Evaluation of Complex Interventions

Diana Elbourne
London School of Hygiene & Tropical Medicine (LSHTM)

for
Helsinki, May 2009
Outline

• What are complex interventions
• Developing complex interventions
• Evaluating complex interventions
• Examples of evaluations coordinated by LSHTM
  – HIM (individually randomised, Russia)
  – BEADI (cluster randomised, England)
  – CHAMPION (cluster randomised, India)
  – CENEX (cluster randomised, Chile)
What are complex interventions?

- Complex interventions are those with multiple components which have separate modes of action, but whose effect depends on the other components.
- ‘built up from a number of components, which may act both independently and interdependently’ (Campbell et al. 2007)
- Many interventions in health care are ‘complex’
Context for complex interventions

• Complex interventions usually involve aspects of service delivery or implementation in health systems
  – For example, a complex intervention of treatment for stroke would include not just the drugs used but also aspects such as ‘investigations, … treatment guidelines, and arrangements for discharge and follow up’

• NB not just health system, but also socio-economic setting/cultural assumptions etc
Developing complex intervention

• Defining/understanding/quantifying the problem
• Identifying possible components of intervention to address problem
  – Theoretical/conceptual underpinnings
  – Existing empirical evidence
• Clarifying population at risk/most likely to benefit
• Exploring appropriate outcomes
• Considering context for implementation
Define problem

Identify possible components of intervention

Define outcomes

Review theory and evidence supporting the components

Seek target population most likely to benefit

Explore context, do baseline and/or pilot studies to guide implementation

Decide whether and how to do a controlled trial
Evaluating complex interventions (1)

• No single formal design for developing and evaluating complex interventions
• More complicated than drug trials
  – the ‘package’ of care
  – the implementation
• But also many similarities with process of developing and evaluating drugs
## Evaluating complex interventions (2)

<table>
<thead>
<tr>
<th>Drug trial phase</th>
<th>Name</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>0</td>
<td>Theory</td>
<td>Explore relevant theory to ensure best choice of intervention</td>
</tr>
<tr>
<td>1</td>
<td>Modelling</td>
<td>Identify the components of the intervention and the mechanisms by which may influence outcomes</td>
</tr>
<tr>
<td>2</td>
<td>Exploratory trial</td>
<td>Investigate the applicability of a preliminary intervention, and pilot-test</td>
</tr>
<tr>
<td>3</td>
<td>Definitive trial</td>
<td>Compare a fully defined intervention with an appropriate alternative</td>
</tr>
<tr>
<td>4</td>
<td>Long term implementation</td>
<td>Impact of the intervention in other settings over the long term</td>
</tr>
</tbody>
</table>
Evaluating complex interventions (3)

• In early stages, qualitative research methods may be particularly appropriate
• Aim to optimise the form of intervention for testing in a trial
• After early stages, may decide
  1. Intervention unlikely to be useful
  2. Evidence supporting intervention has become so strong that just needs to be implemented
  3. Intervention promising but evidence not conclusive so needs evaluation
Evaluating complex interventions (4)

• Needs to be rigorous so provides a definitive answer about whether the intervention is (cost)-effective
• Randomisation to avoid selection bias
• Appropriate size to avoid imprecise answer
• Appropriate design
  – eg individually randomised, cluster randomised, factorial, other
Design

• Standard – individually randomised
• Factorial – to try to tease out different components of complex intervention, or to test more than one intervention
• Cluster - as complex interventions often involve different modes of health care delivery
  – clinic or ward would be typical randomisation units
Generalisability

• If interventions very context-specific, generalisability to other contexts may be problematic

• Important that details of intervention and control groups very well reported to allow readers to assess extent to which could relate to their own context
Example 1
**HIM** (Health for Izhevsk Men) trial

What is the problem?

- Russia one of the very few industrialised countries in the world where life expectancy has been declining
- Alcohol implicated as major contributor
- Particularly marked among working-age men
Hazardous drinking in Russia

• "zapoi“
  – episodes of extended periods of drunkenness during which the participant withdraws from normal life

• Consumption of surrogate alcohols
  – alcoholic substances not intended to be drunk
    - non-beverage alcohols
Vodka: a selection
Surrogate spirits
Alcohol containing medicines
What might reduce alcohol problems?

• Government action
  – to control manufacture and sale of drinkable surrogates and limit the availability
  – to increase price of legitimate alcoholic beverage

• Individual level action
  – individual counselling
  – need to reach beyond specialist treatment services as most hazardous drinkers do not access such provisions
‘Brief’ interventions

• Shown to be effective in many contexts
• Seek to change views of the personal acceptability of excessive drinking and to encourage self-directed behaviour change
• Include both simple forms of advice and brief counselling techniques
• Can be delivered by wide range of generic rather than specialist practitioners
Motivational Interviewing (MI)

- Increasingly prominent brief intervention
  - "A facilitative, patient-centred counselling style for helping people explore and resolve ambivalence"
- Systematic review of 31 trials of MI very promising
- Very little known about the salience and applicability in Russian context
- Early development phase of trial explored adaptations of MI in Russia
RCT in Izhevsk

• Design - individually randomised two-armed parallel group exploratory trial
  – set in context of existing cohort study

• Hypotheses
  – MI will reduce self-reported hazardous drinking at 3 months; self-reported past week beverage alcohol consumption, alcohol dependence and related problems at 3 months and at 12 months
Working-age men living in Izhevsk interviewed

Men with major alcohol problems identified

Consent to medical exam and follow up
RANDOMISED

Up to four sessions of motivational interviewing

Re-interview

Re-interview + medical exam

months 1 to 3
at 3 months
at 12 months

No contact

Re-interview

Re-interview + medical exam
MI intervention

- Adapted MI includes topics such as surrogate drinking and zapoi
- Intervention will be delivered at home or in a clinic by practitioners who have been specially trained and supervised, with a period of practice-based learning following an introductory workshop
- The full intervention comprises up to four sessions
  - two core sessions approximately two weeks apart
  - additional sessions (to a maximum of 2) available upon request
- Approximately 10% of sessions will be audio-recorded for quality control and supervision purposes
Consent

• All initially in the longitudinal study
• Consent requested for medical examination and 3 and 12 month follow up
• After randomisation, men in MI arm asked for their consent to MI sessions
• Control group given ‘usual care’ (not involving MI), and not informed about MI sessions as evidence that this awareness could influence drinking patterns
  – Single consent Zelen design
Sample size

Assumptions
• Based on current MI literature, 25% of participants in the intervention arm will stop hazardous drinking
• Spontaneous reduction in hazardous drinking of more than 5% unlikely in the control arm
• 20% of the participants in the intervention arm will not agree to receive the intervention
  – as randomisation carried out prior to consent to MI
• 20% loss to follow for the 3 month assessment in both trial arms
• 90% power; 5% level of statistical significance

Need overall sample size of between 200 and 250 participants
Practicalities of research

• Collaboration between LSHTM and Izhevsk team of clinicians and researchers
  – Building on earlier collaborations
  – Randomisation and data analysis led from LSHTM
  – Intervention development/delivery and data collection/entry led from Izhevsk

• Funding – from Wellcome trust

• Biggest problems arose from international and local politics
Current status

2041 men re-contacted for longitudinal study
1515 re-interviewed
441 eligible and consented for trial
Randomisation complete
3 month post-randomisation data available
135/221 (61%) 138/220 (63%)
98% of those reaching 3 months
First results likely 2010
Example 2
The BLISS cluster randomised controlled trial of the Effect of ‘Active Dissemination of Information’ on standards of care of premature babies in England (BEADI)
Dominique Acolet
1949-2008
Review of literature

• Gap between research evidence and policy and practice
• Limited effect of traditional ways used by health professionals to keep up to date with their practice
• Systematic reviews showed larger effect with more active dissemination methods
  – audit and feedback
  – interactive workshop
  – educational outreach by experts or trained facilitators (regional champions)
  – multi-faceted interventions
• Most research in N America and in adults
Vermont Oxford Network to promote surfactant therapy

*(Horbar J 2004)*

- Cluster RCT Intervention:
  - audit & feedback
  - evidence reviews
  - interactive training workshop
  - ongoing faculty support via conference calls/emails

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Intervention (%)</th>
<th>Controls (%)</th>
<th>OR</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surfactant in labour ward</td>
<td>55</td>
<td>18</td>
<td>5.4 (2.8-10.2)</td>
</tr>
<tr>
<td>Median time to 1st dose</td>
<td>21 mins</td>
<td>78 mins</td>
<td>p &lt;0.001</td>
</tr>
</tbody>
</table>
Aim of BEADI

• To replicate the Horbar study adapted for NHS in England
• To assess whether an innovative ‘active’ strategy for the dissemination of national neonatal recommendations is more likely to lead to changes in hospital policy and practice in premature babies than the traditional forms of dissemination in English neonatal units
Case Study Project 27/28
Confidential Enquiry Into Maternal and Child Health (CEMACH)

• Quality of care for babies born at 27-28 weeks gestation
• Dissemination to all Trusts
  • Report
  • PowerPoint slide presentation
• Questionnaire survey
  • Respondents reported slides raised local awareness, initiated or consolidated policy changes
  • But low response rate
  • Not a RCT
BEADI Methods

• Cluster RCT
  – all neonatal units in England
  – randomised by hospital (n = 180)
  – stratified by neonatal networks and unit level of care
Criteria for chosen outcomes

1. Needed to be important for babies
2. Had to be an evidence base for interventions to address these outcomes
3. Were collected in parallel study (EPICure 2)
4. *Would have liked to have added that pre-intervention rates were low enough for there to be scope for improvement, but data about these rates from the EPICure 2 study were not available in time to inform this decision, so had to make assumptions*
BEADI outcomes

Focused on 3 main areas of neonatal care shown in Project 27/28 to be associated with death

- timing of surfactant administration
- early temperature control of babies
- skill mix of the resuscitation team present at birth
Sample size

Policy: assuming pre-intervention rates 35% - 60%, 130 units sufficient to detect RR from 1.4 to 1.6, with 80% power, 5% significance

Practice: assumed 1650 annual admissions to NICU from 3,500 births of babies <27 weeks
- Used range of likely intra-cluster correlation coefficients (ICC) to estimate power to detect range of differences in practice between arms
- eg 400 admissions has c80% power to detect a difference from 40% to 55% with ICC of 0.06 – 5% two-sided significance

Allowance for non-compliance/losses to follow up
‘Control’ arm

• Usual dissemination strategies
  – report sent
• PowerPoint slide package
• National position statement on website
‘Intervention’ arm

• Two meetings
  – Autumn 2006

• Benchmarking and feedback on individual policies and practice
‘Intervention’ arm meetings

• 1st meeting: regional ‘champions’
  – training in organisational change principles
  – help in supporting change in intervention centres in their region

• 2nd meeting: consultant leads + champions
  – targeted outcomes: evidence reviews, lectures, agreement on final wording
  – introduction to tools & practice of change
  – examination of current practice
  – drawing up plan for changes and local implementation
Data collection

• Unit policies pre-intervention collected by the EPICure 2 team early in 2006
• Post-intervention data about policies and practice collected by CEMACH for January-March 2007
Policies: flow chart

180 neonatal units randomised

39 not present at intervention workshop

Active arm
N=87

25 with no 2007 policy data

62 units analysed

Control arm
N=93

24 with no 2007 policy data

69 units analysed

Control arm
N=93

69 units analysed

Active arm
N=87

62 units analysed

25 with no 2007 policy data

39 not present at intervention workshop

180 neonatal units randomised
## Baseline units policies
### Jan-March 2006

<table>
<thead>
<tr>
<th>Category</th>
<th>Active N=87</th>
<th>Control N=93</th>
</tr>
</thead>
<tbody>
<tr>
<td>Information available</td>
<td>N=78</td>
<td>N=83</td>
</tr>
<tr>
<td>Policy for hypothermia prevention</td>
<td>75 (96%)</td>
<td>80 (96%)</td>
</tr>
<tr>
<td>Policy for hypothermia prevention involving delivery into plastic bag or wrapping</td>
<td>67 (85.9%)</td>
<td>77 (92.8%)</td>
</tr>
<tr>
<td>Policy for which paediatric staff should be present at extremely preterm birth</td>
<td>64/77 (83.1%)</td>
<td>74/82 (90.2%)</td>
</tr>
</tbody>
</table>
## Policies post-intervention
### January-March 2007

<table>
<thead>
<tr>
<th>Strategies in place</th>
<th>Active N = 62</th>
<th>Control N = 69</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hypothermia prevention n (%)</td>
<td>61 (98)</td>
<td>67 (99)</td>
<td>0.9</td>
</tr>
<tr>
<td>Hypothermia prevention involves plastic bag or wrapping n (%)</td>
<td>58 (94)</td>
<td>63 (96)</td>
<td>0.6</td>
</tr>
</tbody>
</table>
Policies: comments

• No detectable effects of active policy
• Very high rate pre-intervention
  – Ceiling effects
Practice: population
Jan-March 2007

• Babies born at 22 to 26 weeks gestational age

• 169 babies in active arm & 186 in control
Practice: results

<table>
<thead>
<tr>
<th>Practice</th>
<th>Active (N=169)</th>
<th>Control (N=186)</th>
<th>Effect (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surfactant given in labour ward</td>
<td>141 (78.3%)</td>
<td>96 (60.4%)</td>
<td>OR = 1.30 (0.99-1.70)</td>
<td>0.06</td>
</tr>
<tr>
<td>Temperature on admission – mean [SD]</td>
<td>36.5°C [0.08]</td>
<td>36.17°C [0.08]</td>
<td>Mean difference = 0.29°C (0.22,0.55)</td>
<td>0.03</td>
</tr>
<tr>
<td>Trunk delivered in plastic bag</td>
<td>141 (78.9%)</td>
<td>93 (62.0%)</td>
<td>OR = 1.27 (1.01,1.60)</td>
<td>0.04</td>
</tr>
<tr>
<td>Ideal resuscitation team composition at birth</td>
<td>126 (67.7%)</td>
<td>97 (57.4%)</td>
<td>OR = 1.18 (0.97,1.43)</td>
<td>0.09</td>
</tr>
</tbody>
</table>
Comments

• No detectable effects on policy
  – Very high rates pre-intervention (ceiling effects)

• Direction of effect on practice consistently in favour of active arm

• Detectable size of effect potentially diluted by:
  – 48/87 (55%) units allocated to active policy attended one or more meeting
  – Outcome information missing from 27% of units
    • Similar in both arms
Conclusion

• BEADI is first trial of this kind in England
• Feasible within NHS CPD structure
• Active strategy for dissemination of neonatal recommendations is more likely to lead to **practice** changes in preterm babies than current knowledge transfer in England
• A qualitative study is in progress to explore mechanisms
Example 3
CHAMPION (Community Health And Medical Provision: Impact On Neonates)

- Problem – neonatal mortality high in India and especially in state of Andhra Pradesh
- Naandi Foundation based in Hyderabad approached a charity (Effective Interventions - EI) to support an existing programme of maternal and neonatal care in villages in AP
- EI agreed only if part of a rigorous evaluation
- EI asked LSHTM to collaborate on evaluation
Andhra Pradesh
CHAMPION: early preparations (1)

- Identify areas with highest neonatal mortality rates
  - Mahabubnagar District
  - Area suffers from vicious cycle of both poor supply of and low demand for public health care services

- Similar situation in Nepal
  - Trial showed efficacy of community-based interventions such as participatory women’s groups to disseminate health knowledge and support health seeking behaviour

- Then important that health service provision is good
  - ‘Contracting-out’ services to non-public enterprises appears promising but not conclusive
CHAMPION: early preparations (2)

• Initial meeting with representatives of State and local health service providers and researchers
• Ongoing discussions and explorations
  – to refine intervention to be appropriate for AP
  – to agree study design and logistics
• Cluster RCT as intervention delivered at village-level
Aims

• To evaluate whether neonatal mortality can be reduced through systemic changes to provision and promotion of healthcare

• To evaluate cost-effectiveness in order to show feasibility of substantial scaling up in other regions with high neonatal mortality if interventions prove to be effective
Design

• Clusters
  – Villages in Nagarkurnool division of Mahabubnagar district with population of <2,500 people

• Randomisation stratified by
  – distance from the nearest designated health centre
  – village non-tribal; tribal with around 15 families; tribal with around 4-5 families
Inclusion criteria

• Women
  – Married
  – < 50 years old
  – Resident in one of the 464 villages at enumeration
    • or married into the village after enumeration

ENUMERATION IS BEFORE RANDOMISATION
Three tiers of consent

• **State**
  – Approval of the protocol from Department of Health & Family Welfare of the government of Andhra Pradesh

• **Panchayat**
  – The democratically elected body that governs a small group of villages (smallest unit of government in rural India)
  – Will convene their general body meetings and explain the protocol of the trial to the villagers in their local language
  – Consent will be given orally during a Panchayat meeting
  – Written documentation of the approval given by the Panchayat leader ('guardian')

• **Individual**
  – Women who are asked and agree to take part in the enumeration are considered to have given their informed consent to participate in the trial
Interventions

• Community Health Promotion
• Contracting out and subsidising some antenatal/ delivery/ neonatal health services to non-public institutions
• All the services will be provided free to pregnant women and neonates in the intervention communities
Community Health Promotion

• Training Village Health Workers/Midwives visiting fortnightly to provide and co-ordinate antenatal/neonatal services
• Providing health education through a public information campaign
• Organising fortnightly women's participatory discussion groups
Contracting out services to non-public institutions

• Supply of health care inadequate
  – Improvements to public sector estimated to be prohibitively expensive

• Preliminary evidence that private sector may be able to provide superior and cheaper care

• Non-Public Health Centres to provide
  – Coordinated village-based primary care
  – Secondary level care made accessible through enhanced emergency transportation
Control group: Support to Rural India’s Primary Education System (STRIPES)

• No extra maternal/neonatal health intervention
• Primary school education trial
  – Villages eligible if have public primary school
• Randomised to
  – additional after-school instruction and learning materials
  – additional after-school instruction and learning materials plus girls offered school uniform and other ‘kit’
• Children in non-eligible villages given educational materials
• Negligible impact on neonatal mortality but may improve community relations and hence data collection
CHAMPION outcomes

• Primary: neonatal mortality
• Secondary:
  – age and cause of neonatal death
  – neonatal morbidity
  – maternal mortality/morbidity
  – health service usage
  – cost
Sample size

- 330 villages have 80% power (5% 2-sided significance) to detect 25% reduction in neonatal mortality from 4.38% to 3.29%, assuming
  - average population of 659 per village, a birth rate of 23 per 1000 population, and 38 births per village over 30 months
  - Intracluster correlation coefficient (ICC) 0.00644

- Taking into account migration (economic/seasonal; and to mother for 1st birth) and loss to follow up, need 464 villages
Trial design: CHAMPION and STRIPES

464 villages

232 villages randomised to education intervention

190 villages have public schools and will be involved in the trial

INTERVENTION ARM 1
95 villages will receive after-school tutoring only

INTERVENTION ARM 2
95 villages will receive after-school tutoring and eligible girls in the village will also receive materials

232 villages randomised to health intervention

CONTROL ARM
95 villages with public schools will be involved in the education trial as controls
• Important to keep separation between team(s) proving implementation and research trial team conducting evaluation to avoid biased ascertainment
<table>
<thead>
<tr>
<th>CHAMPION TRIAL ACTIVITIES</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
</tr>
<tr>
<td><strong>Intervention Villages</strong></td>
</tr>
<tr>
<td>Initial enumeration of women</td>
</tr>
<tr>
<td>Community health promotion campaign and contracting out healthcare to non-public institutions</td>
</tr>
<tr>
<td>Monthly pregnancy check</td>
</tr>
<tr>
<td>If pregnant, triggers follow up forms</td>
</tr>
<tr>
<td>40-minute interview 6 wks after delivery</td>
</tr>
<tr>
<td>Verbal autopsy if death</td>
</tr>
</tbody>
</table>
Local research team
Current status (1)

- 464 villages enumerated and randomised
  **CHAMPION**
  - Initial training completed
  - 3 non-public health centres established with ambulance; village-level antenatal/intrapartum/neonatal in place; participatory women's groups initiated
  **STRIPES**
  - Initial staff training and baseline assessment of children completed
  - Learning materials and academic support in place
Current status (2)

- STRIPES started later and so introduction of school uniform and other ‘kit’ will only be made available next term.
- Not easy to find and retain appropriate staff for implementation delivery and research for either CHAMPION or STRIPES.
- Research team inexperienced.
- Data collection and processing logistically complicated and very large numbers (c18,000 births) to track.
- Pilot phase has been very important learning!
Example 4
A factorial-design cluster randomised controlled trial investigating the cost-effectiveness of a nutrition supplement and an exercise programme on pneumonia incidence, walking capacity and body mass index in older people living in Santiago, Chile: the CENEX study
Background

• Ageing population
• Older people vulnerable to both macro- and micro-nutrient under-nutrition
• Global policy initiatives designed to promote healthy ageing
• Achieving nutrient intake sufficiency and maintaining moderate physical activity have both been demonstrated to decrease risk of mortality in longitudinal studies
• Evidence from clinical trials is weak and conflicting and comes exclusively from high-income settings
Chile

- Proportion of the population aged 60 years and over increased from 8% to 12% from 1980 to 2005
- Older people in Chile have high rates of pneumonia and other respiratory infections
- 96% of the 65+ years Chilean population are sedentary
• The Chilean Ministry of health established a Health Programme for Older People
  – aim to promote healthy ageing and address the effects of inequalities
  – free health services available to those on low and middle incomes
  – *Programa de Alimentacion Complementaria para el Adulto Mayor* (PACAM) has provided a nutritional supplement to people aged 70 and over since 1998
The policy response (2)

• Stakeholder groups recently proposed
  – PACAM extended to 65+ age group
  – would be enhanced by the inclusion of a physical activity component

• Neither formally evaluated
CENEX

- A 24-month factorial cluster randomised controlled trial designed to evaluate the cost-effectiveness of PACAM, and a specially designed physical exercise intervention for older people of low to medium socio-economic status aged 65.0-67.9 years at baseline attending 28 health centres in Santiago, Chile
CENEX primary outcomes

• Incidence of pneumonia over 24m after initiation of the intervention
• Walking capacity (distance walked in six minutes) 24m after initiation of the intervention
• Body mass index as a measure of potential interaction between the two interventions
CENEX secondary outcomes

• Measures of health, quality of life and depression (SF36 and GDS-15)
• Self-reported incidence of chronic diseases, falls and fractures
• Self reported productive activity
• Anthropometry
• Timed up and go
• Blood indicators of cardiovascular disease risk and insulin resistance
CENEX costing data

*User costs:*
- exit interviews to ascertain costs of accessing interventions
- case-based sampling of pneumonia cases to estimate costs borne by them and caregivers

*Provider costs:*
- defining costs of delivery of interventions
- case-based sampling of pneumonia cases to estimate costs of treatment
- costs associated with changing utilisation of health care services
Implementation

• Ethical approval
• Meetings to explain the study and establish agreed procedures with:
  – Health Services Directors
  – Municipal Health Directors
  – Health Centre Directors
  – Professionals at each health centre
Selecting Health Centres

• 33 potentially health centres visited
• 21 centres selected
  – Interest in participating in the study
  – Not participating in a similar research project
    at same time
  – Good quality of data recording
• 20 HC randomly assigned to 1 of the 4
  treatment arms
  – 1 kept in case of drop out
Fieldworker recruitment

• Qualifications and experience
  – Health professionals
  – Experience in primary health or care of older people
  – PC skills
  – Social skills

• Induction of fieldworkers
  – Deep review of the research protocol
  – Randomly assigned to health centres
  – Formal introduction to each health centre
Baseline

• Questionnaire design and pre-test
• Training of around 10 temporary interviewers
• Training of fieldworkers:
  – Questionnaire application
  – Anthropometry measurements and blood pressure
• Induction of physical activity trainers
  – Coordination with the rest of CENEX team
  – Field visits
  – Training in TUG and 6 minutes walk
Problems/progress (I)

- After 2 months, sampled >6000 houses. Only identified 601 potentially eligible individuals
- Only 351 individuals were willing to take part
- 95% of those potentially eligible via the random geographic sampling procedure were also on health centre clinic lists
- New sampling strategy using names of older people on lists held in clinics
- **2000 individuals recruited with baseline interviews**
Baseline data flow

Screened by the CENEX team  
N = 2928

Contacted by Census N = 376  
Contacted by Health Centre File  
N=2552

Accept to be interviewed  
N=2084

Rejected to be interviewed  
N=492

Detection of some criteria exclusion  
N=233

No reply/Not possible to be contacted  
N=119

Interview done  
N = 2032

Interrupted interview  
N=54

Sign Consent  
N=2032

Rejection during interview  
N=32

Detection of some criteria exclusion during interview  
N=22

Included in CENEX sample  
N=2002

Rejection during 24 hrs. post interview  
N=6

Detection of some criteria exclusion  
N=24
Problems/progress (2)

• Initial sample size based on existing data on incidence of hospitalised pneumonia

• New accurate information on ambulatory and hospitalised cases of pneumonia provided significantly lower estimates of incidence

• Needed to increase size to 28 clusters (2800 people) to maintain power
Interventions
CENEX results late 2009
Conclusions

- Complex interventions reflect complexity of ‘real life’
- (possibly) more difficult than traditional drug-based interventions to develop
- Certainly more complex to evaluate
- But rigorous evaluation IS possible and essential
References (1)


References (2)


