

Project title

Effectiveness trial of day-care (DCA) versus usual care management of severe pneumonia with or without malnutrition in children using the existing health system of bangladesh (Phase I: january 2015 to december 2017; Expansion phase II : 1.7.2017 to 31.1.2019)

Expansion phase II: Start: 1.7.2017

(EAGLE supported) Start of patient enrolment in new study sites: 1.11.2017

Project report III to EAGLE Foundation period 1.1.2019 till 30.06.2019

Date: 20.7.2019

Place of performance

7 study sites in Dhaka city and in rural areas northwest and northeast of Dhaka and Centre for Health and Population Research (icddr), Dhaka, Bangladesh in cooperation with university of Basel, Switzerland and University of Kentucky, Lexington USA.

Investigators

Nur H Alam, Abu SG Faruque, Jubair Chisti, Shahjahan Ali, Tahmeed Ahmed, Shahnawaz Ahmed, George Fuchs, Trevor Duke, Niklaus Gyr

Project brief

Principal Investigator	Dr. Nur Haque Alam, icddr Email: nhalam@icddr.org
Original project duration	January 2015 to January 2019 Expansion phase: July 1st 2017 until January 31st 2019
Donor	UNICEF Switzerland, Botnar Foundation & UBS Optimus Foundation, Switzerland , EAGLE Foundation Switzerland
Implementing Partners	icddr, MoHFW, UNICEF, Pathfinder, PSTC and CWFD
Implementation Location- 7 sites	Urban – Tikatuli, Circular road and Dhalpur Rural – Dhamrai, Karimganj, Pakundia, and Kishoregonj Sadar
Original Target (stat. power 0.85)	3500 children to be treated for severe pneumonia through Day care approach, referral system and existing treatment
Modified Target (stat. power 0.80)	3000 children
Achievement till 18 March 2019 Stop of enrolment	3226 children with severe pneumonia have been enrolled (intervention + control) for treatment under this study protocol
Budget of expansion phase	USD 1 856 282, not including USD 136 815 for the 2 international cooperators and experts G.Fuchs USA and N.Gyr Basel, now partly supported by EAGLE and UNICEF special grant Dissemination credit of USD 142 000 by UBS in 2019

EAGLE Foundation Grant

USD 25 414 for travel, administrative and office expenses of Prof. N.Gyr (no honorarium)

Background of the project

Successful management of children with severe pneumonia (WHO 2013) requires hospitalization for antibiotic and supportive treatment such as pulse oximetry, oxygen therapy, nebulization, nasopharyngeal clearance and monitoring etc. Most, if not all, developing countries including Bangladesh do not have enough paediatric hospital beds to accommodate the demand for admission of all children with severe pneumonia with or without malnutrition and other co-morbidities. It is therefore important to provide some other form of institutional care for those children suffering from severe pneumonia and malnutrition who cannot be hospitalized, but are too sick to be managed in the community.

The project team developed an **innovative and unique model** of Day Care Approach (DCA) as a safe and less expensive alternative to hospital management of severe childhood pneumonia and malnutrition. The new management approach has proven to be efficacious and cost-efficient (>33% less expensive) in several efficacy studies in urban Mirpur, Dhaka, under optimal test conditions (EAGLE study Pediatrics 2010)

Purpose of the study

The aim of the present trial is to prove the safety, efficacy and effectiveness of DCA within the Bangladeshi health system in a large effectiveness trial- on a quasi strategic level

Study design and study locations

The project has been designed as cluster randomized controlled trial involving Primary Health Care Facilities in urban and rural areas under the health system of Bangladesh. The locations are:

Urban location (Wards)	Rural location (Unions)
Intervention and Day Care Clinic	
Tikatuli, Dayaganj, Wari, Jatrabari, Bashabo, Dhalpur, Shantinagar and Circular Road involving the Surjer Hashi Clinics	Dhamrai - Kushura , Sanora , Shombhag , Kulla Karimganj- Baroghoria, Joyka, Niamatpur, Gundhor Pakundia – Patuabhanga, Hosendi, Narandi, Sukhia Kishorgonj Sadar–Baulai, Jasodal, Danaptali, Majkhpan involving the Health and Family welfare Clinics (HFWCs) under the Ministry of MoHFW
Control clinics (existing treatment protocol)	
Gandaria, Begumganj, Muradpur, Lalbagh, Aftabnagar, Maniknagar, Taltola and Badda involving the Surjer Hashi Clinics.	Balia, Jadabpur , Baishakanda , Nannar, Jafrabad, Kadirjongal , Noabad , Dahunda Jangalia, Barudia, Egarasindur, Charfaradi Binnati, Maria, Koshakariail, Chauddasata involving HFWCs under the MoHFW

Case Management of Pneumonia

- Children with pneumonia with/without malnutrition will be identified or those who are self-referred will be treated at home with oral antibiotic for 5 days.
- Those children with pneumonia (i.e., not severe pneumonia) who will fail after two days of oral antibiotic therapy will be referred to hospital/DCA treatment if they fulfill the criteria of **severe** pneumonia.
- Children with **severe** pneumonia are referred directly to the hospitals/Day care clinics.

How Day care management works

Day Care treatment facility is a modified outpatient clinic with facilities similar to a hospital and equipped with trained physicians and nurses, 2-3 pediatric beds, availability of oxygen therapy with pulse oxymetry for measurement of oxygen saturation, long acting injectable antibiotics, nasophayngeal suction, nebulization facilities and calorie dense diet

for the children. The facility operates daily during office hours from 8:30 AM to ~4 PM. Children stay during this period. If not stabilized within this period then the children are referred to the referral hospitals. Cell phone networking is maintained during night hours to guide or refer children to appropriate facilities. There is a regular follow up.

Development 1st half 2019 and situation of the trial per Jun 2019

To cover the cost of remaining enrollment and to successfully complete the trial including diffusion activities additional financial support was required. The issue was discussed with all donors at the Zurich meeting of June 28/29th 2018. UBSOF, who was one of the initial sponsors of this trial, has kindly expressed its willingness to support and early in 2019 contributed USD 142 000 for the completion of the study including diffusion activities.

We now have completed the enrollment on 18 March 2019 and the cumbersome data cleaning process and analysis is in progress. We plan to organize a Steering Committee meeting in September 2019 and a dissemination seminar and workshop in November after the world Pneumonia day 2019. The final reports will be submitted by January 2020 and the first manuscript submission is foreseen in January 2020.

These activities are undertaken in cooperation with UNICEF Dhaka, UN agencies and local Health Authorities in order to obtain maximum public attention.

Enrolment : Since start of the expansion phase in July 2017 1678 additional patients with severe pneumonia have been enrolled in the 24 months period resulting in a total of 3226 patients on 18th March 2019. There is a gap of 274 patients to the original target of 3500 envisaged. Again enrolment was lower than anticipated even after opening of the new study sites. We therefore decided after consultation with statisticians to reduce the statistical power from 0.85 to 0.80 which allowed us to reduce the enrolment target number to 3000 patients plus 2 to 300 patients for compensation of drop outs. The statistical power of 0.80 is well accepted by the scientific community and thus permits a valid result.

Quality of study: Clinical care, data entry and work-up have been checked by the project team and Prof. G.Fuchs during his visit in November 2018 and February 2019 . It appeared well performed promising convincing results.

Clinical outcome: As predicted based on the previous studies the success rate appears to be equal for DCA and control patients, amounting to about 90% in the rural study area and 80% in urban trial sites. Respective data analysis is in progress.

Economic outcome of household expenditure, preliminary (table):

According to the household treatment cost for severe pneumonia, a total of 144.13 US\$ was spent for existent care (ET) which appears around 5 times higher than the Day Care Approach (DCA).

Cost indicators	DCA (n=1581)		ET (n=1474)		Times higher
	Mean (US\$)	SD	Mean (US\$)	SD	
Direct medical cost (i.e., drug, diagnostic)	2.92	9.06	37.01	50.87	12.66
Direct non-medical cost (i.e., transport, tips)	2.34	4.61	11.30	11.72	4.82
Indirect cost	25.99	24.54	95.81	73.46	3.69
Total cost	31.25	32.45	144.13	115.15	4.61

1 US\$=84.45 BDT; DCA – Day Care Approach (DCA); ET- Existent Treatment; US\$ - US dollar

Dissemination: Dr. Khalida Islam, Director of Primary Health and IMCI, was very favorably impressed with the study objectives and its implementation: She is interested having daycare management of pneumonia and malnutrition scaled up throughout the Bangladesh health care system. This view also was shared by the president of the Bangladesh Pediatric Society. The interest of these 2 key persons has been confirmed again.

Trial budget : At the end of September 2018 USD approx. 541 290 were left to finish the trial. The extension to end of 2019 as well as the planned dissemination activities with final symposium and workshop in fall 2019 will require an additional of USD 142 00 which now has been granted by UBSOF.

Activities of N.Gyr during the first year of expansion

N.Gyr was very much involved in the budgeting process and thereafter in budget control for the UNICEF,BOTNAR-EAGLE expansion phase grant as well as for the additional UBSOF grant. He was also involved in follow up of study results. The international communication was maintained with regular skype conferences, direct phone calls as well as e-mails and visits with sponsors in Switzerland eg meeting with new UNICEF CEO Mrs.B. Juncker in Zürich, March 29th 2019.

Last visit of Dhaka in November 2017.

For health reasons N.Gyr was unable to visit Bangladesh in 2018 and 2019 so far.