EUROPEAN MEDICINES AGENCY
SCIENCE MEDICINES HEALTH

How can SmPC and EPAR information contribute to the safe and effective use of medicines in older population?

EMA Worksop: Ensuring safe and effective medicines for an ageing population, 22-23 March 2012

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Patients' needs – Knowledge – Information

- Ageing population

  Diverse health status - Age-related physiological changes - Co morbidity

- Clinical development of medicines vs Real use
  - Data are needed to provide evidence-based information
  - Individual factors (e.g. age, co-morbidity) which may impact on benefits or risks?

- Information on the use of medicines for older people = PRIORITY
  - Full transparent information on available data and limitations if any (EPAR)
  - Practical information for clinical practice (SmPC)
  - Place of SmPC and EPAR as source of information on medicines

Age - Physiological changes - Co morbidity

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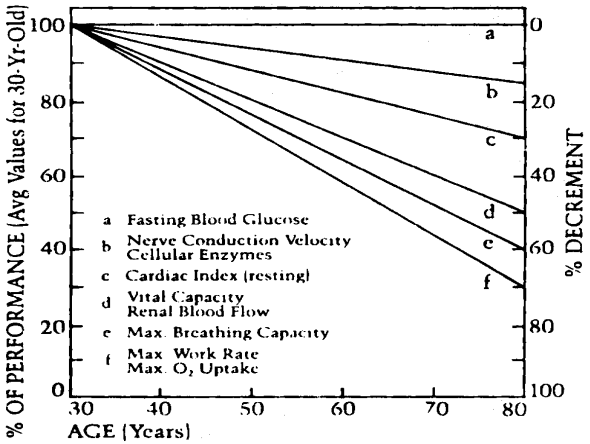
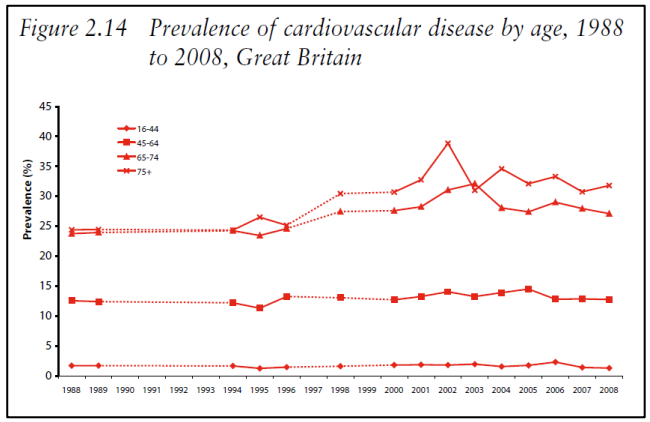
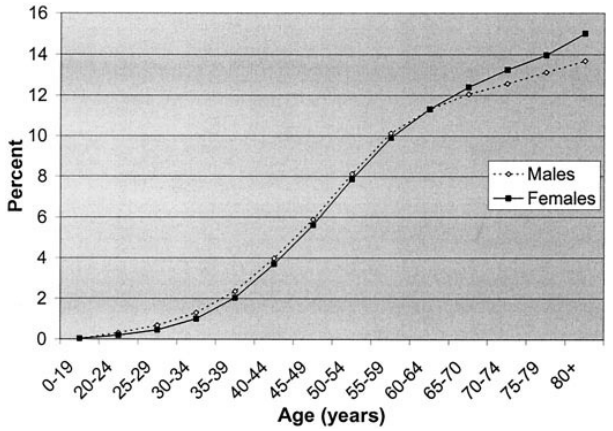


R.C.Cutler, The Biology of Aging, Ed J.A.Behnke et al., 1978



British Heart Foundation Statistics Database



Global diabetes prevalence by age and sex for 2000

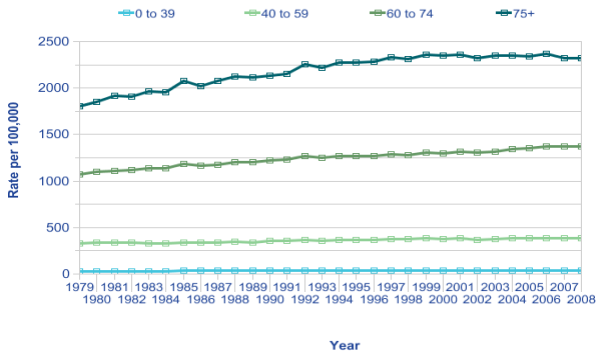
DIABETES CARE, VOLUME 27, NUMBER 5, MAY 2004

Prevalence of doctor-diagnosed arthritis by 10 year age groups, National Health Interview Survey, 2007-2009

Age group	Male	Female
30-59	0,16 %	0,09 %
60-64	1,58 %	0,47 %
65-69	2,17 %	1,10 %
70-74	4,61 %	3,86 %
75-79	5,04 %	6,67 %
80-84	12,12 %	13,50 %
85-89	18,45 %	22,76 %
90-94	32,10 %	32,25 %
95-99	31,58 %	36,00 %

Prevalence of dementia in European countries

EURODEM -*http://ec.europa.eu/health*



All Cancers Excl. Non-Melanoma Skin Cancer: 1979-2008

Great Britain - Cancer Research UK

European Public Assessment Report

- Summary of all submitted data – Discussion – Recommendations:
  - Benefit-risk assessment – population to be treated
  - Need for post-authorisation data (risk management plan)
  - SmPC information to be given to optimise benefits and reduce risks

- 2011 revision of the assessment report template:
  - to focus reviewer attention on presentation and discussion of geriatric data
  - Demographic tables (PK, CT, safety data - >65,>75, >85)
    - "Was the patient population adequately selected (age & inclusion/exclusion criteria)?
  - Discuss B/R, dose adjustment, special warning, RMP/missing data

ICH E7

Can data be extrapolated?

Information on co-morbidity in EPAR

- PK analysis:
  - age, gender, race, smoking status, metabolic polymorphism, renal function and hepatic insufficiency to be considered.
- Secondary pharmacology
  - E.g. blood pressure, biochemistry, ECG, EEG etc.
- Efficacy and safety in subpopulations
  - Subgroup analysis, pooled analysis, dose-effect relationship (weight)
  - "Generalisability" of trial findings, Lack of information in certain groups
- Investigation of drug interactions

Annex I of Directive 2001/83/EC as amended

2.5 Clinical Overview

…

"An interpretation of the way the efficacy and safety findings support the proposed dose and target indications and an evaluation of how the summary of product characteristics and other approaches will optimise the benefits and manage the risks is required."

Summary of product characteristics

European Commission guideline on SmPC

- "The SmPC is the basis of information for healthcare professionals on how to use the medicinal product safely and effectively."
- "Each section of the SmPC should first deal with those issues that apply to the core population for whom the medicine is indicated followed - when necessary – by specific information for any relevant special population (e.g. children or elderly)."

The **package leaflet** should be drawn up in accordance with the SmPC

- More accessible to users than SmPC

SmPC guideline and older population

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4.1 Therapeutic indications	It should be stated in which age groups the product is indicated, specifying the **age** limits
4.2 Posology	**Special populations** Dosage adjustments or other posology related information in specific patient groups should be stated where necessary, in well-defined sub-sections ordered by importance, e.g. regarding: • **elderly** population; it should be made clear whether or not any dosage adjustment is necessary in any subsets of the elderly population, with cross-reference to other sections providing information in elderly, e.g. 4.4, 4.5, 4.8 or 5.2.
4.2 method of administration	When supportive data are available, information on alternative method(s) to **facilitate administration** or acceptability should be given as explicitly as possible (e.g. possibility of crushing tablet, cutting tablet…
4.3 Contraindications	demographic factors (e.g. gender, **age**) - Lack of data alone should not lead to a contraindication.
4.4 Special warnings & precautions for use	Special patient groups that are at increased risk or are the only groups at risk of experiencing product or product class-related adverse reactions (usually serious or common), e.g. **elderly**, children, patients with renal or hepatic impairment (including the degree of impairment, e.g. mild, moderate or severe), patients having an anaesthesic or patients with cardiac failure
4.5 Interaction with other medicinal products & other forms of interaction	If there are patient groups in which the impact of an interaction is more severe, or the magnitude of an interaction is expected to be larger e.g., patients with decreased renal function (in case the parallel pathway is renal excretion), paediatric patients, **elderly** etc, this information should be given here.
4.7? 4.8 Undesirable effects	This section may include information on any clinically relevant differences (i.e. in nature, frequency, seriousness or reversibility of adverse reactions, or need for monitoring) specifically observed in other special populations such as **elderly**, patients with renal impairment, patients with hepatic impairment, patients with other diseases or a specific genotype.
4.9 Overdose	Information specifically observed in special populations such as **elderly**, patients with renal impairment, patients with hepatic impairment, other concomitant diseases etc.
5.1 Pharmacodynamic properties	In the exceptional cases when clinically relevant information from **subgroup** or post-hoc analyses is presented, it should be identified as such in a balanced manner reflecting the limited robustness of both positive and negative secondary observations.
5.2 Pharmacokinetic properties	Variations with respect to factors such as **age**, weight, gender, smoking status, polymorphic metabolism and concomitant pathological situations such as renal failure, hepatic disease, including degree of impairment.

Clinically relevant information in SmPC

Stating "Use with caution" or "There is limited data" only is poorly informative

Effect in older population known	➢ Inform on the conclusions: dose adjustment, warning or precaution for use, or no difference with younger patients	In clinical studies, there has been no indication that patients 65 years of age or older are at increased risk of adverse events compared to patients younger than 65 years old. No dose reductions other than those recommended for all patients are necessary.
Limited information	➢ Inform on available data and uncertainties (consequences)	Clinical studies did not include sufficient numbers of patients aged 65 and over to determine whether they respond differently from younger patients. In an exploratory analysis, increasing age, especially aged 65 years and older, appeared to be associated with increased rates of neurological adverse events.
No information	➢ Inform on lack of information	

Discussion: area for improvement?

- Accessibility, format, structure and content of the EPAR?

  (e.g. post-authorisation data on older people, co morbidity, interactions)
- Could the SmPC better fulfil its objective to be the basis of information for Healthcare Professionals?
- To promote the application of the principles of the SmPC guideline not only for information in older population but also for other special population because of co morbidity
  - Better use of subheadings?
  - Add concept of "frailty"?
  - More CT data in older population in 5.1, 4.8?
  - Clearer information on drug interactions?
- Clear SmPC: a must for a clear package leaflet

Coming soon …

Older population