Acta Tropica 128 (2013) 182–195

Contents lists available at ScienceDirect

Acta Tropica

journal homepage: www.elsevier.com/locate/actatropica

Schistosomiasis research in Africa: how the CONTRAST alliance made it happen☆

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ARTICLE INFO

Article history:
Available online 22 August 2013

Keywords:
Africa
Control
Elimination
Schistosomiasis
Surveillance
Transmission

ABSTRACT

In May 2012, the World Health Assembly passed resolution WHA 65.21, calling upon member states to intensify schistosomiasis control and, wherever possible, to attempt transmission interruption and initiate interventions towards local elimination. It is now clear that CONTRAST – a multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa – was ahead of the game. Indeed, launched in October 2006, this 4-year project funded by the European Commission made important contributions for sustainable schistosomiasis control in the selected African countries through innovation, validation and application of new tools and locally adapted intervention strategies complementary to preventive chemotherapy. Moreover, CONTRAST articulated a research agenda for schistosomiasis elimination, framed by 10 key questions. Here, we provide a rationale for CONTRAST and discuss its overarching goal, the interrelated objectives, establishment and running of a research node network across Africa, partnership configuration and *modus operandi* of the project. A collection of 25 articles is presented that are grouped into five main themes: molecular, biological, spatial, social and cross-cutting issues pertaining to the epidemiology and control of schistosomiasis. We summarize key achievements made by CONTRAST, many of which are featured in this special issue of *Acta Tropica*. Together with an independent view put forth by an eminent schistosomiasis researcher, the current piece provides an umbrella for the 25-article collection, including current gaps and remaining research needs. Finally, post-CONTRAST initiatives are discussed and a speculative viewpoint is given on how schistosomiasis control/elimination will have evolved over the next several years.

1. Introduction

In the mid-1980s, a conceptual shift occurred in the global strategy to control schistosomiasis. There was a change in emphasis from transmission control (i.e. targeting the snail intermediate host) to morbidity control (i.e. treatment of infected people to prevent the negative health consequences of chronic infection) (WHO, 1985). At the root of this strategy change was the advent of safe and efficacious antischistosomal drugs, most importantly praziquantel (Andrews et al., 1983; Gönnert and Andrews, 1977; Groll, 1984). In the late 1980s and early 1990s, research and programmatic experience with schistosomiasis control in different parts of Africa, Brazil and China further consolidated morbidity control as the strategy of choice against schistosomiasis and other helminthiases (Anonymous, 1986, 1989; Savioli et al., 1992; WHO, 1993). By 2001, additional scientific evidence had accrued regarding the impact of regular deworming (Savioli et al., 2002). In parallel, the price of praziquantel plummeted (Fenwick et al., 2003). Hence, in May 2001, the World Health Assembly (WHA) passed resolution WHA 54.19, encouraging member states where schistosomiasis and soil-transmitted helminthiasis are endemic to regularly treat at least 75% and up to 100% of school-aged children at risk of morbidity (WHO, 2002).

From 2002 onwards, catalyzed by a US$ 30 million grant from the Bill & Melinda Gates Foundation, the Schistosomiasis Control Initiative (SCI) embarked on large-scale treatment-based control programmes against schistosomiasis (and soil-transmitted helminthiasis) in selected countries of East and West Africa (Fenwick et al., 2006, 2009). The current vision, global strategy, targets and main indicators of WHO to control schistosomiasis and

☆ CONTRAST is the acronym for "A multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa", a 4-year project funded by the European Commission.

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0001-706X/$ – see front matter © 2013 Published by Elsevier B.V.
http://dx.doi.org/10.1016/j.actatropica.2013.08.011

other neglected tropical diseases were articulated in two widely disseminated documents: "Preventive chemotherapy in human helminthiasis" and "Working to overcome the global impact of neglected tropical diseases", published in 2006 and 2010, respectively (WHO, 2006, 2010).

Colley et al. (2001), shortly after resolution WHA 54.19, expressed concern that large-scale preventive chemotherapy targeting schistosomiasis and other helminthiases might lower enthusiasm, financial commitment, teaching and training of young scientists, and general interest for basic and operational research. It was also emphasized that sustainable control of schistosomiasis requires an integrated, intersectoral approach that goes beyond deworming (Anonymous, 2004; Utzinger et al., 2003). Moreover, experience and lessons from successful schistosomiasis control efforts in Brazil, China and Egypt revealed that an accompanying research component would sustain control interventions and facilitate future progress as the challenges of control change from morbidity control to transmission containment and ultimately local elimination (Bergquist, 2008; El-Khoby et al., 2000a,b; Utzinger et al., 2005; Yuan et al., 2000).

We share Colley and colleagues' concerns and feel that continued research to innovate and validate new and improved tools and strategies that are tailored to specific social-ecological systems are required to enhance the prevention, control and elimination of schistosomiasis and other neglected tropical diseases (Gray et al., 2010; Prichard et al., 2012; Utzinger et al., 2011). Against this background, a consortium of partners from seven African and four European countries was formed that developed a specific targeted research project pertaining to schistosomiasis. Submitted under the acronym CONTRAST, the project was selected for funding by the European Commission (EC) within the Sixth Framework Programme (FP6). CONTRAST was launched in October 2006 and run for 4 years.

Here, we provide an umbrella for a 25-article collection published as a special issue in *Acta Tropica*. We discuss why and how CONTRAST fostered schistosomiasis research in Africa, including the project's overarching goal, interrelated objectives and partnership configuration. Particularly noteworthy features are the highly multidisciplinary nature of CONTRAST, the establishment and running of a network of research nodes across Africa, the large quantity of published research that goes beyond the current state, and effective means of widely disseminating key research findings through different channels and fora. Research conducted by CONTRAST focussed on four main thematic foci – molecular, biological, spatial and social – and hence the collection of articles presented here is grouped accordingly. Additionally, three cross-cutting pieces are featured, which demonstrates that CONTRAST was pushing boundaries. Finally, we briefly summarize important post-CONTRAST initiatives and offer a speculative viewpoint on how schistosomiasis control/elimination will have evolved in the coming years.

2. The CONTRAST alliance

2.1. Initial idea and project development

In March 2005, partners from three European research institutions (DBL – Institute for Health Research and Development, Denmark; Natural History Museum, United Kingdom; and Imperial College London, United Kingdom) had the idea for a new schistosomiasis research project. The partners initiated a 3-day project development workshop in response to an EC call for collaborative projects. The workshop was held in May 2005 at the Helminth Control Laboratory in Zanzibar, Tanzania and the objective was to prepare a draft proposal for the call "INCO-2005-A1.3 – Knowledge and technologies to improve control of neglected communicable diseases". In collaboration with an existing malacological/disease transmission-related network in Africa, a joint draft proposal was developed, entitled "A multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa". In the summer of 2005, a small core writing team finalized the proposal and managed to submit the full package just before 17:00 h Brussels local time on 13 September 2005.

2.2. CONTRAST – it's real!

On Thursday 19 January 2006 – on a cold and snowy day in Copenhagen – happy news reached one of us. Indeed, a letter addressed to Prof. Thomas K. Kristensen, project coordinator, signed by the head of the Community Cooperation Activities, Directorate N2 – International Scientific Cooperation at EC in Brussels, stipulated that CONTRAST was favourably evaluated by EC services with the help of independent experts. The project got an overall score of 27.625 on a scale from zero to 30. The scientific evaluation concluded that "...this is a very strong project that should provide a wealth of data on the population biology of snails and schistosomes in sub-Saharan Africa". The regional evaluation underscored the timeliness and significance of CONTRAST "...(the) project (is) highly relevant to schistosomiasis control strategies. Quality of consortium is of high quality and an SME (small-medium-sized enterprise) is involved". However, four points were offered for consideration: (i) need to clarify intellectual property rights; (ii) identify strategy for laboratory maintenance and cutting-edge status of personal in the developing country laboratories; (iii) need to address imbalance between North-South and South-South resources; and (iv) identify means to encourage females for PhD opportunities. Subsequent contract negotiations based on a slightly amended proposal were successful. Hence, CONTRAST became real. The project was awarded €2.9 million for a 48-month period and was launched in October 2006, during a 5-day kick-off workshop in Entebbe, Uganda.

2.3. Multidisciplinary alliance, goal and objectives

CONTRAST is a multidisciplinary alliance that brought together key skills and expertise from a broad range of individuals and institutions to generate new knowledge on biological, environmental, molecular and socioeconomic factors – at different spatial scales – that govern the frequency, transmission dynamics and burden of schistosomiasis in sub-Saharan Africa. The project aimed to complement ongoing, large-scale preventive chemotherapy campaigns (Fenwick et al., 2009; WHO, 2013) through innovation, validation and application of new and improved tools and strategies for effective and sustainable control of schistosomiasis. Major assets of CONTRAST are (i) the strong involvement and commitment of numerous African partners at all stages of the project – from proposal development to implementation and dissemination of key findings; and (ii) the fact that CONTRAST addresses basic needs of endemic countries to deepen the understanding of schistosomiasis transmission, in order to tailor interventions to specific social-ecological settings and make best use of limited resources for the prevention, control and local elimination.

The overarching goal of CONTRAST was to achieve sustainable schistosomiasis control in selected countries in sub-Saharan Africa. The project covered several inter-related areas. Yet, great strives were made to maintain a clear focus. CONTRAST addressed the following specific research objectives:

- to develop and implement novel molecular DNA assays based upon polymerase chain reaction (PCR) approaches, using

schistosomes and intermediate host snails collected from Central, East and West African environments;
- to investigate schistosome–snail relationships in greater detail in various social-ecological systems in West/Central and East Africa to assess and quantify disease transmission potential;
- to identify risk factors that govern the frequency and transmission dynamics of schistosomiasis and to quantify spatio-temporal disease patterns in selected eco-epidemiological settings across Africa; and
- to assess and quantify the negative effect of schistosomiasis on the daily lives of people in endemic areas, and to measure beneficial effects following local control interventions.

A fifth objective pertained to outreach and dissemination. Hence, a multi-pronged communication strategy was established, consisting of creating an interactive project website (http://www.eu-contrast.eu), regular communication among the project partners, yearly workshops and other means and fora for exchange. Particular efforts were made to harmonize study protocols and to collate all information generated by the project with data made available to project partners in open-access format. Key stakeholders, such as disease control managers, health policy makers and the broader scientific community were informed through policy briefs, presentations at national and international conferences and the peer-reviewed international literature. A special issue of *Parasitology*, entitled "Control of schistosomiasis in sub-Saharan Africa", published in November 2009 (Stothard et al., 2009a), and particularly the current special issue of *Acta Tropica*, underscore the strong outreach and dissemination efforts made by CONTRAST that go far beyond the life-span of the project.

2.4. Consortium and management

Fig. 1 shows the 14 institutions that joined forces and formed the CONTRAST consortium. Thirteen of the partner institutions are

Partner	Logo	Name	Country
1		DBL – Institute for Health Research and Development	Denmark
2	NATURAL HISTORY MUSEUM	Natural History Museum	United Kingdom
3	Swiss TPH	Swiss Tropical and Public Health Institute	Switzerland
4	Imperial College London	Imperial College London	United Kingdom
5		Makerere University	Uganda
6		University of Zambia	Zambia
7	NATIONAL MUSEUMS OF KENYA	National Museums of Kenya	Kenya
8	ISRA	Institut Sénégalais de Recherches Agricoles	Senegal
9	NIGER	Programme National de la lutte contre la Bilharziose	Niger
10		Centre for Schistosomiasis and Parasitology	Cameroon
11		Ministry of Health – Helminth Control Laboratory	Tanzania
12		National Institute of Medical Research	Tanzania
13	CORIS BioConcept	Coris Bioconcept	Belgium
14		Ministry of Health – Vector Control Division	Uganda

Fig. 1. The 14 partner institutions of a European Commission (EC)-funded multidisciplinary alliance to optimize schistosomiasis control and transmission surveillance in sub-Saharan Africa, know under the acronym CONTRAST.

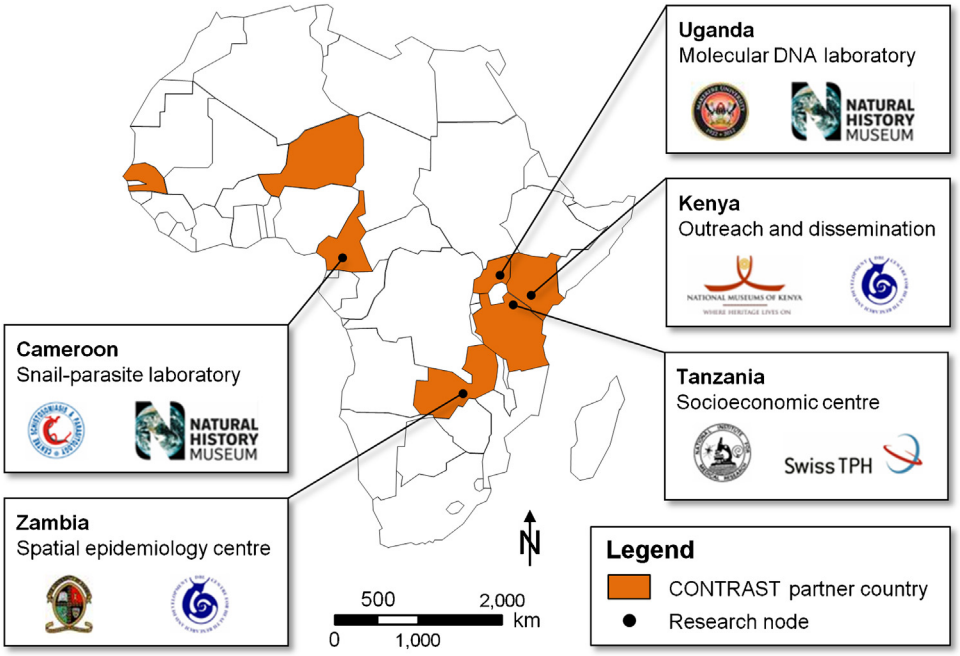

Fig. 2. Map of Africa highlighting the seven partner countries of the CONTRAST project and the five research nodes established through well thought out twinning arrangements between African and European partner institutions (for key of logos, see Fig. 1).

primarily engaged in research, teaching/training and disease control activities, whereas partner #13 (Coris Bioconcept; Belgium) is an SME. Among the research/disease control partner institutions, four are based in three European countries (Denmark, Switzerland and the United Kingdom), whereas the remaining nine partner institutions are from seven African countries (Cameroon, Kenya, Niger, Senegal, Tanzania, Uganda and Zambia) (Fig. 2). The quality of the consortium, including the mix of European and developing country partners, was considered excellent, and hence given the highest rating during the scientific evaluation. The regional evaluation too praised the high quality of the consortium, but would have wished to see an SME also from an Africa country.

DBL – Institute for Health Research and Development acted as the general coordinator of CONTRAST, and also hosted the management secretariat. Throughout the project, the coordinator was the link person between the consortium and the EC, including administrative and financial management and timely dissemination of internal communication. A scientific management committee facilitated the integration of data and new knowledge generated by the different lines of research. The scientific management committee consisted of members from eight of the collaborating institutions, arranged in well thought out twinned arrangements between African and European partners that held overall responsibilities for the specific objectives. The management committe visited at least once every 6 months either face to face or in the virtual space via telephone conferences or Skype exchanges.

2.5. Network of research nodes

A key feature of CONTRAST is the establishment and running of a strong network of research nodes across sub-Saharan Africa. As shown in Fig. 2, juxtaposed on the African collaborating partner countries, five research nodes were created, facilitated by twinning arrangements between African and European partner institutions. The consortium's rationale to invest in the establishment of such a research node network was to ascertain sustainability beyond the project duration of CONTRAST. Five specific research nodes were established with the following purposes:

- Molecular DNA laboratory (Uganda)
  - Establishing innovative molecular tools to characterize schistosomes and intermediate host snails;
- Snail-parasite laboratory (Cameroon)
  - Defining the importance of host-parasite dynamics in different eco-epidemiological settings;
- Spatial epidemiology centre (Zambia)
  - Developing new spatial models for schistosomiasis risk mapping and prediction;
- Socioeconomic centre (Tanzania)
  - Assessing new or improved local control interventions using social science approaches; and
- Outreach and dissemination (Kenya)
  - Ensuring widespread dispersal and access to information generated by the project.

2.6. Annual meetings and beyond

From the very beginning, the management committee recognized the challenge to keep a diverse set of partners and institutions well connected, in order to harness synergies, despite different backgrounds, cultures, scientific disciplines and languages spoken in the respective partner countries. Hence, annual workshops were held and some 30–40 colleagues from the 14 partner institutions convened in one of the African partner countries. With assistance from the general coordinator and his team in Denmark, the partner institutions that volunteered to organize the annual workshops took overall responsibility, including the selection of the venue, specification of the scientific programme and proposing accompanying social events. The workshops usually lasted for 5 days and allowed to debate, exchange and inquire, as well as interact less formally and laugh about CONTRAST-related research, challenges and progress. These in-person meetings turned out to be critical to review achievements made and to jointly plan future activities.

The kick-off workshop took place in October 2006 in Entebbe, Uganda. The format was adapted for the subsequent annual CONTRAST gatherings; in October 2007 in Yaoundé, Cameroon; October

Table 1
Number of citations of 12 previously published articles in a special issue of *Parasitology* with CONTRAST partners figuring as first and/or last author.[a]

Partner in CONTRAST project		No. of citations						Reference
First author	Last author	2009	2010	2011	2012	2013	Total	
Utzinger	–	0	21	24	24	16	85	Utzinger et al. (2009)
–	Utzinger	8	9	12	9	7	45	Brooker et al. (2009)
Simoonga	Kristensen	3	4	10	4	5	26	Simoonga et al. (2009)
Stothard	Utzinger	1	7	7	7	2	24	Stothard et al. (2009a)
Vounatsou	Utzinger	4	2	6	4	3	19	Vounatsou et al. (2009)
–	Utzinger	3	4	3	4	3	17	Danso-Appiah et al. (2009)
Garba	–	1	3	7	3	2	16	Garba et al. (2009)
Webster[b]	–	1	2	3	6	3	15	Webster et al. (2009)
Stothard	Rollinson	1	5	2	5	1	14	Stothard et al. (2009b)
–	Kabatereine	2	1	4	5	2	14	Fleming et al. (2009)
Rollinson	Stothard	2	2	2	1	1	8	Rollinson et al. (2009)
Tchuem Tchuenté	–	2	2	1	2	1	8	Tchuem Tchuenté and N'Goran (2009)

[a] Data obtained from ISI Web of Knowledge (http://apps.webofknowledge.com); access date: 13 September 2013.
[b] Joanne P. Webster (see Fig. 5).

2008 in Livingston, Zambia; October 2009 in Kilifi, Kenya; and, finally, September 2010 again in Kilifi.

In addition to these annual in-person get-togethers by the CONTRAST consortium, the management committee organized virtual mid-term meetings with the various partners, facilitated by telephone conferences and Skype exchanges. Key decisions and next steps were summarized and the minutes circulated to all project partners and made available through the CONTRAST website.

The management committee of CONTRAST also identified suitable national and international venues to feature the multidisciplinary alliance and present key findings to the broader scientific community. For example, in December 2011, a symposium entitled "Toward integrated control of schistosomiasis in Africa: experiences and lessons from CONTRAST" was held at the 60th American Society of Tropical Medicine and Hygiene that met in Atlanta, USA. This 90-min session was chaired by the CONTRAST coordinator and co-chaired by a colleague from Africa. Presentations pertained to the four main domains of research and were delivered by partners from Europe and Africa.

3. An exciting 25-article collection

3.1. A final burst of outreach and dissemination

The fifth objective of CONTRAST is "to collate all information generated by the project and make available to partners and global audience". This plain 16-word sentence was at the root of embarking on the current endeavour that comes to fruition with the publication of this special issue of *Acta Tropica*. We should have known that producing a special issue is no simple task, and might take more than just a couple of extra late-night sessions to have the job accomplished. Indeed, prior experience while moving along a special issue for *Parasitology* should have cautioned us (Stothard et al., 2009a). It took almost 2 years and many hundreds of E-mails and other means of communication to have the *Parasitology* special issue completed, although it was considerably leaner (19 contributions overall) than the current *Acta Tropica* special issue. Yet, the prospects of having more than 250 pages of rigorously peer-reviewed original research uniquely featuring CONTRAST in a one-stop volume was too exciting an option to be ignored. At the closing CONTRAST workshop in Kilifi in September 2010, sharing our ideas of an *Acta Tropica* special issue met with enthusiasm. Moreover, the overwhelmingly positive reactions from the scientific community regarding the aforementioned special issue of *Parasitology*, was additional motivation that tipped the balance to go for another special issue. Table 1 underscores the success and lasting impact of the previous *Parasitology* endeavour. Among the 19 articles, 12 were written by colleagues from the CONTRAST consortium (first and/or last authorship) and, as of September 2013, these 12 contributions obtained 291 citations. Hence, on average, each article has been cited more than five times per year.

Three years have passed since the closing CONTRAST workshop and we now take pleasure in this final burst of project outreach through the dissemination of a 25-article collection. While there were some issues and challenges all along the way, these were countered with solutions – some standard, others somewhat out of the box – and the project turned out to be an enormous amount of fun. Meanwhile, we are truly proud with the final product and we do hope that you – the *Acta Tropica* readership at large– are so too.

3.2. Words of thanks

Clearly, this special issue would never have seen the light of the day without the unconditional support, great guidance and tremendous leadership provided by Dr. Norbert W. Brattig. Of note, Norbert is one of four editors of *Acta Tropica*, and at the same time acts as a co-author on the current piece. Perhaps, this is somewhat unusual, yet it is a small token for our huge respect and recognition of the key role Norbert played over the past 1000+ days. Indeed, it was Norbert who kept the guest editors and the contributing authors on track, the cadre of external referees at high spirit, and hence the project afloat. We have fond memories of Norbert's E-mails, always highly focussed and cheerful, despite – or perhaps because – most of them written late at night or on weekends. Special moments were the occasional three-way Skype exchanges, usually followed by an eruption of E-mails, at times juxtaposed with powerful imagery – those authors who received special attachments might well remember. . . Norbert meticulously kept book on where things stand, pushed us whenever need be (particularly while finalizing the current piece), encouraged the authors and the referees for extra efforts, and skilfully negotiated a few extra days with the production department at Elsevier regarding the final publication date of this special issue. Yet, Norbert and Elsevier at large provided space for editorial freedom that allowed us to push boundaries. We do hope that the current overview article, an independent viewpoint kindly produced by Dr. Robert Bergquist and the exceptional collection of articles is testimony of this stimulating environment.

Second, we are deeply grateful to the 95 contributing authors for contributing some of their most exciting research to the current special issue of *Acta Tropica*. Of course, the true worth of the collection of articles published here is never really known until later – upon further scientific inquiry, confirmation or rebuttal and critical retrospective analyses. Yet, we firmly believe that the research published here will be widely read and cited, and will stimulate

additional scientific inquiry pertaining to the epidemiology and control/elimination of schistosomiasis. We kindly ask all authors, and particularly those who had submitted their chapters in the early days of the project, to accept our most humble apologize for the unordinary delay getting the full package of manuscripts ready for production. Dr. Stefanie Knopp who is now at the Natural History Museum in London, but was still at the Swiss Tropical and Public Health Institute (Swiss TPH) in Basel when she wrote her cross-cutting piece entitled "From morbidity control to transmission control: time to change tactics against helminths in Unguja Island, Zanzibar" (Knopp et al., 2013) must be singled out. Her manuscript was the first submission and the revised version was accepted for publication and became available online on 14 May 2011 – more than 2 years ago. With the final publication of this special issue, we shall get back to our early promise – a bottle of wine for Steffi! In any event, we do hope that the CONTRAST alliance, all contributing authors and the scientific community at large will agree with us that the wait was worth it.

3.3. What's in?

Table 2 gives a summary of the 25 articles that are the core of the current special issue, grouped into the four main areas of research conducted by CONTRAST, namely (i) molecular; (ii) biological; (iii) spatial; and (iv) social aspects of schistosomiasis. Additionally, there are three cross-cutting pieces, two of which go beyond the initial scope of work proposed by CONTRAST (Knopp et al., 2013; Rollinson et al., 2013). Table 2 also shows an analysis of authorship configuration, including provenance of first, last and corresponding authors, and the number of institutions contributing authors are affiliated with. Note that for authors with multiple affiliations or who changed affiliation over the course of the project, only the main or initial institution was considered.

Four issues stand out. First, the current special issue is a true CONTRAST production. Indeed, without exception, first, last and corresponding authors on all 25 articles are part of the CONTRAST alliance. Second, multiple authorship from schistosomiasis-endemic and non-endemic countries is evident throughout. The median number of authors per article is seven with a range from two (one of the two social sciences pieces; Mwanga and Lwambo, 2013) up to 25 (the population genetic structure paper pertaining to *Schistosoma mansoni* and *Schistosoma haematobium* in six African countries; Gower et al., 2013). The fact that only few authors from outside the CONTRAST network were brought in (i.e. 16 co-authorships on the total of 213 co-authorships), perhaps, is testimony of the broad range of expertise, experience and skill sets united through the CONTRAST multidisciplinary alliance. Third, with one exception (Mwanga and Lwambo, 2013), at least two and up to 10 institutions (Webster et al., 2013c) worked in partnership to produce this 25-article collection. The partnerships were by large within the CONTRAST consortium. Fourth, there is a North–South imbalance of authorship. For instance, last authors on 23 of the articles are affiliated with one of the four partner countries in Europe, whilst only two contributions had the senior author affiliated with an African institution; Uganda (Adriko et al., 2013) and Tanzania (Mwanga and Lwambo, 2013). Of particular note is the strong dominance of authors (first, last and correspondence) affiliated with an institution in the United Kingdom, especially among the molecular and biological investigations. In fact, 12 of the 25 articles have United Kingdom as main prominence (Allan et al., 2013; French et al., 2013; Gouvras et al., 2013; Gower et al., 2013; Kane et al., 2013; Levitz et al., 2013; Rollinson et al., 2013; Standley et al., 2013; Stothard et al., 2013a; Webster et al., 2013a,b,c).

Fig. 3 shows the number of co-authors per article, stratified by gender, in ascending order, grouped by the five main themes of research covered in this special issue. Note that the sequence of articles put forth in Table 2 corresponds to the order of the 25 original research contributions featured in this special issue of *Acta Tropica*. Two issues are worth highlighting. First, the collaborative nature of CONTRAST is witnessed by the number of co-authors per article. For example, 22 of the 25 articles have at least five authors. A particularly high number of co-authorship is evident in the molecular domain. These findings corroborate with a 50-year temporal analysis of authorship configuration in the core tropical medicine literature, where trends towards larger number of authors per article and more extensive partnerships have been documented (Keiser and Utzinger, 2005).

Second, female authors figure on all but two of the articles (i.e. the 2-male authored social sciences piece from Tanzania (Mwanga and Lwambo, 2013) and the first cross-cutting contribution put forth by three male European authors (Saarnak et al., 2013)). Taken together, there are a total of 213 co-authorships (shared among 95 unique authors) and females take up one third of these ($n = 71$, 33.8%). Among the 95 unique authors, there are 39 females (41.1%). With regard to gender of the first author, this is well-balanced with 12 females and 13 males. Interestingly, the four articles in the spatial domain all have females as first author. Our findings of a substantial female representation are encouraging. Prior bibliometric analyses revealed that females were strongly under-represented, for example on the editorial boards of general medicine journals, and the lack of female mentors had been highlighted as an important issue (Keiser et al., 2003). Within the CONTRAST network, there are several senior female collaborators and it is conceivable that they serve as role models for upcoming female scientists. The regional evaluation of the CONTRAST proposal emphasized the need to target females for PhD opportunities. The consortium followed this recommendation. Indeed, a considerable number of female PhD students were enrolled and they successfully completed their PhD theses. Moreover, many of these young female scientists produced first-author articles, mostly under the supervision and mentorship of senior female researchers. It is hoped that other projects will be inspired by CONTRAST and offer opportunities for cutting-edge research, teaching and training for the next generation of female scientists.

Fig. 4 shows the results from an analysis regarding the provenance of the contributing authors. Two issues are offered for discussion. First, regardless of whether all contributing authors ($n = 213$; Fig. 4A) or the 95 unique authors (Fig. 4B) are considered, researchers affiliated with institutions in the four European countries contributed most of the research (e.g. 59.2% when considering all co-authorships). Authors affiliated with research institutions in the United Kingdom were the most prolific in terms of published research, as they contributed over a third to the unique and all co-authorships. These findings underscore the key results presented in Table 2 with regard to provenance of first, last and corresponding authors.

Second, about 40% of all co-authorships are linked with an African institution. The highest percentages were observed for Tanzania (8.9%), Niger (8.5%) and Uganda (7.5%). As there were two partner institutions from both Tanzania and Uganda, significant authorship representation from these two countries was expected. In turn, Niger stands out with a relatively higher number of contributions than the other African countries.

Fig. 5 shows those 11 authors who contributed to at least five of the 25 articles published in this special issue of *Acta Tropica*. The champion is Prof. J. Russell Stothard from the Liverpool School of Tropical Medicine (initially associated with the Natural History Museum) with his name on 15 of the 25 articles. There is a slight North-South imbalance; seven authors are affiliated with one of three European counties (United Kingdom, $n = 4$; Switzerland, $n = 2$; Denmark, $n = 1$), whereas four African authors contributed to at least 5 articles, two from East Africa (Tanzania and Uganda) and

Table 2
Summary and key characteristics of the 25 articles published in this special issue of *Acta Tropica*, placing particular emphasis on number of authors and institutions and provenance of the first, last and corresponding author.

Area of research	ID	No. of authors		No. of institutions		Provenance			Reference
		All	CONTRAST	All	CONTRAST	First author	Last author	Corresponding author	
Molecular	Mol-1	6	6	2	2	United Kingdom	United Kingdom	United Kingdom	French et al. (2013)
	Mol-2	6	6	2	2	United Kingdom	United Kingdom	United Kingdom	Webster et al. (2013a)
	Mol-3	6	6	3	3	Denmark	United Kingdom	Denmark	Jørgensen et al. (2013)
	Mol-4	8	8	4	4	Uganda	Denmark	Uganda	Nyakaana et al. (2013)
	Mol-5	9	8	3	2	United Kingdom	United Kingdom	United Kingdom	Allan et al. (2013)
	Mol-6	11	11	3	3	United Kingdom	Belgium	United Kingdom	Kane et al. (2013)
	Mol-7	18	17	10	9	United Kingdom	United Kingdom	United Kingdom	Webster et al. (2013c)
	Mol-8	25	22	9	7	United Kingdom	United Kingdom	United Kingdom	Gower et al. (2013)
Biological	Bio-1	4	4	2	2	Cameroon	United Kingdom	Cameroon	Tchuem Tchuenté et al. (2013)
	Bio-2	5	5	2	2	United Kingdom	United Kingdom	United Kingdom	Levitz et al. (2013)
	Bio-3	7	7	2	2	United Kingdom	United Kingdom	United Kingdom	Webster et al. (2013b)
	Bio-4	7	7	3	3	Uganda	Uganda	Uganda	Adriko et al. (2013)
	Bio-5	9	7	4	3	United Kingdom	United Kingdom	United Kingdom	Gouvras et al. (2013)
	Bio-6	9	6	4	3	Niger	Switzerland	Niger	Garba et al. (2013b)
	Bio-7	9	8	4	3	United Kingdom	United Kingdom	United Kingdom	Stothard et al. (2013a)
	Bio-8	11	9	5	4	Niger	Switzerland	Niger	Garba et al. (2013a)
Spatial	Spa-1	6	5	2	1	Switzerland	Switzerland	Switzerland	Chammartin et al. (2013a)
	Spa-2	7	7	4	4	United Kingdom	United Kingdom	United Kingdom	Standley et al. (2013)
	Spa-3	10	10	4	4	Switzerland	Switzerland	Switzerland	Schur et al. (2013)
	Spa-4	12	12	5	5	Denmark	Denmark	Denmark	Stensgaard et al. (2013)
Social	Soc-1	2	2	1	1	Tanzania	Tanzania	Tanzania	Mwanga and Lwambo (2013)
	Soc-2	5	5	2	2	Tanzania	Switzerland	Tanzania	Mwanga et al. (2013)
Cross-cutting	Cro-1	3	3	2	2	Denmark	Denmark	Denmark	Saarnak et al. (2013)
	Cro-2	7	7	3	3	Switzerland	Switzerland	Switzerland	Knopp et al. (2013)
	Cro-3	11	9	7	5	United Kingdom	Switzerland	United Kingdom	Rollinson et al. (2013)

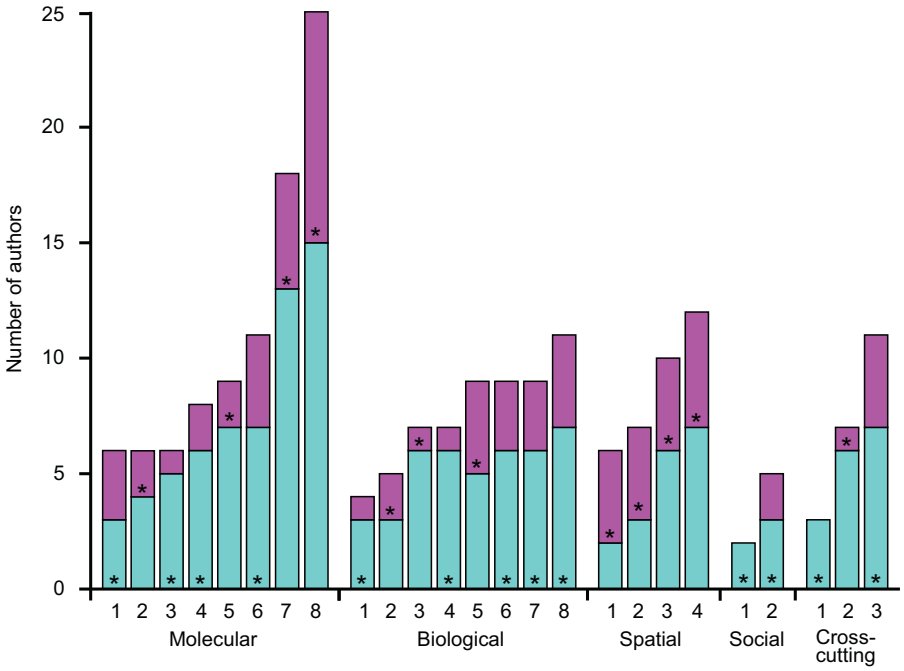

Fig. 3. Number of male (blue) and female (pink) authors on the 25 articles of this special issue of *Acta Tropica*. Articles are stratified by the five main areas of research (molecular, biological, spatial, social and cross-cutting) and follow the same order as in Table 2. Asterisks indicate gender of first author. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of the article.)

two from Central/West Africa (Cameroon and Niger). We also found some evidence for an imbalance between male and female authors who had a least five co-authorships, as there are 8 males, but only 3 females.

3.4. New molecular insight

Shortly before the conception of CONTRAST, important insights had been gained with conserved molecular sequences approaches for the rapid and effective identification of different taxa, and advancing the study of genetic diversity and evolution (Blaxter, 2004). Early on, CONTRAST established the proof-of-concept that sequence diversity within mitochondrial cytochrome oxidase subunit 1 (*cox*1) is able to differentiate between different *Bulinus* snails, the intermediate host of *S. haematobium*, at species group level (Kane et al., 2008).

Presented in this special issue of *Acta Tropica* are further tool developments, specifically the design of DNA probes for real-time PCR assays that target the sequence variation within the ribosomal intergenic spacer (IGS) of schistosome parasites that were ultimately made available in DNA 'dipstick' format (Kane et al., 2013). It has also been shown that molecular markers, particularly compensatory base changes in the secondary structure of nuclear ribosomal internal transcribed spacer (ITS), combined with more traditional methods of species identification, enhances taxonomic work (Jørgensen et al., 2013). However, since the ITS2 sequences are truncated in the terminal end, the secondary structure prediction of the loop IV is still uncertain, and thus the results presented must be interpreted with caution.

The most extensive investigations pertained to employing a DNA barcoding approach to study the genetic diversity of *S. mansoni* and *S. haematobium* in different eco-epidemiological settings, with or without chemotherapeutic pressure and at different spatial scales (Allan et al., 2013; French et al., 2013; Gower et al., 2013; Nyakaana et al., 2013; Webster et al., 2013a,c). For instance, a study in Zanzibar revealed that, despite large-scale administration of praziquantel, there was no obvious change in genetic diversity of *S. haematobium*. This observation has important ramification on drug resistance. Much higher population diversity has been documented for *S. mansoni*, particularly in East Africa, which in turn is important for understanding the local epidemiology of schistosomiasis.

An important spill-over of the DNA barcoding of schistosomes and intermediate host snails, facilitated by additional external funding, was the establishment of a schistosomiasis collection (SCAN in short) at the Natural History Museum in London (Emery et al., 2012). SCAN aims at building up a global repository of schistosomiasis-related specimens (parasites and snails), including contextual data, which in turn provides a resource and public good for new research into schistosomiasis (http://www.nhm.ac.uk/research-curation/collections/curation-groups/scan/).

3.5. Biological studies

A total of eight articles are grouped under this subheading. Of note, one of the studies operated at the interface of biological and molecular investigations (Levitz et al., 2013), whereas one of the articles discussed before under the molecular domain, also included biological tools and approaches (Allan et al., 2013). Of particular relevance are the three studies carried out in Cameroon, Niger and Senegal that assessed the efficacy of two closely spaced praziquantel treatments against *S. mansoni* and *S. haematobium* in single and mixed transmission foci (Garba et al., 2013a; Tchuem Tchuenté et al., 2013; Webster et al., 2013b). Prior research had suggested that a double treatment with praziquantel results in higher cure and egg reduction rates compared to a single treatment against the two main *Schistosoma* species encountered in Africa (N'Goran et al., 2003; Picquet et al., 1998; Utzinger et al., 2000). However, differences in study protocols and setting-specific idiosyncrasies made it difficult to generalize these findings. Hence, from the beginning, CONTRAST paid particular attention to harmonization of study protocols, as discussed elsewhere (Saarnak et al., 2013). In brief, two doses of praziquantel spaced by 3 weeks were administered and

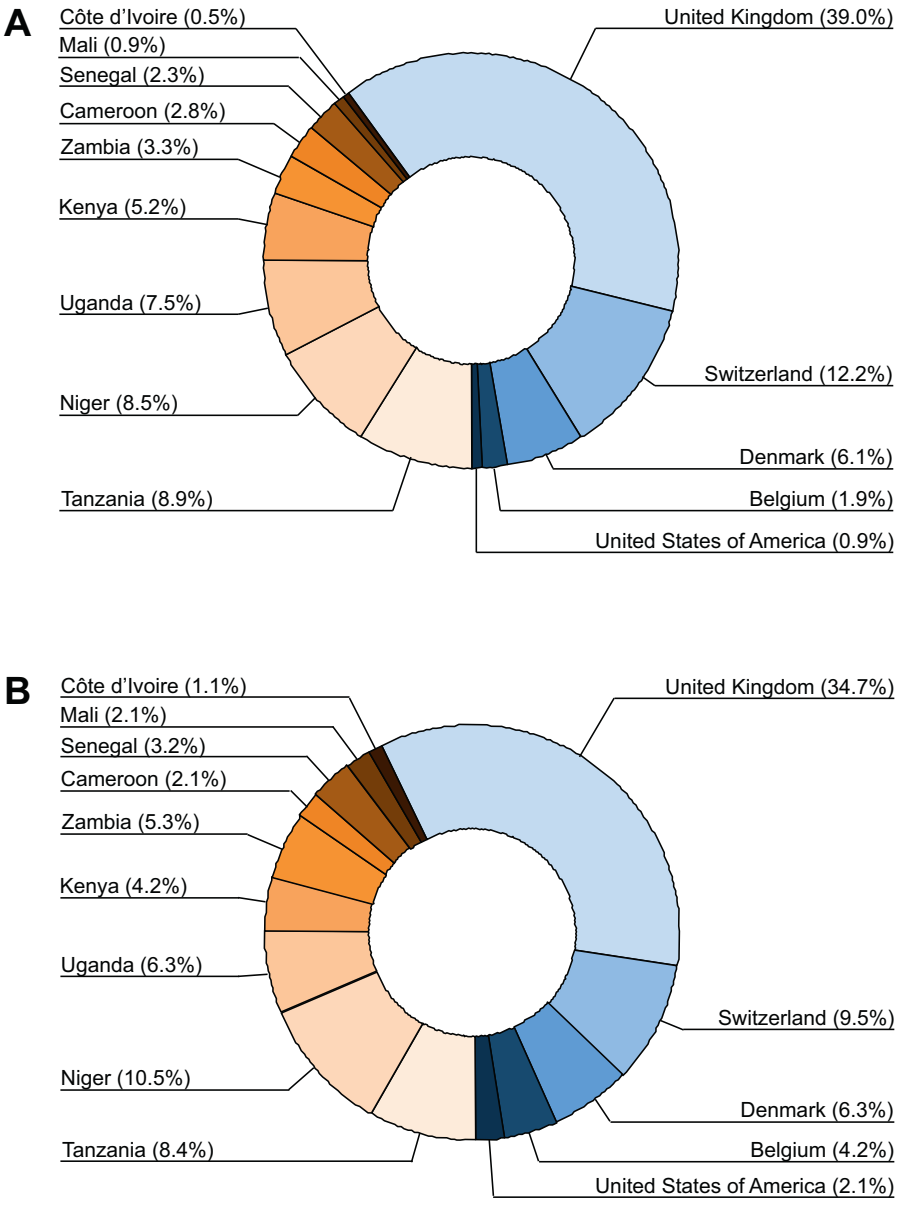

Fig. 4. Provenance of all contributing authors (A; $n = 213$) and unique authors (B; $n = 95$) of the 25-article collection published in this special issue of *Acta Tropica*.

participants were subjected to a reasonably sensitive diagnostic approach with multiple stool and urine examinations before and after praziquantel administration. The studies found that double-treatment consistently resulted in high egg reduction rates against *S. haematobium*, whereas egg reduction rates against *S. mansoni* and cure rates against both species depended on the local setting. The relatively low egg reduction rate against *S. mansoni* is of concern, and warrants further follow-up. Moreover, it will be interesting to compare the results from these CONTRAST studies with findings from a recent systematic review that assessed the incremental benefit of a second praziquantel treatment, including cost-effectiveness and externalities, such as impact on transmission (King et al., 2011).

In view of growing attention paid to the epidemiology and control of schistosomiasis in preschool-aged children (Coulibaly et al., 2013; Ekpo et al., 2012; Stothard et al., 2013b) and the lack of appropriate paediatric formulation of praziquantel (Keiser et al., 2011), one study in Niger tested a syrup formulation. It was found that praziquantel syrup is well tolerated in children aged ≤6 years. A single dose results in moderate-to-high efficacy against *S. haematobium*, whereas considerably lower cure rates were observed against *S. mansoni* (Garba et al., 2013b). Finally, a series of parasite-intermediate host snail compatibility studies, the impact of single *versus* mixed species *Schistosoma* infection on morbidity patterns in school-aged children, and parasitological and malacological studies were carried out in different parts of sub-Saharan Africa, and implications for schistosomiasis transmission and control are discussed (Adriko et al., 2013; Gouvras et al., 2013; Stothard et al., 2013a).

3.6. Spatial risk profiling

One of the most exciting achievements of CONTRAST is the establishment and running of the open-access global neglected tropical diseases (GNTD) database (http://www.gntd.org). Initially set-up as a simple Access database, it was transferred into a state-of-the art mySQL database, that is hosted at Swiss TPH. The development and architecture of the GNTD database has been described in detail elsewhere (Hürlimann et al., 2011). In brief, with an initial focus on schistosomiasis in Africa, the peer-reviewed

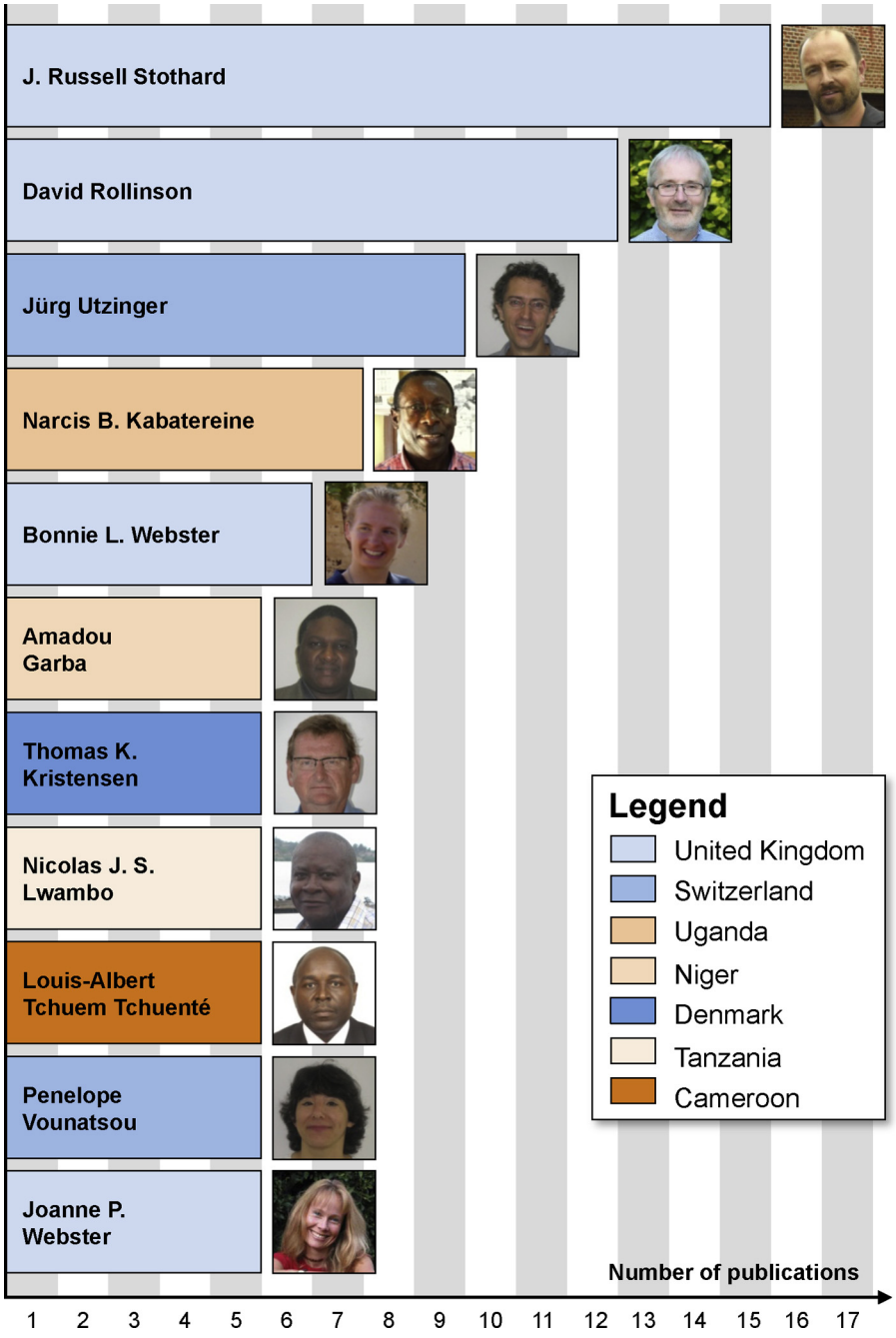

Fig. 5. List of 11 authors (name, portrait and provenance) who contributed each to five or more articles published in this special issue of *Acta Tropica*.

literature was systematically searched for schistosomiasis prevalence surveys, georeferenced and collated into the GNTD database. Standard protocols were adhered to and authors were contacted for missing information. Additionally, Ministry of Health reports and other grey literature (e.g. PhD theses, WHO reports, etc.) were examined for relevant data. Advanced Bayesian geostatistical models were employed for schistosomiasis risk profiling. An important component of this line of scientific inquiry is the identification of risk factors (behavioural, climatic, demographic, environmental and socioeconomic) that govern the spatial and temporal distribution of schistosomiasis.

In this special issue, the first smooth prevalence maps for the two main schistosome species are presented for an ensemble of 13 East African countries (Schur et al., 2013). Hence, the presented risk maps complement previous investigations focussing on West and Central Africa (Ekpo et al., 2013; Schur et al., 2011). The GNTD database, coupled with advanced Bayesian geostatistical modelling, also allows drawing inference regarding the estimated number of infected people, and hence allows calculation of treatment needs at a range of spatial scales (Schur et al., 2012). Importantly, GNTD also contains georeferenced data pertaining to intermediate host snails. Using a modelling approach (i.e. growing degree day model for *S. mansoni* and species distribution models for *Biomphalaria* intermediate hosts), large-scale environmental determinants for the distribution of the *S. mansoni–Biomphalaria* system were investigated, including a potential impact of climate change (Stensgaard et al., 2013). One contribution highlights a number of methodological issues that must be addressed, in

order to further improve schistosomiasis risk profiling. The key issues discussed are challenges of Bayesian computation using large datasets, heterogeneity of historical survey data, stationary and isotropy assumptions, and Bayesian geostatistical variable selection (Chammartin et al., 2013a).

Thanks to additional external funding, the GNTD database has been expanded, both in terms of geography (going global) and disease focus (including several other neglected tropical diseases, such as leishmaniasis and soil-transmitted helminthiasis). A series of recent publications that built upon georeferenced data contained in the GNTD database demonstrates the great utility of this platform that goes far beyond the CONTRAST project life span (Chammartin et al., 2013b,c; Karagiannis-Voules et al., 2013).

3.7. Social sciences approaches

Schistosomiasis is intimately linked to social-ecological systems (Utzinger et al., 2011), and hence the use of social sciences approaches to deepen our understanding of the epidemiology, prevention and control of the disease cannot be emphasized enough (Aagaard-Hansen et al., 2009). CONTRAST developed a participatory hygiene and sanitation transformation (PHAST) strategy that was implemented and validated in a village community in close proximity to Lake Victoria in the Ukerewe district, northwestern Tanzania. *S. mansoni* is highly endemic in this setting. More than 150 community members aged ≥15 years were interviewed for their knowledge, attitudes and practices regarding causes, transmission, signs and symptoms, and health consequences of schistosomiasis. Additionally, human–water contact activities were studied. The PHAST interventions improved people's knowledge about schistosomiasis, whereas the frequency and duration of water contacts decreased (Mwanga and Lwambo, 2013). The improved knowledge of schistosomiasis and the lower risk of becoming infected were accompanied by changing patterns of people's socioeconomic status (Mwanga et al., 2013).

These findings are important and warrant broader validation. Within the CONTRAST project, PHAST has also been implemented in Zanzibar, where *S. haematobium* is endemic, but the data have yet to be fully analyzed and interpreted. It will be interesting to compare findings from two different settings where different schistosome species predominate. Moreover, a cluster-randomized study has been launched in Zanzibar with the ultimate aim of eliminating *S. haematobium* using an integrated approach that consists of drug treatment, snail control and formative research (Knopp et al., 2012). Experience and lessons with implementing a PHAST approach can shed new light on formative research. Hence, a standard protocol for the PHAST approach should be written up and published in the peer-reviewed literature without delay.

3.8. Cross-cutting issues

Three cross-cutting pieces are included in this special issue of *Acta Tropica*. While the first one discusses CONTRAST experiences with regard to the establishment of a project database, and the harmonization of study protocols for collection, verification, sharing and dissemination of data (Saarnak et al., 2013), the other two pieces go beyond the initial scope of work proposed by CONTRAST (Knopp et al., 2013; Rollinson et al., 2013). Indeed, a comprehensive overview of past successful schistosomiasis control/elimination efforts is given, and lessons learned are articulated in a 10-question catalogue that can guide the contemporary schistosomiasis elimination agenda. Additionally, changing patterns of helminth diagnosis and control are discussed in face of repeated large-scale deworming campaigns. These two pieces were instrumental for designing the aforementioned cluster-randomized trial that is now being implemented in the frame of the Zanzibar elimination of schistosomiasis transmission (ZEST) project (Knopp et al., 2012).

4. Post-CONTRAST initiatives

CONTRAST came to an end in October 2010, and hence, it is important to briefly discuss subsequent initiatives that will hopefully keep schistosomiasis research on the radar screen. Of particular note is the Schistosomiasis Consortium for Operational Research and Evaluation (SCORE). Based at the University of Georgia Research Foundation in Athens, United States of America, SCORE was established in December 2008, facilitated by an initial 5-year grant of US$ 18.7 million from the Bill & Melinda Gates Foundation. After a series of expert consultations, SCORE initiated large-scale operational research in different African settings to answer strategic questions about how to gain and sustain schistosomiasis control in moderate and high transmission areas, and how to achieve elimination in low endemicity areas. Layered onto these multi-year investigations are the collection and storage of schistosomiasis-related specimens (Emery et al., 2012), population genetic studies on parasites and snails, and morbidity investigations on selected groups of participants (Samuels et al., 2012).

Additionally, SCORE funded a five-country study to assess the diagnostic accuracy of a point-of-care circulating cathodic antigen (POC-CCA) urine assay for rapid appraisal of the prevalence of *S. mansoni*. Study protocols were harmonized and validation of the POC-CCA urine assay was done against a rigorous diagnostic approach consisting of multiple Kato-Katz thick smear readings. It was found that a single POC-CCA applied on a urine sample is more sensitive than multiple Kato-Katz thick smears from stool samples (Colley et al., 2013). The relevance of these findings for mapping of *S. mansoni* and improved patient management has been discussed and are awaiting policy changes.

While the gaining and sustaining schistosomiasis control studies in Côte d'Ivoire, Kenya, Mozambique Niger and Tanzania, and the *S. haematobium* elimination in Zanzibar are ongoing, SCORE recently received an additional grant of US$ 3.4 million from the Bill & Melinda Gates Foundation. The secretariat is now in the process of identifying a suitable setting to establish the proof-of-concept that *S. mansoni* elimination is feasible. Experiences from CONTRAST with regard to transmission control, and particularly the 10 questions articulated in the schistosomiasis elimination agenda (Rollinson et al., 2013) are of direct relevance for SCORE.

In February 2013, it was announced that the Task Force for Global Health based in Decatur, United States of America, was awarded US$ 28.8 million from the Bill & Melinda Gates Foundation for their grant entitled "Filling the gaps – operational research to ensure the success of the neglected tropical disease control and elimination programmes". The aim of this new grant is to identify and address priority research gaps for a host of neglected tropical diseases, including schistosomiasis. Similar to the early stages of SCORE, the 'Filling the gap' team is currently in the process of convening a series of meetings with expert groups to shape the agenda of operational research on neglected tropical diseases. Lessons learned in the 4-year CONTRAST project – at molecular, biological, spatial and social domains – should be harnessed by the "Filling the gaps" project.

5. Concluding remarks and speculative viewpoint

Retrospectively, CONTRAST can be seen as a path-breaker, guiding the way from schistosomiasis morbidity control to transmission control. On one side, WHO still encourages member states to intensify their schistosomiasis control efforts as the burden remains high and the initial targets from WHA 54.19 of a treatment coverage

among school-aged children of at least 75% are far from being met (WHO, 2013). On the other side, WHO recognizes achievements made, and hence, passed resolution WHA 65.21 in May 2012 that encourages low-transmission countries to initiate interventions towards elimination.

The schistosomiasis elimination agenda, including a comprehensive review of past successful schistosomiasis control/elimination efforts featured in the current CONTRAST special issue is of pivotal importance (Rollinson et al., 2013). Let us be clear, several countries made great strives against schistosomiasis, regardless of whether the disease is due to infection with *S. haematobium*, *S. mansoni* or *S. japonicum* even before the advent and large-scale administration of praziquantel. A multifaceted, integrated and intersectoral control approach, readily adapted to the social-ecological setting and flexible enough to change over time as the challenge of control changes, are key issues identified in analysing past successful control programmes (Gray et al., 2010; Rollinson et al., 2013; Utzinger et al., 2005). Of course, socioeconomic development and modernization, and hence better housing, improved access to clean water and sanitation and strengthened health systems are essential contextual factors. In many African countries, the geographical distribution and burden of schistosomiasis still remains elusive and national control programmes have never been initiated. All efforts possible should thus be made in such circumstances, including advocacy to raise awareness and foster political will. Where control programmes have been initiated, there is a need for rigorous surveillance, so that the impact of control interventions can be documented and the control strategy adapted to the local needs. Whenever resources allow, elimination should be encouraged, and this will need integrated packages of interventions. Much remains to be done, but the prospects of gaining and sustaining schistosomiasis control and moving towards elimination have perhaps never been better. In our view, accompanying research, teaching and training, and surveillance are essential ingredients of successful schistosomiasis control/elimination programmes, so that setting-specific responses can be tailored to address issues identified through the surveillance.

Acknowledgements

We are grateful to all colleagues from the CONTRAST consortium. Their knowledge, expertise, dedication and open spirit to collaborate in this multidisciplinary alliance were key features to render this project a success. We sincerely thank the 95 contributing authors for their hard work and ultimate submission of truly exciting research. We are indebted to the many referees who gave freely of their time and know-how during the external peer-review of the submitted work. Special words of thanks go to Dr. Mirko S. Winkler and Ms. Frédérique Chammartin from the Swiss Tropical and Public Health Institute for expert help with the figures featured in the current umbrella piece. We thank the production team at Elsevier for all their efforts and for accommodating the many special wishes of the authors and particularly the editors. Taken together, this enabling environment facilitated the production of this special issue of *Acta Tropica*. The CONTRAST project was funded by the European Commission within the Sixth Framework Programme (contract no. INCO-CT-2006-03220, Specific Targeted Research Project).

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