THE CONTEXT

Although malignant diseases in children account for less than 2% of the global cancer burden [1], the past 50 years has seen the survival rate in this age group (0–14 years) almost triple, from 30% to 80%, in high income countries (HIC) [2]. A major contributing factor to this success has been the role of clinical trials, now regarded as the standard of care [3,4], despite little addition to the chemotherapeutic armamentarium against malignant diseases in childhood since the National Cancer Act was signed in the USA in 1971 [4]. However, the great majority (exceeding 80%) of children with cancer live in low and middle income countries (LMIC), as defined by the World Bank [5], where their prospects of survival are substantially less overall [6] and very poor (no better than 10%) in the most impoverished countries in which health human resources are markedly deficient (Fig. 1) [7]. It is salutary to note that the burden of cancer in the general population, measured mainly as years of life lost, is increasing faster in LMIC than in HIC [8].

But there is hope for children with cancer in LMIC. Some 2 years ago the United Nations held a high level meeting on non-communicable diseases (www.who.int/nmh/events/un_ncd_summit2011/) that led to a political declaration adopted by the General Assembly in January 2012. While this initiative is to be applauded, no specific mention was made of cancer in children and it must be recognized that attainment of the UN’s Millennium Development Goals, to be accomplished by 2015, has been slow and uneven [6].

Independently of these developments, the global community of pediatric oncology has been engaged in international collaboration for decades. In the spirit of so-called North-South cooperation, the focus has been on twinning programs, engaging partners in HIC and LMIC [6,9]. Most commonly these exercises have involved the pairing of individual institutions with an emphasis on capacity-building. There is insufficient recognition that such activities can have a ripple effect, benefiting children with other conditions [10–12]. Promulgation of a role for twinning is embodied in the Montevideo Document representing the position of the International Society of Paediatric Oncology (SIOP) [13] and in the Margarita Statement from the Latin American Society of Pediatric Oncology [14].

Additional Supporting Information may be found in the online version of this article at the publisher’s web-site.

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THE EVOLUTION OF AHOPCA

The earliest twinning program in pediatric oncology is that of the partnership between the Manuel de Jesus La Mascota Hospital in Managua, Nicaragua (the poorest country in Central America) and three institutions in Europe—initially the Pediatric Clinic of the University of Milano-Bicocca in Monza, Italy followed several years later by the San Giovanni Hospital, Bellinzona, Switzerland and the Istituto Nazionale Tumori (National Cancer Institute) in Milan, Italy [15]. This began in 1986 and was the foundational experience that led to the establishment of the Monza International School of Pediatric Hematology-Oncology (MISPHO) a decade later [16–18]. As stated in a review [19], the fundamental goal of MISPHO was capacity-building, mainly through the vehicles of training and knowledge transfer, while fostering relationships among health professionals, and between health professionals and community-based sources of support. MISPHO convened annually for the next 10 years with the support of the Cariplo Foundation of Milan, providing an educational experience for two participants from each of 14 countries in Latin America—Bolivia, Colombia, Costa Rica, Cuba, Ecuador, El Salvador, Guatemala, Honduras, Nicaragua, Paraguay, Peru, Republica Dominicana, Uruguay, and Venezuela.

Many of the participants from Central America met each other for the first time in MISPHO. Such was the enthusiasm of this geographically tightly knit group, who shared a common language (Spanish), that they formed the Asociación de Hemato-Oncología Pediátrica de Centro América (AHOPCA) in 1998. Initially this consisted of Guatemala, Honduras, Nicaragua, and Costa Rica. Panama joined in 2001 and the Dominican Republic in 2006 (Fig. 2). AHOPCA has held annual meetings, in rotation among its member countries, since its inception. Early evidence of the advantages of forming such a consortium was obtained in comparison of AHOPCA with the other members of the MISPHO family [19]. In particular, the formation of AHOPCA promoted the development of shared clinical protocols, mainly focused on cancer chemotherapy; educational programs, notably for physicians and nurses; a more integrated role for psychologists and social workers; and collaborative research. Appropriately, the establishment of AHOPCA came with the acronym AMOR (AHOPCA–MISPHO–OUTREACH–RESEARCH) [20].

PARTNERS IN PROGRESS

The main source of support for AHOPCA continues to be from the International Outreach Program (IOP) of St. Jude Children’s Research Hospital (SJCRH). The IOP began its engagement with linkages to El Salvador in 1993, subsequently Guatemala and Honduras, then to Costa Rica in 2007. Investments have been made in the provision of salary support for physician leaders and trainees, and in partial funding support for the annual regional meeting, as well as capital outlays in laboratory equipment. Providing secure incomes enables physicians to commit entirely to the development of pediatric hematology/oncology [7] that is appropriately highly centralized in the countries of AHOPCA [21]; with single national centers in the capital cities of Guatemala, Honduras, El Salvador and Nicaragua, and satellite centers so far established in Honduras and in Nicaragua.

The importance of adequate, long-term financial support cannot be over-estimated, for, although the member states of AHOPCA have public health care systems, these do not provide full funding for the centers and such monies as are available are not guaranteed.
This forces the individual countries to rely heavily on philanthropic support, channeled through foundations. For example, in Guatemala, which is the most populous country, Ayudame a Vivir—Help Me to Live—provides almost half of the operating budget of the hospital that now treats more than 400 new children with cancer per year.

Engagement of the IOP in AHOPCA has extended to other activities such as nursing education and training in laboratory technology. Additionally, the IOP facilitates real time consultations and weekly meetings through the medium of Cure4Kids [22]. A contribution of singular importance has been the development of Pediatric Oncology Networked Database (POND) that began as a simple registry and has undergone stepwise expansion to include delivery of protocol-based care, outcome evaluation and assessment of psychosocial support [23]. POND is central to the success of AHOPCA and is complemented by epidemiological and biostatistical support from the Department of Health Science of the University of Milano-Bicocca in Monza [24], and by funding and data management expertise provided for almost a decade by the Pediatric Oncology Group of Ontario (POGO). The ongoing investment by POGO ($50,000 per year for 5 years) has been matched by World Child Cancer from 2013. All of this co-operation has been rewarded by the capture of information on more than 12,000 children with cancer registered in the past decade; information demonstrated to be of high quality [25]. Moreover, these sustained investments have allowed the cadre of data managers to aspire to career progression on a well-defined ladder of advancement (Table I). Now celebrating 15 years of accomplishments, AHOPCA is well supported by a network of partners who collaborate with each other, as evidenced most recently in a formal agreement between SJCRH, POGO, and World Child Cancer. The impact of such twinning activities is well exemplified by the recorded experience over more than two decades of collaboration between Monza and Managua [12].

The Pan American Health Organization (PAHO) has been supportive of AHOPCA since 2007 in several ways, including the strengthening of campaigns for voluntary blood donation while improving the quality of blood banks and the safety of the blood supply.

### FINANCIAL HURDLES

Treatment of cancer in children in developing countries is a demonstrably cost-effective undertaking [26], yet there is limited expenditure by the governments of LMIC on clinical services for children with cancer. Within AHOPCA there is only one self-standing center for pediatric oncology; the Unidad Nacional de Oncología Pediátrica (UNOP) in Guatemala City. The other centers of excellence are within children’s hospitals [27]. In 2012 the operating budget of UNOP, 77.8 million quetzales (US $10 million), was met by its foundation (48%), the national government (44%), and SJCRH (8%). Such detailed information for clinical services devoted to children with cancer are not available for the other centers, but similar distributions of revenue from governmental and philanthropic sources are likely. The importance of parents’ organizations and local foundations cannot be over-emphasized in this regard (Supplemental Table SI).

Yet the World Health Organization (WHO) continues to advocate for universal health insurance [28]. In Mexico, AHOPCA’s neighbor to the north, the introduction in 2006 of health insurance (Seguro Popular) for those previously without coverage (50% of the population) [29] has had a striking effect on the access of children with cancer to care, though still geographically disparate, and on their adherence to treatment [30,31]. Seguro Popular achieved universal coverage in 2012, but it is too early to see a reduction in mortality. There is a clear need to advocate for such investment in the countries of AHOPCA.

In the meantime, additional external sources of funding support are being found. Among these are the My Child Matters program [7], a co-operative venture of Sanofi-Aventis and the International Union for Cancer Control that is engaged in Honduras, Panama and, most recently, Guatemala, and PAHO that provides bulk purchasing of drugs. Other forms of innovative financing, as in a regional value chain framework [32], are worthy of exploration.

### ADVANCES IN CLINICAL OUTCOMES

Despite these financial stringencies, AHOPCA has made considerable progress in improving the survival rates for children with cancer in Central America. By adopting common therapeutic

<table>
<thead>
<tr>
<th>Level</th>
<th>Job title</th>
<th>Roles and responsibilities</th>
<th>Skills required</th>
<th>Training</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Data entry technician</td>
<td>Uses forms created by others Runs pre-prepared reports to assess data completeness</td>
<td>Basic computer skills</td>
<td>Online meetings, AHOPCA meeting, daily supervision</td>
</tr>
<tr>
<td>2</td>
<td>Data manager</td>
<td>Runs quality reports to assess data completeness Adapts POND Quickforms</td>
<td>Computer skills, database experience, Excel (basic)</td>
<td>Online meetings, AHOPCA meeting, daily supervision</td>
</tr>
<tr>
<td>3</td>
<td>Senior data manager</td>
<td>Creates POND Quickforms</td>
<td>Database proficiency, Excel (intermediate), Powerpoint</td>
<td>Online meetings, AHOPCA meeting, daily supervision</td>
</tr>
<tr>
<td>4</td>
<td>Data analyst</td>
<td>Audits forms and data entry Trains and supervises others Presents data Analyzes data with some supervision</td>
<td>Basic statistics, Excel (advanced), Survival curves</td>
<td>Online meetings, AHOPCA meeting, weekly supervision</td>
</tr>
<tr>
<td>5</td>
<td>Senior data analyst</td>
<td>Audits collaborating sites Trains and supervises others Presents data Analyzes data independently</td>
<td>Intermediate statistics, working knowledge of basic functions of statistical analysis software</td>
<td>Online meetings, AHOPCA meeting, monthly supervision</td>
</tr>
</tbody>
</table>

**TABLE I. Career Progression for Data Managers in AHOPCA**

*Used with permission from St. Jude Children’s Research Hospital.*

*Pediatr Blood Cancer* DOI 10.1002/pbc
protocols (Table II), sharing experiences in their implementation and undertaking formal reviews, on a disease-by-disease basis, at annual meetings, stepwise gains have been made. Examples that highlight this progress are an event-free survival rate at 3 years of 65% in acute lymphoblastic leukemia (ALL) with five countries participating [33]; a reduction in the early mortality rate in children with acute leukemia by improving diagnosis, treatment, and the prevention of infections; design and adoption of surgical guidelines for the staging and treatment of solid tumors; earlier diagnosis of retinoblastoma resulting in a reduction in the presentation of children with extra-ocular disease, for example, from 73% to 35% in Honduras [27]; and the successful treatment of Wilms tumor [34] and Hodgkin lymphoma [35] in Nicaragua without radiotherapy. An inventory of the publications and presentations of the activities of AHOPCA are provided respectively in Appendices A and B.

ADDRESSING TREATMENT FAILURE

Although outright refusal of therapy is not common, abandonment of treatment once initiated was a prevalent problem in Central America, as it is across the developing world [36]. Indeed the frequency approached 50% in some countries of AHOPCA, making this the commonest cause of treatment failure. It has even been suggested that abandonment-sensitive survival be used as an outcome measure [37]. However, over the years of its existence, the partnership in Central America has addressed this challenge vigorously and the prevalence of abandonment has been reduced by an order of magnitude, as exemplified in El Salvador and Guatemala where the rate in 2012 was less than 2%. Among the several strategies shown to be successful in mitigating abandonment is financial aid for families, as demonstrated by the impact of Seguro Popular in Mexico.

With such success in limiting abandonment of therapy, there is a new focus in AHOPCA on treatment-related mortality [38]. Recognizing the challenges of adopting regimens of intensive chemotherapy in LMIC [39], AHOPCA has made strides in supportive care, particularly in infection control [40] and nutritional support [41]. Severe malnutrition is evident in more than 50% of children at diagnosis with cancer in Central America [42].

Relapsed disease was all too commonly fatal in children with cancer in the countries of AHOPCA, but even such challenging circumstances are offering glimpses of optimism. Children with relapsed ALL, with relatively favorable predictors (a small group—41/755 patients—who had isolated extra-medullary relapses), had a 3-year overall survival rate of 68% as reported from Guatemala, Honduras and El Salvador [43]. However, the survival rate for the group as a whole was only 28%, in the absence of hematopoietic stem cell transplantation. This exemplifies the need for good palliative and end-of-life care; a challenge as yet largely unmet in Central America, as elsewhere in the developing world. A strategy proposed by WHO [44] has four key components—appropriate policies; adequate drug availability; education of the public policymakers and health care providers; and implementation. There is a recognition of this gap in service provision within AHOPCA and an effort has begun to fill it.

IDENTIFICATION OF THE TOTAL NEED

It has been estimated that only about 20% of the population in Central America is encompassed in cancer registration [45]. With respect to childhood, the observed/expected ratio of incident cases approximates unity only in Costa Rica and then only with an assumed rate of 100 per million per year [42]. At rates of 125 and 150 per million per year (the latter equivalent to rates in HIC) the shortfall is considerable (Table III). That this is not artifactual is evident from the marked increase in accruals of patients across the consortium in the more than a decade of availability of POND (Table IV). Even more dramatically, the number of incident cases at UNOP has increased from 176, when the center opened in 2000, to 403 in 2012!

Under-diagnosis compounds the problem of under-registration [46], to which is added diagnostic delay—a proper target for education of health professionals [47].

NURSING EDUCATION

As noted by others [48], nurses comprise the largest group of health professionals world-wide and so are essential to the provision of the standard of care required to close the survival gap for children with cancer between HIC and LMIC.

The IOP at SJCRH ran an International School for Pediatric Oncology Nursing in El Salvador from 2000 to 2006, enrolling 169 nurses from 15 countries in Latin America (including 84 from the 7 countries of AHOPCA) in 3-month courses. Building on this experience, the IOP has focused on the role of the nurse educator in establishing the Latin American Center for Pediatric Oncology Nursing Education in Santiago, Chile [49]. In an initial evaluation in Guatemala [50], the effectiveness of this approach was assessed in newly hired nurses—86% participated in the chemotherapy course and 93% achieved competency; 57% participated in the course on central venous lines and 79% achieved competency. The nurses completed a mean of 26 hours of continuing education yearly and the annual direct cost of the educator was $244 per nurse.

Subsequently, a before and after study was undertaken using Joint Commission International Standards [48]. In 2006, of 20 standards only 1 was met fully and 2 partially; in 2009, there was marked progress with 16 standards met fully and 1 partially.

POST-GRADUATE MEDICAL EDUCATION

Recognizing the dire shortage of pediatric oncologists in Central America, UNOP devised a training program 10 years ago for fellows in pediatric hematology-oncology. This 3-year program was funded by SJCRH and the Office of International Affairs at the National Cancer Institute in the USA. It is based in Guatemala City.

TABLE II. Therapeutic Regimens in Shared Use in AHOPCA

<table>
<thead>
<tr>
<th>Disease</th>
<th>Year of initiation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Burkitt lymphoma</td>
<td>2000</td>
</tr>
<tr>
<td>Rhabdomyosarcoma</td>
<td>2002</td>
</tr>
<tr>
<td>Nephroblastoma</td>
<td>2004</td>
</tr>
<tr>
<td>Retinoblastoma</td>
<td>2007</td>
</tr>
<tr>
<td>Acute myeloid leukemia</td>
<td>2007</td>
</tr>
<tr>
<td>Acute promyelocytic leukemia</td>
<td>2002</td>
</tr>
<tr>
<td>Acute lymphoblastic leukemia</td>
<td>2008*</td>
</tr>
<tr>
<td>Osteosarcoma</td>
<td>2008</td>
</tr>
<tr>
<td>Malignant germ cell tumors</td>
<td>2011</td>
</tr>
<tr>
<td>Hodgkin lymphoma</td>
<td>2012</td>
</tr>
<tr>
<td>Neuroblastoma</td>
<td>2013</td>
</tr>
</tbody>
</table>

*Except Guatemala and Dominican Republic.
TABLE III. Observed/Expected Ratios of Incident Cases

<table>
<thead>
<tr>
<th>Country</th>
<th>O/E ratio A&lt;sup&gt;a&lt;/sup&gt;</th>
<th>O/E ratio B&lt;sup&gt;b&lt;/sup&gt;</th>
<th>O/E ratio C&lt;sup&gt;c&lt;/sup&gt;</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costa Rica</td>
<td>1.03</td>
<td>0.82</td>
<td>0.69</td>
</tr>
<tr>
<td>Dominican Republic&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.25</td>
<td>0.20</td>
<td>0.17</td>
</tr>
<tr>
<td>El Salvador</td>
<td>0.77</td>
<td>0.61</td>
<td>0.51</td>
</tr>
<tr>
<td>Guatemala</td>
<td>0.50</td>
<td>0.40</td>
<td>0.33</td>
</tr>
<tr>
<td>Honduras</td>
<td>0.62</td>
<td>0.49</td>
<td>0.41</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>0.94</td>
<td>0.75</td>
<td>0.63</td>
</tr>
<tr>
<td>Panama&lt;sup&gt;d&lt;/sup&gt;</td>
<td>0.35</td>
<td>0.28</td>
<td>0.23</td>
</tr>
</tbody>
</table>

<sup>a</sup>Data expanded from Sala et al. [29]; <sup>b</sup>Incident rate 100 per million per year; <sup>c</sup>Incident rate 125 per million per year; <sup>d</sup>Incident rate 150 per million per year; <sup>e</sup>Data from main center in countries with several centers.

and includes rotations in pathology, flow cytometry and radiotherapy as well as 3 months in each of SJCRH and the San Gerardo Hospital in Monza. The facility in flow cytometry is another example of a regional resource, serving El Salvador and Honduras in addition to Guatemala [51].

An additional training program opened at UNOP in January 2013. It is for fellows in intensive care focused on pediatric oncology. These post-graduate training programs are accredited by the School of Medicine of Francisco Marroquin University in Guatemala City. To date, there have been 12 graduates of the first program, all of whom have returned to their countries of origin. An additional nine fellows are in training currently (Supplemental Table SII).

HEALTH-RELATED QUALITY OF LIFE

As expressed by the Task Force on Children and Cancer of the American Cancer Society, the progress achieved in attaining 80% survival in children and adolescents and young adults with cancer can be justified only if their physical, emotional, and social quality of life are protected [52]. Put more cryptically, cure should be determined by survival adjusted for health-related quality of life (HRQL) [53]. A framework for assessing HRQL in children with cancer was the focus of an international workshop that was held in the same year as the establishment of AHOPCA [54]. The purposes of measuring HRQL are several and include a contribution to economic evaluation of health care [55]; a subject of considerable interest to governments in LMIC [56].

Spurred by these considerations, a pilot study was undertaken in Central America of the HRQL of more than 200 survivors of cancer in childhood [57]. This used Spanish language versions of the Health Utilities Index; a family of preference-based instruments that generate utility scores for use, among other purposes, in economic evaluation [58]. Self-assessments were provided by children and complemented by proxy reports from parents and physicians. Overall there was a good inter-rater agreement as determined by intra-class correlation (0.34 < ICC < 0.55). Fewer than 40% of children reported being in perfect health and more than 20% had moderate or severe disabilities [57]. This experience gives support to the recommendation by Feeny that health-related quality of life data should be regarded as a vital sign; measurement of HRQL being undertaken as part of routine clinical practice [59].

FURTHER DEVELOPMENTS

Honduras has been selected by PAHO as one of the sites for a pilot program aimed at educating primary care physicians and other community-based health care providers in the early detection of cancer in children. This is part of the PAHO strategy on Atención Integrada a las Enfermedades Prevalentes en Infancia (AIEPI)—the Integrated Management of Childhood Illness. An approach to diminish the all-too-common presentation of patients with advanced disease has been pursued in Honduras. Since 2003 a retinoblastoma-awareness initiative has been coordinated with the annual country-wide childhood vaccination program, resulting in clear gains with respect to the prevalence of extra-ocular disease [27].

Historically, there has been more than one protocol in use among the countries of AHOPCA for the treatment of ALL. It has been agreed that all countries will adopt a common protocol (see Table II). This will result in an annual accrual of more than 500 patients across the consortium. Expansion of flow cytometry in the region, with a facility in Nicaragua supported by Monza and soon to be available for Costa Rica, will make an important contribution to this development.

The IOP at SJCRH is to expand its financial investment in LMIC on a regional hub and spoke model adopted from the corporate world. The pilot project will be in Central America with UNOP in Guatemala City selected as the hub.

FUTURE CHALLENGES

By its very nature the following list is necessarily incomplete and it is not presented in an order of priority. The continuing education of groups of health professionals, other than physicians and nurses, is an obvious way to strengthen the health care team by

### Table IV. Registration of Incident Cases in AHOPCA

<table>
<thead>
<tr>
<th>Site</th>
<th>2000</th>
<th>2001</th>
<th>2002</th>
<th>2003</th>
<th>2004</th>
<th>2005</th>
<th>2006</th>
<th>2007</th>
<th>2008</th>
<th>2009</th>
<th>2010</th>
<th>2011</th>
<th>2012</th>
<th>Total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Costa Rica</td>
<td>37</td>
<td>93</td>
<td>59</td>
<td>62</td>
<td>86</td>
<td>160</td>
<td>113</td>
<td>89</td>
<td>126</td>
<td>90</td>
<td>92</td>
<td>83</td>
<td>74</td>
<td>1,164</td>
</tr>
<tr>
<td>Dominican Republic</td>
<td>0</td>
<td>15</td>
<td>4</td>
<td>6</td>
<td>39</td>
<td>84</td>
<td>75</td>
<td>75</td>
<td>74</td>
<td>91</td>
<td>86</td>
<td>85</td>
<td>94</td>
<td>728</td>
</tr>
<tr>
<td>El Salvador</td>
<td>45</td>
<td>135</td>
<td>142</td>
<td>155</td>
<td>186</td>
<td>184</td>
<td>180</td>
<td>175</td>
<td>199</td>
<td>194</td>
<td>189</td>
<td>193</td>
<td>209</td>
<td>2,186</td>
</tr>
<tr>
<td>Guatemala</td>
<td>176</td>
<td>214</td>
<td>203</td>
<td>239</td>
<td>304</td>
<td>298</td>
<td>268</td>
<td>278</td>
<td>288</td>
<td>309</td>
<td>314</td>
<td>322</td>
<td>403</td>
<td>3,616</td>
</tr>
<tr>
<td>Honduras</td>
<td>103</td>
<td>137</td>
<td>126</td>
<td>149</td>
<td>177</td>
<td>177</td>
<td>203</td>
<td>188</td>
<td>221</td>
<td>221</td>
<td>222</td>
<td>248</td>
<td>216</td>
<td>2,351</td>
</tr>
<tr>
<td>Nicaragua</td>
<td>115</td>
<td>138</td>
<td>123</td>
<td>145</td>
<td>190</td>
<td>173</td>
<td>191</td>
<td>181</td>
<td>207</td>
<td>195</td>
<td>188</td>
<td>223</td>
<td>193</td>
<td>2,262</td>
</tr>
<tr>
<td>Panama</td>
<td>51</td>
<td>45</td>
<td>54</td>
<td>22</td>
<td>27</td>
<td>40</td>
<td>42</td>
<td>42</td>
<td>44</td>
<td>46</td>
<td>50</td>
<td>33</td>
<td>31</td>
<td>527</td>
</tr>
<tr>
<td>Total</td>
<td>527</td>
<td>777</td>
<td>711</td>
<td>778</td>
<td>972</td>
<td>1,116</td>
<td>1,072</td>
<td>1,028</td>
<td>1,159</td>
<td>1,146</td>
<td>1,141</td>
<td>1,187</td>
<td>1,220</td>
<td>12,834</td>
</tr>
</tbody>
</table>

Pediatr Blood Cancer DOI 10.1002/pbc
building capacity while fostering opportunities for career development. The principles underlying the approach to transformative education, as described by Frenk et al. [60] for physicians, nurses, and public health professionals, are surely applicable to other disciplines. Prime targets are those engaged in behavioral medicine; notably psychologists, social workers and child life specialists. Clinical psychologists from Canada and the United States have participated in annual meetings of AHOPCA, to enthusiastic reception. There is a need to identify a regional leader in this discipline, akin to the model of nursing education, and similar initiatives could be undertaken for social workers and child life specialists. Having the participation of Spanish-speaking colleagues from HIC has been a major advantage. Again, having standards of practice in Spanish from the International Society of Oncology Pharmacy Practitioners is a valuable resource for clinical pharmacists in AHOPCA and elsewhere in Latin America [61]. Furthermore, with the increasing adoption of group-wide protocols and the prospect of engagement in randomized clinical trials (see below), there is an opportunity and a need to train local personnel in study design and biostatistics in a partner institution, such as the University of Milano-Bicocca.

There is a deficit in specific expertise in pediatric neuro-oncology, although there is well-defined capability in pediatric neurosurgery in San Salvador which could serve as a regional center of excellence and a nidus for training. As in other LMIC, there is an apparent paucity of incident cases of brain tumors in children in Central America. Within POND these tumors account for only 3% of registrations, ranging by country from 0.8% to 6.3%. Reasons for this “gap” may include misdiagnosis that is accentuated by a shortage of expertise and equipment in the realm of pediatric neuroradiology [6]. Members of AHOPCA have partnered with colleagues in the US and Canada to begin to design common protocols for patients with low-grade gliomas and medulloblastoma.

The defined burden of nutritional morbidity at diagnosis, coupled with the association of improved nutritional status with better outcomes in children with ALL in Guatemala, demand an approach to nutritional supplementation that is consistent, effective, well accepted, and affordable. Serial measurement of nutritional status by appropriate methods is important [62] and, like supplementation when indicated, should be an integral component of cancer care [63].

To date, the considerable experience that has been accumulated within AHOPCA, using common treatment protocols, has been from single arm studies. From this foundation the consortium is poised to undertake randomized clinical trials. This setting is strengthened by the long established cooperative framework, the availability of POND that has undergone serial expansion and can be adapted further, the complement of data managers and their envisaged career ladder, and the study design and biostatistical expertise provided by colleagues in Monza. The decision to have a uniform protocol for ALL provides a platform for the first study, in which treatment-related mortality could be a primary target for change. Already there is a substantial awareness of attendant ethical issues [64,65]. A longer-term aim could be for AHOPCA to become a member of the Children’s Oncology Group as a consortium and participate in group-wide clinical trials.

Surveillance of survivors for relapses of disease and monitoring for the early detection of late effects of treatment are part of the standard of care for children with cancer in HIC. Given the notable limitation of resources, especially of appropriately qualified health care professionals, in LMIC, the establishment and operation of such programs in AHOPCA pose considerable challenges. The difficulty is compounded by the requirement to have families return to the original centers, often traveling over long distances and at great cost, without a therapeutic intervention or other obvious immediate benefit. Developing satellite centers may provide a solution and offers the additional potential advantages of increasing the identification of incident cases and reducing the rate of abandonment, all as a result of closer proximity to the families’ homes.

Such a network of peripheral centers could also facilitate the delivery of palliative and end-of-life care; a huge problem in LMIC [66]. Agencies such as that described by Chambers et al. [67] can provide useful support and the challenge has been addressed by the International Network for Cancer Treatment and Research [68]. In 2012, it was proposed that patients in palliative care may be offered metronomic chemotherapy with low doses of agents having anti-angiogenesis activity.

There is a manifest need to focus attention on the most socio-economically disadvantaged families in whom strong cultural influences can be barriers to the provision of conventional care. Sociological studies of these challenges should include determinations of success as valued by such families. Models of care can then be developed, with community involvement, to better meet the particular needs in these circumstances.

Attracting further support from national governments, especially in the form of sustainable funding, remains a major hurdle to be overcome. Effective advocacy commonly depends on the involvement of non-health professional groups with a vested interest in the well-being of children with cancer and their families. The International Confederation of Childhood Cancer Parent Organizations (ICCCPO) is such an entity. It was established some 20 years ago and, at present, has 86 member countries. ICCCPO is aligned closely with SIOP and is especially influential in LMIC.

CONCLUSION

The launch of the World Oncology Forum during the 30th meeting of the European School of Oncology in 2012 was a response to the recognition that the war on cancer is far from won [69], and led to an impassioned appeal to world leaders on World Cancer Day this year (February 4, 2013) to STOP CANCER NOW [70]! The community of pediatric oncology has been in the vanguard of the war for decades, serving as a winning example, and should continue to play such a leading role.

Participation in AHOPCA has been a rewarding experience for a large number of individuals and several partner institutions. In various ways, this Central American consortium is a regional example of the new reality of pluralism, as described by Frenk and Moon [71]. As these authors contend, it is important to achieve consensus on the core functions of each major actor; in this instance the partners in AHOPCA. This has been accomplished in a spirit of collegiality and equity, adhering to the principles of clarity and transparency.

The winners are of course the children with cancer and their families. On their behalf much has been accomplished and much remains to be done. A strong foundation has been built, successes have been enjoyed and new achievable goals have been defined. It is our hope that this review will serve as encouragement to others.
engaged in twinning program in pediatric oncology, for these are obviously a mechanism for improving the health outcomes for children with cancer worldwide.

REFERENCES


50. Metzger M, Howard SC, Fu LC, et al. Improving the outcome of childhood acute lymphoblastic leukemia in countries with


APPENDIX B: ABSTRACTS


