Signals. Risk evaluation and management

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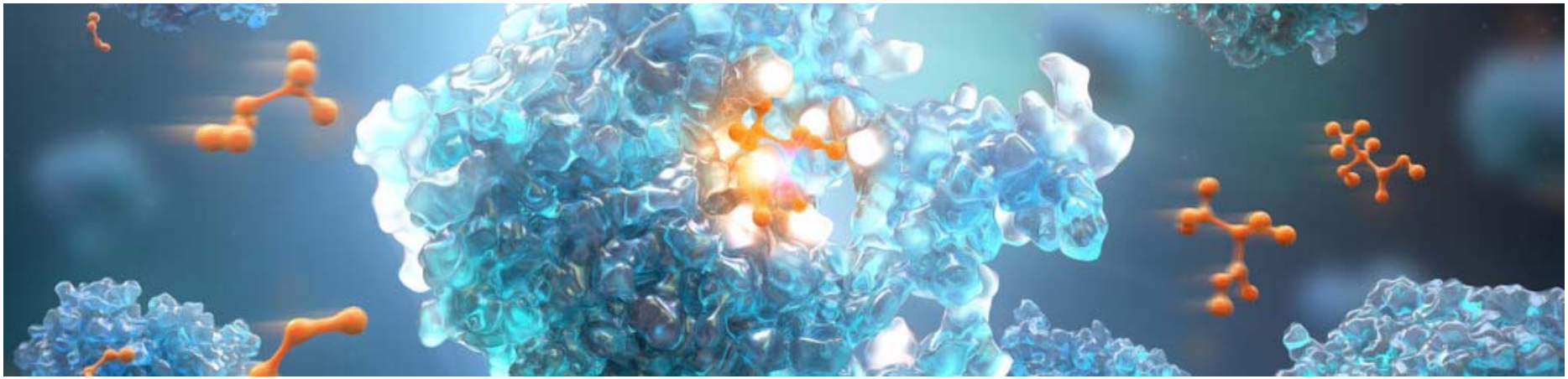
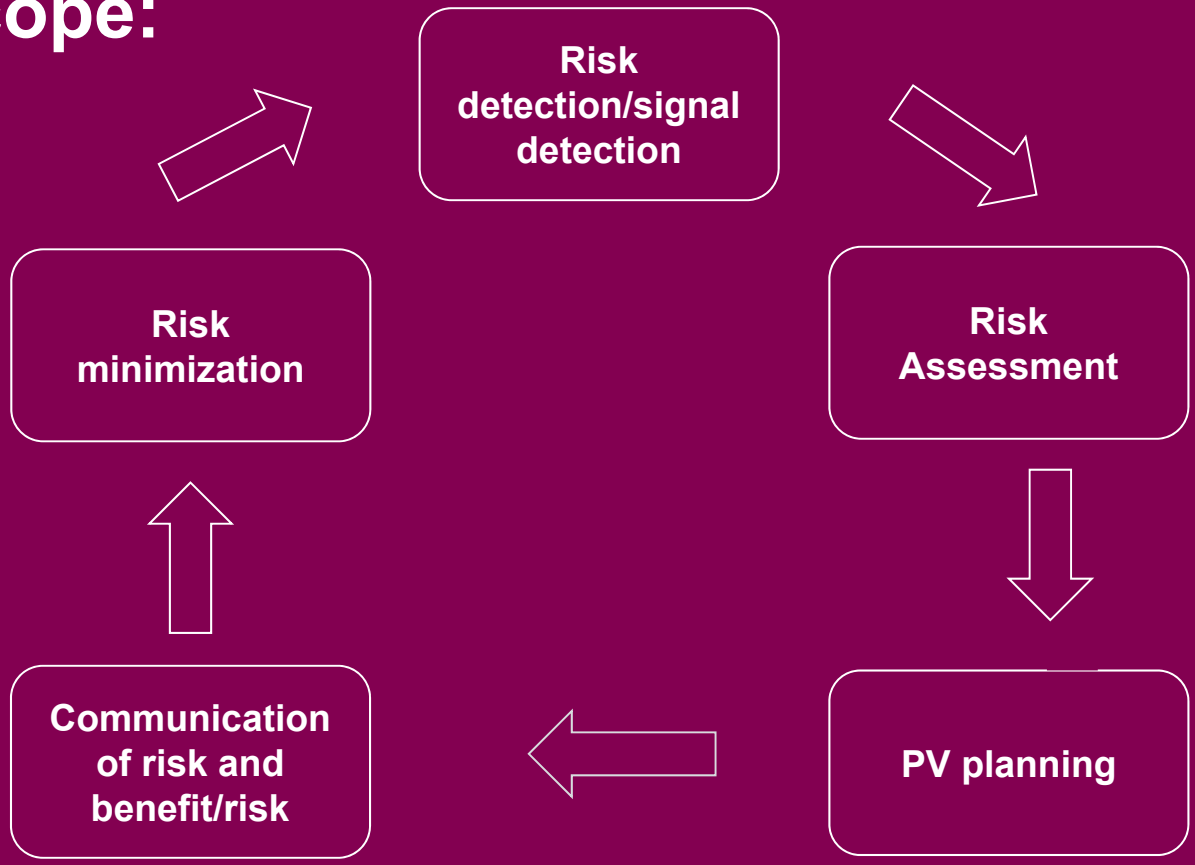


The most effective way is the easiest

'If the average member of the audience can remember with interest and enthusiasm one main theme, the lecture has been a great success.'

Sir William Lawrence Bragg
The youngest person ever to receive a Nobel Prize

The scope:


Risk detection/signal detection
Risk Assessment
PV planning
Communication of risk and benefit/risk
Risk minimization

What is a Signal?

Common association with signal in our daily life:

- beep phone
- alarm
- visual signals on the road etc.

} something is trying to communicate with us

A signal is essentially a **hypothesis** of a risk with a medicine with data and arguments that support it (WHO)

NB! Adequate reaction is needed when something is different compared to prior or expected data

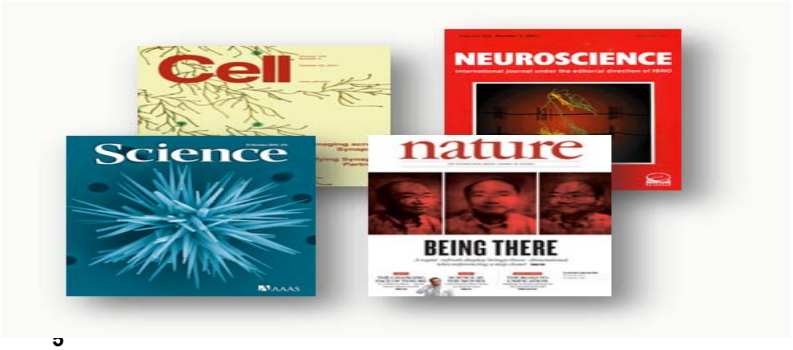
A safety signal is information on a new or known adverse event that **may be** caused by a medicine and requires further investigation (EMA)

Signal Generation:

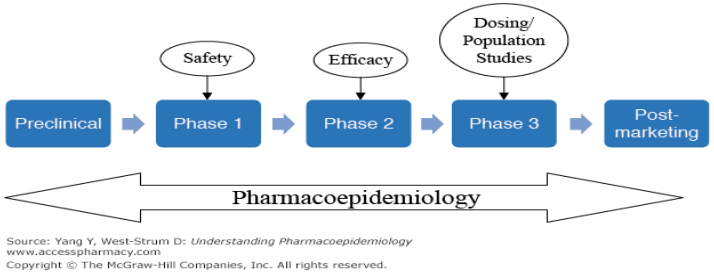
Non-clinical and clinical trial data

Spontaneous reporting systems

Scientific literature



Pharmacoepidemiologic studies



Source: Yang Y, West-Strum D: *Understanding Pharmacoepidemiology*
www.accesspharmacy.com

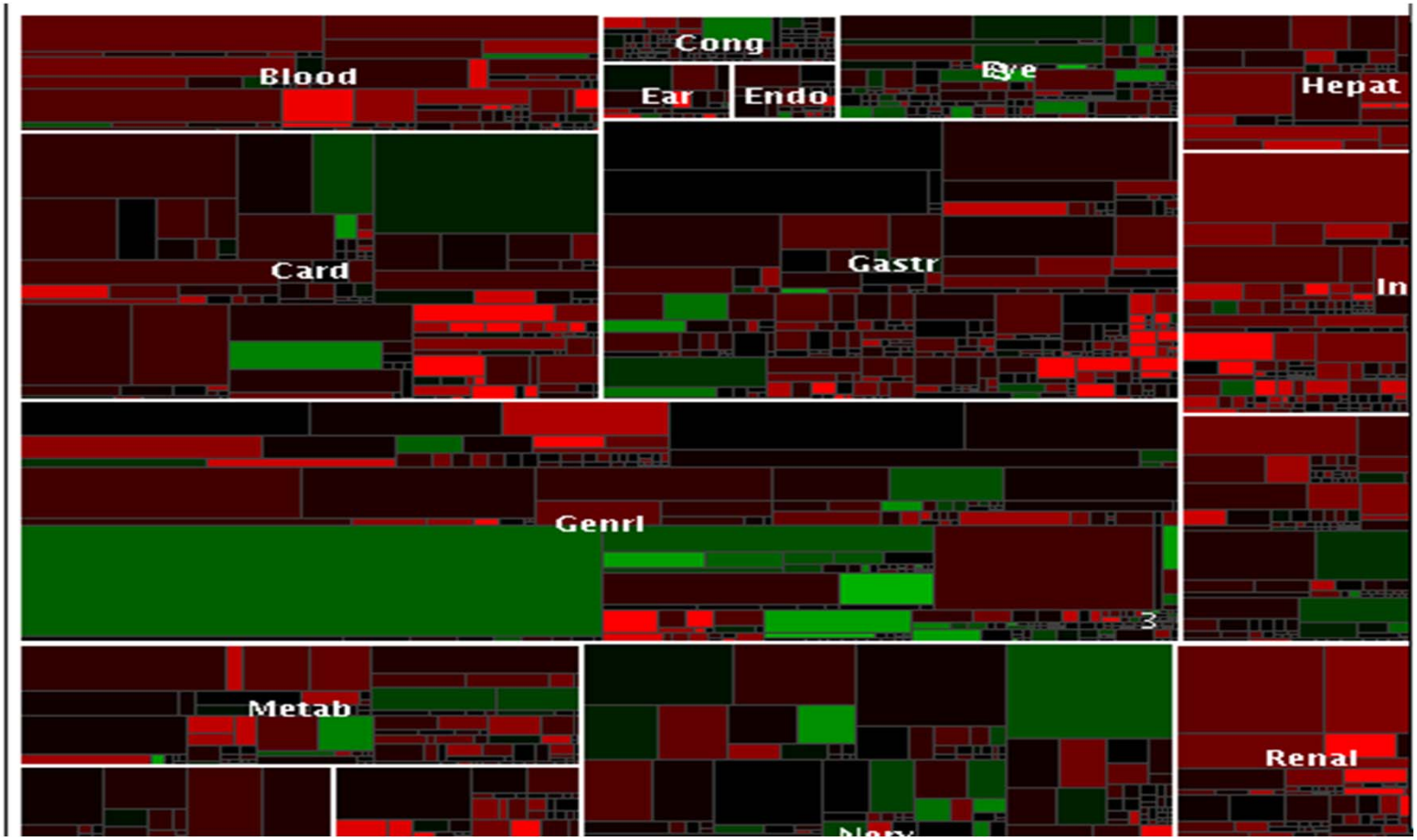
Triggers of signal detection

- life threatening or fatal outcome
- Unexpected ADRs (Unlisted or Unexpected Events) Not on Product Label or RSI of IB
- Specific ADRs (Designated Medical Events or Events Being Closely Evaluated on a Product Level)
- Clusters (groups of the reports from the same source)
- Trending (a significant increase in reporting compared to other events)
- Media attention

Signal detection

When some ADR catching our attention - we need to analyze what is going on. Signal detection involves looking at the adverse reaction data for patterns that suggest new safety information.

Visual presentation of a safety signals



Further signal management

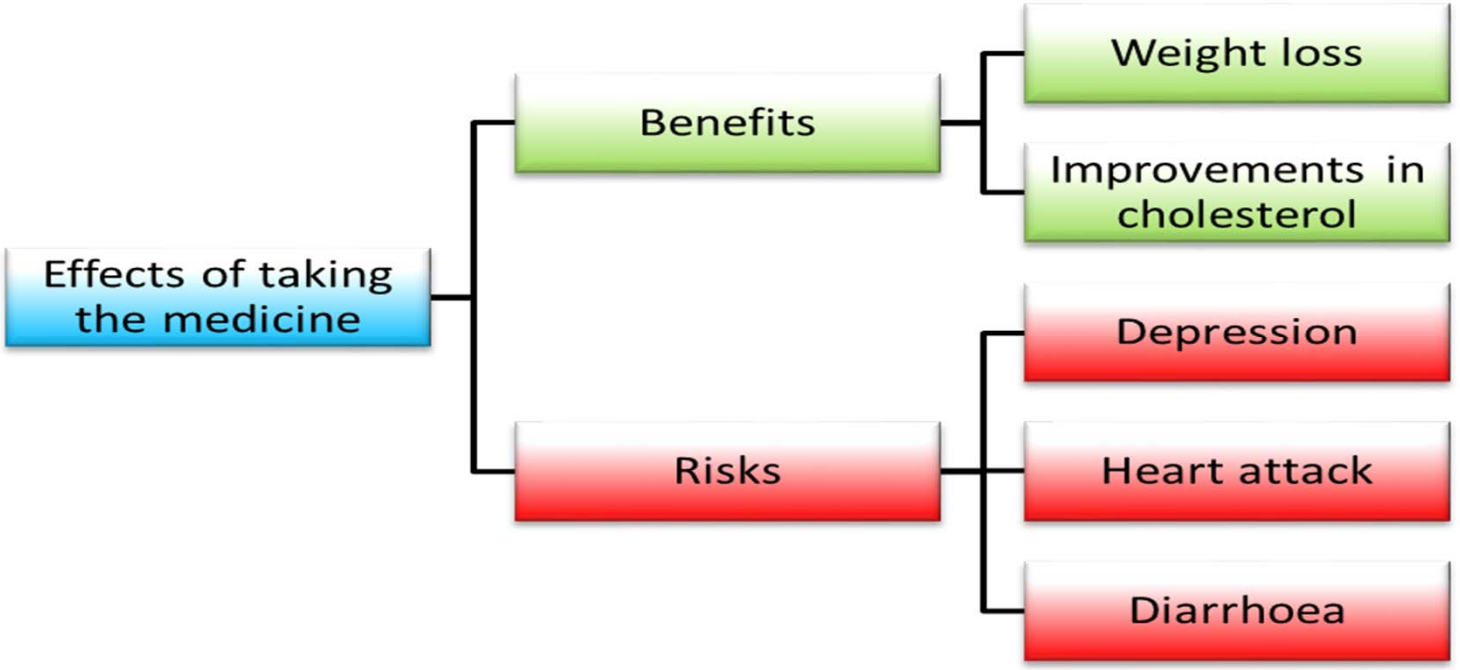
- Validation and Confirmation
- Analysis
- Prioritization
- Assessment
- Recommending action

The idea of risk-benefit balance

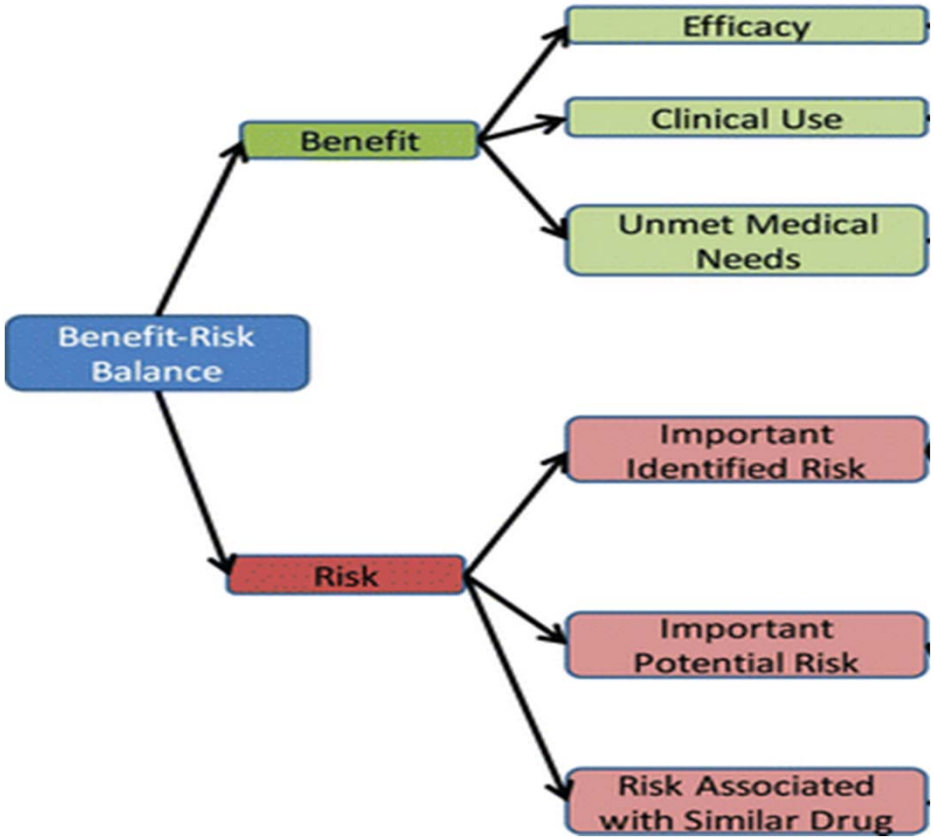
The idea is simple: when the benefits of a given intervention greatly outweigh its risks, this intervention is considered favorable.
Say your car had an 80% chance of spontaneously catching fire while you are driving it… Chances are, you would probably end up walking…
In this case risk-benefit ratio is unfavorable

It's the same thing in healthcare: in selecting a treatment option, you must know if the risk-benefit ration tips in your favor.

Is everything in balance?

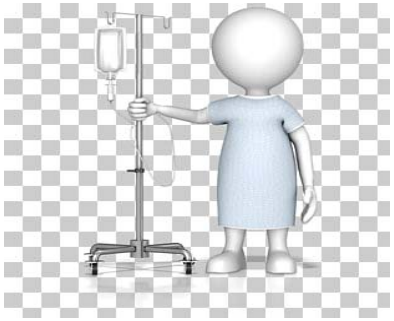


Benefit/Risk Balance



Motivation

To support decision making:
-Licensing decision (enter or remain on market)
-Policy recommendation decisions



-Clinical decisions

Benefit-Risk is not static, it's dynamic

Benefit-risk assessment

Beneficial effect(s):

high proportion
of treated patients

Adverse effects:

small proportion
of treated patients

FDA Benefit-Risk Framework

Decision Factor	Evidence and Uncertainties	Conclusions and Reasons
Analysis of Condition		
Current Treatment Options		
Benefit		
Risk		
Risk Management		
Benefit – Risk Summary Assessment		

Conclusion and communication in risk evaluation:

- BENEFITS MUST ALWAYS OUTWEIGHT THE RISKS
- Condition, population, (condition of use) for which is established that benefits outweigh the risks must be identified
- Benefit-risk assessment final reflection/conclusion must be submitted
- **Communication**: relevant information must be provided to key stakeholders

Risk Management = Risk Assessment + Risk Minimization

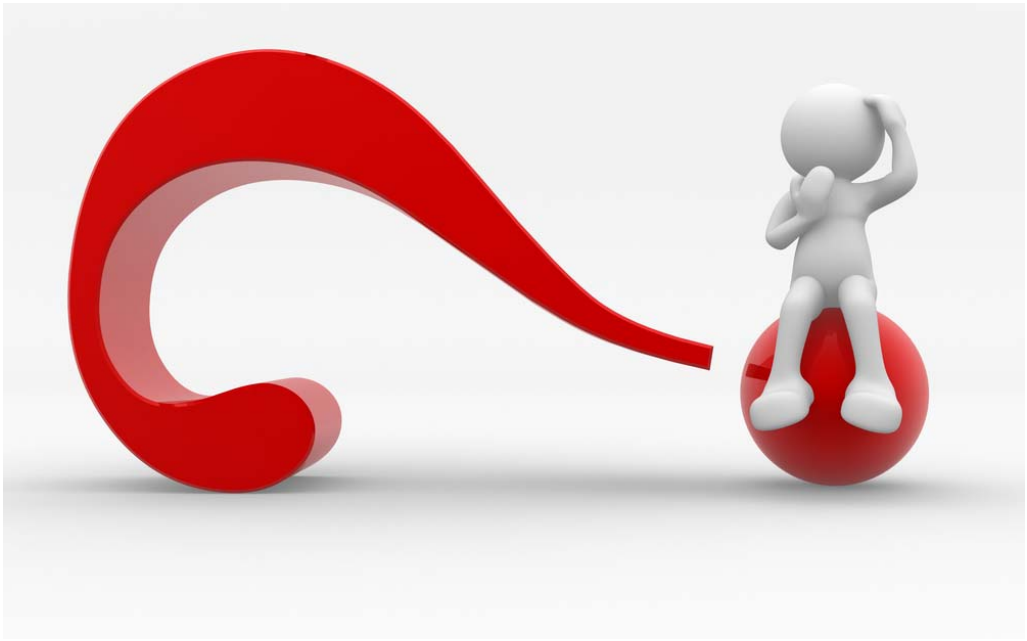
Risk - Management Plan:

Risk-Management plan is detailed description of the Risk-Management system.
It includes all the existing and missing information about the safety profile of the drug.

Conclusion:

In simple terms, working model of Risk Management System should be able to monitor safety of medicines and take steps to reduce the associated risk. Therefore, the assessment of benefit versus risk must begin right from the preclinical evaluation of a medicinal product, and must extend throughout its entire life cycle.

Any questions?



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	http://www.hpra.ie/homepage/medicines/regulatory-information/pharmacovigilance-and-post-authorisation-safety/risk-management-plans-(rmps)
Risk-management system	https://www.ema.europa.eu/en/documents/scientific-guideline/guideline-good-pharmacovigilance-practices-module-v-risk-management-systems-rev-2_en.pdf

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