases, which are corrosive and damaging to intact skin (Vowden et al, 2015). Maceration of the periwound skin typically presents as white, wrinkled soggy tissue at the wound edge.

High-volume and viscous exudate is often associated with unpleasant odour, painful periwound maceration, increased infection risk and exorbidant care costs due to frequent dressing changes. Leakage and/or strikethough onto clothing, furniture and bed linen can lead to feelings of embarrassment and social isolation.

The major categories of dressings are foams, alginates, hydrofibers and super-absorbent dressings (Woo and Smith, 2014). Careful selection of discreet absorbent dressings (avoid bulky materials) will improve the patient’s QoL.

Superficial infection
Complications, such as wound infection, are common, but upsetting. According to analysis of a database comprising approximately 185,000 patients attending family medical practitioners in Wales, 60% of patients with chronic wounds had received at least one antibiotic in a 6-month period for the treatment of wound infection (Braga et al, 2013). Bacteria compete for nutrients and oxygen, which are essential for wound healing, and they stimulate over-production of proteases, leading to degradation of extracellular matrix and growth factors (Woo et al, 2014b).

In patients with DFUs, infection is a major risk factor that precedes amputation. The mortality rate has been reported to be over 50% in patients with bacteraemia secondary to uncontrolled infection in pressure ulcers (Crolla et al, 2012). Being diagnosed with an infection provokes anxiety; patients often fear infection is the beginning of a downward cycle leading to hospitalisation, limb amputation and death. The need to align expectations and dispel misconceptions cannot be underestimated.

As bacterial pathogens proliferate, they may form biofilms, which are encapsulated and protected against host defence and antimicrobial agents by extracellular polymeric substance (Fleming and Wingender, 2010). As many as 60% of chronic wounds contain biofilm (James et al, 2008). It is suspected that biofilm is the primary reason for excessive inflammatory damage in non-healing wounds and recurrent infection.

Clinical assessment is the first step to determine whether superficial or deep infection is a concern. There is no one particular sign or symptom that will accurately confirm the diagnosis of infection, but a combination of possible signs and symptoms should be sought for evaluation of bacterial damage in wounds. Based on review of the literature, the proposed wound infection checklist describes two clusters of signs and symptoms associated with superficial/localised wound infection versus deep soft tissue infection (Figure 3a&b) (Woo et al, 2014b). Immunosuppressed patients may present with a wound that is not healing or worsening when infection is present as other signs and symptoms may be suppressed. Osteomyelitis should be suspected if ulcers probe to bone.

Emotional and psychological state
Isolation and stigma
The bleak feeling of isolation due to wound-related stigma is a recurring theme in the literature. Stigma is often experienced by individuals with chronic and non-healing wounds...
Deep infection/increased bacterial burden should be suspected in the presence of 3 or more signs and symptoms.

Wound Infection Checklist (UPPER)
Local / Superficial Infection - Treat with Topical Antimicrobials

<table>
<thead>
<tr>
<th>Unhealthy tissue</th>
<th>Surface area on wound bed covered by devitalized tissue and unhealthy granulation tissue (thin and friable, bleeds easily, dark red, dull or dusky discoloration, overgranulation, pocketing, and bridging)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Poor healing</td>
<td>Stalled wound healing with no significant change in wound size or volume (approximately 10% in last 7 days)</td>
</tr>
<tr>
<td>Pain</td>
<td>New or increased pain</td>
</tr>
<tr>
<td>Exudate</td>
<td>Increased volume of exudate Change of consistency: viscous and thick exudate</td>
</tr>
<tr>
<td>Reek</td>
<td>Presence of foul odour</td>
</tr>
</tbody>
</table>

Local infection/increased bacterial burden should be suspected in the presence of 3 or more signs and symptoms.

Wound Infection Checklist (LOWER)
Deep Infection - Treat Systemically +/- Topical Antimicrobials

<table>
<thead>
<tr>
<th>Larger in size</th>
<th>Sudden or unexplained increase in wound size or new areas of satellite breakdown</th>
</tr>
</thead>
<tbody>
<tr>
<td>Osseous tissue and/</td>
<td>Wound that probes to bone or deep structures; crepitus may be present</td>
</tr>
<tr>
<td>deep structure</td>
<td>-----------------------------------------------------------------------------------------------------</td>
</tr>
<tr>
<td>Warmth</td>
<td>Increased periwound temperature of more than 3°C compared to areas distant from the wound</td>
</tr>
<tr>
<td>Edema</td>
<td>Increased edema or induration around the wound</td>
</tr>
<tr>
<td>Redness</td>
<td>Redness of &gt;2 cm beyond wound margin</td>
</tr>
</tbody>
</table>

Deep infection/increased bacterial burden should be suspected in the presence of 3 or more signs and symptoms.

References
3. Glaser and colleagues (2005) compared wound healing rates between the slow-healing group (n=120) and the fast-healing group (n=120) using the Perceived Stress Scale, and found that subjects exhibiting higher levels of stress during the study (P<0.05) had lower wound healing rates 7 days after the biopsy (P<0.05). Stress levels reported by the participants via the Perceived Stress Scale were negatively correlated to wound healing rates 7 days after the biopsy (P<0.05). Subjects exhibiting slow healing (below median healing rate) rated higher levels of stress during the study (P<0.05) and had higher cortisol levels 1 day after biopsy than the fast-healing group (P<0.01).

Stress
Stress has a direct impact on QoL. People with chronic wounds tend to experience more emotional problems than people without wounds in the community, and are less capable of coping with stressful events (Woo, 2012). A survey of healthcare practitioners (n=908) acknowledged that mental health issues are common in people with chronic wounds (Upton et al, 2012). Over 60% of survey respondents indicated that between 25% and 50% of people with chronic wounds suffer from mental disorders. Anxiety was rated the most common symptom (81.5%), which is consistent with findings from a pilot study in which over 60% of people living with chronic wounds expressed higher than average anxiety (Upton et al, 2012).

While no one is immune to stress, the impact of a chronic wound on an individual’s perception of wellbeing and QoL depends on personal meanings and values assigned to the demands that arise from living with a chronic wound. Coping is less adaptive or effective if people lack self-esteem, motivation and the conviction they have the aptitude to solve a problem. Woo (2011) evaluated the relationship between self-perception and emotional reaction to stress in people with chronic wounds and found people who are insecure about themselves tend to anticipate more wound-related pain and experience more anxiety.

Chronic stress is not innocuous. Stress activates the hypothalamic–pituitary–adrenal axis, leading to the production of adrenaline, noradrenaline, vasopressin and glucocorticoid (cortisol) (Woo, 2012). Noradrenaline induces vasoconstriction, which can potentially impair normal wound healing by compromising the delivery of oxygen and nutrients. Cortisol attenuates the immuno-inflammatory response to stress. Excessive cortisol suppresses cellular differentiation and proliferation, inhibits the regeneration of endothelial cells and delays collagen synthesis (Woo, 2012).

The body of scientific evidence that substantiates the deleterious impact of protracted stress on wound healing is convincing (Woo, 2012). Ebrecht et al (2004) evaluated healing of acute wounds created by dermal biopsy among 24 healthy volunteers. Stress levels reported by the participants via the Perceived Stress Scale were negatively correlated to wound healing rates 7 days after the biopsy (P<0.05). Subjects exhibiting slow healing (below median healing rate) rated higher levels of stress during the study (P<0.05) and had higher cortisol levels 1 day after biopsy than the fast-healing group (P<0.01). Kiecolt-Glaser and colleagues (2005) compared wound

Figure 3(a). Signs and symptoms of local chronic wound infection: UPPER.

Figure 3(b). Signs and symptoms of deep chronic wound infection: LOWER.
their ulcers through social interaction with expert nurses and peers at Leg Club. Attendance at Leg Club was associated with significant improvement in QoL ($P<0.014$), morale ($p<0.001$), self-esteem ($P=0.006$), pain ($P=0.003$) and functional ability ($P=0.004$). Wound care patients who are affiliated with a religion are also more likely to experience improved QoL (Yamada and Santos, 2005; Yamada et al, 2014).

Financial impact
Patients with chronic wounds are often unemployed, marginalised and isolated. In a study of 21 patients with DFUs, 79% of patients reported an inability to maintain employment secondary to decreased mobility and fear of someone inadvertently stepping on their affected foot (Kinmond et al, 2003). In another study, all patients interviewed felt that the leg ulcer limited their work capacity, with 50% adding that their jobs required them to stand for most of their shift. In that same study, 42% of patients identified the leg ulcer as a key factor in their decision to stop working (Herber et al, 2007). Even for younger patients, leg ulceration was correlated with time lost from work and job loss, ultimately affecting finances (Herber et al, 2007).

Beyond occupational stressors and dilemmas, patients may incur additional out-of-pocket expenses for transportation, parking, telephone bills for medical follow-up, home health aide services, dressing supplies not covered by insurance, and drug costs if they have no prescription plan.

Health care system
Navigating through the healthcare system can be extremely confusing. A trusting and therapeutic relationship between patients and their healthcare providers may serve to buffer the effects of adversity and stress. However, patients sometimes feel rushed during routine wound care clinic visits. It is important to patients that healthcare providers care and display a genuine interest in patient wellbeing (Alvarez et al, 2007). In their description of the key attributes of someone who cares, patients use terms like ‘caring’, ‘holistic’, ‘friendly’, being ‘vigilant’, ‘cheerful’, ‘gentle’ and ‘knowledgeable’. Healthcare providers should provide clear and consistent communication to avoid confusion. In a prospective study, patients attending specialised wound care clinics reported improvement of HRQoL over time (Oliveira et al, 2014).
Conclusion
Inter-professional palliative wound care with goals and outcome measures targeted to the individual with a non-healing or palliative wound can improve QoL and HRQoL. The management strategies detailed in this article are the starting point for an individualised plan of care. When QoL and HRQoL drive the plan of care, non-healing and palliative wound care outcomes are optimised.

References