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**Agenda item 10**

**Development of Strategy 2017 - 2021:  
Strategic Option – Reproductive, Maternal,  
Newborn and Child Health (RMNCH)**

**For Information**  **For Review and Advice**  **For Decision**

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## 1 Executive summary

Significant progress was made in women's and children's health between 1990 and 2015, reducing maternal, child, and newborn mortality in low-income countries by approximately 50%. However, the Millennium Development Goals (MDG 4: reducing under-five mortality by two-thirds and MDG 5: maternal mortality by three-quarters) were not achieved. This is referred to as the unfinished business of the global health MDG agenda.

New ambitions have been set by the Sustainable Development Goals to be accomplished by 2030 (SDG 3.1: reduce the global maternal mortality ratio to less than 70 per 100,000 live births and SDG 3.2: end preventable deaths of newborns and children under five years of age, with all countries aiming to reduce neonatal mortality to at least as low as 12 per 1,000 live births and under five mortality to at least as low as 25 per 1,000 live births) requiring a further reduction of approximately 70%. In addition, reproductive health has been added to the global health agenda (SDG 5.6: ensure universal access to sexual and reproductive health and reproductive rights). To reach these ambitious goals by 2030, the global health community needs to accelerate its efforts.

Since its creation, UNITAID has conducted a large number of projects aiming at improving access to health products for women and children. For instance paediatric formulations or children-adapted diagnostics for HIV/AIDS, TB, and malaria have been a clear area of focus for UNITAID. In the context of developing its strategy for 2017 to 2021, UNITAID has assessed the need for, and the probability of success of, an intervention into women's and children's health beyond HIV/AIDS, TB, and malaria. The analysis focused on issues disproportionately affecting women, children, and newborns in low-income settings. Starting from global goals, it included an assessment of public health need, access to commodities, and innovations, as well as the partner and funding landscape – to identify if there are areas which could potentially be interesting for UNITAID to further explore.

The public health need in women's and children's health is still very high. In 2015, the WHO estimated that more than 500,000 women aged 15 to 69 died from maternal conditions and cervical cancer. Almost half of deaths among children under five were caused by fever conditions (around 2 million deaths). Finally, the vast majority (94%) of 2.3 million newborn deaths were caused by three conditions: birth complications, birth asphyxia, and neonatal sepsis. In conclusion, most women and children in low-income countries are dying from a few conditions only – which are often both preventable and treatable.

To advance towards global goals, these main mortality drivers need to be addressed and coverage of and access to existing commodities and innovations are a key component of the response.

- For existing commodities, the UN Commission on Life-Saving Commodities (UNCoLSC) has conducted extensive work to address health issues and main mortality drivers for Reproductive, Maternal, Newborn and Child Health (RMNCH). A list of 13 life-saving commodities has been defined and recommendations provided to overcome identified barriers and improve access. Progress has been made, but major bottlenecks remain.
- For innovations, there is a rich and promising innovation pipeline with more than 200 relevant innovations, including innovations at the final stage of development for most conditions. The Innovation Working Group (IWG), established in 2010, works to ensure a robust pipeline of innovations. The innovation marketplace established under the leadership of Grand Challenges Canada, is working to transition 20 innovations to scale in a sustainable manner by 2020.

For UNITAID, the opportunity to bring potential interventions to scale is critical. Therefore it is essential to understand the partner and funding landscape, in particular since partners in the health of women and children may differ from the ones UNITAID is accustomed to working with. Mobilization of the global health community has grown over the past years and is now strong, with many partners involved. However, some elements of the landscape are still not fully defined, as the community is transitioning out of the MDG into the SDG era. International support is mainly directed to the 49 lowest-income countries, but the structure of international funding is more fragmented than in HIV/AIDS, TB, and malaria. In addition, key basic drugs are generally funded by domestic rather than international sources, because they are relatively inexpensive. This means that there are relatively few initiatives to leverage global market shaping. This relative lack of global coordination has to be taken into account when considering scalability and potential impact of market-related approaches. In the future, current UNITAID partners such as the Global Fund and PEPFAR are expected to get more involved, particularly in areas adjacent to HIV/AIDS.

Based on this analysis, UNITAID might consider further exploring some areas within women's and children's health and monitoring others. Existing commodities and innovations are both receiving extensive attention by the global health community already. Both should be closely monitored in the future for potential opportunities. UNITAID, as a new player in the field, should initially focus on areas which allow integration into the current delivery channels for HIV/AIDS, TB, and malaria. This approach would enable UNITAID to build on its existing competencies and relationships with partners and would complement current investments in HIV/AIDS, TB, and malaria. During consultations with partners, two areas stood out as potentially interesting: fever conditions and cervical cancer. Fever conditions are closely related to malaria, and cervical cancer is a major co-infection with HIV/AIDS. There may be other areas, but these provide an example of something with which UNITAID could consider getting involved. A preliminary analysis has been conducted and would need to be refined before being presented to the Board for endorsement of these as potential Areas for Intervention.

This document will look at the public health need for, and the challenges and opportunities faced in, reaching the global goals to improve women's and children's health, with a particular focus on RMNCH. Analysis has been performed to assess whether RMNCH is a potential area of interest for UNITAID moving forward, but does not include areas for intervention at this time.

## Introduction

UNITAID has been very active in the field of women's and children's health within HIV/AIDS, TB, and malaria since the early days. Today, nearly 35% of UNITAID's portfolio is dedicated to projects to improve the health of children in the context of HIV/AIDS, TB, and malaria – either with paediatric formulations, or specific diagnostic tools – and to improve the health of pregnant women exposed to malaria.

Currently, UNITAID works with partners in HIV/AIDS (co-infections), TB, and malaria. In the context of a potential expansion into a new area, and given the specificity of UNITAID's business model – in particular the fact that UNITAID relies on partners to scale up its projects – it is critical to understand the partner landscape. Solid understanding of the funding landscape (key sources of funding for commodities and main procurement channels) will be a critical element driving the probability of success for UNITAID in a new field. A dedicated section of this document focuses on assessing the need for UNITAID's intervention and the conditions for success.

## 2 Analysis of the context

This chapter provides an overview of the global goals and public health need in women's and children's health. Global goals are assessed by the progress made throughout the Millennium Development Goals (MDG) period and the ambitions set by the Sustainable Development Goals (SDG) targets until 2030. Public health need is described by looking at reproductive health and at the death burden and main mortality drivers for women, children and newborns.

### 2.1 Global goals

Significant progress was made in reducing maternal, newborn, and child mortality between 1990 and 2015, reducing death burden in low-income countries (LIC) by approximately 50%, as shown in figure 1. Maternal mortality declined by 51%<sup>1</sup> (from 1,020 deaths per 100,000 live births in 1990 to 495 deaths in 2015). Under-five mortality declined by 59%<sup>2</sup> (from 187 deaths per 1,000 live births in 1990 to 76 in 2015). Within that, neonatal mortality<sup>3</sup> declined by 45% (from 49 deaths per 1,000 live births in 1990 to 27 deaths in 2015).

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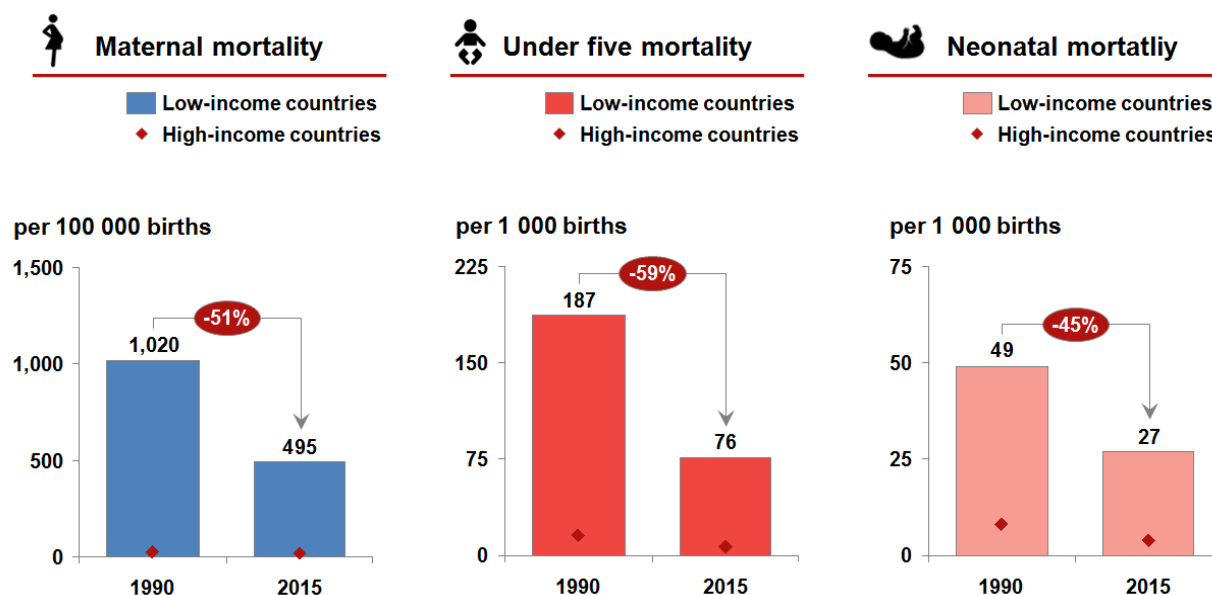
<sup>1</sup> Every Women and Every Child – The Global strategy for women's, children's and adolescents' health (2016-2030)

([http://globalstrategy.everywomaneverychild.org/pdf/EWEC\\_globalstrategyreport\\_200915\\_FINAL\\_WEB.pdf](http://globalstrategy.everywomaneverychild.org/pdf/EWEC_globalstrategyreport_200915_FINAL_WEB.pdf))

<sup>2</sup> WHO data, children under 5 mortality rate, 1990-2015

<sup>3</sup> Neonatal mortality refers to children dying in the first 28 days of life

**Figure 1: Maternal, neonatal, and under-five mortality evolution: 1990 to 2015<sup>4</sup>**

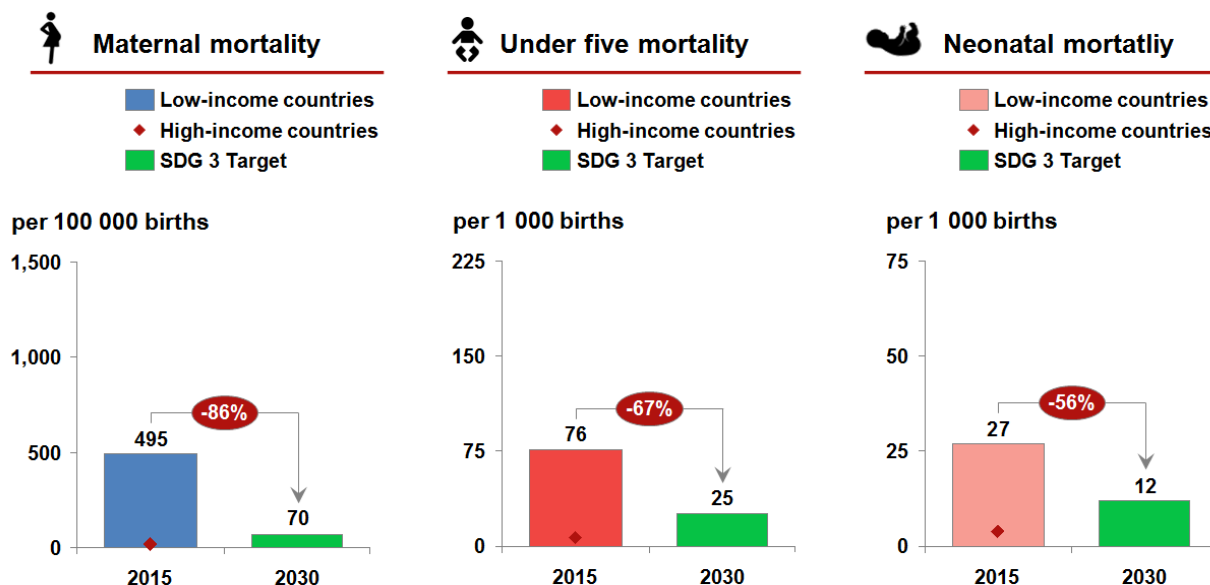


Despite these achievements, the Millennium Development Goals (MDGs) – MDG 4: *Reducing under-five mortality rate by two-thirds* and MDG 5: *Reducing maternal mortality rate by three-quarters* – were not accomplished. This is referred to as the unfinished business of the global health MDG agenda.

Figure 2 shows the Sustainable Development Goals (SDGs) for maternal, newborn, and child mortality for the period until 2030. Targets of SDG 3 include a maternal mortality ratio of less than 70 per 100,000 live births (requires a further reduction by 86% from 495 deaths in 2015), an under-five mortality ratio at least as low as 25 per 1,000 live births (requires further reduction by 67% from 76 deaths in 2015), and a neonatal mortality ratio at least as low as 12 per 1,000 live births (requires further reduction by 56% from 27 deaths in 2015).

<sup>4</sup> World Bank data on Maternal Mortality rate (<http://data.worldbank.org/indicator/SH.STA.MMRT>) and Newborn mortality rate (<http://data.worldbank.org/indicator/SH.DYN.NMRT>), Millennium Development Goals, Sustainable Development Goals

**Figure 2: Maternal, neonatal, and under-five mortality goals until 2030**



In addition, SDG 3 and SDG 5 include a target on reproductive health – to ensure by 2030 universal access to sexual and reproductive health care services, including for family planning, information and education, and the integration of reproductive health into national strategies and programmes. In the context of reproductive health, SDG 5 is closely linked to SDG 3. However, there is no quantitative target defined for reproductive health.<sup>5</sup>

**Key messages:**

Significant progress has been made in the past 25 years, but MDG targets were not achieved. This is referred to as the unfinished business of the MDG agenda and highlighted as an important focus area for the global health community.

The Sustainable Development Goals set ambitious targets until 2030. To reach these targets, the global health community needs to accelerate its efforts.

<sup>5</sup> Sustainable Development Goals (<https://sustainabledevelopment.un.org/sdgs>)



## 2.2 Public health need

### 2.2.1 Reproductive health

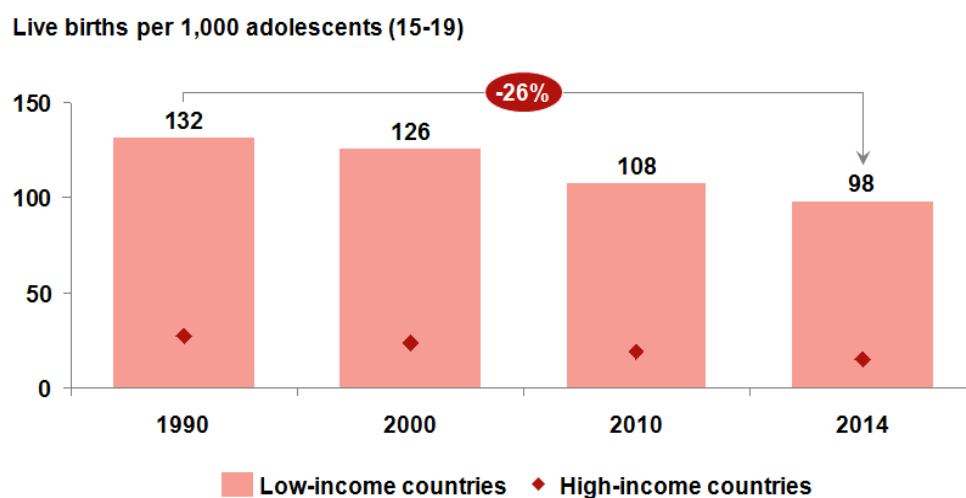
As defined by WHO, Reproductive Health implies that "people are able to have a responsible, satisfying and safe sex life and that they have the capability to reproduce and the freedom to decide if, when and how often to do so".<sup>6</sup> Its importance, in particular in terms of access to family planning, is now well recognized by the global health community. Key indicators for public health need are adolescent birth rate and access to family planning.

Women giving birth under age 20 are a particular area of focus for the global health community as they face higher risks of maternal mortality, and have lower chances of receiving education and obtaining employment:

- Adolescents aged 15 through 19 are twice as likely to die during pregnancy or childbirth as those over age 20<sup>7</sup>
- Girls under age 15 are five times more likely to die during pregnancy or childbirth<sup>8</sup>
- Children born to adolescent mothers face higher risks of mortality, undernourishment, and dropping out of school than their peers

The adolescent birth rate – measured in live births per 1,000 adolescent girls – decreased by 26% in low-income countries between 1990 and 2014 (from 132 in 1990 to 98 in 2014), as illustrated in figure 3. Nevertheless, the global health community recognizes that there is still a long way to go to reach 'acceptable' levels of birth rates.<sup>9</sup>

**Figure 3: Adolescent birth rate in low-income and high-income countries<sup>10</sup>**



<sup>6</sup> WHO topics – Reproductive Health ([http://www.who.int/topics/reproductive\\_health/en/](http://www.who.int/topics/reproductive_health/en/))

<sup>7</sup> Every Women and Every Child – The Global strategy for women's, children's and adolescents' Health (2016-2030)

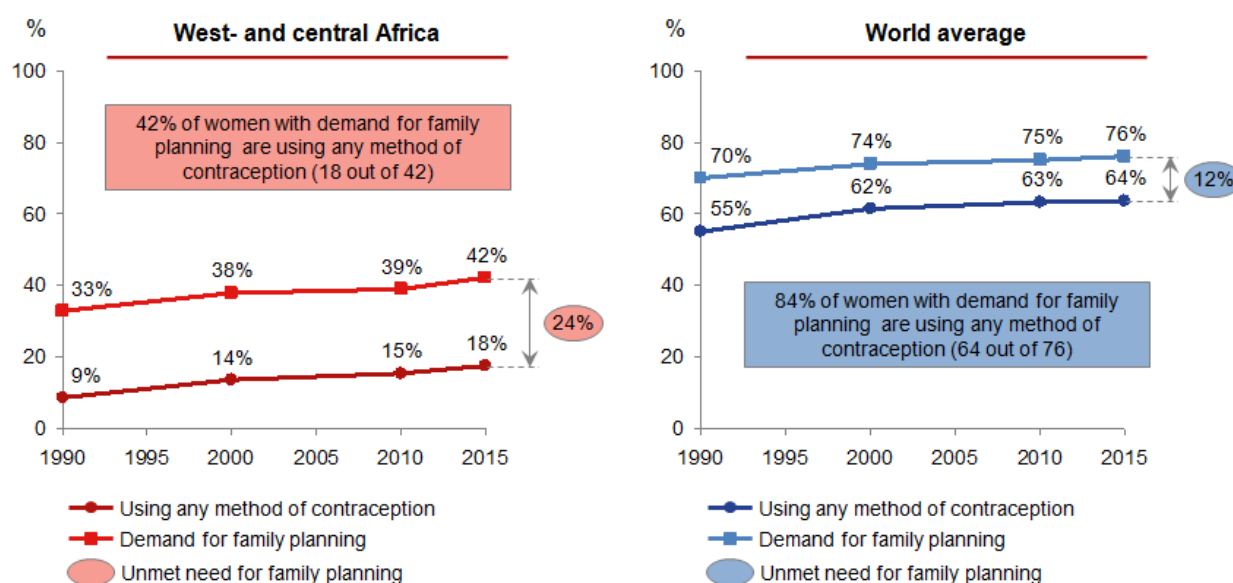
<sup>8</sup> Every Women and Every Child – The Global strategy for women's, children's and adolescents' Health (2016-2030)

<sup>9</sup> Every Women and Every Child – The Global strategy for women's, children's and adolescents' Health (2016-2030)

<sup>10</sup> Universal access to Reproductive Health – Progress & challenges – UNFPA – January 2016

To further decrease adolescent birth rates and unintended pregnancies and pregnancies at short intervals, access to family planning tools and methods of contraception needs to be improved. In the absence of global data, Figure 4 illustrates the situation in West and Central African countries compared with the world average. In general, the demand for family planning is much lower in West and Central African countries compared with the world average (42% versus 76%). Also, the contraceptive prevalence rate – using any method of contraception – is dramatically lower in these countries compared with the world average (18% versus 64%). In addition, the rate of unmet need for family planning is much higher in West and Central African countries than globally (24% versus 12%).<sup>11</sup>

**Figure 4: Proportion of women aged 15-49, married or in a civil union, with a demand for family planning, using any method of contraception, and having an unmet need, by region, 1990-2015<sup>12</sup>**



### 2.2.2 Main causes of death for women aged 15 to 69

The World Health Organization (WHO) estimated that 9.7 million women aged between 15 and 69 years died worldwide in 2015.<sup>13</sup> Some of the main drivers of mortality affect only women, for example maternal conditions or cervical cancer, and in particular women in low-income settings:

- 686,000 women died from HIV/AIDS, the largest single cause of death after ischaemic heart disease and strokes, almost 80% in Africa. It was estimated that 192,000 women died from tuberculosis in 2015, but the latest WHO estimates are even higher (480,000).<sup>14</sup>

<sup>11</sup> Universal access to Reproductive Health – Progress & challenges – UNFPA – January 2016

<sup>12</sup> Note: Numbers are rounded

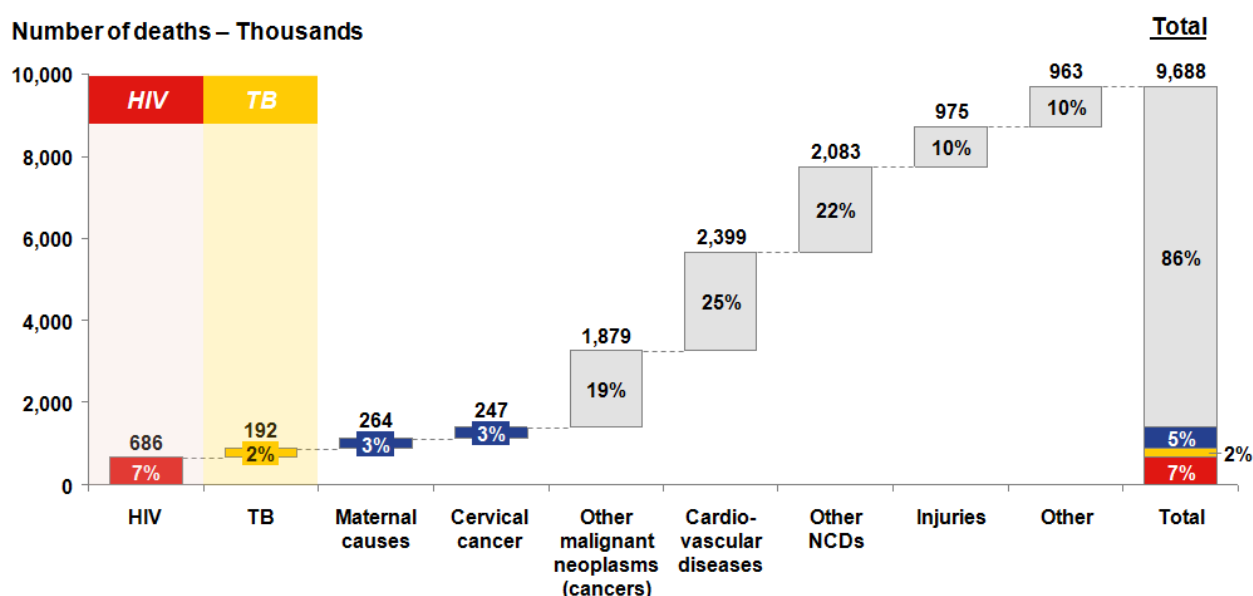
<sup>13</sup> WHO – Global health estimates summary tables, 2013 (Estimates for 2015)

<sup>14</sup> WHO – Tuberculosis in women

([http://www.who.int/tb/publications/tb\\_women\\_factsheet\\_251013.pdf](http://www.who.int/tb/publications/tb_women_factsheet_251013.pdf))

- 264,000 died from maternal conditions. It is estimated that virtually all (99%) of maternal deaths occur in developing countries – nearly 60% in Africa.<sup>15</sup> Four conditions drive 60% of mortality: maternal hemorrhage; hypertensive disorders; maternal sepsis; and unsafe abortion.
- 247,000 died from cervical cancer, approximately 85% of which occur in less developed regions.<sup>16</sup> Cervical cancer is a co-infection with HIV, it more often affects women living with HIV, and women living with HIV progress more rapidly in the disease than others.
- Other main causes of death are a very large number of conditions which in most cases affect both men and women (for instance cardiovascular diseases and injuries).

**Figure 5: Estimated number of death by cause – Women aged 15 to 69 (World 2015)<sup>17</sup>**



### 2.2.3 Main causes of death for children under five (excluding newborns)

WHO estimated that 4 million children under five years of age, excluding newborns, died worldwide in 2015. Almost half of the death burden is caused by fever conditions. In low-income countries the share of fever-related death is even higher – for example, in Africa, 55% of death burden in children under five is caused by fever conditions: malaria, diarrhoeal diseases, respiratory infections (mainly pneumonia).<sup>18</sup> Tuberculosis death in kids are often reported as part of HIV deaths and have recently also been re-estimated by WHO at much higher levels.

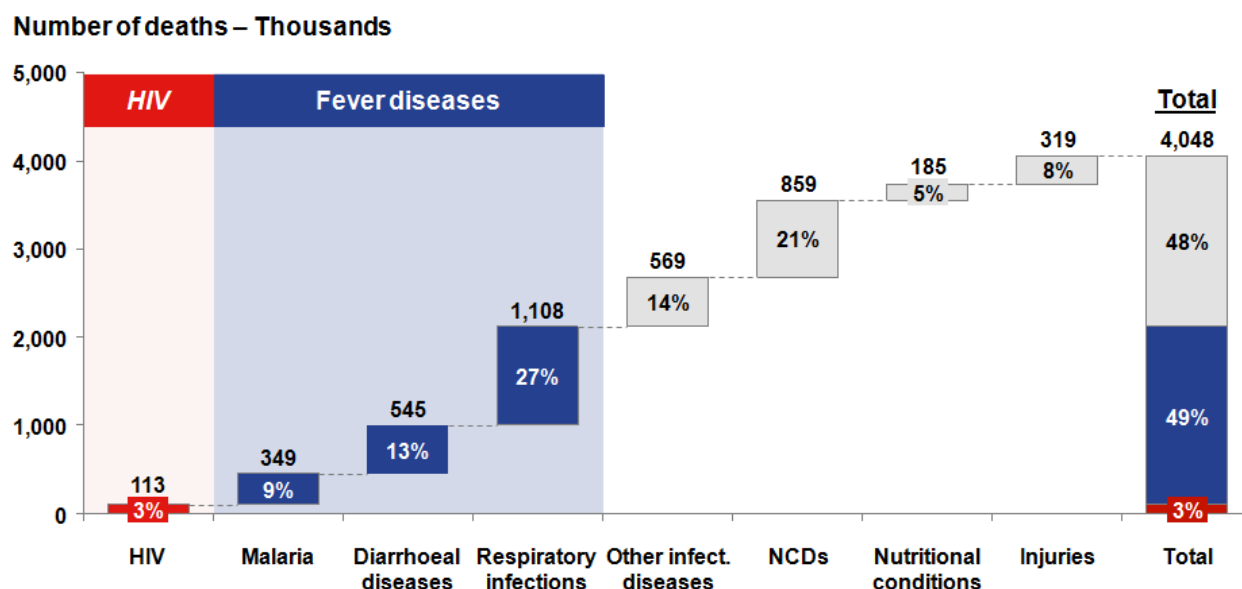
<sup>15</sup> WHO – Maternal mortality (<http://www.who.int/mediacentre/factsheets/fs348/en/>) – Developing countries as defined by the UN country classifications, mainly Africa, East Asia, South Asia, Western Asia, and Latin America and the Caribbean ([http://www.un.org/en/development/desa/policy/wesp/wesp\\_current/2012country\\_class.pdf](http://www.un.org/en/development/desa/policy/wesp/wesp_current/2012country_class.pdf))

<sup>16</sup> WHO – Vaccines and diseases (<http://www.who.int/immunization/diseases/hpv/en/>) – Less developed regions as defined by Globocan are: all regions of Africa, Asia (excluding Japan), Latin America and the Caribbean, Melanesia, Micronesia and Polynesia

<sup>17</sup> WHO – Global health estimates summary tables, 2013 (Estimates for 2015)

<sup>18</sup> WHO – Global health estimates summary tables, 2013 (Estimates for 2015); Note: Estimates for Tuberculosis have been adjusted by WHO in 2014, when it has been reported that 140,000 children died from Tuberculosis, but no specific number has been published for children under five.

**Figure 6: Estimated number of death by cause – Children under five, excluding newborns (World 2015)<sup>19</sup>**



#### 2.2.4 Main causes of death for newborns<sup>20</sup>

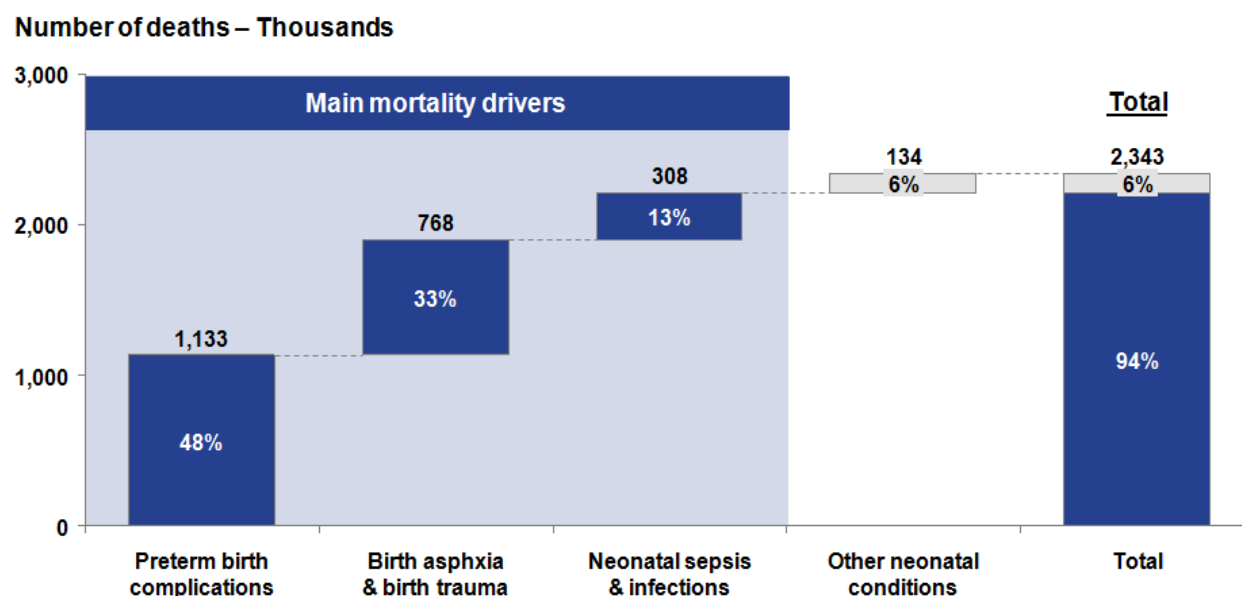
WHO estimated that 2.3 million newborns died within the first 28 days of life worldwide in 2015. The vast majority of deaths (94%) were caused by three conditions: preterm birth complications; birth asphyxia and birth trauma; and neonatal sepsis and infections. In general, virtually all newborn deaths (99%) occur in low- and middle-income countries, especially in Africa and South Asia.<sup>21</sup>

<sup>19</sup> Other infectious diseases include STDs, childhood-cluster diseases, meningitis, encephalitis, acute HCV and HBV, other parasite and vector diseases, and intestinal infections

<sup>20</sup> Every Women and Every Child – The Global strategy for women's, children's and adolescents' health (2016-2030)

<sup>21</sup> WHO – The Partnership for Maternal and, Newborn and Child health ([http://www.who.int/pmnch/media/press\\_materials/fs/fs\\_newborndealth\\_illness/en/](http://www.who.int/pmnch/media/press_materials/fs/fs_newborndealth_illness/en/))

**Figure 7: Estimated number of death by cause – Newborns in the first 28 days of life (World 2015)<sup>22</sup>**



**Key messages:**

Significant progress was made in maternal and child health between 1990 and 2015, reducing death burden by approximately 50%. However, the MDGs 4 and 5 (reducing maternal mortality rate by three-quarters and under-five mortality by two-thirds) were not achieved.

Despite this progress, public health need is still very high and death burden is driven by a limited number of conditions:

- In 2015, more than 500,000 women aged 15 to 69 died from female-specific conditions, disproportionately affecting women in low-income settings. Deaths were listed as maternal causes (264,000 deaths) and cervical cancer (247,000 deaths).
- Moreover, approximately 4.0 million children under five (excluding newborns) died in 2015 – almost half from fever related conditions.
- In addition, more than 2.3 million newborns died within their first 28 days of life in 2015 – with the vast majority of deaths (94%) caused by three conditions: preterm birth complications, birth asphyxia, and neonatal sepsis.

<sup>22</sup> WHO – Global health estimates summary tables, 2013 (Estimates for 2015) and EWEC, the global strategy for women's children's and adolescents' health (2016-2030)

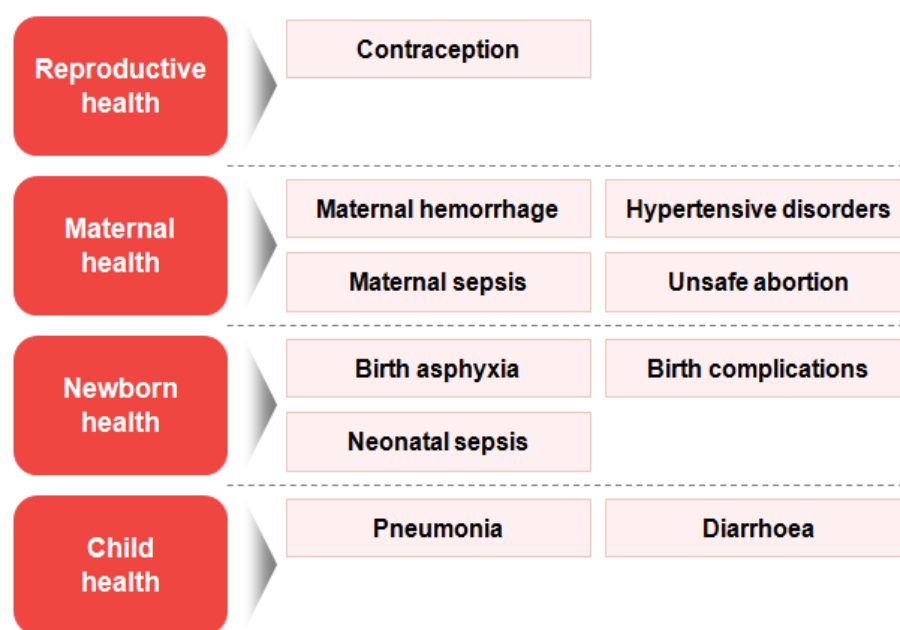
### 3 Tools to prevent, diagnose, and treat the main causes of death

This chapter looks at the health products available to prevent, diagnose, and treat the previously identified main causes of death (maternal conditions, fever conditions, conditions driving newborn deaths) and for contraception. For this analysis, products have been grouped along two dimensions:

- Development status: which products are available now (existing commodities), and which are yet to be developed (innovation pipeline)
- Categories / Causes of death: which causes of death they address, for instance, maternal conditions, fever conditions, newborn main conditions, or contraception for reproductive health

The first section looks at existing commodities for RMNCH, and in particular those analyzed by the UN Commission on Life-Saving Commodities. The second section looks at the innovation pipeline for all conditions.

**Figure 8: Major categories for RMNCH**



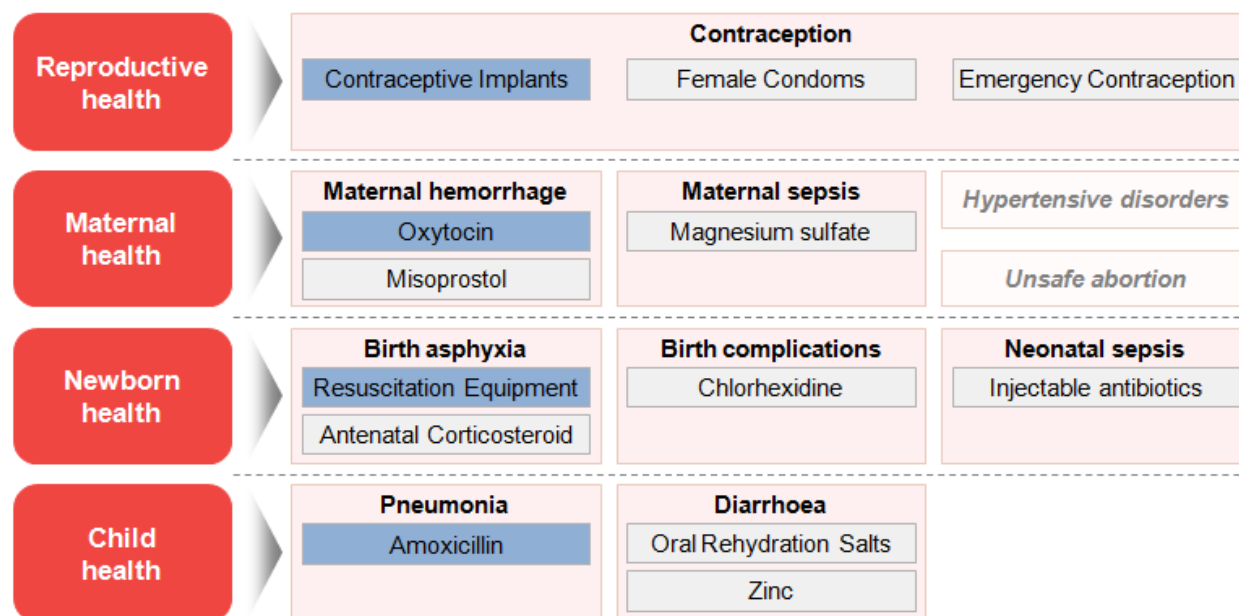
#### 3.1 Coverage of and access to existing RMNCH commodities

The UN Commission on Life-Saving Commodities (UNCoLSC) established in 2012, has conducted extensive work on commodities addressing reproductive health issues and the main mortality drivers in maternal health, newborn health, and child health.<sup>23</sup> The work and organization of the commission are further detailed in the section on Partner landscape.

The work of the Commission was to identify the commodities and make recommendations to improve their accessibility. Figure 9 provides an overview of the 13 lifesaving commodities along main conditions and mortality drivers in RMNCH.

<sup>23</sup> UN Commission on Life-Saving Commodities for Women and Children – Commissioners' Report 2012

**Figure 9: UN Commission on Life-Saving Commodities – 13 overlooked commodities<sup>24</sup>**



The detailed analyses conducted by the technical teams under the umbrella of the commission highlighted different situations and market-related challenges:

- Drugs are generally cheap, but face quality and delivery issues, mainly due to manufacturing or delivery challenges and a lack of global standards – examples of this are oxytocin or amoxicillin.
- Devices are usually expensive, require trained healthcare workers and present longevity issues implying supply chain challenges to replace parts at the right time – an example of this are resuscitation devices.
- Access at the point of care seems to be a challenge for both drugs and devices, as commodities are generally not available in remote locations.
- Across all categories, the need for innovation is high, as innovation could circumvent larger health system challenges and/or facilitate delivery. For example, heat-stable formulations not requiring refrigeration along the supply chain could increase access.

<sup>24</sup> Life-saving commodities – Improving access, saving lives  
(<http://www.lifesavingcommodities.org/about/lifesaving-commodities/>)

An example for the analysis is provided below, with the summary of challenges identified for oxytocin.

### **Oxytocin**

Oxytocin is a first-line drug for prevention and treatment of postpartum hemorrhage caused during labor. It must be administered through injection by a qualified health care worker. Postpartum hemorrhage causes 60,000 deaths per year. Oxytocin is procured from domestic budgets, so there are no global standards.

**Innovation and availability:** Oxytocin is registered in most UNCoLSC countries, even though it is not widely available in remote locations, due to a lack of the required cold chain. Many research projects have been initiated to develop alternative forms of oxytocin. Most of them could address both low adoption and delivery issues.

**Quality:** There is only one WHO prequalified product – Syntocinon, produced by Novartis. Studies in markets show that available oxytocin is often of substandard quality. For example, 65.5% of oxytocin sampled in Ghana did not meet quality standards. In addition, there are many local manufacturers often without quality controls due to substandard manufacturing processes.

**Affordability:** Oxytocin is a very cheap commodity, with an average price of \$0.20 for a ten-dose ampoule. This low price is a result of the high level of competition of the market.

**Demand and adoption:** Adoption of oxytocin is often limited because its administration by injection requires sterilized equipment and trained health care workers, which are often in short supply. Moreover, more than half of women give birth at home where the resources required are not available.

**Supply and delivery:** Oxytocin must be kept refrigerated all along the supply chain. Different manufacturers apply different labels and storage requirements, resulting in misunderstandings and disregard of storage and transportation requirements. Storage is also challenged by a lack of constant electricity. These issues induce a degradation of the product.

Progress has been made since 2012, but major bottlenecks remain (just over half of the 13 lifesaving commodities were in stock at the point-of-service at the time of assessment)<sup>25</sup>. During the past year, several initiatives have been launched to address a number of critical areas, such as the inclusion of commodities on the WHO Essential Medicines List, the tracking of registration in countries, the enhancement of quality through prequalification and Good Manufacturing Processes (GMP), the negotiation of price reductions, the regional market shaping particularly of the East African Community, the supply chain strengthening, the demand generation or the increase of product innovation. Commodities particularly addressed with these initiatives include oxytocin, chlorhexidine, contraceptive implants, antenatal corticosteroids, resuscitation devices and amoxicillin DT.<sup>26</sup> The initiatives are too recent to measure the impact they may have and should be monitored in the future.

<sup>25</sup> RMNCH Landscape Synthesis conducted by the UN Commission on Life Saving Commodities for the 2014 progress report was carried out in 10 countries in sub-Saharan Africa (Cameroon, Ethiopia, Kenya, Nigeria, Senegal, Sierra Leone, Tanzania, Uganda, Mali and Malawi)

<sup>26</sup> 2014 PROGRESS REPORT UN Commission on Life Saving Commodities (May 2015)



**Key messages:**

The UN Commission on Life-Saving Commodities for Women and Children (UNCoLSC) identified and endorsed an initial list of 13 overlooked lifesaving commodities. The commission identified barriers that prevent access to and use of the 13 lifesaving commodities and recommended ten actions to address them.

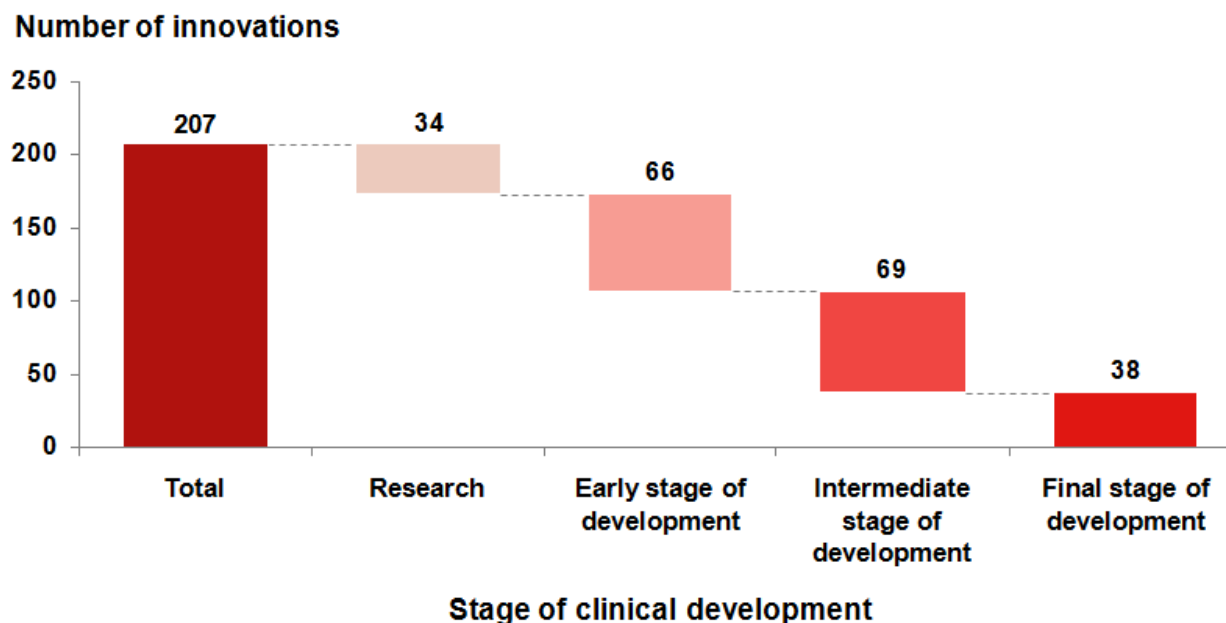
The analysis of selected commodities identified different trends for drugs (usually cheap and lacking in quality) and devices (often expensive tools with a low adoption levels due to technical requirements). Availability appears to be a major challenge for both drugs and devices, as commodities are generally not available in remote locations or at home.

Recently several initiatives have been launched to address a number of critical issues, including pre-qualification, registration and quality. The initiatives are too recent to measure the impact they may have and should be monitored in the future. See section on partner landscape for more details.

### 3.2 RMNCH innovation pipeline

Beyond existing commodities there is a strong innovation pipeline in RMNCH with more than 200 relevant innovations identified in medicines, diagnosis, and devices. Figure 10, provides an overview of the innovation pipeline from research on, the early and intermediate stages of development to the final stage of development.

**Figure 10: Innovation pipeline in RMNCH – from research to final stage of development<sup>27</sup>**

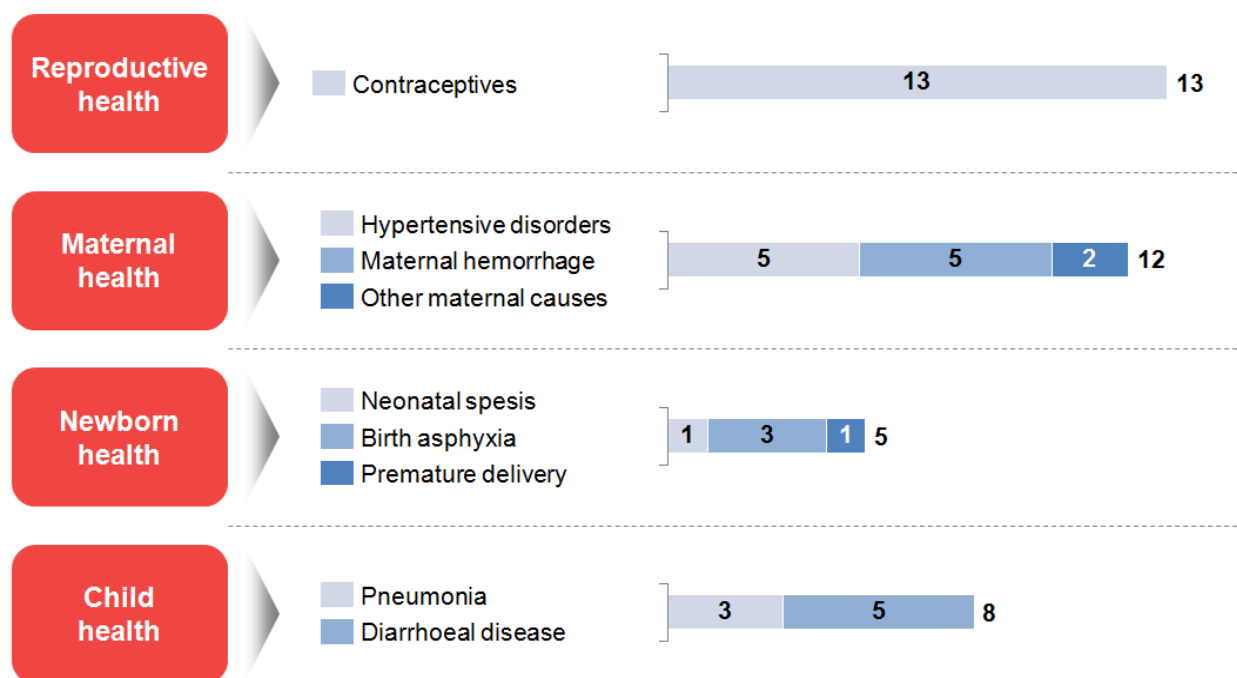


Final stage of development refers to innovations which have successfully passed phases I, II, and III, and have been filed with a Stringent Regulatory Authority (SRA). SRA members are European Union member states, Japan, and the US. Observers are Switzerland and Canada, and associates are Australia, Norway, Iceland, and Liechtenstein.<sup>28</sup> At this stage, an innovation can either be already approved (in need of scale-up) or still in the approval process (not yet commercialized). The 38 final stage of development innovations have been allocated to the main mortality drivers along the RMNCH categories, as illustrated in figure 11. There is a rich and promising pipeline of final-stage innovations for all major areas.

<sup>27</sup> Sources analyzed: R&D for RMNCH, 2014; PLOS medicine, 2015; EWEC, Global Strategy, 2015; EWEC, Technical Paper, 2015; ic2030 report, 2015; Clinical Trials; EvaluatePharma; Global Innovation Fund; Saving Brains Innovation; Saving Lives at Birth

<sup>28</sup> List of countries considered as Stringent Regulatory Authorities (SRA) from 1st July 2009 ([http://www.stoptb.org/assets/documents/gdf/drugsupply/List\\_of\\_Countries\\_SRA.pdf](http://www.stoptb.org/assets/documents/gdf/drugsupply/List_of_Countries_SRA.pdf))

**Figure 11: Innovations in the final stage of development – allocated to RMNCH categories and main mortality drivers<sup>29</sup>**



At this stage, it is difficult to assess whether this pipeline would deliver promising innovations for RMNCH in low-income countries or resource-limited settings. A closer analysis would be required. However, the number of products, the breadth that they cover and the stages of development indicate that this should be monitored.

**Key messages:**

There is a rich innovation pipeline in RMNCH with more than 200 relevant innovations identified – 38 final stage innovations addressing all major areas.

At this stage it is difficult to assess which of these innovations are the most promising but it should be monitored for future opportunities.

<sup>29</sup> Sources analyzed: R&D for RMNCH, 2014; PLOS medicine, 2015; EWEC, Global Strategy, 2015; EWEC, Technical Paper, 2015; ic2030 report, 2015; Clinical Trials; EvaluatePharma; Global Innovation Fund; Saving Brains Innovation; Saving Lives at Birth

## 4 Partner and funding landscape

Because of the way UNITAID operates, it relies on others for scale-up of the projects it supports. Therefore, understanding the evolution and current focus of the global response to women's and children's health builds the foundation for a potential engagement of UNITAID into RMNCH. This chapter provides an overview of the partner and funding landscape.

### 4.1 Global mobilization

#### 4.1.1 Mobilization before 2010

Mobilization for women's and children's health began growing around Millennium Development Goals 4 and 5, with the UN network which primary advocates and promotes RMNCH.

In 2008, the H4+ partnership – now known as H6 – was formed by the UN agencies UNFPA, UNAIDS, UNICEF, WHO, and the World Bank (UN Women was added to the group after its creation) to help countries strengthen their health systems for RMNCH. Working together, the agencies intend to build on long-term and trusted relationships with each other and with governments committed to RMNCH progress.<sup>30</sup>

#### 4.1.2 Acceleration from 2010 onwards

In 2010, the first Every Women Every Child (EWEC) strategy was launched to set out the "key areas where action is urgently required to enhance financing, strengthen policy, and improve service delivery."<sup>31</sup> This strategy has triggered further mobilization of the UN community.

The same year, the Muskoka initiative was launched at the G8 summit in Muskoka, Canada – committing \$7.3 billion, on top of existing commitments, to accelerate progress in RMNCH. Contributors were mainly the G8 countries (under the leadership of Canada and with the strong contribution of France), plus other governments (the Netherlands, New Zealand, Norway, the Republic of Korea, and Switzerland), and foundations (the Bill & Melinda Gates Foundation (BMGF) and the UN Foundation).

In 2012, The Family Planning 2020 initiative was launched to support EWEC strategy with core partners; DFID, BMGF, UNFPA, and USAID. The goal of this initiative is to have 120 million more women using contraception by 2020.<sup>32</sup>

In 2012, the UN Commission on Life-saving Commodities described previously was established. To overcome the identified barriers and improve access to the 13 life-saving commodities, the UN Commission on Life-Saving Commodities has developed recommendations and a detailed implementation plan. This plan assigns clear responsibilities to the multiple stakeholders (BMGF, CHAI, DFID, WHO, USAID, UNFPA, PATH, country governments) involved.<sup>33</sup> To date, \$202 million has been committed to the RMNCH fund to support the mandate of the UNCoLSC, helping 19 high-burden countries to

<sup>30</sup> Every Women and Every Child – Strategy foreword (2010)

<sup>31</sup> UNFPA website on H4+ partnership

<sup>32</sup> Family planning 2020 (<http://www.familyplanning2020.org/>)

<sup>33</sup> Implementation Plan of the UN Commission on Life-Saving Commodities (September 2012)

develop and implement plans to reach women and children with lifesaving commodities.<sup>34</sup> As of April 2015, \$117 million has been disbursed to the countries – nearly half of which went towards systems strengthening interventions, such as supply chain improvement or integrated RMNCH health worker training. Approximately 20% of funds were used to procure commodities – largely in DRC, Ethiopia and Kenya.<sup>35</sup>

Progress has been achieved since 2012, as outlined in the UNCoLSC 2014 progress report, but major bottlenecks remain. Progress is measured by the RMNCH Landscape Synthesis tool, which focuses on identifying systems-related and commodity-specific barriers of the 13 lifesaving commodities. Between January 2013 and May 2015, the RMNCH Landscape Synthesis was carried out in ten sub-Saharan Africa countries (Cameroon, Ethiopia, Kenya, Nigeria, Senegal, Sierra Leone, Tanzania, Uganda, Mali, and Malawi). The key challenge observed was the limited downstream transfer of updated standards, guidelines, and training, as well as the transfer of commodities themselves, from the national-level warehouses to service delivery points where they are needed most.<sup>36</sup>

To support this initiative, an RMNCH Trust Fund was established in 2013 by WHO and UNFPA, and notably also with support from Norway and the UK. This fund has been very active in identifying effective market issues and financing high impact, priority catalytic interventions in order to accelerate progress towards MDGs 4 and 5, including life-saving commodities. However, it is expected to be finished by the end of 2016 and discussions are ongoing on how to transition the work of this group to other entities.<sup>37</sup>

The UNCoLSC recommendations are carried forward by a network of Technical Resource Teams (TRTs). Each TRT is a consortium of global experts from UN agencies, non-governmental organizations, government partners and academic institutions. Originally, one TRT was formed for each of the 13 commodities and 10 recommendations, and an advocacy working group was dedicated to advancing their cross-cutting goals. Later the TRTs were consolidated to eight groups currently focusing on commodities related to family planning; maternal health; newborn health; child health; as well as on demand, access and performance; global markets, quality and regulation; supply chain and local markets; and advocacy. The TRTs are coordinated by a multi-agency RMNCH Strategy and Coordination Team supported by UNICEF, UNFPA and WHO and housed by UNICEF.<sup>38</sup>

#### 4.1.3 Transition from MDGs to SDGs

Over the past two years, the transition out of the MDG into the SDG era has been driving more changes in the landscape:

- In 2014, the Global Financing Facility (GFF) was created to support financing of RMNCH for 49 countries in the longer term. As stated in the GFF strategy, the Global Financing Facility (GFF) supports *Every Woman Every Child* by ensuring mobilizing financing for investment cases, and ensuring that the GFF Trust Fund uses its resources to provide financing in ways that achieve results while being catalytic and driving sustainability. The GFF governance is constituted of 4 platforms: The GFF Investors Group acts as a steering committee for the GFF, The Trust Fund Committee ensures the effective use of funds, a secretariat coordinates the GFF activities, and

<sup>34</sup> Life-saving commodities – Improving access, saving lives (<http://www.lifesavingcommodities.org/>)

<sup>35</sup> 2014 PROGRESS REPORT UN Commission on Life Saving Commodities (May 2015)

<sup>36</sup> 2014 PROGRESS REPORT UN Commission on Life Saving Commodities (May 2015)

<sup>37</sup> Commission on Life-Saving Commodities for Women and Children – Commissioners' Report 2012 and Every Women Every Child – Resources (<http://www.everywomaneverychild.org/resources/10-networks>)

<sup>38</sup> Life-saving commodities (<http://www.lifesavingcommodities.org/about/>)

country-level platforms implement the programs with local partners. These multi-stakeholder committees operate under the leadership of national governments. Funding is provided by constituents of the Trust Fund Committee (DFID, JICA, and USAID who have explicitly aligned their investments to the GFF's). Allocation & secretariat budgeting approvals are decided by the Trust Fund Committee. Monitoring is overseen by the Trust Fund Committee. So far, \$895 million have been raised by the GFF from the Bill & Melinda Gates Foundation, Norway and Canada, with an additional \$570 million of funding aligned to GFF investments.

- In 2015, the second EWEC strategy further increased global health mobilization on RMNCH topics and the creation of the Innovation Marketplace as described below.

#### 4.1.4 RMNCH innovation marketplace

In 2010, the Innovation Working Group (IWG) was created under the UNSG's Every Women Every Child initiative – in support of the Global Strategy for Women's and Children's Health. The vision of the IWG is to create “A world in which a robust pipeline of RMNCAH innovations goes to scale in a sustainable manner to save and improve the lives of the world's most vulnerable women and children and thereby plays a critical role in helping to reach the MDGs and the Sustainable Development Goals (SDGs).”<sup>39</sup>

Today, a robust pipeline of innovations exists with more than 200 innovations, as described above, but still only few of these innovations transition to scale. To smooth the pathway to scaling innovation in a sustainable manner, an innovation marketplace has been established, to coordinate across four interlinked elements; (1) pipeline, (2) curation, (3) brokering, and (4) investment.<sup>40</sup> The marketplace is hosted at Grand Challenges Canada and seeking Scientific Associates (SA) to support its operations. The work of SAs will grant the innovations exposure to partners within the Innovation Marketplace including the Grand Challenges Global Network, which encompasses the United States Agency for International Development (USAID), the Bill & Melinda Gates Foundation, and domestic organizations such as Grand Challenges Brazil, India, Peru, South Africa, Thailand, Japan, Israel, Africa, and China.

The goals of the marketplace are “to transition to scale 20 Women's, Children's and Adolescents' Health (WCAH) investments by 2020, and by 2030 to see at least ten of these innovations widely available and having significant impact on women, children and adolescents.”<sup>41</sup> In addition, by 2020, it aims to generate more than 500 new RMNCH innovations to refresh the pipeline and selectively fill gaps based on results that move towards the goals.

The IWG's key strategy going forward is “... to contribute to a global marketplace for RMNCAH innovations, where innovations meet investors to help them transition to scale in a sustainable manner and achieve widespread impact.”<sup>42</sup> In this context, it could be interesting for UNITAID to explore a potential collaboration.

<sup>39</sup> EWEC – Innovation Working Group (STRATEGY DOCUMENT, September 2014)

<sup>40</sup> EWEC – Innovation Working Group

(<http://www.everywomaneverychild.org/networks/innovation-working-group>) and Innovations for Women's, Children's and Adolescents' Health: Every Woman Every Child Innovation Marketplace ([http://www.everywomaneverychild.org/images/13\\_GC\\_Innovations\\_Technical\\_Paper\\_March\\_23\\_2015\\_CLEAN\\_2015-03-23.pdf](http://www.everywomaneverychild.org/images/13_GC_Innovations_Technical_Paper_March_23_2015_CLEAN_2015-03-23.pdf))

<sup>41</sup> EWEC – Innovation Working Group

(<http://www.everywomaneverychild.org/networks/innovation-working-group>)

<sup>42</sup> Innovations for Women's, Children's and Adolescents' Health: Every Woman Every Child Innovation Marketplace

([http://www.everywomaneverychild.org/images/13\\_GC\\_Innovations\\_Technical\\_Paper\\_March\\_23\\_2015\\_CLEAN\\_2015-03-23.pdf](http://www.everywomaneverychild.org/images/13_GC_Innovations_Technical_Paper_March_23_2015_CLEAN_2015-03-23.pdf))

**Key messages:**

Mobilization of the global health community for RMNCH has grown over the past years and is now very strong. Some elements of the landscape are still not fully defined, as the community is transitioning out of the MDG era and must define a new structure to take over the work conducted by the UN Commission on Life-Saving Commodities and the RMNCH Trust Fund.

The UN Commission on Life-Saving Commodities has initiated significant work and mobilized many partners around the 13 commodities. This work has recently been started and should be monitored in the medium term.

An Innovation Working Group (IWG) was established in 2010 to ensure a robust pipeline of RMNCAH innovations. In addition, an Innovation Marketplace has been established, led by Grand Challenges Canada, with the objective of transitioning 20 innovations to scale in a sustainable manner by 2020 and of seeing at least ten of these innovations widely available and having significant impact on women, children, and adolescents by 2030.

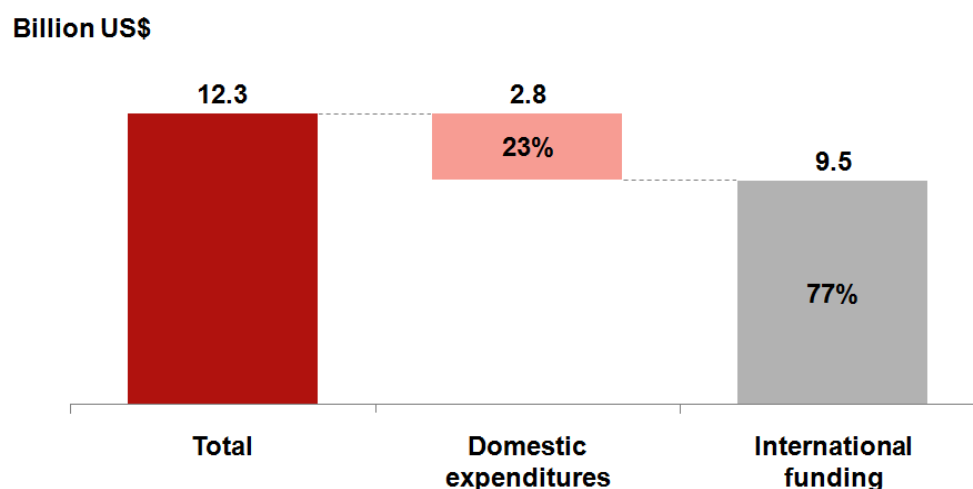
## 4.2 Funding landscape

Understanding the funding landscape is a prerequisite for assessing potentially interesting areas for UNITAID. Given UNITAID's business model and the strong reliance on partners to scale up the interventions UNITAID invests in, it is essential to identify and analyze potential funding partners. This chapter provides an overview of the funding landscape in RMNCH, in particular the funding sources and structure as well as expected changes in the near future.

### 4.2.1 International funding

The first EWEC Strategy (Global Strategy for Women's and Children's health) tracks financing for RMNCH in 75 countdown countries, of which 49 are identified as lowest-income and priority countries. In these 49 lowest-income countries, financing depends mainly on international funding, as illustrated in figure 12. In fact, these countries receive the bulk of international funding – approximately \$10 billion out of \$12 billion total international funding in 2013 – and contributed only about \$3 billion in domestic expenditures.<sup>43</sup>

**Figure 12: Sources of RMNCH funding in 49 lowest-income countries (2013)<sup>44</sup>**



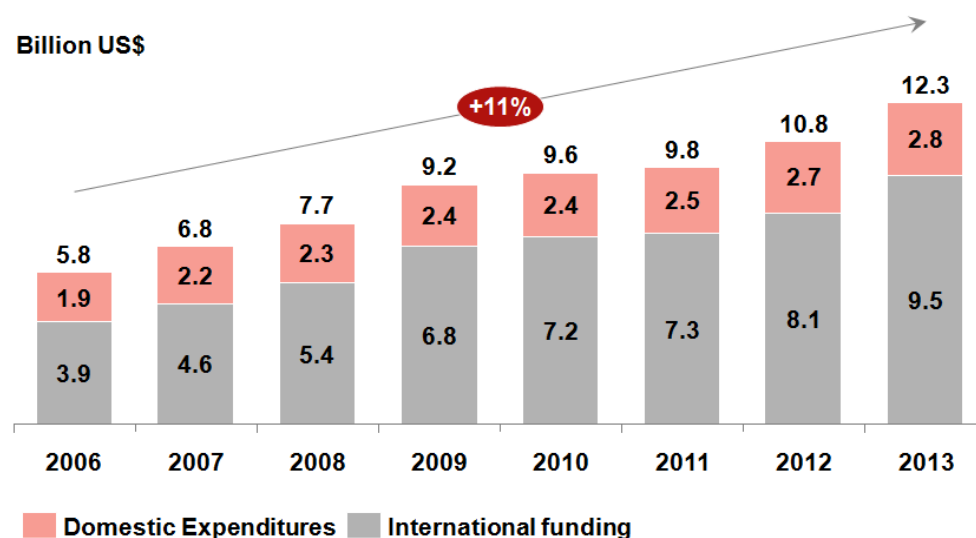
Since 2006, total RMNCH funding in the 49 lowest income countries has grown continuously at an average rate of 11% per year, doubling from \$6 billion in 2006 to \$12 billion in 2013, as illustrated in figure 13. This growth was mainly driven by international funding – domestic expenditures increased much more slowly, averaging only 6% per year.<sup>45</sup>

<sup>43</sup> The Partnership for Maternal, Newborn & Child Health – 2015 Accountability Report

<sup>44</sup> Note: Numbers are rounded

<sup>45</sup> The Partnership for Maternal, Newborn & Child Health – 2015 Accountability Report



**Figure 13: Evolution of RMNCH funding in 49 lowest income countries (2006 – 2013)**<sup>46</sup>

Beyond the current funding situation, the Global Financing Facility (GFF) in support of Every Women Every Child estimated a funding gap of approximately \$27 billion in 2015, mostly in 63 low- and lower-middle-income countries.<sup>47</sup>

#### 4.2.2 Structure of international funding

There are two characteristics of the international funding for women and children's health, in particular when compared to HIV/AIDS, TB, malaria where UNITAID is used to operate:

- The level of fragmentation
- The type of support (commodity purchase vs. other support)

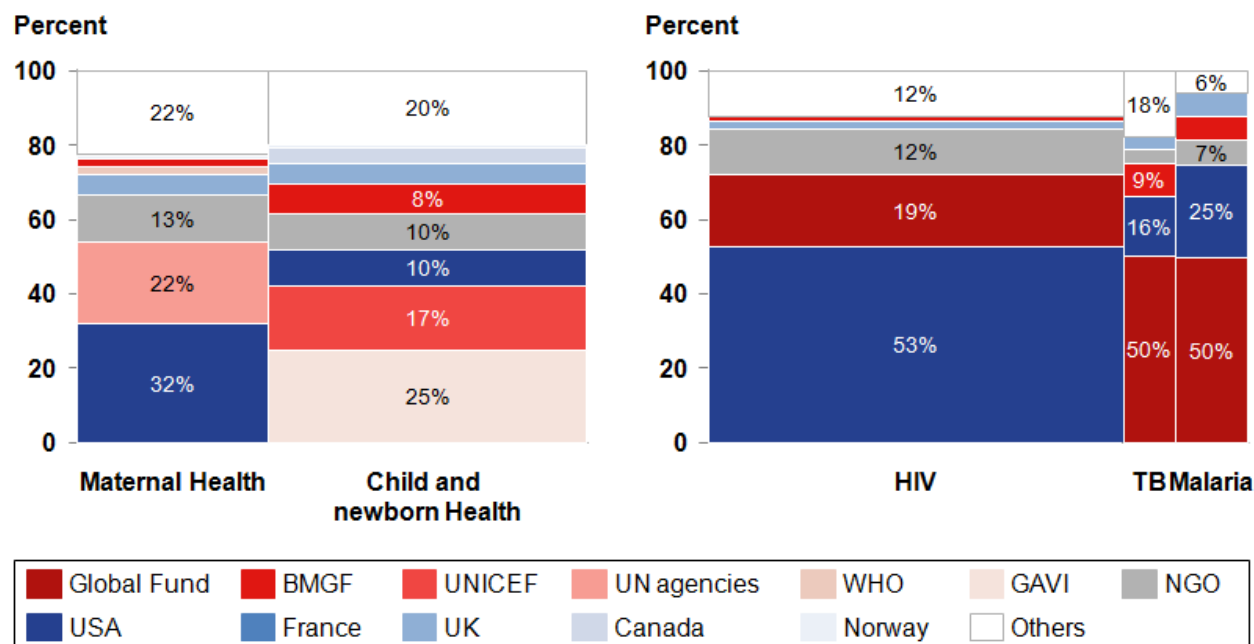
The sources of international funding are more fragmented than for HIV/AIDS, TB, and malaria, as illustrated in figure 14. In HIV/AIDS, TB, and malaria, the top two donors account for 70%, on average, of the funding:

- For maternal health, the top two donors account for 54% of total funding.
- For child and newborn health, the top two donors account for 42% of total funding. GAVI alone making up 25% of the funding, with a sole focus on immunization.

<sup>46</sup> The Partnership for Maternal, Newborn & Child Health – 2015 Accountability Report

<sup>47</sup> Concept note: a global financing facility in support of every women and every child (2014)

**Figure 14: Development assistance for health by channel and health area (2000-2014)**<sup>48</sup>



Finally, international financial support is in general not focused on commodity purchase because of their very low costs. Beyond the roles that GAVI plays in vaccines and that UNICEF and UNFPA are playing in specific areas (e.g., contraceptives) and for a limited share of commodities, there is no coordinated procurement mechanism. This difference from the environment in which UNITAID traditionally operates has an impact on the potential market-shaping levers. Global coordination is a key success factor in influencing the quality of products procured and/or their prices.

#### 4.2.3 Expected changes in the funding landscape

The global health community expects to see additional partners becoming more involved. Most interestingly for UNITAID, international funders which historically focused on HIV, TB, and malaria have progressively extended their scope to include RMNCH topics. As an example, the Global Fund and PEPFAR have recently committed more strongly to RMNCH.

The Global Fund has explicitly included several co-infections of HIV relevant to maternal health, including cervical cancer. It has also committed to focus on women’s and girls’ health, including making keeping girls at school a priority (and potentially ensuring access to family planning). Within its new strategy, which is currently being developed, the Global Fund is strongly considering to support interventions that affect reproductive, women’s, children’s, and adolescent health, for example by integrating RMNCH services into HIV, TB, and malaria services. As stated in the draft Strategy of the Global Fund "Global Fund support may be used for antenatal care, childbirth, postpartum care, sexual health and family planning, and preventive and curative care for newborns and children, as well as care for survivors of gender-based and intimate partner violence".<sup>49</sup>

<sup>48</sup> IHME database

<sup>49</sup> The Global Fund – Maximizing Impact through Strategic Investments, Improving the Health of Women and Girls (2015) and Draft Global Fund strategy – 2017-2021. January 2016 Draft

PEPFAR has invested in several programs, the most notable being the “DREAMS” initiative, an ambitious \$385 million partnership – that includes the Bill & Melinda Gates Foundation, Girl Effect, Johnson & Johnson, Gilead Sciences, and ViiV Healthcare – to reduce HIV infections among adolescent girls and young women in ten sub-Saharan African countries. The goal of DREAMS is to help girls develop into “Determined, Resilient, Empowered, AIDS-free, Mentored, and Safe women.”<sup>50</sup> Another example is "Saving Mothers, Giving Life" – a public-private partnership to dramatically reduce maternal and newborn mortality in three sub-Saharan African countries (Uganda, Zambia, and Nigeria). Launched in 2012, the five-year initiative employs a health systems approach to ensure every pregnant woman has access to clean, safe childbirth services, including emergency care reachable within two hours. To date, the partnership – which includes the governments of Uganda, Zambia, Nigeria, the US, and Norway as well as Merck for Mothers, Every Mother Counts, Project C.U.R.E., the American College of Obstetricians and Gynecologists, and the Centers for Disease Control and Prevention (CDC) – has pledged more than \$280 million in financial resources.<sup>51</sup>

**Key messages:**

Women’s and children's health is mostly supported by international funding in the lowest-income countries. This funding is more fragmented than in HIV/AIDS, TB, and malaria. The lack of a global coordination mechanism for the procurement of some products (in particular the basic health products for maternal and child health) must be taken into account when considering the probability of success of market-related approaches.

In the future, current UNITAID partners such as the Global Fund, PEPFAR and others may get more involved in women and children's health, particularly in areas adjacent to HIV/AIDS.

<sup>50</sup> PEPFAR – Dreams: Working Together for an AIDS-free Future for Girls and Women (<http://www.pepfar.gov/partnerships/ppp/dreams/>)

<sup>51</sup> PEPFAR 3.0 strategy – Controlling the epidemic: Delivering on the promise of an AIDS-free generation and "Saving mothers, giving life" website (<http://savingmothersgivinglife.org/>)

## 5 Proposed areas to be further explored by UNITAID

Using the approach developed for HIV/AIDS, TB and malaria, UNITAID has looked at prioritizing potential areas for intervention.

### 5.1 Prioritization process

UNITAID can prioritize areas for potential investment in this field using the same criteria as for HIV/AIDS, TB, and malaria. Given the specificities of women and children health, the criteria have been reordered here:

- **Potential public health impact:** focus on challenges for which there is strong evidence of high public health impact
- **UNITAID's expertise:** focus on challenges that are inherently commodity access issues
- **Feasibility:** focus on challenges for which the necessary technology can be available in the relevant timeframe
- **Optimized use of resources:** focus on challenges for which critical gaps exist in the global response and where scale-up is possible

**Public health need** – The analysis above highlights a high public health need, with a very high number of deaths from a limited number of conditions and preventable causes remaining in low-income countries. The main causes of death beyond HIV/AIDS, TB, and malaria, are maternal hemorrhage, hypertensive disorders, maternal sepsis, unsafe abortion, neonatal conditions, fever for children, and NCDs including cervical. Reproductive health is also a matter of high public health need, even if not directly linked to mortality.

**UNITAID's expertise** – Health products have been identified as a major means to improve the health of women and children. Access is critically low in low-income countries. Health products can be classified in two groups:

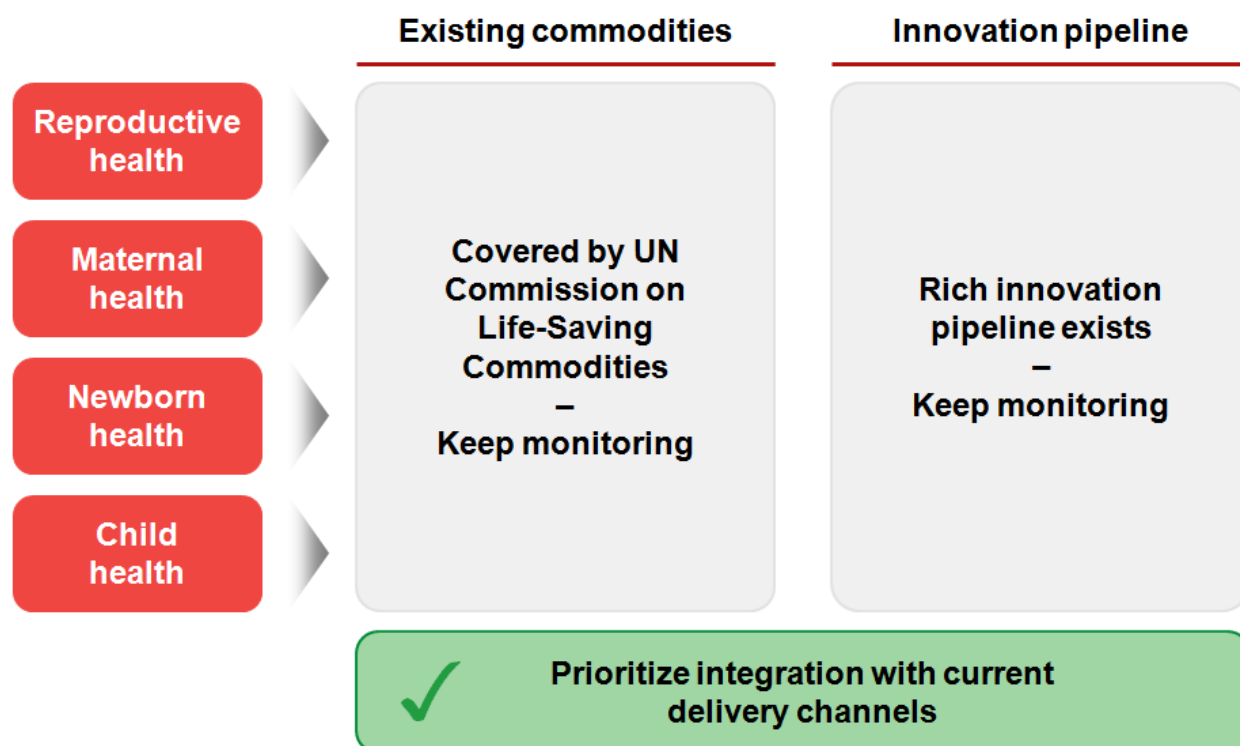
- Existing commodities – for which challenges are often related to quality, in particular for cheap drugs, or to affordability for devices.
- Innovations – for which access needs to be accelerated in low-income settings

**Feasibility** – Most of these products exist, but are not accessible in countries where they are needed at the appropriate level of quality. In addition, there is a strong pipeline for innovation with more than 200 products being developed.

**Optimized use of resources** – This criteria is particularly critical, because RMNCH is a rather new field for UNITAID and it is important to understand how UNITAID's potential action would add value to the response:

- For the 13 life-saving commodities, many partners are actively improving access as this was highlighted as an issue by the UN Commission on Life-Saving Commodities and dedicated task forces have been set up for each commodity. The full impact of their work is yet to be assessed as they have been started recently.
- For innovation, the Innovation Marketplace is a major player, acting as a convening partner and seeking to ensure that innovations reach scale. The leaders of the innovation marketplace have indicated that they are seeking additional support and would be interested in exploring a partnership opportunity with UNITAID.

**Figure 15: Priority areas for UNITAID would initially aim at integration with current delivery channels**



This analysis indicates that UNITAID should maintain engagement with partners in RMNCH to monitor the evolution of the landscape and need for further involvement. UNITAID can continue to explore potential areas where RMNCH is linked to HIV/AIDS, TB and malaria because these areas are less covered by the RMNCH community than others, UNITAID's expertise on HIV/AIDS TB and malaria would add more value, and the link with existing partners would maximize the chances of success of UNITAID's projects.

Links with HIV/AIDS, TB and malaria can be of two kinds:

- Same providers: When the same provider would see a patient for RMNCH and a patient for HIV/AIDS, TB and malaria. For instance, when a child presents to a nurse with fever for suspected malaria but turns out not to have malaria.
- Same patients: A condition which affects the same people as HIV/AIDS, TB or malaria, typically co-infections. An example would be HPV known as a major co-infection with HIV/AIDS.

These two examples stood out during the consultation process and have therefore been detailed. They would require further investigation before UNITAID would consider potential investments.

## 5.2 Examples for potential areas of interest for UNITAID

This section provides preliminary elements of analysis for UNITAID's potential role in these two exemplary areas. Further analysis is needed before considering them as potential areas for intervention.

### 5.2.1 Fever conditions

Fever conditions account for more than half of all deaths among children under five in low-income countries – with two main conditions apart from malaria being pneumonia and diarrhoea.<sup>52</sup>

Pneumonia<sup>53</sup> is the single largest cause of death in children worldwide. It killed an estimated 922,000 children under the age of five in 2015. Pneumonia can be caused by viruses, bacteria, or fungi. But it can be prevented with immunization and adequate nutrition, and by addressing environmental factors such as air pollution. Pneumonia can be treated with antibiotics, but only one-third of children with pneumonia receive the antibiotics they need.<sup>54</sup>

Diarrhoeal disease<sup>55</sup> is the second leading cause of death in children under five. Each year, diarrhoea kills around 760,000 children under five. Key treatments for diarrhoea are simple, and include zinc, rehydration with oral rehydration salts (ORS), and supplementing the diet with nutrient-rich foods – but as with pneumonia, the coverage rate is low and only one-third of children receive the treatment they need<sup>56</sup>. In addition, a vaccine is available.

Generally, fever conditions are both preventable and treatable. For example, a significant share of diarrhoeal diseases could be prevented through provision of safe drinking water and adequate sanitation and hygiene. In addition, diagnostics are often a challenge – especially in low-income settings and for non-malaria fever causes. Pneumonia, for instance, is often misdiagnosed by health care providers in resource-poor settings until it develops into a severe stage.<sup>57</sup> This often leads to the wrong treatment and therefore increased resistance to the drugs wrongly provided (for instance ACTs or pneumonia antibiotics).

The global health community is strongly engaged, as child survival has been an early priority for UN agencies, bilateral donors, civil society organizations, and WHO.

In this context, the incomplete diagnostics landscape is an area which could potentially be interesting for UNITAID to further explore. Improved diagnostic tools would better guide the decisions made in providing treatment. For example, new and improved Acute Respiratory Infection Diagnostic Aid (ARIDAs – or fast breathing timers) would help community and primary health care workers accurately diagnose pneumonia. Presently there is no effective way to differentiate viral pneumonia from bacterial pneumonia outside

<sup>52</sup> Health in 2015 – From MDGs to SDGs – WHO – Child Health p.87

<sup>53</sup> WHO – Pneumonia factsheet n°331 (<http://www.who.int/mediacentre/factsheets/fs331/en/>)

<sup>54</sup> WHO and UNICEF – Ending preventable child deaths from pneumonia and diarrhoea by 2025 – The integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD) – ([http://www.who.int/maternal\\_child\\_adolescent/documents/global\\_action\\_plan\\_pneumonia\\_diarrhoea/en/](http://www.who.int/maternal_child_adolescent/documents/global_action_plan_pneumonia_diarrhoea/en/))

<sup>55</sup> WHO – Diarrhoeal disease factsheet n°330 (<http://www.who.int/mediacentre/factsheets/fs330/en/>)

<sup>56</sup> WHO and UNICEF – Ending preventable child deaths from pneumonia and diarrhoea by 2025 – The integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD)

<sup>57</sup> World Health Organization, Key Problems in Pneumonia Diagnosis and Management, WHO, Geneva, June 2014

of a laboratory. Innovation is needed to develop a rapid point of care (POC) diagnostic that would enable health care workers to identify bacterial pneumonia in children and give them appropriate treatment.

**Key messages:**

Public health need is high with fever conditions accounting for more than half of all deaths among children under five in low-income countries. Two main mortality drivers apart from malaria are pneumonia and diarrhoea.

Prevention mainly depends on environmental factors, such as provision of safe drinking water and adequate sanitation and hygiene. The diagnostic landscape is challenging and incomplete, with many non-malaria fever causes misdiagnosed in developing countries. Misdiagnoses often lead to the wrong treatment, resulting in poor health outcomes and contributing to the development of drug resistance.

As an example, the incomplete diagnostics landscape is an area which could potentially be interesting for UNITAID to explore further.

### 5.2.2 Cervical cancer

Cervical cancer is mainly caused by the human papillomavirus (HPV)<sup>58</sup>, a group of extremely common viruses, mainly transmitted through sexual contact. Persistent infection with specific types of HPV may lead to genital warts or cancers (the most frequent being cervical cancer). HPV and HIV are co-infections – each acts in a manner that favors the other infection at the cellular level.

As 87% of HPV-related cancers are cervical cancers, women are the most vulnerable population. Cervical cancer is the fourth most frequent cancer in women with an estimated 530,000 new cases in 2012 representing 7.5% of all female cancer deaths, therefore the public health need is dire worldwide.<sup>59</sup> Of the estimated more than 270,000 deaths from cervical cancer every year, more than 85% occur in less developed regions. The global health community has not established specific goals with regard to HPV-related conditions. Some efforts are underway nevertheless, either regarding cancers in general<sup>60</sup> or at national levels.

There is no treatment for the virus itself. Prevention is the most effective way to deal with HPV. There are currently two WHO prequalified HPV vaccines being marketed in many countries throughout the world. Screening is the easiest way to diagnose cervical cancer and there are three different types of tests: conventional (Pap) test, visual inspection with Acetic Acid (VIA), and HPV testing for high-risk HPV types. Acetic Acid tests are still the most used in LMICs.

Global efforts currently primarily address affordability issues for vaccines.<sup>61</sup> GAVI, for example, is acting to decrease prices of vaccines. In addition, WHO is working to develop guidance on how to prevent and control cervical cancer, including through vaccination and

<sup>58</sup> WHO – Human papillomavirus (HPV) and cervical cancer factsheet n°380 (<http://www.who.int/mediacentre/factsheets/fs380/en/>)

<sup>59</sup> WHO – Globocan 2012 ([http://globocan.iarc.fr/Pages/fact\\_sheets\\_cancer.aspx](http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx))

<sup>60</sup> WHO – Global Action Plan for Prevention and Control of Non-communicable Diseases (NCDs)

<sup>61</sup> President's Cancer Panel Annual Report, 2012-2013, "Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer" (<http://deainfo.nci.nih.gov/advisory/pcp/annualReports/HPV/>)

screening. Others, such as the PAHO Revolving Fund and CDC<sup>62</sup>, are acting on a smaller scale, to provide many GAVI-ineligible middle-income countries with HPV vaccines at reduced prices.

The innovation pipeline for HPV/cervical cancer features fifteen relevant innovations of which five have reached the final stage of development, addressing prevention, diagnosis and treatment. Recent research has mainly focused on the utility of alternative screening approaches in resource-poor environments, including the use of rapid HPV testing to triage high-risk women. CareHPV is an example of a new diagnostic test specifically developed for use in the developing world. It is battery-powered bench-top instrument which requires neither electricity nor running water. Therefore, it has enormous potential for use in LMICs as it is specifically designed to be rapidly processed by inexperienced personnel under.<sup>63</sup> Another promising test is Cepheid's Xpert HPV<sup>64</sup>, a 60-minute test for cervical cancer. The test runs on Cepheid's GeneXpert system, technology supported by UNITAID and partners in current projects.

In this context, development and potential scale-up of new diagnostic tools is an area which could potentially be interesting for UNITAID to further explore. Work in this area could aim to amplify the impact of research and development efforts by accelerating uptake of emerging diagnostic options.

**Key messages:**

Public health need is high for cervical cancer mainly caused by the human papillomavirus (HPV) – with an estimated 270,000 deaths every year; more than 85% of which occur in less developed regions.

Prevention is addressed through vaccination programmes worldwide. Modern diagnostic methods are often not available in low- and middle- income countries, where visual inspection and the Acetic Acid test are still most common. Diagnosis is of paramount importance, as it allows for the detection of pre-cancerous lesions which can easily be treated. Treatments for developed cancers are onerous and often not available in developing countries.

The development and potential scale-up of new diagnostic tools is an area which could potentially be interesting for UNITAID to explore further.

<sup>62</sup> Centers for Disease Control and Prevention (<http://www.cdc.gov/vaccines/who/teens/for-partners/index.html>)

<sup>63</sup> Science direct – Molecular Oncology Testing in Resource-Limited Settings (<http://www.sciencedirect.com/science/article/pii/S1525157814001494>)

<sup>64</sup> Cepheid, Press Release, April 2014 (<http://ir.cepheid.com/releasedetail.cfm?releaseid=837096>)



## 6 Conclusion

Based on the analysis provided above, there is a potential for UNITAID's intervention:

- Existing commodities for reproductive, maternal, newborn and child health have been thoroughly analyzed by the UN Commission on Life-Saving Commodities. Progress has been made since 2012, but major bottlenecks remain. Challenges have been identified that are in the scope of what UNITAID typically funds. Taskforces coordinated by the UN Commission are addressing the bottlenecks and several initiatives have been launched recently so their impact is yet to be seen. In addition, these commodities are mostly sourced through domestic funding, which limits the potential leverage of or need for international funding, including that of UNITAID. In conclusion, progress in access to existing commodities should be closely monitored in the future for potential opportunities.
- Innovations in women's and children's health show a strong pipeline and the innovation marketplace seeks to play a key role in coordinating actions to ensure scale-up of innovation. The marketplace is in search for additional partners and UNITAID could explore a potential collaboration.
- This analysis suggests that UNITAID should monitor closely the needs related to existing products and to innovations. Given that it is a new player in the field, UNITAID should initially focus on areas which allow integration into the current delivery channels for HIV/AIDS, TB and malaria. This approach would enable UNITAID to build on its existing competences and relationships with partners and would be complementary to current investments in HIV/AIDS, TB and malaria.

### Request to the Executive Board:

The Executive Board takes note of this analysis and requests that UNITAID Secretariat includes RMNCH in the scope of the new strategy 2017-2021.

The Board supports that the Secretariat continues to monitor the innovation landscape.

The Board requests the Secretariat to bring potential areas for intervention for Board endorsement in RMNCH linked with HIV/AIDS, TB and malaria.

## 7 Appendix

### 7.1 RMNCH interviews and consultations

We conducted 15 interviews on RMNCH topics in order to gather information about the main conditions and causes of death among women and children, and the existing associated commodities and innovations and partner landscape:

- Anshu Banerjee and Frederik Kristensen, Assistant Director-General Family, Women's and Children's Health at WHO
- Viviana Mangiaterra, Executive Director/Head of Technical Advice and Partnerships at the Global Fund
- Andrew Storey and his team, Vice Chairman and Chief Executive Officer of the Clinton Health Access Initiative
- The HPV team from the Bill and Melinda Gates Foundation
- The RMNCH team from the Bill and Melinda Gates Foundation
- Alan Court, Senior advisor at the UN Special Envoy for the Financing of the Health MDGs and for Malaria
- Sophie Biacabe, Focal point for Maternal and Child Health at the AFD
- Christophe Douat, President of MedinCell
- John Gaffney, Humanitarian health advisor at Save the Children
- Amy Lin from USAID
- Pascal Bijleveld from the RMNCH Trust Fund
- John Skibiak, director of the Reproductive Health Supplies Coalition
- Bjørg Sandkjær, Senior Advisor, Global Health Initiatives at NORAD
- Peter Singer, Chief Executive Officer of the Grand Challenges Canada
- The Family Planning team of the Bill and Melinda Gates FoundationThree from French NGOs
- Sami Asali from Coordination Sud
- Marguerite Bannwarth from Equilibre & Populations
- Sandrine Simon and Anne Sinic from Médecins du Monde
- Celina Schocken from Pink Ribbon Red Ribbon
- Jan-Willem Scheijgrond from Philips
- Pascal Bijleveld from the RMNCH Trust Fund (consulted twice)
- Monique Vledder from the World Bank
- Amy Lin from USAID

## 7.2 Further information on fever conditions

### 7.2.1 Disease introduction/Public health need

The vast majority of deaths in children under five in low-income countries are caused by infectious diseases and aggravated by poor nutrition.<sup>65</sup> Fever conditions account for 55% of these deaths. Fever conditions are the most preventable cause of death, with two main conditions apart from malaria being pneumonia and diarrhoea.

Pneumonia<sup>66</sup> is the largest cause of death in children worldwide, having killed an estimated 922,000 children under the age of five in 2015. Pneumonia can be treated with antibiotics, but only one-third of children with pneumonia receive the antibiotics they need. The disease can be caused by viruses, bacteria, and fungi and can be spread in a number of ways:

- The viruses and bacteria commonly found in a child's nose or throat can infect the lungs if inhaled.
- They may also spread via airborne droplets from a cough or sneeze. Pneumonia can spread through contact with blood, especially during and shortly after birth.
- More research needs to be done on the different pathogens causing pneumonia and the ways they are transmitted, as this is of critical importance for treatment and prevention.

Diarrhoeal disease<sup>67</sup> is the second leading cause of death from fever in children under five. Each year, diarrhoea kills around 760,000 children under five, even though it is both preventable and treatable. Diarrhoeal diseases have various causes:

- Infection: By bacterial, viral, and parasitic organisms, most of which are spread by faeces-contaminated water. Infection is more common when there is a shortage of adequate sanitation and hygiene and safe water for drinking, cooking, and cleaning.
- Malnutrition: Children who die from diarrhoea often suffer from underlying malnutrition, which makes them more vulnerable to diarrhoea. Each diarrhoeal episode, in turn, exacerbates their malnutrition.
- Source: Water contaminated with human faeces, for example, from sewage, septic tanks, and latrines, is of particular concern. Animal faeces also contain microorganisms that can cause diarrhoea.
- Other causes: Diarrhoeal disease can also spread from person-to-person, aggravated by poor personal hygiene. Food is another major cause of diarrhoea when it is prepared or stored in unhygienic conditions.

The most severe threat posed by diarrhoea is dehydration. During a diarrhoeal episode, water and electrolytes (sodium, chloride, potassium, and bicarbonate) are lost through liquid stools, vomit, sweat, urine, and breathing.

### 7.2.2 Global Goals and associated strategy

There is consensus that the global health community and all countries must continue to accelerate the reduction of the mortality rate for children under five in order to reach the SDG targets by 2030. To do this, partners are advocating for a change in the way interventions are carried out. The MDG era has yielded impressive results, but global health partners agree that ending preventable deaths in children under five will require more patient-centered, integrated, and innovative approaches.



<sup>65</sup> Health in 2015 – From MDGs to SDGs – WHO – Child Health p.87

<sup>66</sup> WHO – Pneumonia factsheet n°331 (<http://www.who.int/mediacentre/factsheets/fs331/en/>)

<sup>67</sup> WHO – Diarrhoeal disease factsheet n°330 (<http://www.who.int/mediacentre/factsheets/fs330/en/>)

Specific goals of the global health community with regard to pneumonia and diarrhoea are illustrated in figure 16.

**Figure 16: Goals by the global health community for pneumonia and diarrhoea<sup>68</sup>**

		<b>2025</b>
Reduce mortality from pneumonia in children<5	$\leq 3$ per 1000 live births	
Reduce mortality from diarrhoea in children<5	$\leq 1$ per 1000 live births	
Reduce the incidence of severe pneumonia in children<5 vs. 2010	$\geq 75\%$	
Reduce the incidence of severe diarrhoea in children<5 vs. 2010	$\geq 75\%$	
Reduce the global number of children<5 who are stunted vs. 2010	$\geq 40\%$	

### 7.2.3 Tools to prevent, diagnose, and treat

#### **Prevention and treatment of pneumonia<sup>69</sup>**

Preventing pneumonia in children is an essential component of any strategy to reduce child mortality:

- Immunization against Hib, pneumococcus, measles, and whooping cough (pertussis) is the most effective way to prevent pneumonia.
- Adequate nutrition is key to improving children's natural defenses.
- Addressing environmental factors such as indoor air pollution and encouraging good hygiene in crowded homes decreases pneumonia risks.
- In children infected with HIV, daily use of antibiotic cotrimoxazole decreases the risk of contracting pneumonia.

Pneumonia should be treated with antibiotics. The antibiotic of choice is amoxicillin dispersible tablets. Most cases of pneumonia require oral antibiotics, which are often prescribed at a health centre – but could also be diagnosed and treated with inexpensive oral antibiotics at the community level by trained community health workers. Hospitalization is recommended only for severe cases of pneumonia.

<sup>68</sup> WHO – UNICEF Ending preventable child deaths from pneumonia and diarrhoea by 2025 – The integrated Global Action Plan for Pneumonia and Diarrhoea (GAPPD)

<sup>69</sup> WHO – Pneumonia factsheet n°331 (<http://www.who.int/mediacentre/factsheets/fs331/en/>)

## **Prevention and treatment for diarrhea<sup>70</sup>**

A significant proportion of cases of diarrhoeal diseases can be prevented by providing safe drinking water and adequate sanitation and hygiene.

Key treatments for diarrhoea are simple, and include zinc, rehydration with oral rehydration salts (ORS), and supplementing the diet with nutrient-rich foods, but as with pneumonia, the coverage rate is low and only one-third of children receive the treatment they need. A vaccine is available as well.

### **7.2.4 Partner landscape**

Since 2010, following the launch of the UN first Global Strategy for Women's and Children's Health 2010-2015,<sup>71</sup> many initiatives have emerged and many countries have accelerated their actions. Examples of global initiatives for children include the Child Survival Call to Action, the UN Commission on Life-Saving Commodities, and the global action plan for pneumonia and diarrhoea.<sup>72</sup>

As highlighted in global health partners' recent strategies and statements, a shift in strategic direction will be necessary to increase access and coverage, and improve quality of child health services:

- EWEC advocates a life-course and patient-centered approach. The global strategy *"aims at the highest attainable standards of health and well-being."*
- In addition, the UN Commission on Life-Saving Commodities highlights the critical role of innovation to help reach more children, clearly stressing that, *"there has been an insufficient focus on optimizing innovative approaches to product formulation, packaging and delivery devices."*
- Finally, the WHO – UNICEF integrated global action plan for pneumonia and diarrhoea proposes that an integrated approach is the only way to end these two preventable diseases, stating that, *"it is now clear that pneumonia and diarrhoea must be addressed in a coordinated manner."*

### **7.2.5 Main challenges to be addressed**

Three main types of issues impede progress on child health, and specifically on fever diseases like pneumonia and diarrhoea:<sup>73</sup>

- Social determinants: linked to topics other than health (nutrition, environment, education, etc.).
- Access to services: ensuring that children have access to health care services at the community and health care facility level.
- Access to disease-specific products: ensuring that when children are taken to seek care in their community or at a health care facility, they have access to medicines and tools to better prevent, diagnose, and treat pneumonia and diarrhoea.

A number of issues impeding progress against pneumonia and diarrhoea are expected to be commodity-related. Expanding access to lifesaving commodities for children will only come about by leveraging upstream and downstream market-shaping interventions. Examples of interventions could include bringing to market innovations suitable for low-income settings and increasing availability of existing commodities.

<sup>70</sup> WHO – Diarrhoeal factsheet n°330 (<http://www.who.int/mediacentre/factsheets/fs330/en/>)

<sup>71</sup> EWEC movement grown out from this strategy (could be referenced as the first EWEC strategy)

<sup>72</sup> Health in 2015 – From MDGs to SDGs – WHO – Child Health p.87

<sup>73</sup> EWEC – The Global strategy for women's, children's and adolescents' Health (2016-2030)

## 7.3 Further information on cervical cancer

### 7.3.1 Disease introduction/Public health need

Cervical cancer is mainly caused by the human papillomavirus (HPV)<sup>74</sup> – a group of extremely common viruses. There are more than 100 types of HPV, of which at least 13 are cancer-causing (also known as high-risk type):

- HPV is mainly transmitted through sexual contact and most people are infected with HPV shortly after the onset of sexual activity.
- The majority of HPV infections do not cause symptoms or disease and resolve spontaneously. However, persistent infection with specific types of HPV may lead to pre-cancerous lesions. If untreated, these lesions may progress to cervical cancer, but this progression usually takes many years. Genital warts and other cancers (anus, vulva, vagina, penis, and oropharynx) can also develop due to HPV.
- Two HPV types (16 and 18) cause 70% of cervical cancers and pre-cancerous cervical lesions.
- Symptoms of cervical cancer tend to appear only after the cancer has reached an advanced stage and may include: irregular or inter-menstrual bleeding, or abnormal vaginal bleeding after sexual intercourse; back, leg, or pelvic pain; fatigue, weight loss, loss of appetite; vaginal discomfort or odorous discharge; and a single swollen leg.
- HPV and HIV are co-infections: each displays interactions favoring the other infection at the cellular level:
  - HIV-positive people are more seriously affected by HPV-induced conditions. They are more likely to have HPV, carry more different HPV types on average, and are less likely to spontaneously clear that virus, leading to greater risk of cancer due to progressive immune suppression.
  - HPV infection favors HIV acquisition in both women and men.

Worldwide, cervical cancer is the fourth most frequent cancer in women with an estimated 530,000 new cases in 2012 representing 7.5% of all female cancer deaths. Of the estimated more than 270,000 deaths from cervical cancer every year, more than 85% occur in less developed regions:<sup>75</sup>

- In developed countries, programs enable women to get screened, making most pre-cancerous lesions identifiable at stages when they can easily be treated. Early treatment prevents up to 80% of cervical cancers in these countries.
- In developing countries, limited access to effective screening means that the disease is often not identified until it is further advanced and symptoms develop. In addition, prospects for treatment of such late-stage disease may be poor, resulting in a higher rate of death from cervical cancer in these countries.
- The high mortality rate from cervical cancer globally (52%) could be reduced by effective screening and treatment programs.

<sup>74</sup> WHO – Human papillomavirus (HPV) and cervical cancer factsheet n°380

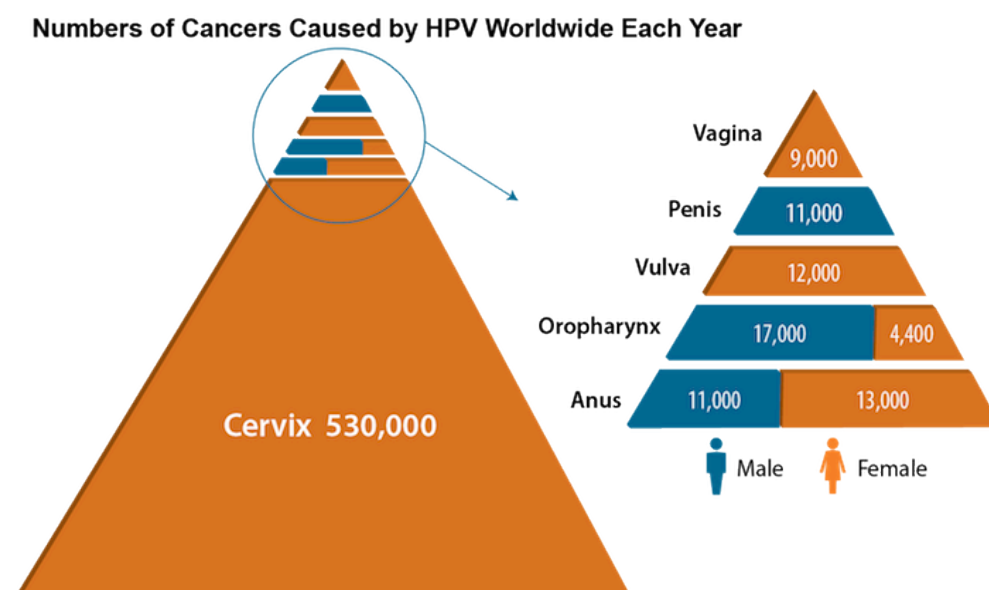
(<http://www.who.int/mediacentre/factsheets/fs380/en/>)

<sup>75</sup> WHO – Globocan 2012 ([http://globocan.iarc.fr/Pages/fact\\_sheets\\_cancer.aspx](http://globocan.iarc.fr/Pages/fact_sheets_cancer.aspx))

Women are the most vulnerable populations, but men can be contaminated too, as illustrated in figure 17:<sup>76</sup>

- HPV is mainly responsible for cervical cancer (87% of the HPV-related cancers), which is a female-only cancer.
- Men can only be stricken by anus, oropharynx, and penis cancers. They represent only 6.4% of HPV-related cancers.

**Figure 17: Number of cancers caused by HPV worldwide each year<sup>77</sup>**



### 7.3.2 Global goals and associated strategy

No clear global goals have been established specifically regarding HPV-related conditions (warts and cancers, mainly cervical), but some efforts have been made either regarding cancers in general or at the national level.

WHO released in 2013 a Global Action Plan for Prevention and Control of Non-communicable Diseases (NCDs) aimed at reducing mortality from several NCDs, including cancers. The WHO global monitoring framework includes several targets and indicators related to prevention and control of cancers. These include decreasing premature mortality due to cancer by 25% by 2025, improving HPV vaccine coverage, monitoring cancer incidence, and increasing the proportion of women who are screened for cervical cancer. These goals remain very vague, mainly concerning cancers, and not specifically targeting cervical cancers or other HPV-related cancers. In the US, the federal goal is to vaccinate 80% of boys and girls against HPV by 2020.<sup>78</sup>

<sup>76</sup> President's Cancer Panel Annual Report, 2012-2013, "Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer"

(<http://deainfo.nci.nih.gov/advisory/pcp/annualReports/HPV/Part1.htm#sthash.w7wUPjbp.dpbs>)

<sup>77</sup> President's Cancer Panel Annual Report, 2012-2013, "Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer"

(<http://deainfo.nci.nih.gov/advisory/pcp/annualReports/HPV/Part1.htm#sthash.w7wUPjbp.dpbs>)

<sup>78</sup> The Wall Street Journal, Nov 2014 (<http://www.wsj.com/articles/federal-goal-is-to-vaccinate-80-of-boys-and-girls-against-hpv-by-2020-1415647100>)



### 7.3.3 Tools to prevent, diagnose, and treat

There is no treatment for the virus itself. However, there are treatments for the health problems that HPV can cause. Prevention is the most effective way to deal with HPV, and early detection through efficient diagnosis is necessary as early as possible.

#### **Prevention through HPV vaccination**<sup>79</sup>

Primary prevention begins with HPV vaccination of girls aged 9 to 13, before they become sexually active. There are currently two WHO prequalified HPV vaccines on the market, both preventing HPV types 16 and 18, which are known to cause at least 70% of cervical cancers:

- Gardasil is a quadrivalent (Types 6, 11, 16, 18) vaccine produced by Merck
- Cervarix is a bivalent (Types 16, 18) vaccine produced by GSK

HPV vaccination does not replace cervical cancer screening. In countries where HPV vaccine is introduced, screening programs may still need to be developed or strengthened, as it only covers 70% of cervical cancer types. GAVI is supporting the roll out of HPV vaccines.

#### **Comprehensive approach**

WHO recommends a comprehensive approach to cervical cancer prevention and control. The recommended set of actions includes interventions across the life course. It should be multidisciplinary, including components from community education, social mobilization, vaccination, screening, treatment, and palliative care. Primary prevention begins with HPV vaccination of girls aged 9 to 13 years, before they become sexually active.

Other recommended preventive interventions for boys and girls as appropriate are:

- Education about safe sexual practices, including delayed start of sexual activity.
- Promotion and provision of condoms for those already engaged in sexual activity.
- Warnings about tobacco use, which often starts during adolescence, and which is an important risk factor for cervical and other cancers.
- Male circumcision.

#### **Diagnostics – screening for cervical cancer**

Screening is used to diagnose cervical cancer and pre-cancer conditions. It can detect cancer at an early stage when treatment has still a high potential for cure. Early detection is critical especially in low-resource settings, where treatment options are not available. Because pre-cancerous lesions take many years to develop, screening is recommended for every woman aged 30 to 49, at least once in a lifetime and ideally more frequently. There are currently three different types of screening tests available:

- Conventional (Pap) test and liquid-based cytology (LBC) require sophisticated laboratories and highly trained technical staff and are therefore mainly used in high-income countries.
- Visual inspection with Acetic Acid (VIA) is a simpler, easy to administer test developed especially for use in low-income settings.
- HPV testing for high-risk HPV types requires collecting vaginal cells and sending them to a laboratory for examination under a microscope to see if the cells contain genetic material from types of HPV that cause cancer.

However, effective HPV testing strategies are not used as much as they should be, resulting in many affected not knowing their status. Symptoms are often not pronounced before an advanced stage. Diagnosis also often occurs late, due to infrequency of screenings.

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<sup>79</sup> WHO – Human papillomavirus (HPV) and cervical cancer factsheet n°380 (<http://www.who.int/mediacentre/factsheets/fs380/en/>)



**Treatment**<sup>80</sup>

There is no treatment for the virus itself. However, there are treatments for the health problems that HPV can cause:

- Genital warts can be treated by the patient or a physician. If left untreated, genital warts may go away, stay the same, or grow in size or number.
- Cervical pre-cancer lesions can be treated. Women who get routine Pap tests can identify problems before cancer develops. If treatment is needed, cryotherapy (destroying abnormal tissue on the cervix by freezing it) is recommended.
- If signs of cervical cancer are present, treatment options for invasive cancer include surgery, radiotherapy, and chemotherapy.

Treatments for cancer are quite onerous, requiring appropriate equipment and trained health workers. These treatments are not accessible for many women in low- and middle-income countries.

In addition, there is a pipeline of innovations for HPV/cervical cancer, including innovations especially designed for resource-poor environments. The research conducted identified fifteen relevant innovations of which five have reached the final stage of development, addressing prevention, diagnosis and treatment.

**Prevention:** There is a new HPV vaccine, addressing more cancer-causing HPV types and a test to understand effects and develop the vaccine scheme for this new vaccine:

- *9vHPV vaccine* by Merck targets five additional cancer-causing HPV types and can offer protection from more than 80% of cervical cancers. The vaccine is approved by the Food and U.S. Drug Administration (FDA) in December 2014, but not yet WHO pre-qualified.
- *Test on 9vHPV vaccine* by NCEZID (The U.S. National Center for Emerging and Zoonotic Infectious Diseases) to measure the immune system response to the nine types of HPV in the 9vHPV vaccine. The test, a high-throughput multiplex serology assay, uses one sample to provide much-needed answers to questions about how many doses of vaccine are necessary, when they need to be given, and whether giving other vaccines at the same visit will affect the immune response to the HPV vaccine.<sup>81</sup>

**Diagnostics:** Two diagnostic tools are currently in development, especially for resource-poor environments, including the use of rapid HPV testing to triage high-risk women:

- *CareHPV* by Qiagen is a new test specifically developed for use in the developing world and designed to be rapidly processed by inexperienced personnel.
- *Xert HPV* by Cepheid is a quick (60-minute) test for cervical cancer that runs on Cepheid's GeneXpert system, which UNITAID already worked with in the context of Tuberculosis.

**Treatment:** *CryoPop* by Jhpiego, an affiliate of Johns Hopkins University, is an efficient cryotherapy device. It is a low-cost, sustainable, portable cryotherapy device that uses dry ice to treat pre-cancerous cervical lesions. This treatment relies only on compressed CO<sub>2</sub>, and is 10 times cheaper and 30 times more efficient than other cryotherapy devices.<sup>82</sup>

<sup>80</sup> Centers for Disease Control and Prevention (<http://www.cdc.gov/std/hpv/stdfact-hpv.htm>)

<sup>81</sup> National Center for Emerging and Zoonotic Infectious Diseases – Innovative Technologies (<http://www.cdc.gov/ncezid/pdf/innovative-technology-2015.pdf>)

<sup>82</sup> (<https://www.newglobalcitizen.com/impact-and-innovation/innovations-in-diagnostics-treatment-and-monitoring-could-eradicate-cervical-cancer-worldwide>)

### 7.3.4 Partner landscape

**WHO** has developed guidance on how to prevent and control cervical cancer, including through vaccination and screening.<sup>83</sup> The Organization works with countries and partners to develop and implement comprehensive programs. By the end of 2012, 45 countries had introduced HPV vaccination. Most of these are developed countries, but given that the global burden of cervical cancer falls most heavily on developing countries, there is still a great need for more countries to introduce the HPV vaccine as part of a national public health strategy that includes a comprehensive approach to prevention and control of cervical cancer.

**CDC** encourages partner organizations and state programs to promote adolescent vaccinations within their communities by increasing awareness about the importance and benefits of adolescent vaccination, through communication with nearby schools.

**GAVI** announced in June 2013 successful negotiation for a sustainable supply of HPV vaccine for use in developing countries at an unprecedentedly low price of \$4.50 per dose for Gardasil and \$4.60 per dose for Cervarix.<sup>84</sup> The lowest previous public-sector cost was \$13 per dose. The goal is that by 2020, 30 million girls in 40 countries get the vaccines at or below these prices.

**The PAHO Revolving Fund** provides a mechanism for many GAVI-ineligible, middle-income nations in Latin America and the Caribbean to procure HPV vaccines at reduced prices. Revolving Fund Member States pool their resources to purchase vaccines and related supplies at discounted bulk rates. The fund also provides countries a 60-day line of credit for purchases and assists with the logistics of vaccine procurement. As of 2012, four countries had introduced HPV vaccines with PAHO Revolving Fund support.

### 7.3.5 Main challenges to be addressed

Two main areas deserve the attention of the RMNCH community in order to answer to the public health need created by HPV: (1) vaccines and (2) diagnostics.

Vaccines challenges are mainly around the increase of coverage through vaccination programmes and the development of alternative and innovative forms of vaccines to address technical issues such as administration, transportation, and storage.<sup>85</sup> Many interventions are already underway, mainly driven by GAVI – which is developing a new HPV vaccine.

Diagnostic challenges for HPV are mainly focused around increasing their access in developing countries, and developing new diagnostic tools:

- The implementation of HPV screening programs in low- and middle-income countries (LMICs) is of paramount importance. Indeed, in developing countries, limited access to effective screening means that the disease is often not identified until it is further advanced. In addition, prospects for treatment of such late-stage disease may be poor, resulting in a higher rate of death from cervical cancer in these

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<sup>83</sup> WHO – Cancers (<http://www.who.int/reproductivehealth/topics/cancers/en/>)

<sup>84</sup> President's Cancer Panel Annual Report, 2012-2013, "Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer" (<http://deainfo.nci.nih.gov/advisory/pcp/annualReports/HPV/Part5.htm>)

<sup>85</sup> President's Cancer Panel Annual Report, 2012-2013, "Accelerating HPV Vaccine Uptake: Urgency for Action to Prevent Cancer" (<http://deainfo.nci.nih.gov/advisory/pcp/annualReports/HPV/Part5.htm#sthash.O6SzOxQY.dpbs>)

countries. The high global mortality rate from cervical cancer (52%) could be reduced by effective screening and treatment programs.<sup>86</sup>

- The development and scale-up of new diagnostic tools would help to spread efficient screening of cervical cancer. Work in this area would aim to amplify the impact of upstream research and development by accelerating the uptake of emerging diagnostic options. Recent research has mainly focused on the utility of alternative screening approaches in resource-poor environments. Promising tests are being developed and innovations will probably have to be tested through pilots and brought to markets before being scaled-up.

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<sup>86</sup> WHO – Human papillomavirus (HPV) and cervical cancer factsheet n°380 (<http://www.who.int/mediacentre/factsheets/fs380/en/>)