



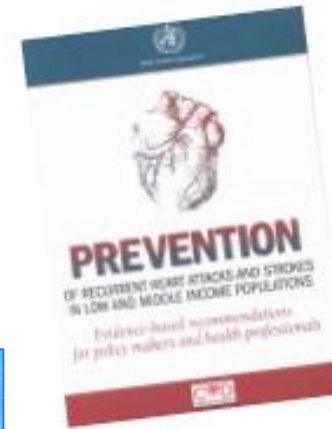


# **Challenges and opportunities in international evidence based guideline development**

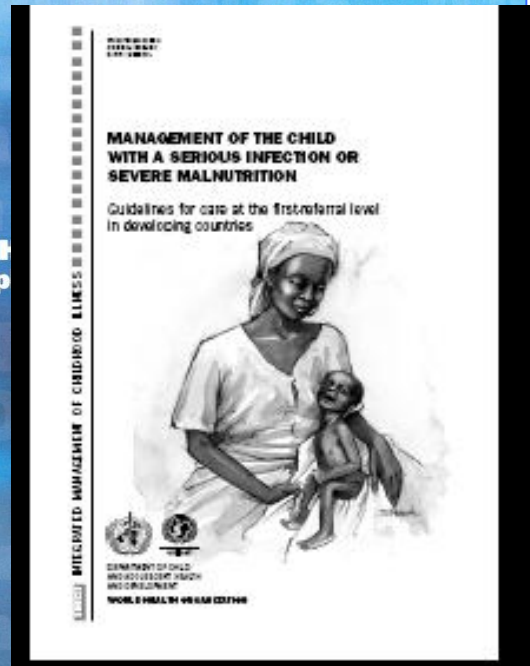
**Suzanne Hill**

**October 2006**

Evidence-based recommendations for  
Policy Makers and Health Professionals



World Health Organization  
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***'Critical appraisal of the JNC VI, WHO/ISH and BHS guidelines for essential hypertension.'***

**'These differing recommendations between JNC VI and BHS, and WHO/ISH cannot be reconciled and they are of such magnitude as to carry serious implications for clinical practice, not least among which is that acceptance of the WHO/ISH levels of 'normality' for blood pressure would result in some 45% of the population of all ages and nearly 60% of elderly people being classified as 'hypertensive'.'**

*O'Brien & Staessen, 2000*



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## ***Implementation of WHO/ISH Guidelines: role and activities of WHO.***

**'In order to increase its impact, however, an implementation strategy is needed that includes advocacy, dissemination, training and evaluation as its major components.'**

*Martin, Clin Exper Hypertens, 2000*

*'World health organisation-international society of hypertension (WHO/ISH) hypertension guidelines.'*

**'Since the publication of the 1999 WHO/ISH Guidelines for the Management of Hypertension, WHO determined in 2000 that in future the evidence base for all of its guidelines will be explicitly documented according to a defined methodology. '**

*Whitworth JA, Chalmers J. Clin Exper Hypertens  
2004*

## Progress report?

- Essential Medicines List
- Opioid dependence
- Avian influenza

# Essential medicines

- **The concept of essential medicines**

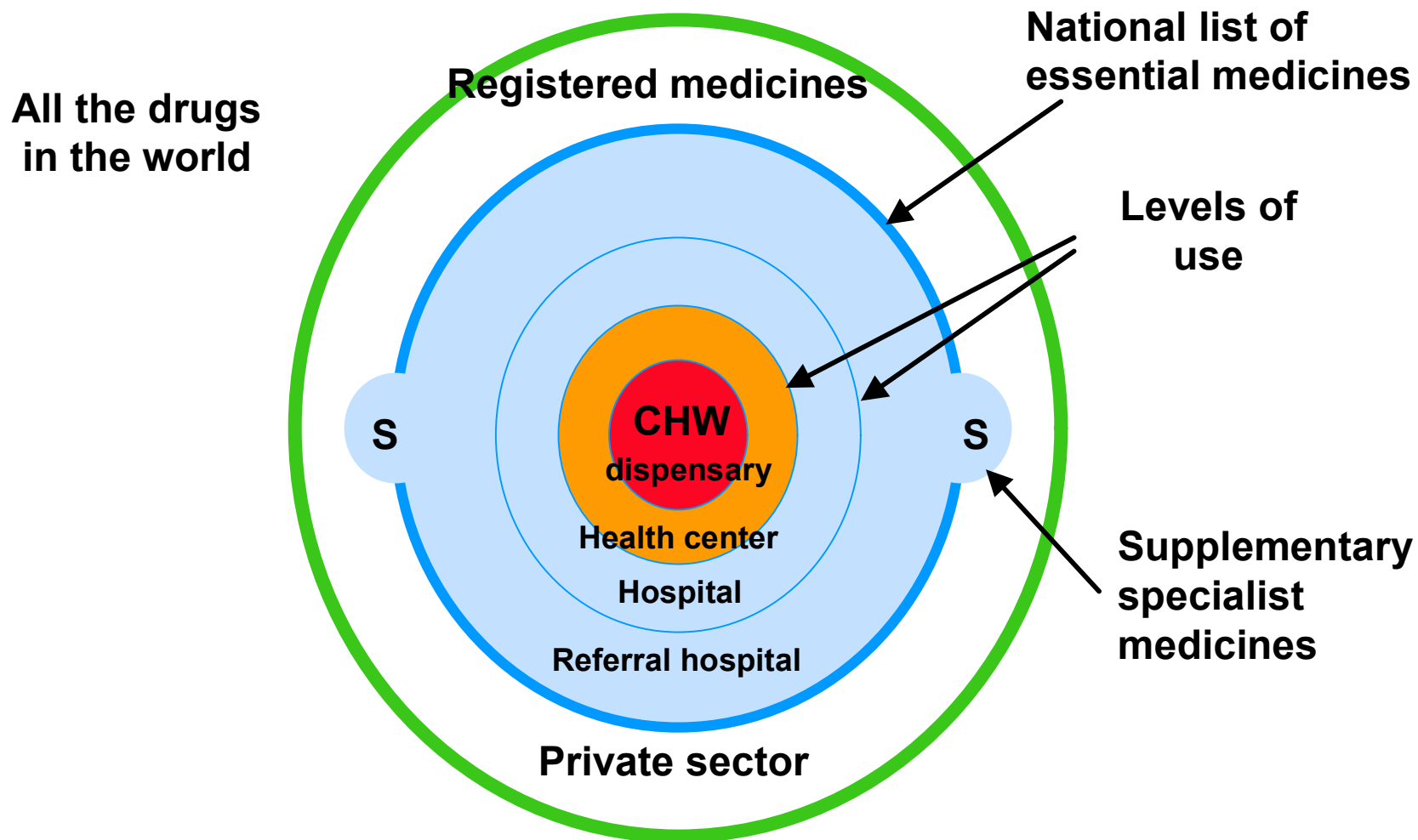
**A limited range of carefully selected essential medicines leads to better health care, better drug management, and lower costs**

- **Definition of essential medicines**

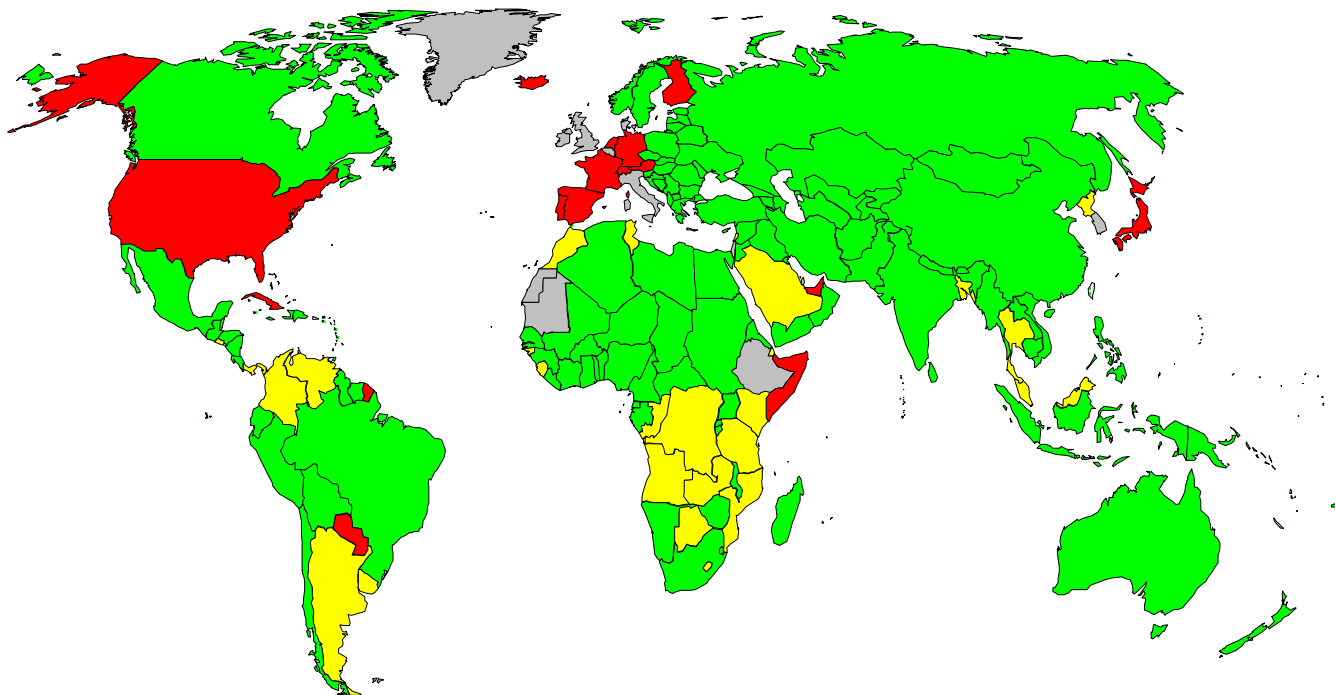
**Essential medicines are those that satisfy the priority health care needs of the population**

**(Report to WHO Executive Board, January 2002)**

# The Essential Medicines Target



# Global application



Countries with an official selective list for training, supply, reimbursement or related health objectives. Some countries have selective state/provincial lists instead of or in addition to national lists.



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## Evidence for the 15<sup>th</sup> list?

- 306 medicines
- Over 50% of drugs have a relevant Cochrane review
- Some reviews raise questions over inclusion on the list  
eg. antacids, allopurinol
- Linked through Essential Medicines Library





- WHO Model List of Essential Medicines
  - [Medicines in alphabetical order](#)
  - [Medicines by section](#)
  - [Historical changes](#)
  - [Published lists](#)
  - The WHO Model Formulary (WMF)**
    - [Edition 2004](#)
  - [Links](#)
    - [WHO related links](#)
    - [Other useful sites](#)

### Medicine Use(s) : ACETYLSALICYLIC ACID

SECTION	FORMULATION	ATC CODE(S)	LIST	DISEASE/INDICATION	RATIONALE FOR INCLUSION
<a href="#">02.01.00.00</a>	tablet, 100-500 mg; suppository, 50-150 mg	N02BA01	Core List	Analgesic - mild to moderate pain and antipyretic.	Date added: 1977.
<a href="#">07.01.00.00</a>	tablet, 300 - 500 mg	N02BA01	Core List	Acute migraine attacks.	Date added: 1988.
<a href="#">12.05.00.00</a>	tablet, 100 mg	B01AC06	Core List	Low dose aspirin used to prevent platelet aggregation (prophylaxis of cerebrovascular disease or myocardial infarction).	Date added: 1992.

- MEDICINE REFERENCES**
- [Cochrane review: Anticoagulants versus antiplatelet agents for acute ischaemic stroke.](#)
  - [Cochrane review: Antiplatelet agents versus control or anticoagulation for heart failure in sinus rhythm.](#)
  - [Cochrane review: Antiplatelet and anticoagulation for patients with prosthetic heart valves.](#)
  - [Cochrane review: Antiplatelet therapy for acute ischaemic stroke.](#)
  - [Cochrane review: Antiplatelet therapy for preventing stroke in patients with non-valvular atrial fibrillation and no previous history of stroke or transient ischemic attacks.](#)

**And the gaps...**

Primaquine tablet	Used as a supplement to standard treatment for <i>P vivax</i> and <i>ovale</i> to eradicate dormant parasites from the liver and prevent relapses.
Nicosamide chewable tablet	Treatment of tapeworm
Triclabendazole tablet	Treatment of fascioliasis and paragonimiasis.
Vancomycin powder for injection	Treatment of infections with susceptible organisms including: methicillin-resistant staphylococcal pneumonia, staphylococcal meningitis, endocarditis treatment and prophylaxis.
Clofazamine capsule	Treatment of multibacillary leprosy
Dapsone tablet	Treatment of leprosy as part of combination therapy, (paucibacillary and multibacillary).
Cycloserine capsule or tablet	Second line treatment of multi-drug resistant TB
Ethionamide tablet	Treatment of multi-drug resistant TB
Potassium iodide saturated solution	Treatment of cutaneous sporotrichosis.
Melarsoprol injection	Treatment of African trypanosomiasis.
Suramin sodium powder for injection	Treatment of African trypanosomiasis.
Eflornithine injection	2nd line therapy for late stage African trypanosomiasis due to <i>Trypanosoma brucei gambiense</i> .
Pentamidine powder for injection	Treatment of African trypanosomiasis and visceral and cutaneous leishmaniasis.

## **And gaps for additions.....**

- **Viral haemorrhagic fevers – ribavirin**
- **Evidence for paediatric formulations**
- **Reviews for old cardiovascular drugs**
- **Review for a statin**



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# Opioid dependence

- Comprehensive guideline
- Target audience policy makers and clinicians
- Potential for significant change
  - Access to medications
  - Access to health care service
  - Reduction in blood-borne disease

# Process

- Guideline group
- Identification of evidence
- Systematic reviews
- Evidence profiles
- Recommendations
- Consultation

## GRADE Evidence Profile

**Author(s):** Amato L

**Date:** 02/02/2006 16.01.56

**Question:** Should methadone vs buprenorphine be used in all opioid dependent patients?

**Patient or population:** any opioid dependent patients wishing to detox

**Settings:** outpatients

**Systematic review:** Gowing. Buprenorphine for the management of opioid withdrawal Amato Methadone at tapered doses for the management of opioid withdrawal

Quality assessment						Summary of findings					
No of studies	Design	Limitations	Consistency	Directness	Other considerations	No of patients		Effect		Quality	Importance
						methadone	buprenorphine	Relative (95% CI)	Absolute (95% CI)		
<b>completion of treatment</b> (number of people that completed the treatment Follow up: 14 to 30 days)											
2	Randomised trials	No limitations	No important inconsistency	Some uncertainty (-1) <sup>1</sup>	Imprecise or sparse data (-1) <sup>1</sup>	21/30 (70%)	26/33 (78,8%)	RR 0.88 (0.67 to 1.15)	100/1 000 (290 less to 100 more)	⊕⊕○○ Low	1
<b>side effects</b> (objective measures Range: to . Better indicated by: lower scores)											
1	Randomised trials	No limitations	No important inconsistency	No uncertainty	Imprecise or sparse data (-1) <sup>4</sup>			-	WMD -5.1 <sup>3</sup> (-14 to 5.3)	⊕⊕⊕○ Moderate	1

### Footnotes:

1. imprecise or sparse data

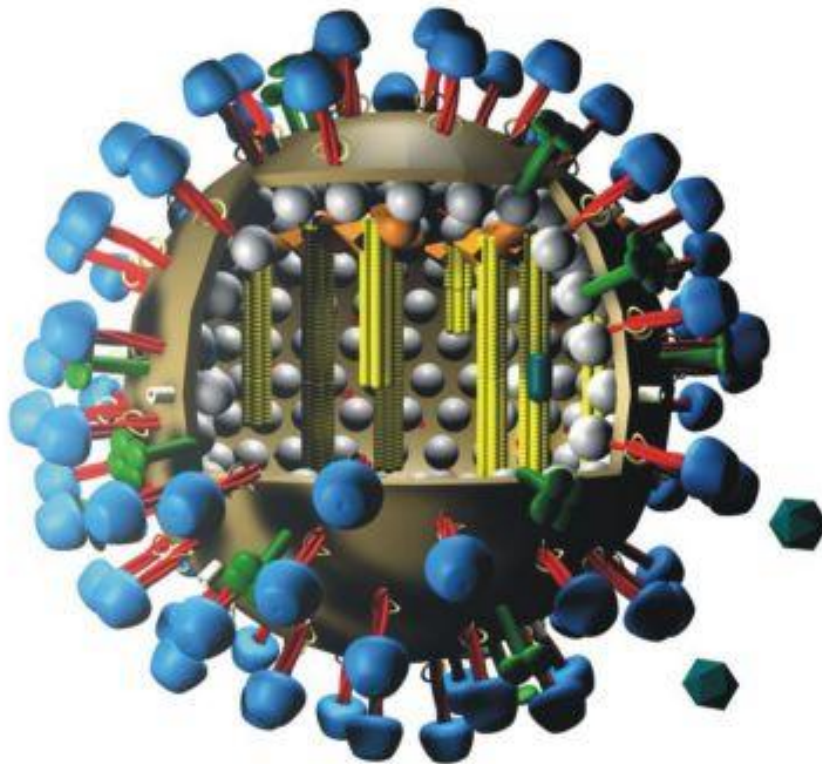
2. imprecise or sparse data: only 63 patients









3. difference in systolic blood pressure

4. only one study with 39 patients

# Problems

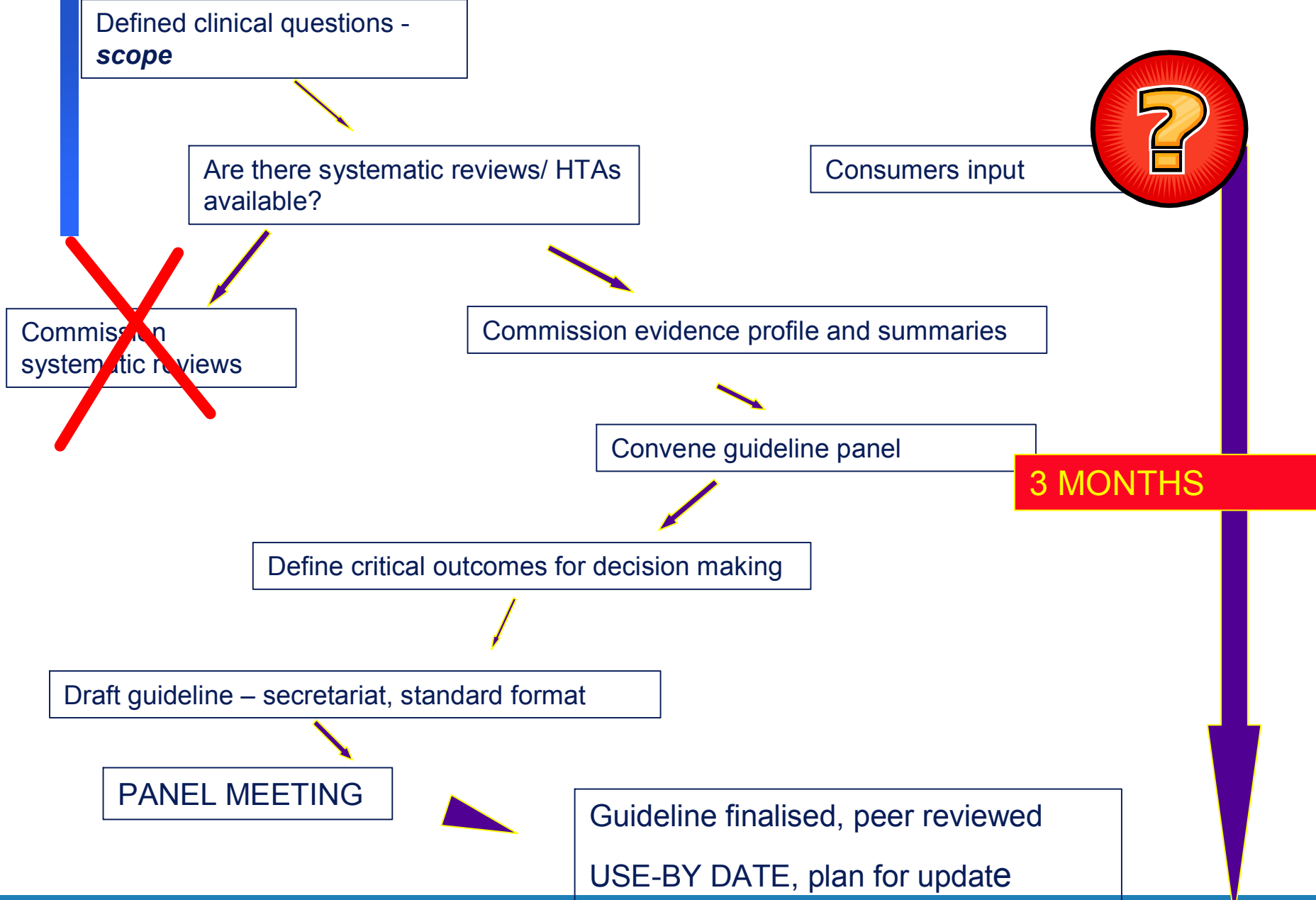
- Studies mostly come from developed world settings
- Research gaps
- Reviews do not report outcomes relevant for decision-making
  - summary estimates of symptom scores
  - harms / adverse events
- Time spent going back to original studies
- Time spent commissioning extra reviews
  
- ....guideline still going.....



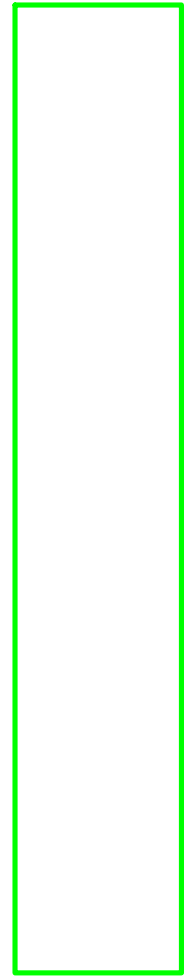
-  PB1, PB2, PA
-  HA
-  NP
-  NA
-  M1
-  M2
-  NS2
-  NS1

# Avian influenza

- **Needed in a hurry – clinical uncertainties**
- **Money available**
- **Flexible process**
- **Extensive collaboration**



# Evidence summaries



# Recommendations

*Context: Treatment of patients with confirmed or strongly suspected infection with avian influenza A (H5N1) virus in a non-pandemic situation where neuraminidase inhibitors are available for therapy.*

**Rec 01: In patients with confirmed or strongly suspected H5N1 infection, clinicians should administer oseltamivir treatment as soon as possible (strong recommendation, very low quality evidence).**

*Remarks:* This recommendation places a high value on the prevention of death in an illness with a high case fatality. It places relatively low values on adverse reactions, the development of resistance and costs of treatment. Despite the lack of controlled treatment data for H5N1, this is a strong recommendation, in part, because there is a lack of known effective alternative pharmacological interventions at this time. The recommendation applies to adults, including pregnant women and children. Until further information becomes available, the current treatment regimen for H5N1 is as recommended for early treatment of adults, special patient groups (e.g. those with renal insufficiency) and children with *seasonal* influenza.



## **Clinical uncertainty**

- **Cochrane review in seasonal influenza – reported relative results only**
- **Clinical evidence in H5N1 accruing on the basis of case reports**
- **Clinical trials planned but not yet recruiting**
- **Role of animal studies**



**WHO Rapid Advice Guidelines  
on pharmacological management  
of humans infected with  
avian influenza  
A (H5N1) virus**



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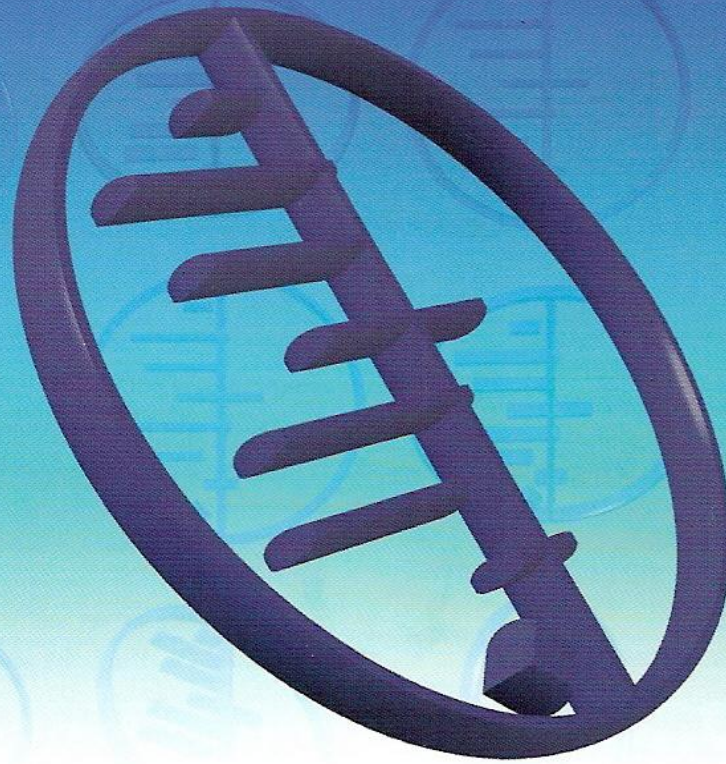
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# What about the rest?

- **Prevention of post partum haemorrhage**
  - **Drafted last week**
  - **Based on systematic reviews and GRADE**
  - **Needed re-analysis**
  - **Problems with trials, not reviews - evidence for harms**
- **Oncology**
  - **Reviews for some priority diseases**
  - **Gaps for developing world studies**
  - **Gaps for new products**
- **Acute care in children**
  - **300 questions**
  - **30 reviews**



*Could do better.....*



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# Challenges for Cochrane

- Not just ‘what works’?
- Or what is interesting?
- Better reviews
- And more of them







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