Review

Scabies: update on treatment and efforts for prevention and control in highly endemic settings

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Abstract
Scabies is a contagious parasitic skin disease caused by Sarcoptes scabiei infestation which can be transmitted through direct or indirect contact. WHO classified scabies as a neglected tropical disease. The prevalence of scabies is high in certain countries ranging from 32.1% to 74%, especially in crowded conditions such as prisons, boarding schools, and orphanages. Indonesia is one of the most heavily affected countries worldwide. Scabies might cause great impact on patients, which includes decreased concentration and academic achievement at school, social stigma, sleep disturbances, and decreased economic productivity in community. Management of scabies with anti-scabies needs to be carried out appropriately, accompanied with treatment for all contacts. Mass treatment with permethrin cream or ivermectin can be given directly to patients. Prevention is conducted by providing medical treatment and breaking the chain of transmission. Source elimination and disinfection of fomites is very important. Participation of non-medical personnel such as teachers, cadres, and parents together with the local health workers (primary health care) is highly recommended. Using checklists or application can aid non-medical personnel to determine suspected cases, thus contributing to scabies elimination. Cooperation between patients, patient's family, health workers and other non-medical personnel will greatly reduce the prevalence of scabies and ultimately improve patient's quality of life. The aim of this review is to provide an update on scabies treatment and efforts for prevention and elimination, with focus on the situation in Indonesia.

Key words: Scabies; treatment; elimination; prevention; non-medical personnel.

Introduction

Scabies is a skin infestation of the mite, Sarcoptes scabiei, which manifests as a pruritic skin eruption and can be transmitted directly through person-to-person contact and indirectly through bedsheets, clothing, or other fabric material. Scabies infection is particularly prevalent in overcrowded environment such as orphanages and public boarding schools [1]. The World Health Organization (WHO) stated that scabies is one of the most neglected diseases in the world [2]. It is estimated that 200 million people in the world have suffered from a scabies infection at least once in their lifetime. The prevalence of scabies ranges from 0.2 to 71%. A Global Burden of Disease Study in 2015 reported that Indonesia ranks first, among the 195 countries of the world, in scabies infection [3]. The aim of this review is to provide an update on scabies treatment and new efforts for prevention and elimination, with focus on the situation in Indonesia.

Causative Agent

Scabies is a parasitic skin infection caused by the human-specific mite Sarcoptes scabiei var. hominis. Adult mites are approximately 0.4 mm in size, which requires imaging instruments to visualize them [4,5]. The life cycle of scabies infestation starts when a pregnant female mite creates a burrow on the human epidermis, producing 2–3 eggs daily. Most eggs deposited in the burrows hatch into larvae after 48–72 hours. Larvae excavate other burrows and reach the adult stage in 10–14 days. Adult mites then reproduce, ultimately repeating the life cycle. The incubation period is estimated to be between 4–6 weeks after primary infection. Route of transmission includes predominantly via direct skin-to-skin contact [5-7] and rarely via indirect contaminated fomites, particularly in patients with crusted scabies [5,6,8]. Without residing the human host, scabies mites remain to survive around 24–36 hours at room temperature, enabling further infection [6,7].

Epidemiology and risk factors

An estimated 130 million people worldwide are infected by scabies, at any given time. This estimate is supported by the high number of cases reported throughout the world every year, reaching 300 million
cases [9]. A cross-sectional analysis on the 2015 Global Burden of Disease Study found that Indonesia is one of the top five countries with greatest scabies burden followed by China, Timor-Leste, Vanuatu, and Fiji [3]. The prevalence of scabies varies from 0.2 to 71% in each country.

In Indonesia, a report by the Ministry of Health in 2011 revealed that 2.9% of 69,15,315 people, were infected with scabies. In 2012, the proportion increased to 3.6%. Scabies was frequently observed in children as compared to adults [10]. Reports from community health centres or ‘Puskesmas’ across Indonesia found that scabies is the third most commonly found skin disease [11]. The prevalence ranges from 5.6% to 12.9%. In 2012, the number of scabies cases amongst orphans and religion-affiliated boarding schools in East Jakarta were 51.6% and 68% in South Jakarta the following year [11].

Appropriate treatment per se is not adequate to eradicate scabies. A physician must consider environmental factors and patient’s habits, which are pivotal for preventing reinfection. A study conducted in 2017 found that the availability of hot water as well as living conditions in religion-affiliated boarding schools were important factors related to scabies reinfection [12]. While clean water was available in the property, hot water was not available for washing clothes. A water temperature of at least 50°C is essential to ensure mite and egg elimination. This finding was supported by Yasin et al., which reveals that personal hygiene consists of bathing frequency, towel, and clothes sharing were not a significant factor for scabies infection, instead clean water availability or room sanitation was correlated with scabies [13].

In addition to personal hygiene, bedding conditions was another problem encountered in the study. Since several students occupied beds that were not covered by bed-sheets, thus allowing direct skin contact. Mites would drop on the mattress surfaces and since the mattresses are not washed, parasites stayed longer and were able to infect other people promptly [12]. Widuri et al. reported that sleeping together in closed spaces increased the risk of getting scabies by 21 times [14]. Personal habits comprises of towel-sharing, clothes-sharing, and prayer-attire sharing are recurrently noticed in students at religion-affiliated boarding schools [12]. Furthermore, towel-sharing increased the risk of scabies by 3.4 times [14]. Widaty et al. found that the practice of clothes-sharing and prayer-attire sharing might be driven by socioeconomic reasons, as study participants admitted to not having spare items [12]. Participants did not frequently wash their attire thus increasing the risk of prolong contact with infectious materials. Akmal et al. who conducted a study in Sumatra also reported that poor personal hygiene was strongly correlated to scabies [11]. In addition to behavioural habits, knowledge level was another significant factor correlated to scabies prevalence. However, it was not clearly defined what constituted the knowledge [12].

Clinical Manifestation and Diagnostic Criteria

A recently modified Delphi study involving 34 worldwide experts proposed consensus criteria for the diagnosis of scabies, known as The 2020 International Alliance for The Control of Scabies (IACS) criteria. Three levels and eight subcategories of diagnosis are established as per diagnostic certainty, which is confirmed, clinical, and suspected. (Table 1) [5].

A confirmed diagnosis of scabies (level A) is established based on the presence of any stage of scabies’ lifecycle (eggs, larvae, nymphs, or adults) or feces (scybalas). Visualization devices and samples affect the diagnostic subcategory, for instance, A1 if the eggs, mites, or feces are discovered on the skin sample using light microscopy; A2 if the eggs, mites, or feces are visualized in vivo using high-powered magnifying devices; A3 if the mites are visualized in vivo using dermoscopy [5]. The most recognized and suitable method to confirm scabies diagnosis is by identifying the skin sample using light microscopy. However, the result accuracy is operator-dependent, especially in

<table>
<thead>
<tr>
<th>Diagnostic Level and Subcategories of Scabies</th>
<th>A: Confirmed Scabies</th>
<th>B: Clinical Scabies</th>
<th>C: Suspected Scabies</th>
</tr>
</thead>
<tbody>
<tr>
<td>A1: Minimum fulfil one criterion</td>
<td>A1: Mites, eggs, or feces depicted through light microscope on skin specimen</td>
<td>B1: Scabies burrows</td>
<td>C1: Typical lesions affecting typical distribution along with one history feature*</td>
</tr>
<tr>
<td>A2: Mites, eggs, or feces visualized in vivo through high-powered imaging device e.g. video-dermoscopy</td>
<td>B2: Typical lesions involving male genitalia</td>
<td></td>
<td>C2: Atypical lesions affecting atypical distribution along with two history features*</td>
</tr>
<tr>
<td>A3: Mites identified in vivo through dermoscopy</td>
<td>B3: Typical lesions affecting typical distribution along with two history features*</td>
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</tbody>
</table>

*History Features; H1: Itch (pruritus); H2: Positive contact history.
obtaining the burrows and preparing the materials. Although a positive test validates the diagnosis of scabies, a negative test does not eliminate it, given that patients with clinical scabies often have negative results [5,15,16]. High-powered magnifying devices allow the identification of scabies mites, in vivo, in a detailed manner. Magnification using these devices (e.g., reflectance confocal microscopy and video dermoscopy) can achieve more than 70x amplification [5,9]. Identification of scabies mites through dermoscopy in vivo confirms the diagnosis of scabies [5,16-19]. Several hallmarks can be observed through dermoscopy. S-formed burrow demonstrated as a curvilinear trail of scale. Brown triangular V-formed arrangement is analogous to the head and set of legs, commonly mentioned as the triangle sign, delta-wing jet, delta glider, jet plane, or spermatozoid configuration. Visualization of mite at the edge of the burrow is frequently referred to as the jetliner with its trail [17,20,21]. Furthermore, the ovoid forms resting inside the burrows indicated the appearance of scabies eggs [17,18].

Based on the clinical evaluation, such as the patient’s history features and dermatological examination, scabies can be diagnosed as clinical scabies (level B) or suspected scabies (level C). If the attributes meet the criteria, then a diagnosis of clinical scabies can be established. However, if the characteristics are less specific, a diagnosis of suspected scabies can be achieved [5].

Itch (pruritus) is frequently observed in infected patients [5,19]. Following primary infection, itch starts to develop [4,5]. Itch intensity can vary between individuals, ranging from extreme-itch impairing quality of life to mild manifestation [5,22-24]. Typically, the itch is often exacerbated at night [5,25,26]. However, numerous pruritic skin diseases demonstrate a similar pattern; hence nocturnal pruritus is inadequate as a diagnostic feature [5,24,27]. Itch can be localized, confined on the noticeable scabies lesions, or generalized, affecting other body regions. Constant scratching on the lesions, which manifests as excoriating, also fulfils the itch criterion, particularly in the pediatric population [5,28].

As a rule, skin-to-skin contact facilitates scabies transmission [5-7]. Fomite-mediated transmission hardly occurs in common scabies, except for crusted scabies [5,6,8]. Multiple factors that influence the risk of common scabies transmission are duration, frequency, and body surface area of skin contact [5,29]; hence bed-sharing individuals and children are at higher risk [5]. Previous literature suggested that the minimum skin-to-skin duration for mites infection is approximately 20 minutes [4,7]; however, it is still undetermined.

Detailed positive contact history and close contact are defined as per the 2020 IACS. A positive contact history with high-risk transmission includes any contact with a patient diagnosed with crusted scabies, close contact with a patient diagnosed with common scabies, close contact with a patient with inexplicable pruritus, and close contact with a patient with typical scabies lesion affecting typical distribution with inexplicable condition. Close contact is described as: persons who sleep together in the same residence; persons who share a bed or sleeping surface, e.g., couples, children in the same teaching space or who play together; and adults with documented skin-to-skin contact, e.g., workplace exposure (health professionals, assisted living caregivers, teachers of schoolchildren) and leisure exposure (contact sports, e.g., wrestling) [5].

Clinical signs of common scabies between each patient are extensive depending on the skin manifestation of individual lesions, grouped or clustered lesions, and various secondary changes including excoriation, lichenification, impetiginisation, and eczematisation, which ultimately complicate the primary scabies infestation. If the definite signs of scabies such as burrows or lesions affecting male genitalia are lacking, clinical judgment to determine whether a lesion is considered typical for scabies depends on morphology and number [5].

The most frequent morphological lesions are papules [5,30], which are erythematous or hyperpigmented in darker skin tone [5]. Nodules are more likely to appear in particular body areas (axillae, breasts, groins, genitalia, and torsos in infants) [5,31,32], for few months even after the mites have been completely exterminated [5]. Although less common in adults [5], vesicles and pustules can be observed in infants, particularly in the palmoplantar regions. If the predominant lesions are vesicles, pustules, or blisters, the differential diagnosis should be considered [5,33]. Furthermore, superimposed infection by S. aureus or S. pyogenes causes impetiginized lesions characterized by demonstrating inflammation along with ulceration and yellowish crust. Groups of lesions typically emerge on a particular body area, although widespread lesions may occur [5].

Scabies is classified as typical if there are three minimum lesions on a particular body area or contained in diameter of around 10 to 20 cm. If the lesions do not demonstrate typical morphology or the number of
lesions is below 3 in any body area, then the lesions are classified as atypical. Typical distribution of scabies lesions are described as per Figure 1. Lesions of common scabies appear in several body areas [5], while severe infestation results in multiple body areas that can be symmetrical between left and right sides [5,34]. Atypical distribution includes lesions observed on the head, scalp, neck, and tends to be asymmetrical [5,35].

Hyperinfestation of mites in immunodeficient host causes a severe and rare manifestation of scabies, known as crusted scabies [36,37]. It was formerly called ‘Norwegian scabies’, although the term should no longer be applied [36 -40]. Comprising up to 4,000 mites per gram of skin, crusted scabies is highly infectious. It is characterized by abundant hyperkeratotic skin crusts and fissures, which have a significant mortality rate compared to common scabies [36,37,41,42]. Contrary to common scabies, the itch is relatively mild or even absent in crusted scabies [38]. Jouret et al. [37] proposed a comparison of the pathophysiologic characteristics between common and crusted scabies (Table 2).

Furthermore, a recent clinical grading scale of crusted scabies was established by Davis et al. [36], which classified clinical severity into three grades: Grade 1 (mild crusted scabies), Grade 2 (moderate crusted scabies), and Grade 3 (severe crusted scabies) (Table 3).

<p>| Table 2. Comparison of pathophysiologic characteristics between common and crusted scabies. |</p>
<table>
<thead>
<tr>
<th>Indicator</th>
<th>Common Scabies</th>
<th>Crusted Scabies</th>
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<tbody>
<tr>
<td>Type of immune response</td>
<td>Th1 lymphocytes</td>
<td>Th2 lymphocytes</td>
</tr>
<tr>
<td>Infiltrate along the epidermal</td>
<td>Predominantly CD4+ T cells</td>
<td>Predominantly CD8+ T cells</td>
</tr>
<tr>
<td>junction</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Consequence</td>
<td>Type IV hypersensitivity reaction</td>
<td>Local IL-17 secretion: induces keratinocyte proliferation, acanthosis, hyperkeratosis, appearance of thick scabs</td>
</tr>
<tr>
<td></td>
<td>Protective response: limitation of the number of mites</td>
<td>Ineffective inflammation: cytotoxic lesions of keratinocytes (by CD8+ T cells); proliferation of mites</td>
</tr>
<tr>
<td>Histological characteristic</td>
<td>Similar to atopic dermatitis</td>
<td>Similar to psoriasis: acanthosis, parakeratotic hyperkeratosis, keratinocytic apoptosis, dermal lymphocytic infiltrate, basal mitosis</td>
</tr>
</tbody>
</table>

Table 3. Clinical grading scale for crusted scabies.

A: Distribution and Extent of Crusting
1. Wrist, web spaces, feet only (< 10% Total Body Surface Area)
2. Point 1 plus forearms, lower legs, buttocks, trunk, or 10-30% TBSA
3. Point 2 plus scalp or > 30% TBSA

B: Crusting / Shedding
1. Mild crusting (< 5 mm depth of crust), minimal skin shedding
2. Moderate (5-10 mm) crusting, moderate skin shedding
3. Severe (> 10 mm), profuse skin shedding

C: Past Episodes
1. Never had it before
2. 1-3 prior hospitalizations for crusted scabies or depigmentation of elbows, knees
3. ≥ 4 prior hospitalizations for crusted scabies or depigmentation as above plus legs/back or residual skin thickening/ichthyosis

D: Skin Condition
1. No cracking or pyoderma
2. Multiple pustules and/or weeping sore and/or superficial skin cracking
3. Deep skin cracking with bleeding, widespread purulent exudates

Grade 1: Total score 4-6; Grade 2: Total score 7-9; Grade 3: Total score 10-12.

Figure 1. Predilection site of scabies lesions.
Treatment

Various effective scabicides are available, which can be topical or oral, depending on patients’ characteristics, disease conditions, treatment cost and accessibility, and physicians’ preference. Treatment regimens should be given at every stage of diagnostic levels; not only limited to clinical or confirmed scabies, but also to patients with suspected scabies [6].

A recent network meta-analysis of 52 studies was conducted by Thadanipon et al. [43] to determine the relative efficacy and safety of anti-scabies agents. Permethrin, as the first-line of treatment option, demonstrated a statistically significant higher cure rate than sulphur, malathion, lindane, crotamiton, and benzyl benzoate [38,44,45]. A higher cure rate, although insignificant, was obtained when comparing a combination of topical permethrin and oral ivermectin to single topical permethrin [38,46]. Based on the curative perspective, a combination of topical permethrin and oral ivermectin showed the uppermost ranking [46]. Topical ivermectin ranked highest concerning pruritus improvement [47]. However, synergized pyrethrins revealed the most adverse events [48]. Conclusively, there is no single anti-scabies agent that was superior in all aspects such as cure rate, pruritus improvement, and adverse events; hence, physicians’ judgment depends on the drug’s efficacy-safety and convenience [43].

The latest guideline for the management of scabies was established in 2017, known as the European Guideline for the Management of Scabies. Several new recommendations were updated since the 2010 edition. A summary of the general principles of treatment are described in Table 4 [38].

Topical agents should be applied to all skin parts nocturnally, including scalp, navel, groin, fingers, interdigital areas, and skin underneath the nails’ terminal part. Topical treatment should remain in contact with affected skin for 8 to 12 hours. Skin condition should be cool and dry while on the treatment. Following the application of the topical treatment, clean apparel should be worn. Close contact persons should also be treated concurrently to prevent the spread of infection and the host’s reinfection [38,49]. To date, the application of lindane is not suggested due to the possible risk of neurotoxicity [38,50] and production of hazardous pollutants in waste-water [51].

All apparel, bed sheets, towels, and other fomites should be machine washed at a temperature over 50 °C, dry-cleaned, or wrapped in a plastic container for one week (level of evidence: VI; grade C recommendation) [40,52]. Furthermore, a comprehensive written explanation of scabies infestation should also be provided for the patients (level of evidence: IV; grade C recommendation) [38,50]. Successful treatment is indicated by the absence of active scabies manifestation following one week of final treatment, which is the non-appearance of active lesions and convalesced nocturnal itch. However, post-treatment itch may remain until 2 to 4 weeks. Reapplication of emollients, oral antihistamines, and mild-potency topical corticosteroid should be given to alleviate post-treatment itch [38].

### Table 4. General Principles of Scabies Treatment.

<table>
<thead>
<tr>
<th>Anti-scabietic Agent*</th>
<th>Instruction</th>
<th>Level of Evidence (LoE); Grade Recommendation</th>
</tr>
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<tbody>
<tr>
<td><strong>Recommended treatments</strong></td>
<td></td>
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</tr>
<tr>
<td>Permethrin 5% cream [32,38]</td>
<td>Apply head-to-toe, repeat after 7-14 days.</td>
<td>Ib; A</td>
</tr>
<tr>
<td>Oral ivermectin 200 mcg/kg [32,39]</td>
<td>Consume along with food.</td>
<td>Ib; A</td>
</tr>
<tr>
<td>Benzyl benzoate 10-25% lotion [32,46]</td>
<td>Two doses with a one-week interval.</td>
<td>IV; C</td>
</tr>
<tr>
<td><strong>Alternative treatments</strong></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Malathion 0.5% aqueous lotion [32,39]</td>
<td>Apply once weekly for two weeks, cleanse after 24 hours.</td>
<td>IV; C</td>
</tr>
<tr>
<td>Ivermectin 1% lotion [32,41]*</td>
<td>Apply once as a single application</td>
<td>Ib; A</td>
</tr>
<tr>
<td>Sulphur 6-33% cream, ointment, or lotion [32,43]</td>
<td>Apply once daily for three consecutive days.</td>
<td>Ib; A</td>
</tr>
<tr>
<td>Synergized pyrethrin foam [32,44]*</td>
<td>Apply once daily for three consecutive days.</td>
<td>IIa; B</td>
</tr>
<tr>
<td><strong>Crusted scabies [32,45]</strong></td>
<td></td>
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<tr>
<td>Topical scabicide (Permethrin 5% cream or benzyl benzoate 25% lotion) and oral ivermectin 200 mcg/kg</td>
<td>Apply topical scabicide once daily for seven days, followed by twice-weekly until healed.</td>
<td>IV; C</td>
</tr>
<tr>
<td></td>
<td>Consume oral ivermectin on days 1, 2, and 8. Extra ivermectin might be required in severe cases, given on days 9 and 15 or days 9, 15, 22, and 29.</td>
<td></td>
</tr>
</tbody>
</table>

*All topical agents should be applied to all skin parts nocturnally and remain in contact with the skin for 8 to 12 hours [32]; †Demonstrated equal efficacy to permethrin cream 5% [32].
Following treatment completion, a follow-up visit within two weeks is essential to evaluate the affected skin through microscopic examination (level of evidence: IV; grade C recommendation) [38,50].

Permethrin [38,49], benzyl benzoate, and sulphur [38,50,53,54] are considered safe during pregnancy (level of evidence III; grade B recommendation). Furthermore, permethrin is permitted for children above two months of age [38,55]. For pregnancy, lactation, and children below two years of age, permethrin application should be restricted to no more than two hours between two doses with a one-week interval [56]. Ivermectin should not be given to pregnant women and children weighing below 15 kg [38,57].

Failure to scabies treatment has recently been reported [58]. Sunderkotter et al. proposed several reasons underlying the failure of scabies treatment such as improper application of permethrin, reinfection because of the partial management of environs, including contact with individuals and fomites, and resistance of mites toward permethrin. Several circumstances might affect the improper application of permethrin, including a short exposure period to permethrin, not trimming the fingernails which may hide the subungual mites following scratching, ineffective treatment of hyperkeratotic skin, or failure to employ permethrin in the head area in toddlers [58,59]. Reinfestation because of incomplete eradication of mites in surroundings can result in treatment failure. Unrecognized or incompletely treated contacts are commonly encountered in a paediatric population who share the same surroundings [58,60]. Furthermore, several plausible explanations might address the resistance to permethrin and ivermectin [58]. Mounsey et al. reported an extended survival of scabies after exposure to permethrin and associated with greater glutathione-S-transferases' transcription [61]. Several studies report resistance of mites to ivermectin, due to genetic changes of the mites structure that regulate the glutamate-directed chloride gate [62,63] or a P-glycoprotein membrane transport protein [64]. However, it is improbable that scabies mites are insensitive to both permethrin and ivermectin [58].

**Scabies prevention**

Although scabies is not regarded as a deadly disease, it largely affects the patient’s quality of life [65]; therefore, elimination and prevention efforts are important. A way to eliminate scabies is by increasing community awareness and knowledge regarding the diseases and the preventive measures, for instance proper handling of contaminated materials (bedsheets, clothing, towel). To ensure mite elimination, contaminated materials must be washed in hot water and dried with a hot dryer. If hot water is not available, sterilization can be performed by keeping infected materials in a plastic bag for 7 days, as the survivability of mites only last 3 days outside of the host. As scabies are frequently encountered in boarding schools, participation of non-medical personnel in scabies screening might be beneficial for early detection of cases. The utilization of a screening checklist for scabies’ signs and symptoms might be practical for early detection and thus promoting prompt treatment [66].

A screening checklist, known as “Deskab” in Indonesia, comprises of simplified history taking and physical examination that can be performed by a non-medical personnel. This checklist was based on the established criteria for diagnosing scabies such as, nocturnal pruritus, history of itchiness in exposed individuals, and presence of lesions suggestive of scabies. We investigated the application of this screening tool and the results showed that there was no statistically significant difference between students who were examined by dermatologists and those who were assessed by non-medical personnel using the Deskab form [66]. Deskab has been used in a number of boarding schools throughout Indonesia. We found that by training non-pharmacological intervention such as, involvement of non-medical personnel, contributes to the significant decrease of scabies incidence rate [67].

**Conclusions**

Scabies is a skin disease that affects an individual’s quality of life. Diagnosis is established clinically or through additional supporting examinations deemed necessary. It is important that all members of the affected household are treated and their surroundings are sterilized properly to ensure mite elimination and ultimately preventing further transmission. The role of non-medical personnel in performing screening for scabies and providing surveillance in over-crowded communities will aid scabies eradication.

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### Conflict of interests:

No conflict of interests is declared.