

Herb-Drug Interaction

中西藥相互作用

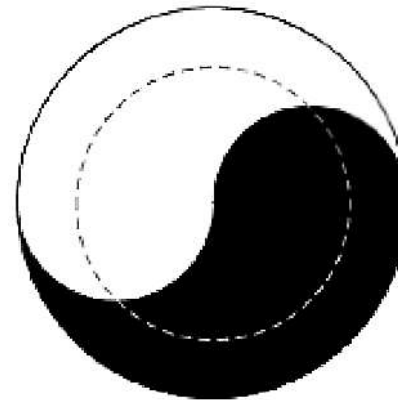
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Committee on Research and
Development of Chinese Medicines

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Credentials & Affiliations

- Clinician
- CMP
- Service Developer
- Hospital Authority
- Schools of Chinese Medicine, CPO, HACMD
- HK Association for Integration of Chinese-Western Medicine
- Inductive Thinking:
Contradictions within
Unity 矛盾中的統一



Questions & Issues

in an era when mainstream WM is faced with emerging CM

Public & Industries

- I am taking drugs x, y and z. Can I take herbal medicine?
- One, due to fear of side-effects of WM drugs despite being high effective, insists to take CM herbal medicine.
- There is no public database on HDI that is Chinese-oriented.

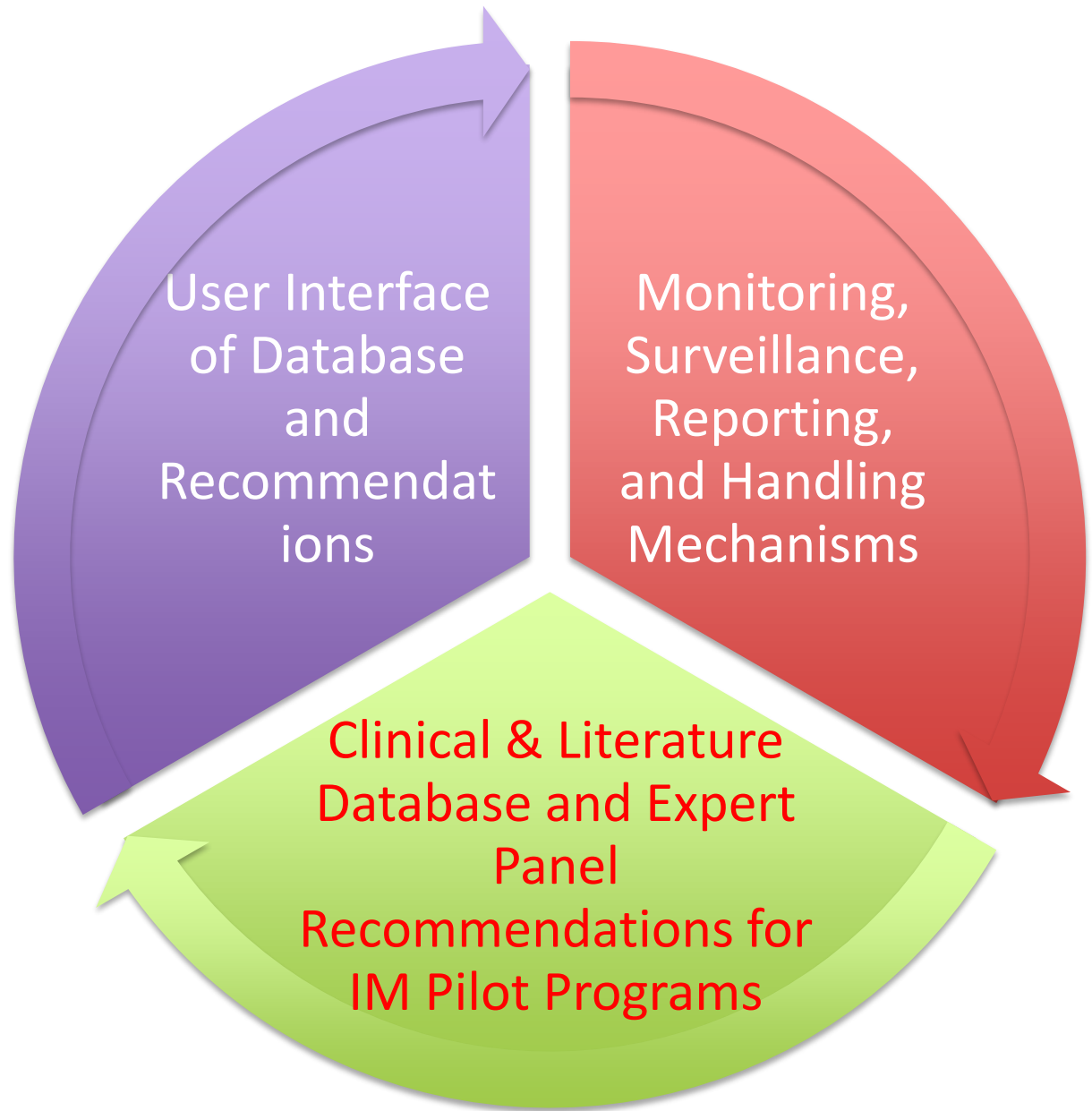
WM & **CM** Professional

- This patient presents with symptom A. Is it herb-related?
- What is the scientific basis to separate the administration of herb and drug by at least 2 hours?
- WM: I have not received training on CM herbs.
- CM: I prescribe herbal medicine according to CM principles. My traditional CM training does not include HDI.

Herb-Drug Interaction **Chinese** Reference Standard:
A **Public Service** & Industry Development Based on Clinical
Surveillance & Literature Review

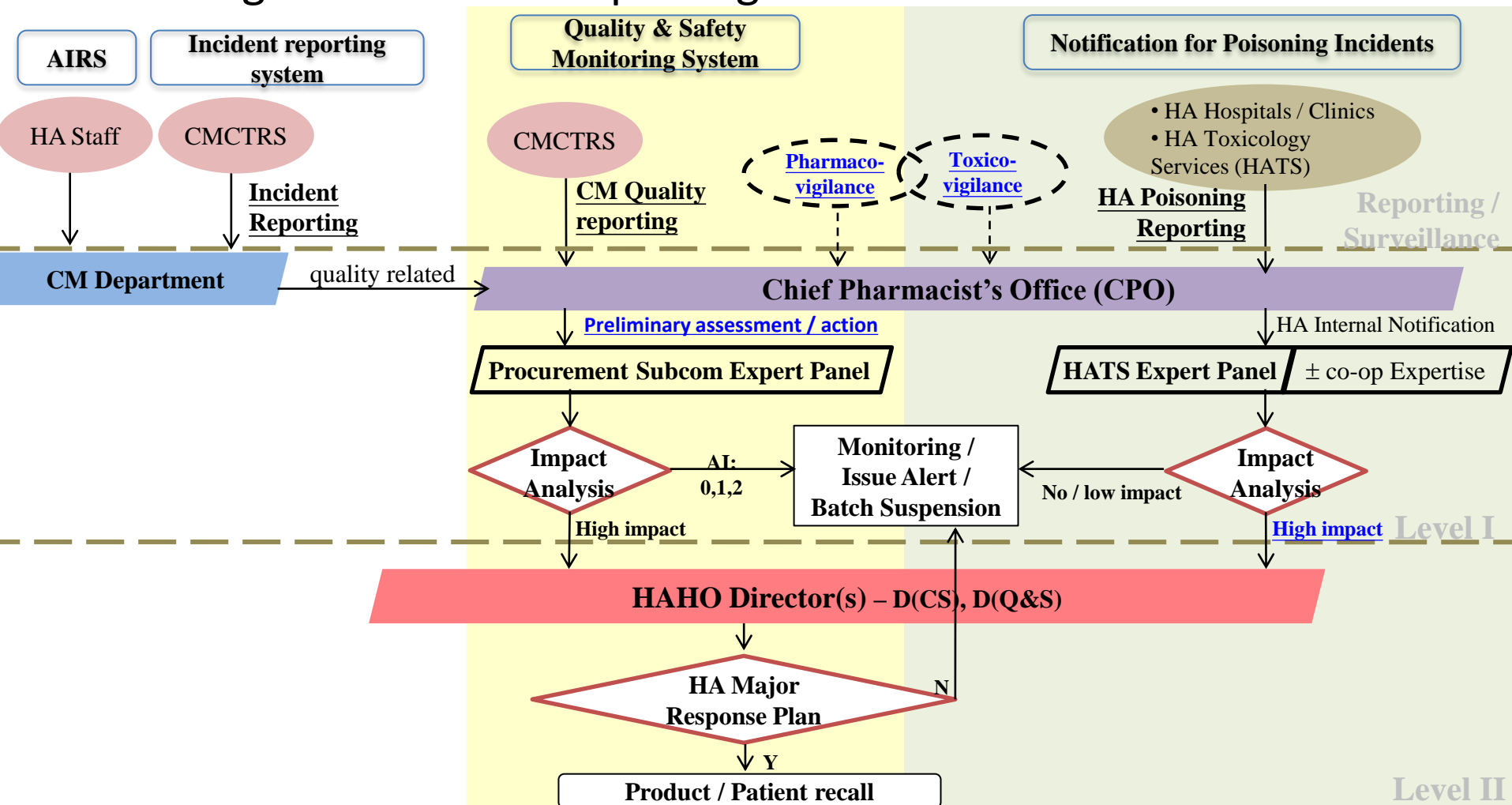
VISION, ULTIMATE GOAL & DIRECTION

Existing HA Herb-Drug Interaction & Herbal Safety Services



Clinical Risk Management

- CM drug related issues reporting



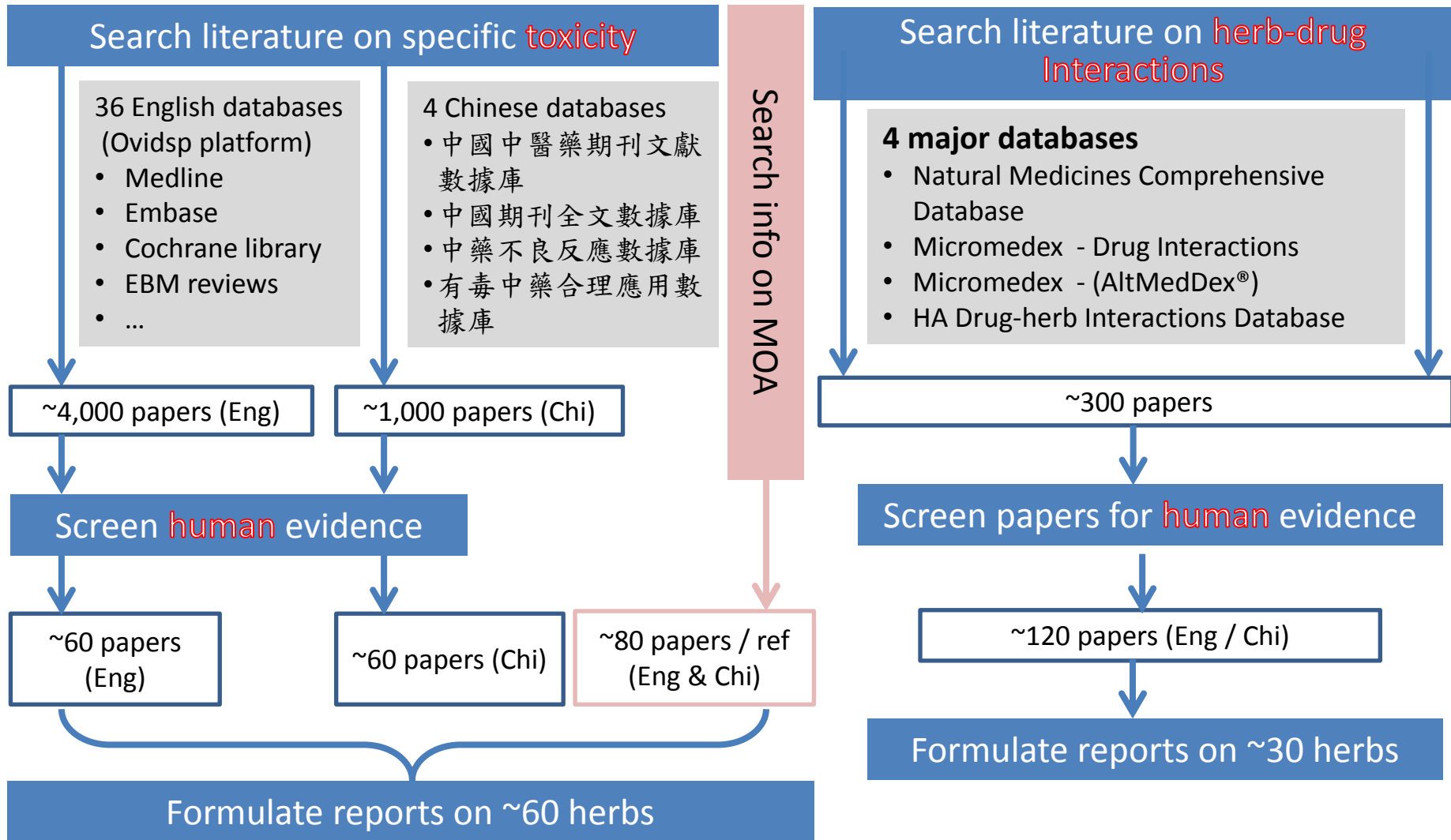
Action Index (AI):

- 0 – quality reporting that doesn't diminish therapeutic effect
- 1 – quality reporting that may diminish therapeutic effect but doesn't cause harmful effect
- 2 – quality reporting that may cause harmful effect

Level of Response:

- Reporting / Surveillance -- Pharmacovigilance / Toxicovigilance
- Level I -- Alert / Monitoring
- Level II -- Major Response Plan

Search Methodology



Search:

 [Advanced Search](#)**NATURAL MEDICINES**
COMPREHENSIVE DATABASE

Unbiased, Scientific Clinical Information on Complementary, Alternative, and Integrative Therapies

Level of Significance: Stop-Light Rating System Occurrence/Severity

	Likely	Probable	Possible	Unlikely
High				
Moderate				
Mild				
Insignificant				

Major = Do not use combination; contraindicated; strongly discourage patients from using this combination; a serious adverse outcome could occur.

Moderate = Use cautiously or avoid combination; warn patients that a significant interaction or adverse outcome could occur.

Minor = Be aware that there is a chance of an interaction; advise patients to watch for warning signs of a potential interaction.

Likelihood of Occurrence

Likely = Clinical research indicates that this interaction is likely to occur in most patients.

Probable = Clinical research or pharmacokinetic studies in humans suggests that this interaction will occur in a significant portion of patients.

Possible = Clinical research, pharmacokinetic data in humans or animals, or in vitro research suggest that this might occur in some patients.

Unlikely = Clinical research, pharmacokinetic data in humans or animals, or in vitro research suggest that this interaction can occur, but is not likely to occur in many patients.

Severity

High = Life threatening or severe impairment possible

Moderate = Moderate impairment or significant discomfort possible

Mild = Mild impairment or mild discomfort possible

Significant = Drug levels may be affected, but a clinically significant interaction is not likely.

[Close Window](#)**Level of Evidence****Level** **Definition**

A	High-quality randomized controlled trial (RCT)
A	High-quality meta-analysis (quantitative systematic review)
B	Nonrandomized clinical trial
B	Nonquantitative systematic review
B	Lower quality RCT
B	Clinical cohort study
B	Case-control study
B	Historical control
B	Epidemiologic study
C	Consensus
C	Expert opinion
D	Anecdotal evidence
D	In vitro or animal study
D	Theoretical based on pharmacology



- Tools: [Drug Interactions](#) | [Trissel's™2 IV Compatibility](#) | [Drug Identification](#) | [Tox & Drug Product Lookup](#) | [Drug Comparison](#) | [Calculators](#) | [CareNotes®](#) | [NeoFax® / Pediatrics](#)

SEARCH

Example Searches



Clinical News:

[Sublingual Allergy Extract Approved](#)

DEFINITIONS

Severity:

- Contraindicated**
The drugs are contraindicated for concurrent use.
- Major**
The interaction may be life-threatening and/or require medical intervention to minimize or prevent serious adverse effects.
- Moderate**
The interaction may result in exacerbation of the patient's condition and/or require an alteration in therapy.
- Minor**
The interaction would have limited clinical effects. Manifestations may include an increase in the frequency or severity of the side effects but generally would not require a Major alteration in therapy.
- Unknown**
Unknown.

PRINT CLOSE

DEFINITIONS

Documentation:

Excellent	Controlled studies have clearly established the existence of the interaction.
Good	Documentation strongly suggests the interaction exists, but well-controlled studies are lacking.
Fair	Available documentation is poor, but pharmacologic considerations lead clinicians to suspect the interaction exists; or, documentation is good for a pharmacologically similar drug.
Unknown	Unknown.

PRINT CLOSE



HA Drug-herb Interactions Database

Introduction

Drug List

Search

eKG

significance

Level of Significance

Severity

Description of interaction

Brief summary on content of the reference(s)

Effects: The combination of St. John's wort¹ with statins may decrease the drug efficacy of statins in tumor cells and animal models and cause poison in vivo.

Mechanism: The combination of St. John's wort¹ with statins may affect the pharmacokinetics of statins.

Management: Concomitant administration of statins and St. John's wort should be avoided.

Discussion: The combined treatment of statins and St. John's wort¹ was investigated in animal model and human studies. Results showed that statins-induced neuronal damage, pro-inflammatory cytokines production and neuronal apoptosis were attenuated by the pretreatment of St. John's wort (SJW). This inhibition of pro-inflammatory cytokines and neuronal apoptosis appears partly explained by protective effect of SJW against statins-induced oxidative stress. However, other recent studies reported that although the co-administration of SJW with statins resulted in lower toxicity induced by statins, the excessive plasma concentration (C_{max}) of statins and SJW (active metabolite of statins) had significantly decreased after a long time exposure to SJW for consecutive 14 days (2, 3). Similar results were obtained from another long-term RCT, in which two patients had subclinical rhabdomyolysis, long half drug release and low half toxicity, but the plasma levels of SJW in patients were significantly reduced by 47% following co-treatment of statins and SJW (4).

References:
1. Hu ZP, Yang XS, Chen YF, Su AL, Ding W, Zhu YZ, et al. St. John's wort attenuates statins-induced oxidative DNA damage via down-regulation of specific pro-inflammatory cytokines and

Table 1. Level of Significance

Severity	Level of Evidence	A	B	C	D	E
		High	1	1	1	2
Moderate		1	1	2	2	3
Mild		2	2	2	2	3
Insignificant / Uncertain		3	3	3	3	3
Not known		*	*	*	*	*

Severity

High	Potentially life-threatening or capable of causing permanent damage
Moderate	May cause deterioration in the physiological / clinical status. Drug levels or effects will be affected, a clinical significant interaction is likely.
Mild	Clinical mild impairment or mild discomfort possible. Drug levels or effects maybe affected, a clinical significant interaction is probable.
Insignificant / Uncertain	Drug levels or effects maybe affected, but a clinical significant interaction is not likely / uncertain.
Not known	Adverse DHI not studied or no proven adverse DHI shown

Level of Evidence

A	High quality RCT or meta-analysis (quantitative systematic review)
B	Non-randomized clinical trial; non quantitative systematic review; lower quality RCT; clinical cohort study; case-control study, historical control; epidemiologic study
C	Case series, more than one case report
D	Consensus of expert panel
E	Anecdotal evidence (single case report); <i>in vitro</i> or animal study; theoretical based on pharmacology; A or B without statistical data analysis



Risk-stratification Methodology

- Level of evidence
- Quality (validity, applicability, size etc of studies) of the information
- Severity of reaction
- Expert opinion

I	a - Meta-analysis of RCT b - At least one RCT
II	a - At least one well designed non-R CT b – At least one well designed experimental trial
III	Case, correlation, and comparative studies.
IV	Opinion from panel of experts

Risk Stratification Matrix – Herb X

Level of Evidence				
Quality of studies	I	II	III	IV
Good	1	2	2	2
Fair	2	2	3	3
Poor	2	3	3	3
Recommendation				
Other remark				

1 = high risk
 2 = moderate risk
 3 = low risk
 4 = No reported risk

Recommendations on Use of Chinese Medicines in ICWM Pilot Project

- Toxicity
 - Risk Rating on CM Toxicity (by Physiological Systems):
 - e.g. “High”: 枳實 (Hypertension, tachycardia, may prolong QTc if taken with QT interval-prolonging drugs)
- Herb-Drug Interaction
 - a. Risk Rating on Herb-Drug Interactions (by CM Class):
 - e.g. “Moderate”: 丹參 with Warfarin (May increase INR)
 - b. Risk Rating on Herb-Drug Interactions (by Drug Class):
 - e.g. “Low”: Antihypertensives with 甘草 (May reduce effectiveness of antihypertensive drugs)

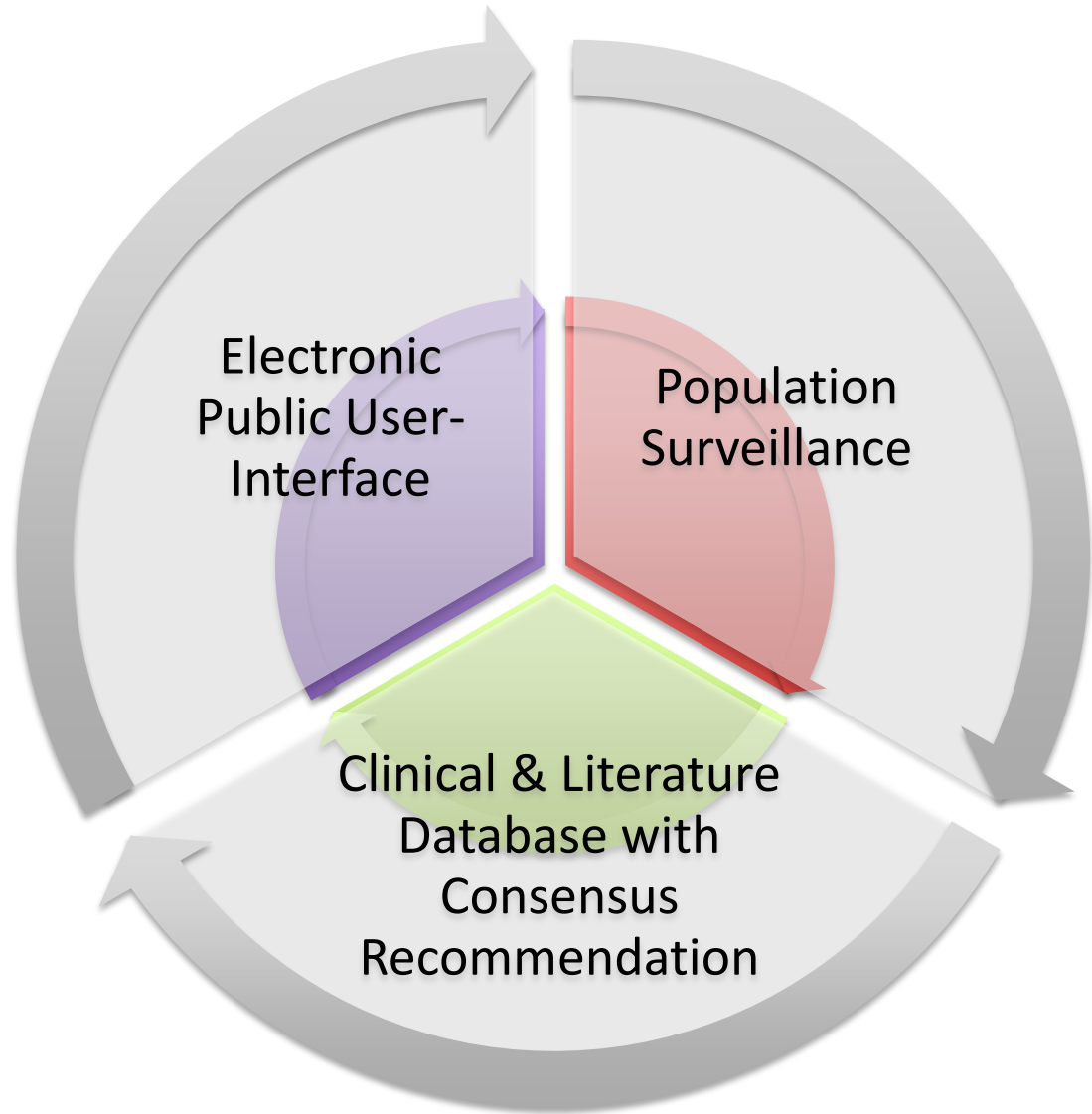
Short- & Medium-Term Tasks



Database Maintenance
and Regular Updates
on Recommendations

Electronic User-
Interface

**Long-term
Goal:
Chinese
Public
Reference
Standard on
Herb-Drug
Interaction
& Herbal
Safety**



Strategic Intentions & Partners

Short, Medium, and Long-term

HA

- Toxicology
- CPO
- Clinicians
- NGO CMP

CM

Hosp/Dept

- HA IT
- NGO
- SCM

Public

- IT for Public UI
- Herbal Industry
- Private Doctor
- Private CMP



Thank You