How to secure high fidelity and quality of delivery of the intervention(s) in RCTs

CISMAC webinar 4th April
Outline

• Background
• Monitoring fidelity and quality in the
  • cKMC-study
  • RISE-study
  • B12-study
  • BCG-study
• Discussion
Background

- RCTs test the effects of specific intervention(s) on selected outcomes of interest.
- Should make sure the intervention(s) is implemented properly so the hypothesis about it being effective can be tested.

Two important aspects of the implementation:
- Fidelity (whether intervention is delivered as intended)
- Quality of intervention delivery

Can be monitored as part of a process evaluation.
• If an intervention is found to be ineffective, data from process evaluation can help determine whether the failure is attributable to:

1. failure of intervention concept or theory

2. specific intervention design not working, but basic concept right
   • content of components
   • delivery mode,

3. aspects of trial design, delivery or context precluding detection of real effect, but basic concept right
Aspects of implementation that can influence whether effects on outcomes can be measured:

• adherence to protocol,
• quality of delivery,
• exposure/coverage,
• risk of contamination
• any interventions in the control arm?
Studying the implementation process

• Process evaluations not only concerned whether an intervention is implemented correctly
• But also increasingly concerned with the mechanisms through which fidelity and quality is achieved,

• Can inform efforts to incorporate the intervention into routine practice after the evaluation
Monitoring fidelity and quality in different CISMAC trials
Process Evaluation

Impact of Promoting Community Initiated Kangaroo Mother Care (KMC) for Low Birth Weight Infants
Aim:

**Monitor intervention:**
Implemented as intended
Assess fidelity and quality

**Understand factors associated with success or failure**
Specific Objectives:

• Compliance of KMC community supervisors (KCS) and community workers (KCW) to the desired intervention content and delivery
  o Messages
  o Counselling
  o Demonstration
  o Problem solving

• Documentation of enablers, barriers and solutions
  o Experiences and feedback of mothers/family members
  o Feasible, acceptable, effective solutions
  o Update counselling guide
Methods:

**Observation**: Accompanied visits

**Study protocol visit schedule**:

- KCS and KCW make joint home visits for first 3 days of enrolment
- Independent visits by KCW:
  - at infant age 5 and 7 days
  - once a week in subsequent weeks till 28 days of age

**PE Team**: Senior experienced members of study team
Methods:

**Periodicity of visit:**
12 KCS; 25 KCW, each observed once in 3 months

**Tool: Observation checklist**
- Appearance of worker appropriate for home visit, ID card
- Preparedness: Job aids, photographs, message sheet, counselling guide, registers, electronic compliance form, hard copies of forms
- Appropriate introduction to family
- Behaviour and rapport with family
- Recapitulation of messages of previous visit
- Clean hands, use of soap water/hand sanitiser
Tool: Observation checklist (contd...)

- Observation of SSC: position, clothing of baby and mother, ascertainment of duration day, night

- Observation of BF: position, attachment, sucking, ascertainment of exclusive BF, frequency of BF.

- Hands on demonstration

- Problem identification, aptitude in resolving

- Counselling skills, alertness, responsiveness, involvement with family members, praising mother/family members, asking checking questions

- Ability to observe home ambience, family dynamics and support, interaction, mothers condition and stress [obtained from examination of notes]
Reporting:

Summary report submitted to study coordinator within 2 days.

Observations in qualitative format
Preliminary Findings:

- Fidelity to planned implementation high

- Intervention delivery team well prepared: technical and effective counselling skills

- Gained expertise and confidence with time to resolve barriers, provide feasible solutions

- Comprehensive counselling guide
Interesting Observations:

- Compliance higher than expected
  Most compelling reason: emotional bonding, feeling of closeness to baby

  Other reasons: visible benefits motivate
  - Baby more playful
  - Feeds better
  - Sleeps peacefully
  - Skin smooth
  - Face glows
  - Becoming heavier, healthier

- Two way learning process
  Context specific examples by families from daily life
  Study team uses the same to motivate other families
RISE interventions

- Economic support
  - Monthly cash to adolescent girls
  - Annual grants to their guardians (in 2017 and 2018)
  - Payment of school fees for grade 8 and 9 (in 2017 and 2018)

- Community dialogue
  - Youth club meetings
  - Community meetings

- Material support
  - Writing materials
RISE process evaluation

Methods for evaluating fidelity to economic support components:

• Lists where recipients sign are scrutinized by Trial supervisors the following month
  • Authenticity of signatures compared
• Girls asked whether they have received cash in biannual interviews
• Guardians asked for feedback about economic support during annual meetings
RISE process evaluation

Methods for evaluating fidelity to community dialogue components:
• Log forms filled in by facilitators (teachers and community health workers (CHWs))

• Observations
  • Monitoring of all community meetings and 15-20% of youth club meetings by Trial supervisors
    • Some meetings also monitored by PMT members
  • «Qualitative» reports during first implementation year
  • Introduced «Quality indicator score» sheet in the second implementation year

• Qualitative interviews
  • IDIs with the implementers (teachers and CHWs)
  • IDIs and FGDs with participating girls, boys and parents
Monitor scores meeting from 0 to 2 on

• 20 items for youth club meetings and
• 17 items for community meetings

*Items include:*

• Whether activities as outlined by the manual are adequately covered
• Presentation skills
• Whether participants were fully engaged and said something
• Organisation of group work
• Activity level among boys and girls

• Feedback given to facilitators after meeting.
• PMT members and Trial supervisor compare scores when monitored same meeting
RISE process evaluation: Preliminary findings

• Fidelity to economic component high
  • But some cases of misuse of funds by cash teachers or school management have been discovered
  • Schools appreciate school fees – headteachers send multiple reminders to make sure we pay school fees

• Community dialogue:
  • Training appreciated, seemed to prepare teachers and CHWs well
  • Most teachers and CHWs motivated and follow manuals,
    • But some struggle to engage all the learners
    • Boys tend to dominate meetings
    • Group work often done with very big groups
    • -> may reduce effects on knowledge, attitudes and behaviour
B12 supplementation for pregnant mother

Supplementation - 50 µg per day till 6 months after delivery - ~ 12 months

Main outcomes:
- Bayley scores at 6 and 12 months of age
- Growth of infants and hemoglobin concentration

Status: Screening-335

Enrollment started - 27th March 2017

Total enrollment - 191

Total drop-out - 10

Total deliveries - 94
Completed - 3
## During enrolment and follow up

<table>
<thead>
<tr>
<th>Visit</th>
<th>Strategies</th>
<th>Monitoring plan</th>
</tr>
</thead>
<tbody>
<tr>
<td>• During enrolment</td>
<td>• Counselling on dose, timing, reminder</td>
<td>• 5% weekly visits monitoring by supervisors</td>
</tr>
<tr>
<td>• Weekly visit</td>
<td>• Weekly visit form-refill supplementation</td>
<td>• Independent check of diary records; review when requested for next packet of supplement</td>
</tr>
<tr>
<td>• Timely supply of supplement and co-interventions (Iron, folic acid, Calcium)</td>
<td>• Diary record of supplement and co-interventions (includes total amount of supplement with participant which roughly indicates the date before which the next visit has to be made)</td>
<td>• 10% monthly visits monitoring by supervisors; update in Viber groups and register after completion of activities.</td>
</tr>
<tr>
<td>• Timely conduction of activities prescribed in the protocol/manual</td>
<td>• List of activities along with dates</td>
<td></td>
</tr>
</tbody>
</table>
Strategies considered for fidelity and quality in current study

<table>
<thead>
<tr>
<th>Activities</th>
<th>Strategies</th>
<th>Remark</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Training of practitioners in conducting activities/tests and Standardization</td>
<td>• Training on activities/tests and Standardization conducted before every new activity/test.</td>
<td>• Discussions on the process of conducting activities are regular but informal</td>
</tr>
<tr>
<td>• Orientation to the activity specific forms (paper/electronic based)</td>
<td>• Forms discussed routinely.</td>
<td>• Forms and errors are discussed regularly</td>
</tr>
<tr>
<td>• Orientation and exercise on Diary record keeping of supplement and cointervention; monthly record submission of cointervention</td>
<td>• Orientation on diary record keeping, cointervention monthly record submission and requisition of new packet of supplement.</td>
<td>• Frequent/Need-based diary record discussions, monthly record review and feedback by supervisor, calculation of errors (number of supplement pieces missed by participants) while requesting for next packet and counselling, if needed, to participants with errors more than 10%</td>
</tr>
</tbody>
</table>
The BCG Trial

• **Study design:** An individually randomized controlled trial

• **Study population:** 2,200 HIV exposed infants

• **Intervention:** 0.05 ml of BCG vaccine within 24 h of birth

• **Comparator:** 0.05 ml of BCG vaccine at 14 weeks of age

• **Our main threat to Fidelity:** Children in the comparator arm (to receive BCG at 14 weeks of age) receiving the vaccine *before* 14 weeks of age because the WHO/Ugandan guideline is “as soon as possible after birth” and usual timing is on the day of birth
**Threat to Fidelity:** Receipt of the vaccine earlier than scheduled in the comparison arm because 14 weeks after birth is an unusual timing (usual on the day of birth)

**Solution:** Explicit labelling of the study participants’ vaccination cards

---

<table>
<thead>
<tr>
<th>VACCINE</th>
<th>PROTECTS AGAINST</th>
<th>MODE OF ADMINISTRATION</th>
</tr>
</thead>
<tbody>
<tr>
<td>AT BIRTH</td>
<td></td>
<td></td>
</tr>
<tr>
<td>BCG</td>
<td>Tuberculosis</td>
<td>Intradermal injection on Right Upper Arm</td>
</tr>
<tr>
<td>Polo 1</td>
<td>polo</td>
<td>2 Oral drops</td>
</tr>
<tr>
<td>Polo 2</td>
<td>polo</td>
<td>2 Oral drops</td>
</tr>
<tr>
<td>DPT</td>
<td>diptheria, whooping cough, tetanus</td>
<td>Intramuscularly, outer aspect of Left Thigh</td>
</tr>
<tr>
<td>PCV</td>
<td>Pneumoniae Pneumoniae</td>
<td>Intramuscularly, outer aspect of Right Thigh</td>
</tr>
<tr>
<td>Polo 3</td>
<td>polo</td>
<td>Dull Sow administration, inner aspect of the cheek</td>
</tr>
</tbody>
</table>

| AT 6 Weeks|                                      |                        |
| DPT      | diptheria, whooping cough, tetanus | Intramuscularly, outer aspect of Left Thigh |
| PCV     | Pneumoniae Pneumoniae | Intramuscularly, outer aspect of Right Thigh |

| AT 10 Weeks|                                      |                        |
| DPT       | diptheria, whooping cough, tetanus | Intramuscularly, outer aspect of Left Thigh |
| PCV      | Pneumoniae Pneumoniae | Intramuscularly, outer aspect of Right Thigh |

| AT 14 Weeks|                                      |                        |
| DPT      | diptheria, whooping cough, tetanus | Intramuscularly, outer aspect of Left Thigh |
| PCV      | Pneumoniae Pneumoniae | Intramuscularly, outer aspect of Right Thigh |

| 6 Months|                        |                        |
| Measles | measles               | Subcutaneously, Left Upper Arm |

---

**Child’s vaccination card**

**Messages to vaccination health care workers under a highly visible highlight**
Threat to Fidelity: Receipt of the vaccine earlier than schedule in the comparison arm because 14 weeks after birth is an unusual timing (usual is at birth)

Solution: Explicit labelling of the children’s vaccination cards

14 week vaccination date written twice on top of the vaccination card so that it can be easily seen by vaccinating health care workers

Message to health care workers to send study participants with labels to the BCG study clinic for verification before vaccination

This baby eventually received the vaccine on the 17/10/2017 which was within 1 day of the schedule 16/10/2017. This was in agreement with the study protocol. Overall, fidelity is very high.
## Actual compliance BCG trial Kampala (until mid-Dec 17)

**Compliance in Early BCG trial arm:** 528 of 528 babies arm received BCG on the day they were born: 100%

**Compliance in Delayed BCG trial arm:**

<table>
<thead>
<tr>
<th>Received BCG as per protocol, i.e. within 13 weeks (91 days) and 15 weeks (111 days) of age</th>
<th>311</th>
</tr>
</thead>
<tbody>
<tr>
<td>n (% of 360)</td>
<td>Age when vaccinated</td>
</tr>
<tr>
<td>12 (3.3%)</td>
<td>7 days or less</td>
</tr>
<tr>
<td>3 (0.8%)</td>
<td>8-13 days</td>
</tr>
<tr>
<td>5 (1.4%)</td>
<td>14-30 days</td>
</tr>
<tr>
<td>13 (3.6%)</td>
<td>30-90 days</td>
</tr>
</tbody>
</table>

33 babies received BCG *before* 13 weeks of age despite being randomized to late BCG vaccination

| n (% of 360) | Age when vaccinated |
| 12 (3.3%) | 7 days or less |
| 3 (0.8%) | 8-13 days |
| 5 (1.4%) | 14-30 days |
| 13 (3.6%) | 30-90 days |

16 babies received BCG *later than* 15 weeks of age despite being randomized to late BCG vaccination

| n (% of 360) | Age when vaccinated |
| 14 (3.9%) | 16-25 weeks |
| 1 (0.3%) | 26-41 weeks |
| 1 (0.3%) | 42-52 weeks |

Children who by mid-Dec 2017 were less than 13 weeks of age (will receive BCG as per protocol.)

| 161 |

Missing Vaccination Cards, age at vaccination is being ascertained by other means

| 7 |
Dealing with challenged fidelity

- Major threats: Jeopardizes trial, makes interpretation difficult

- Small (e.g. BCG trial) and moderate threats: Compare Intention-to-treat (ITT) with per protocol (PP) analysis and with Instrumental Variable Analysis (IVA)
Questions for discussion

What are the advantages and disadvantages of

- Involving independent monitors in assessing fidelity and quality?
- Using information from monitoring of intervention delivery to strengthen the implementation versus just analyzing process data at the end?
- Separating or integrating process and outcome evaluation teams?