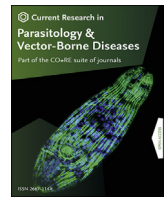


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# Current Research in Parasitology & Vector-Borne Diseases

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## Understanding the current state-of-the-art of long-lasting insecticide nets and potential for sustainable alternatives



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### ABSTRACT

Long-lasting insecticide-treated nets (LLINs) are widely distributed to communities where malaria is a major cause of mortality, especially to those under the age of 5 years-old. To protect people from this illness, LLINs provide physical and chemical barriers by containing insecticides within the matrix of the polymer fibers or on the surface. Synthetic polymers including polyethylene and polyester are common material choices for these nets, and pyrethroids, along with other additives, are the insecticides of choice for this application. Many studies have shown the effectiveness of these nets on the impact of malaria is highly significant, but there is a demand for more durable nets that last longer than only a few years as the available products are rated for 2–3 years of use. Improvements in this area would increase cost effectiveness, because better durability would reduce the frequency of manufacturing and worldwide shipping. Additionally, due to the plastic fibers, the waste can build quickly, damaging the environment. To deal with the sustainability and durability issues, biodegradable and renewable materials should be chosen as an alternative.

### 1. Introduction

Long-lasting insecticide-treated bednets (LLINs) have been proven to be the most effective intervention tool to control malaria. They function as knitted polymer filaments that contain or are coated with insecticide allowing for this mosquito-killing effect to be maintained longer than alternative methods of protection. To initiate the exploration of potential improvements to LLINs, it is essential to understand the relationship between the materials, insecticides, and manufacturing processes. Issues like durability have been an obstacle to the longevity of the nets from both structural and insecticidal perspectives, and because these are being distributed in mass quantities all over the world, cost is an important element that must also be considered when looking for new alternatives. Focusing on the current products on the market and the recent studies in the field of eco-friendly fiber formation will provide necessary information to begin development of more sustainable and effective malaria prevention options. Bio-based polymers encountered in nature such as cellulose offer an alternative to traditionally used polymers such as high-density polyethylene and will contribute to sustainability efforts as well

as the overall performance of the nets. Here, we provide an overview of current conventions of LLINs and ongoing sustainable material research in LLINs (U.S. provisional patent 63/248,060).

### 2. Background of malaria and LLINs

Despite technological and medical developments available, illnesses like malaria remain a serious problem in certain regions of the world where economic resources are limited. The highest rates of malaria infection and death occur in poor communities, where identification of the disease is weak, and therefore preventative measures are less common (WHO, 2021). Thus, malaria remains in the top ten causes of mortality in low-income countries. The World Health Organization (WHO) has designated 11 countries, named the high burden high impacts countries (HBHI), that are the most affected and the most at risk for the malaria endemic. These countries include Burkina Faso, Cameroon, Democratic Republic of the Congo, Ghana, Mali, Mozambique, Niger, Nigeria, Uganda, United Republic of Tanzania, and India, the first 10 located in sub-Saharan Africa (WHO, 2021). The WHO African region

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reports 228 million cases in 2020 which account for 95% of all malaria cases (WHO, 2021). Despite a population increase of 435 million in this area, cases decreased from 363 to 225 per 1000 people from 2000 to 2019 which is a decline of 29%, due to the widespread use of the LLINs (WHO, 2020a). This is a significant decrease, but the progress has slowed in recent years despite steady distribution of insecticidal nets from 5% to 65% coverage of people in the sub-Saharan African countries (WHO, 2021). Unfortunately, in 2020 and 2021, cases of malaria have begun increasing again. Malaria remains a significant health burden in many parts of the world with 229 million cases and 409,000 deaths occurring in 2019 and 243 million cases and 456,000 deaths occurring in 2020 (WHO, 2021). Therefore, to keep these nets working towards the goals of malaria remediation, improvements are incredibly necessary.

Innovations in mass production have allowed the unit cost of nets to remain low. Although it varies from manufacturer to manufacturer, in 2021 one unit can be as low as \$1.71/net versus over \$4 when they first were being made before 2012 (Pulkki-Brännström et al., 2012), so despite the rising issues, LLINs are still the most effective approach for preventing malaria transmission in high-risk areas. The economic burden of malaria is also significant. An estimated 10% reduction in malaria incidence would result in a 0.3% increase in economic growth in highly affected countries (Gallup & Sachs, 2000).

LLINs, the most popular malaria intervention method, contributed to 62–72% of the decline in cases (Bhatt et al., 2015). In fact, after 70 years, China has eliminated malaria, and this is widely attributed to the consistent distribution of insecticidal nets since the 1980s (Chen et al., 2021). Although this effectiveness has decreased recently, LLINs remain widely utilized for their cost and coverage when compared to other options. In 2020, 229 million LLINs were delivered, and as of the year 2020, over 2.3 billion LLINs have been produced and distributed globally at the rate of 300–400 million per year (Lorenz et al., 2020). In 2020, access to nets is at 51%, not having fluctuated much in recent years, but rate of use has risen from 71.3% in 2004 to 87.1% in 2020 (Bertozzi-Villa et al., 2021). Although it is important that nets are being distributed in mass quantities for maximum population coverage and protection, this produces a great deal of plastic waste that will be disposed of after only a few years, and if not done properly, can pollute water sources with microplastics and insecticides (WHO, 2014a).

Even if old nets are discarded appropriately or burned, the synthetic polymers from which they are constructed will contribute plastic pollution in the environment. Overall, the resources needed to continuously supply these nets worldwide means that nets should remain affordable; however, the environmental impacts suggest that manufacturers of LLINs should consider longer lasting and sustainable alternative LLINs. Additionally, recycling can still be an option, but the facilities for this purpose have not yet received enough support and it remains an unviable solution to date.

The progress against malaria is slowing, and there is much interest in improving the effectiveness of existing interventions as well as developing new ones (WHO, 2021). For LLINs, improvements have focused primarily on introducing new active ingredients in response to emerging insecticide resistance. In this paper, we will discuss opportunities for improving the fabric substrate in durability, the environmental impacts of production, and its disposal.

### 3. Current practices for long-lasting insecticide nets (LLINs)

Due to their significant role in malaria prevention, LLINs distribution and use is widespread; however, not all nets provide the same physical and biological protection from bites of infected mosquitoes. Nets differ in their material composition, insecticide used, and methods and means of production and processing. The materials commonly used for the nets vary from polyester to composites of high-density polyethylene and low-density polyethylene. However, to date, synthetic polymers are the primary material used for modern LLINs. This is due to the fact that complex structures can be created with polyesters, although they are far

from sustainable and green practices. Before LLINs became widely used, it was standard to have fabrics that were simply dipped or sprayed with an insecticide (Gopalakrishnan et al., 2018). Many LLINs are still coated using technology that involves an insecticidal resin that binds to the surface of the net, which has proven to be effective (Kilian et al., 2008), while others are incorporated with the insecticide during fiber formation (Bhatt et al., 2015).

#### 3.1. Insecticides and additives

Due to increased development of insecticide resistance in mosquitoes, different additives have been commercially employed to counteract resistance through various modes of action. Currently, only two types of insecticides are approved for net use (CDC, 2022).

The original insecticides used in LLINs nets are called pyrethroids (WHO, 2014b, 2020b, 2020c). Examples of the used pyrethroids are permethrin, alpha-cypermethrin, and deltamethrin which are used because they are readily available, cost-effective, and have been widely studied and used for many years (Shafer et al., 2005). Commonly used additives include piperonyl butoxide (PBO) and pyrroles. Pyrroles are used as insecticidal additives, but not all additives are insecticides on their own. Some additives, such as PBO, may act as synergists which can serve to enhance the functional role of the insecticide by restoring susceptibility to pyrethroids. These structures can be seen in Fig. 1.

Pyrethroids act quickly to kill the insect. It is important for the chemical used in malaria vector control measures to show various means of insecticidal activity, otherwise unharmed mosquitoes will continue to seek hosts, and transmission throughout the community would not be stopped. Insecticidal properties also help control the overall mosquito population. A knock-down effect is a good strategy for these nets where the goal is to kill the insect, also known as “knockdown response (kdr)”, which can result in the death of the insects if the dose is high enough (Rehman et al., 2014; Bowman et al., 2018). Excito-repellency and irritation are important properties of active ingredients for LLINs, because they direct mosquito activity away and modify the ability to detect hosts. Another sub-lethal effect is feeding inhibition, a mode of action that affects the attraction behavior (Ogoma et al., 2014). Most pyrethroids, though, only have a slight repellent effect, their main function being insecticidal. The main way in which pyrethroids function is by blocking the voltage-gated sodium channels (VSSC) that promote the potential difference necessary for synapsis (Shafer et al., 2005; Field et al., 2017).

Due to the continued use of these insecticides, there has been a decline in efficacy of LLINs from resistance built up by the mosquitoes in regions where pyrethroids have been used. Thus, synergist compounds are currently being added to LLINs to mitigate this issue. These synergist molecules may be insecticidal on their own or not, but in combination with one of the pyrethroids, they have shown increased efficacy of an LLIN by enhancing susceptibility to pyrethroids.

One additive commonly found in combination with permethrin or deltamethrin is piperonyl butoxide (PBO), a synergist that inhibits the cytochrome P450 enzymes from detoxifying the pyrethroid (Protopopoff et al., 2018). In effect, it reverses the natural defense mechanisms and allows the pyrethroid to attack the system as it normally would without a built-up resistance. Because of this mechanism of inhibiting the enzymes, the addition of PBO results in higher mortality rates than early LLINs (Gleave et al., 2018). For an unwashed net, deltamethrin on its own against pyrethroid-resistant insects only resulted in a mortality rate of 238 per 1000 mosquitoes and the addition of PBO results in 438 deaths per 1000 mosquitoes (Che-Mendoza et al., 2021; Gleave et al., 2021). Many of the newer distributed LLINs contain this synergist, but these nets come with a slightly higher cost, in both production and retail (Shepard et al., 2021), which is likely to decrease with increased demand.

Some newer models of LLINs have different types and compositions of insecticides on different parts of the net. For example, PermaNet 3.0 has synergist PBO and deltamethrin on the top of the nets and only deltamethrin on the sides (Tungu et al., 2010). The justification of this is that

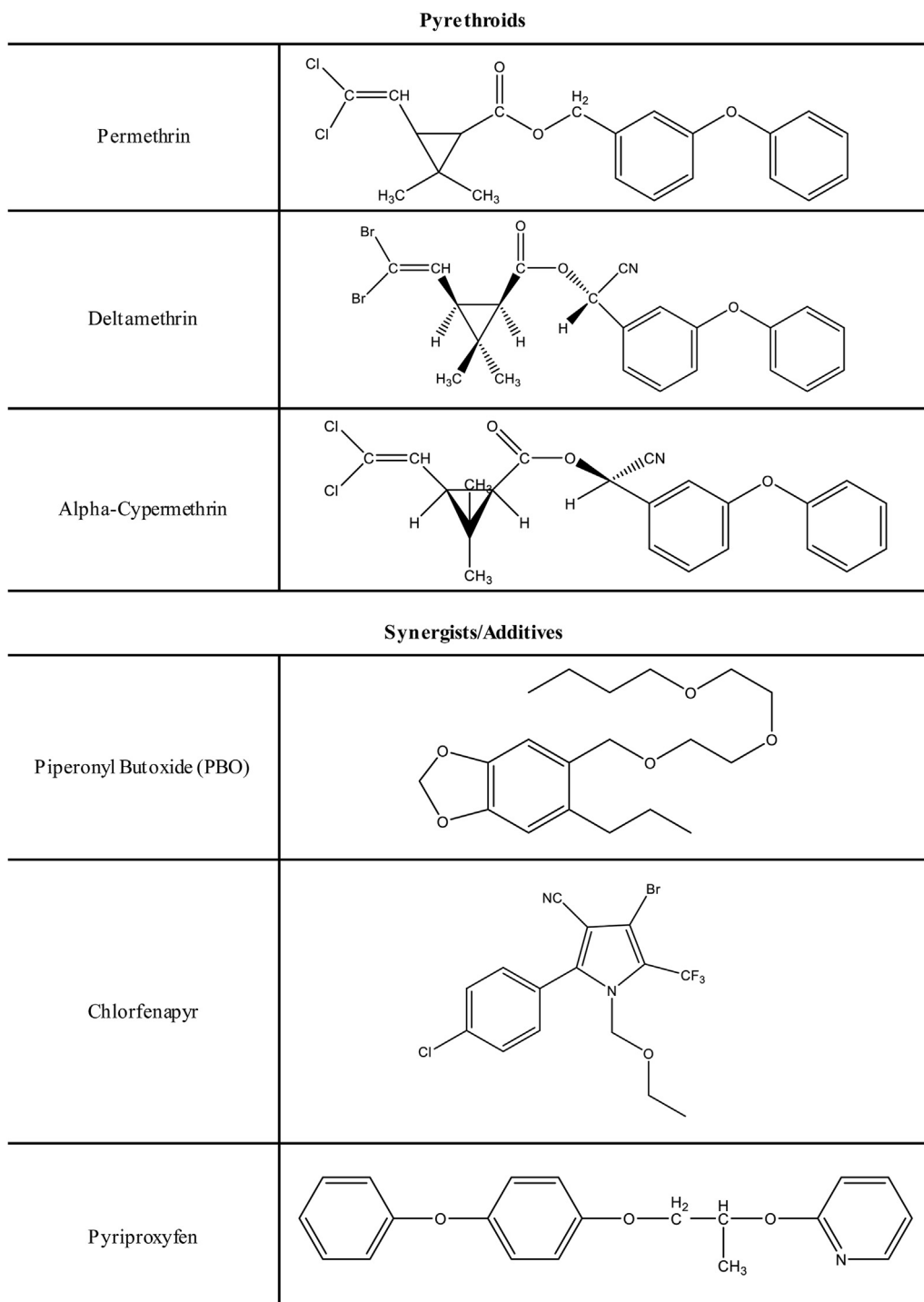


Fig. 1. Insecticides and additives.

the mosquitoes will encounter the top of the net first (Tungu et al., 2010). This helps with cost reduction, because the mosquito should still encounter the necessary synergist prior to the insecticide while reducing the amount of PBO necessary to ensure the insect makes contact.

Another example of an effort to reduce pyrethroid resistance is the use of chlorfenapyr, a pyrrole additive to nets containing alpha-cypermethrin (N'Guessan et al., 2016). Unlike PBO, chlorfenapyr itself is an insecticide, so the idea is that the mosquito will likely not be resistant to both chlorfenapyr and the pyrethroid (N'Guessan et al., 2016). These nets with two insecticides are called dual active ingredient (AI) LLINs. Interestingly, the efficacy of chlorfenapyr may be decreased by the addition of

PBO, so these two may not be an effective combination (Raghavendra et al., 2011). An important detail is that the function of chlorfenapyr is an adulticide which disrupts oxidative phosphorylation in the mitochondria (N'Guessan et al., 2016). Because this mode of action differs from that of pyrethroids, no cross-resistance is expected (N'Guessan et al., 2016).

Pyriproxyfen (PPF) is a commonly used juvenile hormone mimic and growth inhibitor which can be added to nets to sterilize any mosquitoes that survived contact with the net, so the more resistant mosquitoes cannot multiply; it can also be effective at reducing their lifespan (Toé et al., 2019). Studies have shown that over time, average mosquito mortality for PPF-permethrin nets is 8.6% higher than for nets with only permethrin

(Toé et al., 2019). Additionally, this compound is safe for humans and effective to mosquitoes at low concentrations (Tiono et al., 2015).

### 3.2. Manufacturing processes

Out of the 23 LLINs currently prequalified by WHO, the insecticides in 14 of them are incorporated, seven are coated, and two use incorporated netting for the roof and coated netting for the sides. After the manufacture of the LLINs, pyrethroids and other additives are released by the fibers of the nets through diffusion (WHO, 2007) for the nets to have slow release and long-lasting properties. Polyethylene nets are incorporated with active ingredient and polyester nets are impregnated, meaning they are coated with a suspension that contains the insecticide and other additives.

For polyethylene nets, the method of infusing active ingredients into the fibers of LLINs can be explained by melt spinning. The mode of action is so that the insecticide can remain within the fiber and migrate to the surface when needed. As shown in Fig. 2, through this extrusion process the active ingredient migrates through the matrix of a solid. For polymeric materials, natural and synthetic, this rate is dictated by the initial concentration the active ingredient, and the particles diffusion is driven by a concentration gradient seen in the cross-section of the polymer filament (Skovmand et al., 2021). In this process, the insecticide is mixed with the polymer and both components are coextruded into a fiber or filament. Incorporating the insecticide and other additives is done through mixing pellets of polymer and a combination of the active ingredients in the form of a powder or a liquid.

While this is true of polyethylene nets, polyester nets are assembled in a different manner. They are treated, or coated, with insecticide after the multiple filaments are knitted into a fabric by including ingredients that bind the insecticide to the material. A polymer and insecticide mixture are suspended in a bath, then the multifilament polyester yarn is run through the bath so the suspension can bond to the surface. Then, the net must be dried so the polymer can cure, and the insecticide can crystallize in at the interfaces of the filaments. When the insecticide migrates to the surface, it moves through the coating in its amorphous form.

### 3.3. Materials: microstructure and macrostructure

The material used for LLINs needs to be carefully chosen and its properties understood, as the material itself will act as the interface between the mosquitoes and the active components. The nature of the

material has an impact on the physical and chemical properties the resulting LLINs will display. In combination with insecticide and additives after processing, the choice of material will also have an impact on the kinetics and efficacy of the final product. Many of the early insecticide nets were made from cotton or cotton-polyester blends (Gopalakrishnan et al., 2018). The way LLINs are manufactured nowadays, however, allows the surface to remain insecticidal even after multiple washings. Extrusion process requires the given material to have certain mechanical, thermal, and chemical properties for the insecticide infusion and production of the fibers.

For the most used LLINs, when they are said to be 100% polyester and not specifically labeled as some variation of polyethylene, it can be assumed that polyethylene terephthalate (PET) is being used (see Fig. 3 for chemical structures). Polyesters generally have a high melting temperature, close to 250 °C, so the process of melt spinning with a pyrethroid with a lower vaporization temperature may be inefficient, especially compared to polyethylene (Girija et al., 2005).

It has been claimed that polyester nets are preferable because of their softness, but polyethylene has been proven to have a higher bursting strength by weight (Skovmand & Bosselmann, 2011). Bursting strength is defined by how the strength of these fibers can be measured, where the pressure is noted at the point of rupture (UNHCR, 2011). Table 1 shows some differences in requirements for these two categories of LLINs sourced from the United Nations High Commissioner for Refugees (UNHCR) which was adapted from the WHO.

Material is not the only choice that must be made during the manufacturing that will affect the overall quality. There are some factors that lead to preferable characteristics of the final net, which can have a significant impact on the usage of the net such as culture and environmental conditions. For example, it has been found that when nets are available, people may choose to not sleep under one. The mechanisms behind net use and sleeping under them are complex. One explanation has been discomfort involving heat and lack of air flow while sleeping under the net (Pulford et al., 2011). Heat buildup due to lack of airflow within a fabric barrier is likely correlated to the weave pattern and mesh size of the netting, because larger gap in between fibers would allow for more air exchange. Unfortunately, this could also expose the sleeping person to mosquitoes that penetrate through the less dense fabric. A study examined nets with the following mesh sizes: 24 holes/cm<sup>2</sup>, 30 holes/cm<sup>2</sup> plus a 75 cm border of fine cloth, and they were all effective at keeping out mosquitoes, but in this study the users disapproved of the fine mesh due to experienced discomfort (Singh et al., 2016). Studies have also analyzed different patterns and gap concentrations to evaluate the relative bursting strength (Skovmand & Bosselmann, 2011).

Furthermore, nets can be monofilament or multifilament, meaning that they can have one extruded strand knitted into a net or they can be further processed so that many fibers will be included in a single strand. This will contribute to the bursting strength of the nets. Much like tensile strength, bursting strength of the individual strands are important to the overall physical durability of the net (Skovmand & Bosselmann, 2011), but certain weave patterns and mesh sizes can be optimized to use an appropriate amount of material while still displaying good strength. Denier of the fabric is the weight of 9000 m of the thread or filament and can vary depending on the product. Physically, it can be interpreted as linear mass density, which makes it also dependent on the material itself. For the same monofilament material, however, a larger denier indicates a larger diameter. For a multifilament yarn, denier refers to the weight of the filament bundle, not of the individual filaments. As previously discussed, the ability for the insecticide to move to the surface at an appropriate rate depends on the microstructure, but it also can change based on the cross-sectional area of the fiber (Skovmand & Bosselmann, 2011). Factors that can affect user experience are texture, gap shape, and denier. Texturizing the fibers by creating a rough surface instead of a smooth one has proven to make fibers feel softer and more comfortable (Skovmand & Bosselmann, 2011). This also reduces the weight of the fiber, therefore saving some product, which is significant even

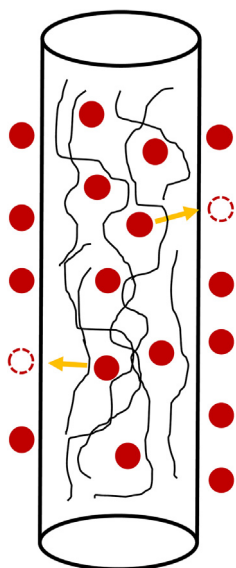
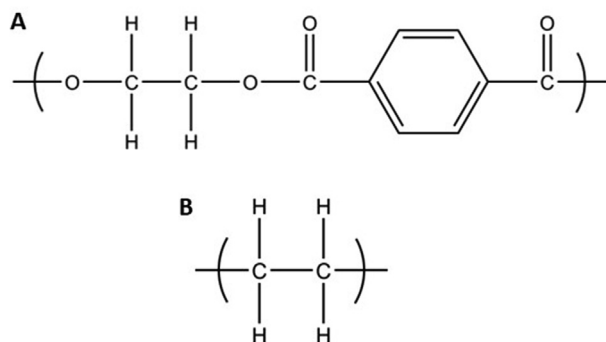


Fig. 2. Diffusion mechanism of active ingredient in a filament.





**Fig. 3.** Main monomers of commercial bednets. **A** Polyethylene terephthalate (PET). **B** Polyethylene (PE).

considering the slight reduction in strength. The fibers can be turned into a net in a variety of ways. With mesh size around 8.7 holes/cm<sup>2</sup> for polyethylene and 24 holes/cm<sup>2</sup> for polyester, they are typically either knitted with rhomboid or hexagonal holes (see Fig. 4). Nets with atlas pattern display a higher elasticity, and 4-sided gaps exhibit a higher bursting strength than equivalent 6-sided gaps. During manufacturing, resistance to tearing can be positively affected by turning the knitting direction of the net by 90° before sewing, so the upward forces that are usually the cause of tears will be parallel to the orientation of the fibers (Skovmand & Bosselmann, 2011).

### 3.4. Available nets

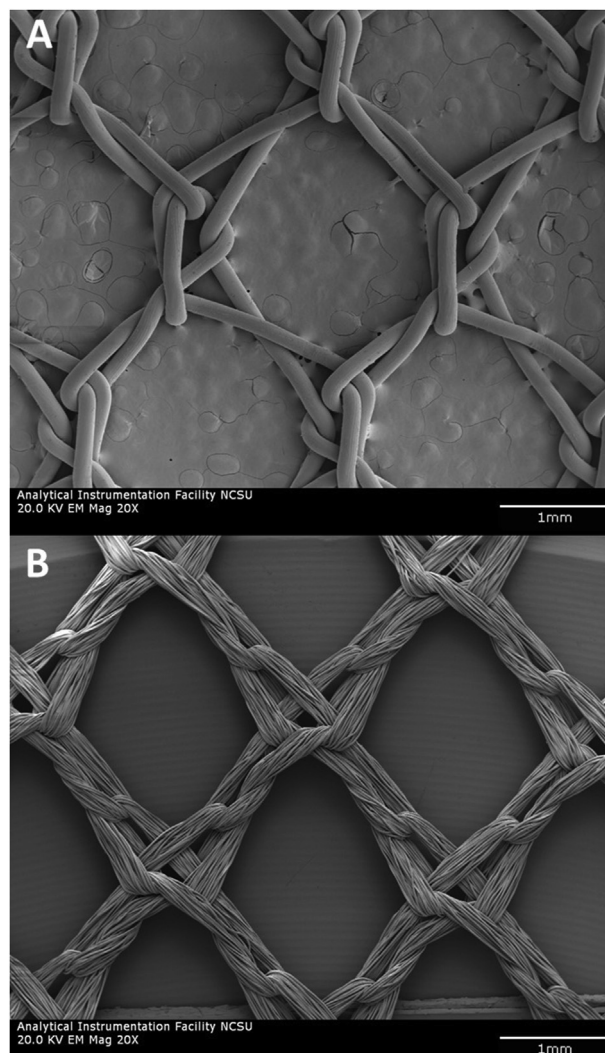
Data on currently commercially available LLINs and their effectiveness are compiled in Table 2. Some are currently being distributed only if they have been prequalified by the WHO. They meet the specifications in terms of insecticide, material, impurities, efficacy, and specific physical properties. Others, though, have either not gone through the approval process yet or failed to meet the requirements. Only 100% polyester and 100% polyethylene have been approved as per material, and only pyrethroids and pyrethroids have been approved as per active ingredients. The recommended concentration of these, though, varies based on the specific chemical being used, denier, and the overall net design.

## 4. Challenges related to utilization of LLINs

Despite being such a crucial tool in the global control and elimination of malaria, the available LLINs still have plenty of room for improvement. Chemical and physical durability relating to the longevity of the infused insecticide and the material being used are not the only challenges. When insects gain resistance to pyrethroids, there may still be some residual contact irritancy but in general, the main component becomes the physical aspect. Additionally, the sustainability of the products used to produce LLINs can be improved by using materials other than synthetic polymers, which are difficult to recycle and do not biodegrade, leaving behind considerable amounts of waste. Considering the current costs of nets, extending the lifespan for one or two extra-years would save malaria control costs between \$500 and \$700 million over the next five

**Table 1**  
UNHCR net requirements by material (UNHCR, 2011)

Net requirements	Polyethylene	Polyester
Material (%)	100	100
Size	180 × 160 × 150 cm	180 × 160 × 150 cm
Denier	100–150	75–100
Filament	Mono	Multi
Mesh Size	8.7 holes/cm <sup>2</sup>	24.2 holes/cm <sup>2</sup>
Shrinkage	± 5%	± 5%
Bursting strength (min)	250 kPa	250 kPa



**Fig. 4.** Incorporated polyethylene monofilament (A) and coated polyester multifilament (B). Courtesy of S. Smith.

years (Lorenz et al., 2020). Because sustainability efforts usually have a higher price point, the extension of the useable time of the nets while using sustainable materials could be cheaper for the user due to more infrequent manufacturing and shipping. It is important to note that there are many different factors between households that may affect all aspects of the durability of the nets (Kilian et al., 2015).

LLINs are cheap and effective, but currently have a maximum lifespan of only around three years. In fact, despite the requirement by WHO for them to have insecticidal effects for three years, studies analyzing the efficacy of nets by three separate manufacturers show that the most common LLINs only prove to be effective against malaria for around 2–2.6 years (Lorenz et al., 2020).

The ability of LLINs to provide protection for multiple years of use is an important performance criterion for economic reasons. Often the biggest expense for distribution programmes comes from making deliveries to users in remote locations. A long-life product not only reduces the volume of products purchased over a given period, but also the number of deliveries. When LLINs first emerged, no longevity data were available, so use-life was estimated using laboratory wash testing. For approval, WHO requires that LLINs be able to withstand 20 wash/rinse cycles in a standardized wash test and still be able to kill 80% of susceptible mosquitoes in a standard bioassay (WHO & WHOPES, 2013). Further assumptions about how frequently the nets were washed by users, and results from a handful of small field studies, led some

**Table 2**  
Summary of commercially available LLINs

Name	Material	Insecticide	Dose (g/kg)	Denier	Reference
World Health Organization qualified/prequalified					
Olyset Net	Polyethylene	Permethrin	20.0	150	Tarimo & Cosmas (2018); WHO (2020d)
Olyset Plus	Polyethylene	Permethrin	20.0	150	Oumbouke et al. (2019); WHO (2020d)
Veeralin	Polyethylene	PBO	10.0	130	Oumbouke et al. (2019); WHO (2020d)
		Alpha-cypermethrin	6.0		
		Piperonyl butoxide	2.2		
MAGnet	HDPE	Alpha-cypermethrin	5.8	150	Oumbouke et al. (2019)
Permanet 2.0	Polyester	Deltamethrin	1.8	75	Wills et al. (2013); WHO (2020d)
			1.4	100	
			6.7	75	
Interceptor	Polyester	Alpha-cypermethrin	6.7	75	Lissenden (2020); WHO (2020d)
Interceptor G2	Polyester	Alpha-cypermethrin	3.2	75	Bayili et al. (2017); Lissenden (2020); WHO (2020d)
			2.4	100	
		Chlorfenapyr	6.4	75	
			4.8	100	
Royal Sentry	HDPE	Alpha-cypermethrin	5.8	150	Lissenden (2020); WHO (2020d)
Royal Sentry 2.0	HDPE	Alpha-cypermethrin	5.8	120	Lissenden (2020); WHO (2020d)
Royal Guard	HDPE	Alpha-cypermethrin	5.5	120 or 150	Lissenden (2020); WHO (2020d)
Permanet 3.0	Polyester	Deltamethrin	Roof: 4.0	75 or 100	Tungu et al. (2010); Lissenden (2020); WHO (2020d)
			Side: 2.8	75	
			Side: 2.1	100	
		Piperonyl butoxide	Roof: 25	75 or 100	
Duranet	HDPE	Alpha-cypermethrin	5.8	150	Lissenden (2020); WHO (2020d)
Duranet Plus	HDPE	Alpha-cypermethrin	6.0	150	Lissenden (2020); WHO (2020d)
		Piperonyl butoxide	2.2		
Miranet	HDPE	Alpha-cypermethrin	4.5	135	Lissenden (2020); WHO (2020d)
Yahe	Polyester	Deltamethrin	2.3	50	Lissenden (2020); WHO (2020d)
			1.85	75	
			1.4	100	
Safenet	Polyester	Alpha-cypermethrin	6.7	75	Lissenden (2020); WHO (2020d)
			5.0	100	
			1.8	75	
Yorkool	Polyester	Deltamethrin	1.8	75	Ketoh et al. (2018); Lissenden (2020)
			1.4	100	
Panda Net 2.0	Polyethylene	Deltamethrin	1.8	75	UNICEFF (2020); WHO (2020d)
			1.4	100	
Tsara	Polyethylene	Deltamethrin	2.5	120	Lissenden (2020)
Tsara Boost	Polyethylene	Deltamethrin	3.0	130	Kasinathan et al. (2019); Lissenden (2020)
		Piperonyl butoxide	11.0		
Tsara Soft	Polyester	Deltamethrin	2.7	75	Lissenden (2020); WHO (2020d)
			2.0	100	
				150	
Reliefnet Reverte	Polyethylene	Deltamethrin	1.8	120	WHO (2021)
Tsara Plus	Polyester	Deltamethrin	Roof: 3.0; Sides: 2.5	Roof: 130; Sides: 100	Lissenden (2020); WHO (2020d)
		Piperonyl butoxide	Roof: 11.0		
Not approved					
Dawaplus	Polyester	Deltamethrin	3.0	130	Kasinathan et al. (2019)
		Piperonyl butoxide	11.0		
NetProtect	Polyethylene	Deltamethrin	1.8	118	Randriamaherijaona et al. (2017)
LifeNet	Polypropylene	Deltamethrin	8.5	100	Djènontin et al. (2018)
Olyset Duo	Polyethylene	Permethrin	20.0	150	Tiono et al. (2018); Toé et al. (2019)
		Pyriproxyfen	10.0		

manufacturers to claim that their products would last up to seven years in the field.

Later, studies of LLINs recovered from the field often found nets so physically damaged that even if they retained insecticidal potency, they provided no physical barrier against mosquitoes (Smith, 2007; Tsuzuki, 2011). Studies into the causes of damage and attempts to correlate damage to protection loss are difficult and imperfect (WHO, 2013; Kse & Russell, 2014), but nonetheless have led to the consensus that a realistic median LLIN use-life is closer to 2–3 years.

Since there is little room for making the product less expensive, there has been some effort to find ways to make LLINs more physically durable, such as to capture savings by lengthening the time-to-replacement. Progress in this area has been slow, for both technical and organizational reasons, such as identification and development of testing methods that could predict multi-year use life relies on confirmation from actual multi-year experience with prototype materials (Skovmand & Bosselmann, 2011; Smith et al., 2012; WHO, 2015; Wheldrake et al., 2021). LLINs that last for e.g. five years are likely to be more expensive than current products, and procurement agencies are

reluctant to spend more per product unless there is convincing evidence of a long-term overall cost savings. Still, considering the huge volumes of LLINs purchased each year, the introduction of a demonstrably more durable product could lead to enormous cost savings to malaria control programmes (Pulki-Brännström et al., 2012).

The main factors for chemical durability are wash resistance, indicated by the retention index, and diffusion rate of the insecticide in the polymer matrix. The definition of washing is determined by the WHO Pesticide Evaluation Scheme (WHOPES) to be a very thorough washing and drying process with specific types and amounts of soap down to details like pH and scrubs per minute, but it is unlikely that the users follow these exact steps so variation in the results is to be expected (Gladbach et al., 2015). Retention index is used to measure this (Eqn. (1)):

$$r = n \sqrt{\left(\frac{t_n}{t_0}\right)} \quad (1)$$

where  $t_n$  is the active ingredient content (g/kg) after  $n$  washes,  $t_0$  is the active ingredient content (g/kg) after 0 washes, and  $n$  is the number of

washes.

For the Permanet 3.0, a deltamethrin- and PBO-based net, 20 washes reduced the knockdown and mortality rates from 54% and 80% to 19% and 20%, respectively (Birhanu et al., 2019). In MAGNet LN, the retention of alphacypermethrin remained at 95% at 20 washes and 90% at 25 washes (Kasinathan et al., 2019). Another study looked at Permanet 2.0, Yorkkool, and Interceptor LLINs, and an inverse relationship between mortality rates and chemical retention was found. This study determined the Interceptor net to be inferior to the performances of the other two, despite it being the most recommended product in 2012, highlighting the need for continuous studies and the differences between results with different test parameters (Ghimire et al., 2020).

Physical durability of the nets is analyzed by the size of holes and tears found in the net after a monitored period of use by the proportional hole index. In a study of many PermaNet 3.0 nets, holes were found all over the nets after three years from a few main sources including children, rodents, and sleeping mats, primarily (Birhanu et al., 2019). In fact, 27% were determined to be too damaged after the three-year period (Birhanu et al., 2019). Mechanically generated holes from snagging, tearing, and seam ripping makes up for most holes found in nets (Wheldrake et al., 2021). Although all nets experience a decrease in physical integrity, they can usually be still considered effective to a certain degree because of the insecticidal activity or the type of damaged sustained (Herrera-Bojórquez et al., 2020). Kse & Russell (2014) showed that holes ripped at the corners of the net, likely at the supports, allowed twice as many mosquitoes inside than comparable tears in the center and several small holes throughout. Often, holes can form near the bottom of nets where the bedframe or floor meet the fabric, and snags are likely to occur Sutcliffe. A two-year-long assessment in Uganda of various polyester nets showed holes in 85% (Ghimire et al., 2020). It has also been studied that the rate of repair by the user is very low when damage does occur (Wills et al., 2013).

Through these durability monitoring studies nets can be evaluated for their overall effectiveness. Physical durability and bioefficacy are factors that have been monitored under various conditions, and physical durability has been proven to be impactful against malaria infection even when the insecticides are not providing full protection (França et al., 2021). Studies have concluded that while insecticidal activity discourages mosquito biting and protects others in the community, the effects are negligible if the net cannot withstand daily wear and tear proving the importance of a physically durable net along with long-lasting insecticidal effect (Lindsay et al., 2021). Before the introduction of LLINs and ITNs, untreated bednets that were not treated with insecticides could be found in many communities, and they had a great impact on malaria infections (Lindsay et al., 2021). There are studies that refer to this time of untreated nets to support the idea that the nets without insecticide are also helpful due to the physical barrier created (Lindsay et al., 2021). These are no longer recommended by the WHO. Rather than negating the importance of insecticide, this idea shows the significance of high physical durability of these nets in the case of reduced bioefficacy of insecticide on nets or in the face of widespread insecticide resistance.

In summary, as a malaria control intervention, LLINs are a cost-effective strategy due to the reduced cost of manufacturing and the cost of delivery models that have been examined to optimize control efforts (Arroz et al., 2019). Distribution costs can be reduced by improving the overall product so that they remain effective and useable for longer periods of time. The materials in use to produce the nets themselves are already very inexpensive, but as previously mentioned, the additives that are used to combat pyrethroid resistance create additional cost. Conversely, prolonged chemical and physical durability may make them even longer lasting which may reduce the overall costs of LLIN interventions. An analysis via proportional hole index of more physically durable nets being chosen over less physically durable nets showed a 20% decrease in equivalent annual cost (Lorenz et al., 2020).

## 5. Recent and ongoing potential improvements

Despite the many effective LLINs on the market, there are some possible variations to this approach to malaria control. There are great opportunities to extend the length of insecticidal activity and the physical durability of nets. Ideally, this should be done sustainably and inexpensively. By focusing on the application of biopolymers such as cellulose as the primary material for LLINs, the issue of sustainability can be addressed. By making improvements on the material and process techniques, the overall physical and chemical durability can also be reassessed.

Composites, materials that combine two or more different materials to achieve new properties, are an important consideration in the field of materials engineering, and the use of a new composite to make a more sustainable LLIN is a valid option to be explored. An example of a composite for this purpose is an insecticidal cotton fabric that was coated with pyrethroid-infused polymer matrix (Hebeish et al., 2010). Polyvinyl acetate was used as the polymer cross-linking agent for the cotton and insecticide. In other words, the insecticide, cypermethrin, was bonded to the surface with a polymer. This method showed insecticidal effect, but the chemical durability was not monitored over a long period (Hebeish et al., 2010). Similarly, some fibers have been developed that use a core polymer that has been infused with an active ingredient and a plain sheath polymer. The inner polymer is ethylene-vinyl acetate (EVA) with repellent DEET, and the outer coating is HDPE. Processed similarly to other LLINs, a modified extrusion method was used. The idea is that the lack of chemical on the sheath will drive the active ingredient to the surface in a controlled manner. Although no long-term studies were conducted to conclude anything about the effectiveness of this approach, it is a new way to look at the potential for different types of LLINs that improve on the challenges of the current ones (Sibanda et al., 2019).

Likewise, biodegradability is an important factor to consider. One net on the market currently is called the Reliefnet Reverte, and it uses a pro-oxidant additive to allow for the biodegradation of their polyethylene nets. This additive is often a transition metal (Co, Mn, Fe, Ni, or Cu), and metal salts (Fe, Mn, and Co), and it may accelerate the process depending on the type of polyethylene. A comparison between the polyethylene has shown that low density polyethylene is more susceptible to degradation than high density (Al-Salem et al., 2019). While these nets are biodegradable after UV and heat treatment, they are still originally made from petroleum-based polymers which are from a non-renewable source. It is also unknown if all microorganisms can successfully break down the polymer fully along with all the other additives present in the net, or if they will result in the liberation of microplastics.

## 6. Perspectives and opportunities with bio-based polymers utilization and outlook

Beside the research done for the full development of LLINs, there has also been research in how biopolymers can interact with pesticides. Understanding these interactions can also help to identify other materials that could be used for LLINs if formation of fibers can be obtained. For example, carboxymethyl cellulose has been used to form nanoparticles to slowly deliver avermectin (Chen et al., 2020).

Cellulose is an abundant, renewable, and biodegradable natural polymer that has been studied for its use as fibers by using green chemistry. It is found in many different crystalline allomorphs and its surface can be functionalized to serve a particular purpose. The interactions of cellulose and active components are currently studied for the development of slow-release systems, mostly for fertilizers (Pang et al., 2019; França et al., 2021). Moreover, there has been some studies of the interaction of cellulose-based materials and pesticides, mostly for its removal and control after non-point and point sourcing contamination (Rana et al., 2021). Some other efforts in the generation of polymeric and cellulose-based repellent fabrics have also been reviewed (Elsayed et al., 2021a; Sun et al., 2020).



There, the surface modification of cellulose and its nano-formulation seem to be the most cited approach for obtaining active fabrics; however, they keep relying on synthetic polymers to increase surface interaction with the active components rather than imbedding them.

Based on those studies, its abundancy, renewability, and other physicochemical properties, cellulose-based materials are a practical replacement for the current LLINs on the market. However, to develop filaments imbedded with active ingredient, the cellulose must be first dissolved, and filaments regenerated as other synthetic polymers are. Cellulose is insoluble in common solvents like water and typical organic solvents due to the formation of a strong hydrogen bond network between the hydroxyl groups within and with other adjacent chains; as well as the hydrophobic crystalline face that is naturally formed in the ensemble of the fibers (Medronho et al., 2012). Advances in the understanding of this material has led to the identification of some solvents that aim to break this network to successfully dissolve cellulose, allowing processing and regeneration. These new solvents including deep eutectic solvents (DESs) and ionic liquids (ILs). Once the cellulose is dissolved, the insecticide can be incorporated and the solution spun into strong yarns, achieving the end goal of a sustainable LLIN (Elsayed et al., 2021b). Furthermore, this process is not restricted to the use of cotton, jute, or other long cellulose fibers, allowing for the utilization of any lignocellulosic biomass as raw material, even agroforest byproducts. Some biobased products, like cotton, are less sustainable than others due to the high water demand and use of valuable farmland, so the source should be considered. Additional biodegradable cellulose derivatives could also be considered, such as cellulose esters to better tune the diffusion rates and material interactions. Inherently, many bio-based materials show great mechanical properties and controlled-release ability, allowing for a durable and effective net which can translate into overall cost savings.

Beside the formation of the cellulose yarns, coating them with other biopolymer-pesticide layers can be done, especially, when emerging techniques like electrospinning - both AC and DC - are considered (Balogh et al., 2016), or the formation of double layer spinners are utilized (Reyes et al., 2020). This coating would allow for the selective application of additives in strategic areas of the nets, as well as the modification of the release rates. Further studies on the interactions of the pesticides and the solvents used for the cellulose dissolution are needed, as well as the optimization of the regeneration processes to assure the insecticides will still be active after formation. However, cellulose-based yarns and fabrics seem to be a clear path to obtain alternative and more sustainable LLINs.

## 7. Conclusions

Despite the room for improvement that has been identified through the analysis of all types of nets, LLINs have proven to be an important strategy in the mitigation of malaria around the world. Knowing what materials, insecticides, and processing techniques are available and how they may be modified and optimized will help the development of nets with improved physical and insecticidal properties and lower environmental impact. Looking ahead, bio-based polymers are replacing synthetics in many industries and have been proven successful in other applications as mediums for the controlled-release. Furthermore, advances in the processing of cellulose from different raw materials and its transformation into yarns opens the possibility to imbed them with active molecules. Thus, these sustainable tools highlight encouraging opportunities for the development and distribution of bio-based polymers in LLINs and complementary vector control tools in the global fight against malaria.

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## CRedit author statement

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## Declaration of competing interests

The authors declare that they have no known competing financial interests or personal relationships that could have appeared to influence the work reported in this paper.

## Data availability

The data supporting the conclusions of this article are included within the article.

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