Mobile phone devices and handheld microscopes as diagnostic platforms for malaria and neglected tropical diseases (NTDs) in low-resource settings: A systematic review, historical perspective and future outlook

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**Abstract**

The accurate, rapid, and cost-effective diagnosis of malaria and neglected tropical diseases (NTD) in low-resource settings may benefit by significant technological advances in handheld and mobile phone microscopy. We systematically review the available literature in this field and discuss the future directions in which these technologies may be applied. English-language studies from the PubMed, Embase, and Web of Sciences were searched through April 2018 for observational and interventional studies reporting diagnostic characteristics of handheld and mobile phone microscopy devices as compared to field-established gold standard reference tests. Seventeen studies were included in the analysis. Findings included the high performance of the Newton Nm1 microscope in the diagnosis of *Plasmodium* species, *Schistosoma mansoni*, and soil-transmitted helminths (STHs), exhibiting sensitivity and specificity values often greater than 90%. Similarly, the CellScope was shown to have excellent diagnostic characteristics in the detection of *Loa loa* and *Schistosoma* species. Fluorescent microscopy was found to have high specificity and sensitivity in the diagnosis of *Plasmodium* species.

Mobile phone technologies and handheld microscopes hold significant promise in the rapid and effective diagnosis of malaria and NTDs in areas where accurate diagnosis is vital. Although many of these technologies have yet to be securely embedded within the health system and studied directly in this context, the foundations for significant healthcare advances and impact have already been laid by several studies conducted within the last decade.

**Introduction**

Malaria and neglected tropical diseases (NTD) continue to cause significant morbidity and mortality worldwide (Murray *et al.*, 2012; Snow *et al.*, 2017; Vos *et al.*, 2017). Several interventions are needed to combat these diseases effectively including integrating effective and low-cost diagnostic tools into routine clinical and public health practice. However, routine diagnosis of malaria and NTDs remains challenging due to the paucity of specialized equipment and need for specialist or highly trained individuals in many low-resource settings. To tackle these complex issues, implementation research involving several complimentary approaches is needed, including publicly and privately funded ventures to develop new inexpensive diagnostic platforms, tools, and protocols that improve diagnostic accuracy for common medical conditions of clinical and public health significance. Within this realm, there have been several recent developments involving handheld microscopes and mobile phone microscopes (Coulibaly *et al.*, 2016a; Rajchgot *et al.*, 2017). Some advantages of these technologies in low-resource settings include low handling costs, portability, battery power, image capture with telemedicine possibilities, and low equipment training requirements.

Specific to portable microscopy, mobile phone devices converted into microscopes provide a distinct advantage due their built-in high-resolution cameras which are continually being improved and refined. Furthermore, mobile phones are already widely used even in low-resource settings and their use is familiar even to un-trained personnel (Bastawrous and Armstrong, 2013). Mobile phones can also be modified or customized to act as microscopes with newly developed applications or added-on hardware. These features, along with increased storage space, access to powerful computing capabilities, connectivity with global positioning system (GPS), and improved access to the internet provide mobile phones with numerous appealing features that make them ideal platforms in low-resource settings.

While there were some early innovations in handheld microscopes [Meade Instruments, 2018], recent innovations and improvement in the realms of optics, design, and engineering have produced devices with the potential to be effective in real-world clinical and public health practice in low-resource settings. The field remains in its early stages of development and continues to see a rapid evolution of novel devices harnessing creative methods to image pathogens of global health significance. In this article, we first outline a brief history of handheld microscopy. We then present the first systematic review of handheld and mobile phone microscope technologies to evaluate their effectiveness, compared to gold-standard diagnostic methods for NTD diagnosis in low-resource clinical settings. We also summarise future applications of mobile technologies that have been tested in laboratory settings but have not yet been examined in the field.

**Historical Perspective**

The growth of mobile and handheld devices in the field of microscopy has mirrored the rapid development of diagnostics and treatment in the field of parasitology (Stothard and Rollinson, 2018). The history of portable microscopy with traditional light optics can be traced back over seventy-five years to a particularly influential clinical pioneer named John Norris McArthur (b. 1901 d. 1996) who promoted their application in parasitic disease detection and diagnosis. While a medical student in London shortly before WWII, McArthur conceived and designed a particularly revolutionary format with inverted optics and carefully placed prisms that radically shortened the reflected light path. First fashioned inside wood and then later metal housings, these devices were essentially self-contained monocular microscopes small enough (10.2cm x 6.4cm x 5.1cm) to be held in one hand and carried inside a coat pocket (Dunning and Stothard, 2007).

The McArthur microscope and its derivations (**Figure 1**), which bore his name, could deliver as much optical performance with more versatility than the traditional bench-top compound microscope. Originally fashioned to use external natural light and later an internal bulb from either a battery or main supply, the McArthur microscope set the industry standard for portable microscopy for several decades. Its use by UK-based medical practitioners such as Murray Longmore advanced the concept of ‘bedside’ microscopy alongside miniaturization of diagnostic testing and streamlined staining protocols (Longmore, 1983, 1986). A particularly seminal study by Collier and Longmore (1983) assessed the performance of the McArthur microscope in the field-diagnosis of malaria in the Solomon Islands (Collier and Longmore, 1983). Whilst proven useful, MacArthur’s microscope fell out of regular commercial production upon his death largely due the loss of its strongest advocate and its increasing expense owing to individual-tooling.

The late 1980s saw advances in computer design and mouldable plastic technology leading to the original ambition of the McArthur microscope being reinvigorated. This included the production and commercial retail of low-cost portable microscopes such as the ‘Enhelion’ in 1988 originally priced at £99 UK with magnifications of x80 and x200. This unit was produced by Science of Cambridge, conceived and designed by Keith Dunning and Rick Dickinson (Kreindler, 2013a; b). Over the next two decades, there were several fluctuations in supply, demand, and commercial production of similar portable microscopes (Kreindler, 2013a). However, the field of portable microscopy within clinical application was significantly advanced by an initiative from the Wellcome Trust in 2009 to make the Newton Nm1 microscope. This device used light emitting diode (LED) technology, which offered magnifications at x100, x400 , and even higher at x600 (dry) and x1000 (oil emersion), for application in peripheral health clinics in low and middle income countries (Kreindler, 2013b).

**Systematic Review Methods**

Reporting conformed to PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) guidelines (Moher *et al.*, 2009). The study’s protocol has not been published or registered elsewhere.

**Data Sources and Searches**

We searched the Web of Science, PubMed, and Embase from inception through 15 April 2018, including only English-language literature. The key concepts included in our search strategies were mobile phone and handheld devices, tropical infections and NTDs, and microscopy (see Supplemental Table 1 for details). We excluded conference proceedings. We also conducted hand search reviews of literature cited by relevant articles and reviews.

**Study Selection**

Two investigators (AV and IB) independently screened titles and abstracts. We included interventional and observational studies that compared a handheld, point-of-care, or mobile phone diagnostic tool with a reference or gold standard diagnostic tool in the diagnosis of a NTD and malaria. We also only included studies that were conducted in low-resource field settings. Demonstration studies, and/or studies conducted in high-resource settings were excluded. Two investigators then independently evaluated the full-text articles and disagreements were resolved by consensus.

**Data Extraction and Quality Assessment**

One investigator extracted study data, including setting, population, the diagnostic measures, and descriptions of the mobile technology. The primary outcomes were the sensitivity and specificity, including confidence intervals, of the diagnostic tool of interest compared to a gold standard. Positive and negative predictive values were also extracted from the studies. Due to significant study heterogeneity in terms of the infections being investigated, the types of diagnostic tools, and reference standards, we did not perform a meta-analysis. One reviewer independently assigned each study a level for risk of bias (low, high, or unclear) on the basis of the Quality Assessment of Diagnostic Accuracy Studies (QUADAS2) criteria (Whiting, 2011) (Supplemental Table 2). The four domains of bias that were judged were patient selection, index testing, reference standard, and flow and timing. Studies that randomly selected their samples from a representative population were deemed low risk of bias. Similarly, studies that chose well-defined and well-established testing methods as their gold standard comparison were deemed low risk of bias. Lastly, studies that blinded evaluators and had multiple evaluators were also deemed to be low risk from bias according to these criteria.

**Results**

With removal of duplicate records, the search strategies identified 462 studies, 71 of which we evaluated as full-text articles (**Figure 2**. We chose a total of 17 reports in the final selection for inclusion in the review (**Table 1**). All studies except for one (Bogoch *et al.*, 2016) were conducted in Africa. Eight of the studies were conducted exclusively in a paediatric population, the most common subgroup to be studied (Stothard *et al.*, 2005; Nkrumah *et al.*, 2011a; Bogoch *et al.*, 2013, 2014a; b; Ephraim *et al.*, 2015; Coulibaly *et al.*, 2016a; Bogoch *et al.*, 2017a). The most common organisms studied were *Plasmodium* species (Hassan *et al.*, 2010; Sousa-Figueiredo *et al.*, 2010; Nkrumah *et al.*, 2011a; Hassan *et al.*, 2011a; Birhanie, 2016a), and the most commonly studied mobile technologies were the Newton Nm1 portable microscope (Stothard *et al.*, 2014; Bogoch *et al.*, 2014b, 2016, Coulibaly *et al.*, 2016a; b) and Cyscope (Hassan *et al.*, 2010; Sousa-Figueiredo *et al.*, 2010; Nkrumah *et al.*, 2011a; Hassan *et al.*, 2011a; Birhanie, 2016a). Gold standard comparisons were most commonly with conventional light microscopy using standard Kato-Katz thick smear tests (Katz *et al.*, 1972) for helminth and thick Giemsa stain smears for studies examining malaria, . The number of samples studied in the selected papers ranged from 33 to 16 259. The number of reviewers/microscopists for each study ranged from 1 to 4 with an average of 1.25 reviewers per study. The technologies roughly divided into four categories: first-generation ball lens-mounted mobile phone devices, second-generation mobile phone devices, handheld light microscopes, and the Cyscope.

*First Generation Ball Lens-Mounted Mobile Phone Devices:*

The results of two studies using first generation ball lens-mounted devices for microscopy are shown in **Table 2A**. These studies (Bogoch *et al.*, 2013, 2014a) developed a novel tool for portable microscopy by mounting a 3-mm ball lens onto a mobile phone. This was used to diagnose *Schistosoma haematobium* eggs in the urine that resulted in poor sensitivity for low intensity infections (29%) and moderate sensitivity for high intensity infections (78.3%). For all infection intensities, the specificity was moderate at 64% with high positive predictive value but very poor negative predictive value. In these two studies, the test characteristics were poor for the diagnosis of *T. trichiura* – particularly the sensitivity (30 – 55%) and negative predictive value (26 – 61%).

*Second Generation Mobile Phone Devices:*

This group of mobile phone-related devices included the reverse-lens CellScope and Foldscope devices as well as other 3D printed devices (**Table 2B**). The reversed-lens CellScope is a microscope that is operated in conjunction with an unmodified mobile phone. Users of the device place the lens such that it aligns with the camera of the mobile phone, and capture images by holding the mobile phone microscope directly above a sample and manually adjusting the focus. Use of this device was studied for the diagnosis of *Schistosoma* species by two studies (Ephraim *et al.*, 2015; Coulibaly *et al.*, 2016a), which found that the tool provided a high degree of specificity (upwards of 99%) and had a high negative predictive value, indicating a very high proportion of true negatives. A modified version of the CellScope, now known as the LoaScope, was studied in the diagnosis of *Loa loa* in two other investigations (D’Ambrosio *et al.*, 2015; Kamgno *et al.*, 2017). The LoaScope uses a similar modified lens that is attached to mobile phones but also provides the benefit of automatically quantifying microfilariae in the collected samples. Notably, the LoaScope had a sensitivity ranging from 93-100% and specificity close to 100%. The Foldscope, a device that is similarly added to a mobile phone, consists of a paper device harnessing a 2.38 mm ball lens and an LED. Ephraim et al. (Ephraim *et al.*, 2015) investigated the use of this device for the diagnosis of *Schistosoma haematobium* in a paediatric population in Ghana. Compared to the CellScope, the Foldscope had both poorer sensitivity (56% vs 68%) and specificity (93% vs 100%).

The third technology using a novel mobile phone design (Bogoch *et al.*, 2017a) focused on the diagnosis of *Schistosoma haematobium* in rural Ghana. Here, the authors used a lightweight 3D printed custom-designed optomechanical unit that was attached to the camera unit on a mobile phone. The regular mobile phone camera application was used to capture images of the sample. Although the sensitivity of the device was only 72%, the specificity and positive predictive value were estimated to be 100%. Thus, there were no false positives in the study.

*Handheld Light Microscopes Used With and Without Mobile Phone Attachments:*

The best studied of the portable microscopy devices is the Newton Nm1 microscope. This monocular light microscope is a commercially available and lightweight (~0.5 kg) device that can be secured onto mobile phones. Similar to the CellScope and Foldscope, this technology relies on the mobile phone’s camera to examine specimens on slides. As seen in **Table 2C**, a wide variety of organisms have been studied using this device. Of note, the microscope performed well with regard to the diagnosis of *Plasmodium* species (Stothard *et al.*, 2014), *A. lumbrocoides* and *T. trichiura* (Bogoch *et al.*, 2014b), and *Schistosoma mansoni* (Bogoch *et al.*, 2014a; Coulibaly *et al.*, 2016a) infections, exhibiting sensitivity and specificity values often greater than 90%. Furthermore, the device appears to have high specificity but poor sensitivity for the diagnosis of intestinal protozoa (Coulibaly *et al.*, 2016a).

A second device, the Meade Readview handheld microscope, is an inexpensive and lightweight monocular microscope that is portable and uses an LED as a light source. Only one study investigated its use in the diagnosis of schistosomiasis*,* and it performed reasonably well, with a sensitivity of 85% and specificity of 96%.

*Cyscope:*

Several studies focused on the use of Cyscope for the diagnosis of *Plasmodium* species, all of which were conducted in Africa. This device is a portable battery-operated fluorescent microscope with long life even in high power modes. Practically classified as a rapid detection test (RDT) for the diagnosis of malaria due to its ability to provide a result in under 10 minutes, it has the advantage of also being able to quantify parasitemia from blood specimens. Although the technology has been used in the diagnosis of tuberculosis, we did not include those articles here (Chaidir *et al.*, 2013; Chang *et al.*, 2015). Additionally, studies performed in dense population centers with greater resources were also excluded (Ogouyèmi-Hounto *et al.*, 2013). We identified five studies investigating this technology in rural and low-resource settings in Africa. Except for one study (Sousa-Figueiredo *et al.*, 2010), the device showed high sensitivity (>90%) and specificity (>87%) in the diagnosis of *Plasmodium* species, mostly *P*. *falciparum* (Hassan *et al.*, 2010; Nkrumah *et al.*, 2011b; Hassan *et al.*, 2011a; Birhanie, 2016a). The exceptional study (Sousa-Figueiredo *et al.*, 2010) had very high rates of false positives for unclear reasons.

**Discussion**

Our review is the first to systematically search the available literature to determine the effectiveness of handheld and mobile phone devices for the microscopic diagnosis of malaria and NTDs in low-resource settings. While this field of research is rapidly evolving and the technologies are expected to be modified and improved in the near-future, our review provides a baseline for future systematic assessment of the topic. Our article builds on one prior review focused mobile phone devices in the diagnosis of parasitic diseases that included studies in controlled laboratory settings (Saeed and Jabbar, 2018).

Overall, the quality of the articles selected in our review were low in bias on the basis of the QUADAS2 criteria, a widely used tool for the assessment of diagnostic tests (Whiting, 2011). For example, all articles chose gold standard comparisons that are well-accepted in the field of microscopy, including thick Giemsa stains for the diagnosis of malaria and the Kato-Katz thick smear for the diagnosis of *S. mansoni* and STHs. Additionally, with regard to patient selection, studies generally chose random subjects from general populations in endemic settings to study rather than individuals with suspected high or low burdens of disease. Such a wide distribution of individuals lends to the validity of using these devices in the field. Thirdly, for nearly all samples studied in these investigations, the authors reported that both the experimental tool and index standard were tested and few samples were lost or remained untested. A notable exception to the high quality features of the articles were that three of the five studies examining the Cyscope did not blind their microscopists to the results of the reference standard. This lack of blinding may threaten the validity of some of these findings.

We found that the wide range of test performance characteristics varied depending on organism and setting. Notable examples of effective devices included the high specificity of CellScope in the diagnosis of *Schistosoma* species and *Loa loa*; the high sensitivity and specificity of the Newton Nm1 microscope for the diagnosis of schistosomiasis and STH; and the generally high specificities of using fluorescent microscopy (Cyscope) for the diagnosis of malaria. Although positive and negative predictive values are summarized in our review, it is important to interpret these values based on local disease prevalence. Thus, high predictive values in one setting may not translate to other settings with differing disease prevalence.

There are several important implications from our findings. Firstly, reasonable evidence exists that the Foldscope provides excellent specificity but low sensitivity in the diagnosis of *S. haematobium.* Secondly, the LoaScope has shown promise in the diagnosis of *Loa loa* infection in highly endemic regions of Africa. Because rapid and accurate diagnosis of *Loa loa* is also critical to the treatment and elimination of onchocerciasis in areas where these two parasites are co-endemic, this device may have a dramatic impact on public health programs in various regions across Africa. Thirdly, based on numerous studies, the Cyscope appears to be an accurate method of identifying malaria infection with rapid turnaround time in various low-resource settings, including hospitals and field clinics. This holds the advantage over traditional RDTs due to its ability to quantify parasitemia as well as reliably diagnose *P.* *falciparum* infections.

An important limitation to our review was the inability to conduct a mathematical analysis of the data to generate a summary measure of the effectiveness of the studied technologies. This is because the settings, diseases, diagnostic tools, and reference tests varied widely between the studies. Such an analysis may be possible once future additional research is performed to validate the use of these diagnostic tools for different diseases in several settings.

While the current study only evaluated devices tested in real-world low-resource settings, there are many new diagnostic tools that have demonstrated potential utility in early, laboratory-based proof-of-concept studies. Several creative approaches have recently been taken to image pathogens, including tomography, fluorescence, and holographic imaging modalities (Seo *et al.*, 2009; Isikman *et al.*, 2011; Zhu and Ozcan, 2013; Tapley *et al.*, 2013; Zuo *et al.*, 2015). Additionally, the use of high resolution wide-field lenses may be a more effective mechanisms to scan samples (Zhu *et al.*, 2011). One device harnesses the buoyant properties helminth eggs to concentrate them in a small area and visualize them in a single field of view (Sowerby *et al.*, 2016), and another device detects the movement of miracidia for schistosomiasis diagnoses (Linder *et al.*, 2016). While these creative approaches demonstrate promise in the field of mobile microscopy, the next major step will be to transform them into modalities that can be evaluated in field settings with comparison to gold standard diagnostic tests.

Many of the devices discussed here rely on innovative imaging technology for users to better visualize samples. However, the field of handheld and mobile phone microscopy is now angling towards a promising direction where software may help visualize, identify, and quantify specific organisms independent of human observers. For example, machine learning may permit better image contrast to help identify organisms on mobile phones in addition to automating the diagnosis of giardiasis (Ceylan Koydemir *et al.*, 2017), eggs of STH and *Schistosoma* (Linder *et al.*, 2013; Slusarewicz *et al.*, 2016; Holmström *et al.*, 2017), and malaria parasites (Rosado *et al.*, 2017). Much of the software has already been integrated onto the mobile phones for diagnosis, which may be a challenge for remote settings with limited local hard-drive storage and computing power. However, harnessing the power of cloud-based analyses and advancing the concept of telemedicine may be a solution to this barrier, whereby data processing may occur distant from where images are captured, and results are rapidly and electronically relayed back to front-line personnel (Linder *et al.*, 2008).

An important aspect of successful mobile phone and handheld microscope technologies must be its ability to accommodate a broad array of samples and be sturdy enough to maintain high-level diagnostic performance in rugged conditions. While many of these devices are being designed for use in low-resource settings, more attention on the preparation of samples in such settings is required such that rapid point-of-care diagnoses can be made (Rajchgot *et al.*, 2017; Bogoch *et al.*, 2017b). An interdisciplinary approach to device design and evaluation will likely result in better microscopes that are useful in real-world settings.

**Conclusion**

Handheld microscopes and mobile phone devices have the potential to improve the quality of clinical care and public health care for NTDs in low-resource settings. Current devices are slowly being integrated into routine practice and newer innovations such as computer vision and machine learning may aid in automating diagnoses. The latter holds great promise in bringing equitable laboratory diagnostic support to areas most in need. The field continues to rapidly evolve as more novel lens and lighting technologies are being developed and studied. Future investigation in the area will likely result in more accurate, portable, and economical tools used in the diagnosis of NTDs.

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**Dedication**: We would like to dedicate our article to the memory of a dear friend and recently departed colleague Rick Dickinson who has left us much enriched by his wisdom and wonderful legacy of innovative portable microscope designs.

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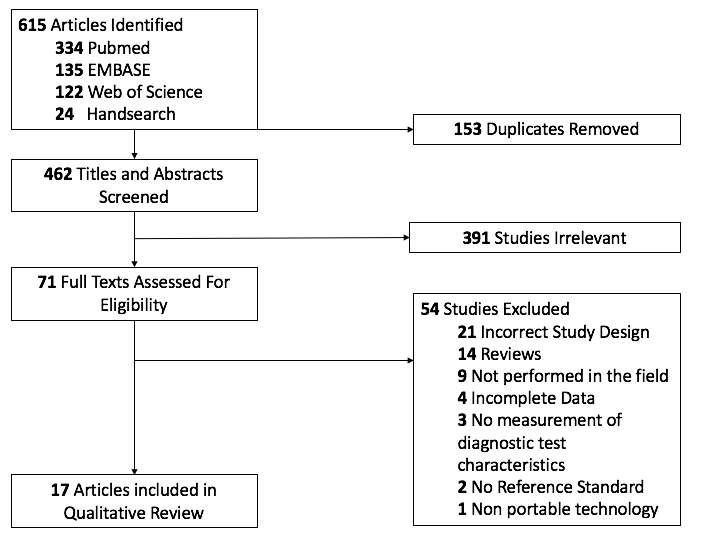
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**Figure 1:** Three handheld microscopes illustrative of advances in microscope design and tooling beginning with the McArthur (left), Lensman (centre) and Newton Nm1 (right), with the carry box of each depicted. For scale, the coin seen on the left image is a €1 coin.



**Figure 2: Flow chart of study selection for diagnostic devices used to diagnose neglected tropical diseases in low-resource settings.**

**Table 1:** Overview of the studies included in the qualitative review, by device type and year.

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Setting | Number of Samples Tested | Population | Organism | Mobile Technology | Gold Standard | Reviewers |
| Bogoch et al., 2013 (Bogoch *et al.*, 2013) | Pemba Island, Tanzania | 199 | Paediatric | *T. trichura, A. lumbricoides* | iPhone add-on | Kato Katz Method, Olympus CX21 microscope | 1 |
| Bogoch et al., 2014 (Bogoch *et al.*, 2014a) | Azaguie, Côte d'Ivoire | 180 | Paediatric | *Schistosomiasis spp., T. trichura* | iPhone add-on, Newton Nm1 | Kato Katz Method, Olympus CX21 microscope | 1 |
| Bogoch et al., 2017 (Bogoch *et al.*, 2017a) | Central Region, Ghana | 60 | Paediatric | *S. haematobium* | Novel Mobile phone device | Olympus CX21 microscope | 1 |
| Bogoch et al., 2014 (Bogoch *et al.*, 2014b) | Pemba Island, Tanzania | 182 | Paediatric | *T. trichura, A. lumbricoides* | Newton Nm1 | Kato Katz Method | 1 |
| Stothard et al., 2014 (Stothard *et al.*, 2014) | Uganda | 50 | Women and children | *Plasmodium spp,* | Newton Nm1 | Olympus CX22 microscope | 4 |
| Coulibaly et al., 2016 (Coulibaly *et al.*, 2016b) | Grand Moutcho, Côte d'Ivoire | 223 | General | *P. falciparum* | Newton Nm1 | Olympus CX22 microscope | 2 |
| Bogoch et al., 2016 (Bogoch *et al.*, 2016) | Laos | 104 | Adult | *O. viverrini* | Newton Nm1 | Kato Katz Method, Olympus CX21 microscope | 1 |
| Coulibaly et al., 2016(Coulibaly *et al.*, 2016a) | Grand Moutcho, Côte d'Ivoire | 226 | Paediatric | *S.hematobium/mansoni, G. intestinalis, E. histolytica/dispar,* | Newton Nm1, reversed lens CellScope | Kato Katz Method, Olympus CX21 microscope | Unclear |
| Stothard 2005 (Stothard *et al.*, 2005) | Hoima and Mayuge districts, Uganda | 685 | Paediatric | *Schistosoma spp* | Meade Readview | Kato Katz Method | 4 |
| Ephraim et al., 2015 (Ephraim *et al.*, 2015) | Central Region, Ghana | 49 | Paediatric | *Schistosoma spp* | CellScope and Foldscope | Conventional light microscopy | Unclear |
| D'Ambrosio et al., 2015 (D’Ambrosio *et al.*, 2015) | Cameroon | 33 | General | *Loa loa* | CellScope Loa | Giemsa Stained Thick Smear | 2 |
| Kamgno 2017(Kamgno *et al.*, 2017) | Okola District, Cameroon | 16 259 | General | *Loa loa* | LoaScope | Thick Smear | 2 |
| Sousa-Figueiredo et al., 2010 (Sousa-Figueiredo *et al.*, 2010) | Uganda | 1530 | Women and children | *Plasmodium spp.* | Cyscope | Thick Giemsa Smear | Unclear |
| Hassan, et al., 2010 (Hassan *et al.*, 2010) | Sinnar, Sudan | 293 | Adult | *P. falciparum* | Cyscope | Thick Giemsa Smear | 1 |
| Hassan, et al., 2011(Hassan *et al.*, 2011b) | Central Region, Sudan | 128 | Pregnant Women | *P. falciparum* | Cyscope | Thick Giemsa Smear | 1 |
| Nkruma, et al., 2011 (Nkrumah *et al.*, 2011b) | Ashanti Region, Ghana | 263 | Paediatric | *P. falciparum* | Cyscope | Thick Giemsa Smear | 2 |
| Birhanie, 2015 (Birhanie, 2016b) | Metema District, Ethiopia | 180 | General | *Plasmodium spp.* | Cyscope | Thick Giemsa Smear | 1 |

**Table 2:** Summary of diagnostic characteristics of the devices studied. CI=confidence interval; PPV=Positive predictive value; NPV=Negative predictive value; NR=Not reported.

**Table 2A:**  First-generation ball lens-mounted mobile phone devices

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Organism | Sensitivity (95%CI) | Specificity (95%CI) | PPV (95%CI) | NPV (95%CI) | Pearson R | Device |
| Bogoch et al., 2014 1](Bogoch *et al.*, 2014a) | *S. mansoni* (all infections) | 68.2 (60.1-75.5) | 64.3 (35.1-87.2) | 95.4 (89.5-98.5) | 15.8 (7.5-27.9) | NR | iPhone Add-on |
|  | *S. mansoni* (low intensity infection) | 29 (14.9-48.2) | NR | NR | NR | NR | iPhone Add-on |
|  | *S. mansoni* (high intensity infection) | 78.3 (70-85.1) | NR | NR | NR | NR | iPhone Add-on |
|  | *T. trichiura* (all infections) | 30.8 (19.9-43.4) | 71 (61.1-79.6) | 40.8 (27-55.8) | 61.2 (51.7-70.1) | NR | iPhone Add-on |
|  | *T. trichiura* (low intensity infection) | 26.3 (15.9-39.9) | NR | NR | NR | NR | iPhone Add-on |
|  | *T. trichiura* (moderate/heavy intensity infection) | 62.5 (25.9-89.9) | NR | NR | NR | NR | iPhone Add-on |
| Bogoch et al., 2013 0](Bogoch *et al.*, 2013) | STHs (all infections) | 69.4 (61.8-76) | 61.5 (40.7-79.1) | 92.3 (85.9-96) | 23.2 (14.2-35.2) | NR | iPhone Add-on |
|  | *A. lumbricoides* (all infections) | 81 (65.4-90.9) | 87.3 (80.7-91.9) | 63 (48.7-75.4) | 94.5 (89.1-97.4) | NR | iPhone Add-on |
|  | *A. lumbricoides* (low intensity infection) | 74.5 (53.4-88.1) | NR | NR | NR | NR | iPhone Add-on |
|  | *A. lumbricoides* (moderate/heavy intensityinfection) | 93.3 (66-99.7) | NR | NR | NR | NR | iPhone Add-on |
|  | *T. trichiura* (all infections) | 54.4(46.3-62.3) | 63.4 (46.9-77.4) | 85.1 (76.4-91.2) | 26.5 (18.4-36.6) | NR | iPhone Add-on |
|  | *T. trichiura* (low intensityinfection) | 43.9 (34.5-53.8) | NR | NR | NR | NR | iPhone Add-on |
|  | *T. trichiura* (moderate/heavy intensityinfection) | 76.5 (62.2-86.7) | NR | NR | NR | NR | iPhone Add-on |
|  | Hookworm (all infections) | 14.3 (8.3-23.1) | 89.1 (81-94.2) | 56 (35.3-75) | 51.7 (44.1-59.3) | NR | iPhone Add-on |

**Table 2B:** Second-generation mobile phone devices

|  |  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- | --- |
|  | Organism | Sensitivity (95%CI) | Specificity (95%CI) | PPV (95%CI) | NPV (95%CI) | Pearson R | Device |
| Ephraim et al., 2015 (Ephraim *et al.*, 2015) | *S. haematobium* | 55.9 (38.1-72.4) | 93 (66-99.7) | NR | NR | NR | Foldscope |
|  | *S. haematobium* | 67.6 (49.4-82) | 100 (74.7-100) | NR | NR | NR | CellScope |
| D'Ambrosio et al., 2015 (D’Ambrosio *et al.*, 2015) | *Loa loa* | 100 | 94 | NR | NR | 0.96 | CellScope |
| Coulibaly et al., 2016 (Coulibaly *et al.*, 2016a) | *S. mansoni* | 50 (25.4-74.6) | 99.5 (97-100) | 85.7 (42-99.2) | 97.3 (93.9-98.9) | NR | CellScope |
|  | *S. haematobium* | 35.6 (25.9-46.4) | 100 (96.6-100) | 100 (86.7-100) | 70.1 (63.1-76.3) | 0.92 | CellScope |
| 1Kamgno et al., 2017 (Kamgno *et al.*, 2017) | *Loa loa* | 92.8 | 99.7 (99.6-99.8) | 92.8 | 99.7 (99.6-99.8) | NR | LoaScope |
| Bogoch et al., 2017(Bogoch *et al.*, 2017a) | *S. haematobium* (all infection) | 100 (59.8-100) | NR | NR | NR | NR | Novel Mobile Phone Device |
|  | *S. haematobium* low intensity infection | 72.1 (56.1-84.1) | 100 (75.9-100) | 100 (86.3-100) | 57.1 (37.4-75) | NR | Novel Mobile Phone Device |
|  | *S. haematobium* (high intensity infection) | 65.7 (47.7-80.3) | NR | NR | NR | NR | Novel Mobile Phone Device |

1Threshold for positive *L. loa*microfilariae was a density below 20,000 mf per milliliter of blood

**Table 2C**: Handheld microscopes with and without mobile phone attachments

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Organism | Sensitivity (95%CI) | Specificity (95%CI) | PPV (95%CI) | NPV (95%CI) | Pearson R |
| Bogoch et al., 2014 (Bogoch *et al.*, 2014b) | *A. lumbricoides* | 99.2 | 96.4 | 98.4 | 98.2 | 0.90 |
|  | *T. trichiura* | 93.8 | 81 | 97.4 | 63 | 0.94 |
| Stothard et al., 2014 (Stothard *et al.*, 2014) | *Plasmodium spp.* | 93.5 (78.6-99.2) | 100 (82.4-100) | 100 (88.1-100) | 90.5 (69.6-98.8) | 0.98 |
| Coulibaly et al., 2016 (Coulibaly *et al.*, 2016b) | *P. falciparum* | 80.2 (73.1-85.9) | 100 (92.6-100) | 100 (96.4-100) | 65.6 (54.9-74.9) | 0.997 |
| Bogoch et al., 2016 (Bogoch *et al.*, 2016) | *Opisthorchis viverrini* | 70.6 (59.6-79.7) | 89.5 (65.5-98.2) | 96.8 (87.8-99.4) | 40.5 (26-56.7) | 0.98 |
| Bogoch et al., 2014 (Bogoch *et al.*, 2014a) | *S. mansoni* (all infections) | 84.8 (78-90.1) | 85.7 (57.2-98.2) | 98.5 (94.6-99.8) | 34.3 (19.1-52.2) | NR |
| *S. mansoni* (low infection intensity) | 45.2 (27.8-63.7) | NR | NR | NR | NR |
| *S. mansoni* (high infection intensity) | 95 (89-98) | NR | NR | NR | NR |
| *T. trichiura* (all infections) | 81.5 (70-90.1) | 93 (86.1-97.1) | 88.3 (77.4-95.2) | 88.6 (80.9-94) | NR |
| *T. trichiura* (low infection intensity) | 80.7 (67.7-89.5) | NR | NR | NR | NR |
| *T. trichiura* (moderate/heavy infection intensity) | 87.5 (46.7-99.3) | NR | NR | NR | NR |
| *S. haematobium* (all infection intensity) | 78.6 (49.2-95.3) | 91 (85.5-94.9) | 42.3 (23.4-63.1) | 98.1 (94.4-99.6) | NR |
| *S. haematobium* (low infection intensity) | 72.7 (39.3-92.7) | NR | NR | NR | NR |
| *S. haematobium* (high infection intensity) | 100 | NR | NR | NR | NR |
| Coulibaly et al., 2016 (Coulibaly *et al.*, 2016a) | *S. mansoni* | 91.7 (59.8-99.6) | 99.5 (97-100) | 91.7 (59.8-99.6) | 99.5 (97-100) | NR |
| *S. haematobium* | 81.1 (71.2-88.3) | 97.1 (92.2-99.1) | 94.8 (86.5-98.3) | 88.6 (82.1-93) | 0.98 |
| *E. histolytica/dispar* | 83.3 (36.5-99.1) | 100 (96-100) | 100 (46.3-100) | 99.1 (94.6-100) | NR |
| *G. intestinalis* | 84 (63.1-94.7) | 100 (95.2-100) | 100 (80.8-100) | 96 (89.5-98.7) | NR |
| *S. mansoni* | 85 | 96 | 95 | 88 | NR |
| Stothard et al., 2005 (Stothard *et al.*, 2005) |  |  |  |  |  |  |

**Table 2D:** CyScope

|  |  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- | --- |
|  | Organism, age group | Sensitivity (95%CI) | Specificity (95%CI) | PPV (95%CI) | NPV (95%CI) | Pearson R |
| Sousa-Figueiredo et al., 2010 (Sousa-Figueiredo *et al.*, 2010) | *P. falciparum,* Adults | 86.7 (79.3-92.2) | 38.8 (33.6-44.1) | 32.8 (27.7-38.3) | 89.4 (83.4-93.8) | NR |
|  | *P. falciparum,* Children | 92.1 (89.6-94.1) | 28.6 (22.8-34.9) | 77.1 (73.9-80.2) | 57.9 (48.3-67.1) | NR |
| Hassan et al., 2010 (Hassan *et al.*, 2010) | *P. falciparum*, Adults | 98.2 (90.6-100) | 98.3 (95.7-99.5) | 93.3 (83.8-98.2) | 99.6 (97.6-100) | NR |
| Hassan et al., 2011 (Hassan *et al.*, 2011a) | *P. falciparum*, Pregnant women | 97.6 (92.2-99.6) | 89.1 (77.5-95.9) | 94.1 (87.4-97.8) | 95.3 (85.4-99.2) | NR |
| Nkrumah et al., 2011 (Nkrumah *et al.*, 2011b) | *P. falciparum,* Children | 100 (96.6-100) | 97.4 (93.6-99.3) | 96.4 (91-99) | 100 (97.6-100) | NR |
| Birhanie, 2015 (Birhanie, 2016b) | *Plasmodium spp.,* Adults and Children | 93.8 (87.1-100) | 87.9 (79.7-96.1) | 86.4 (77.2-95.5) | 94.6 (88.7-100) | NR |