CANCER GUIDELINES: CURRENT GAPS

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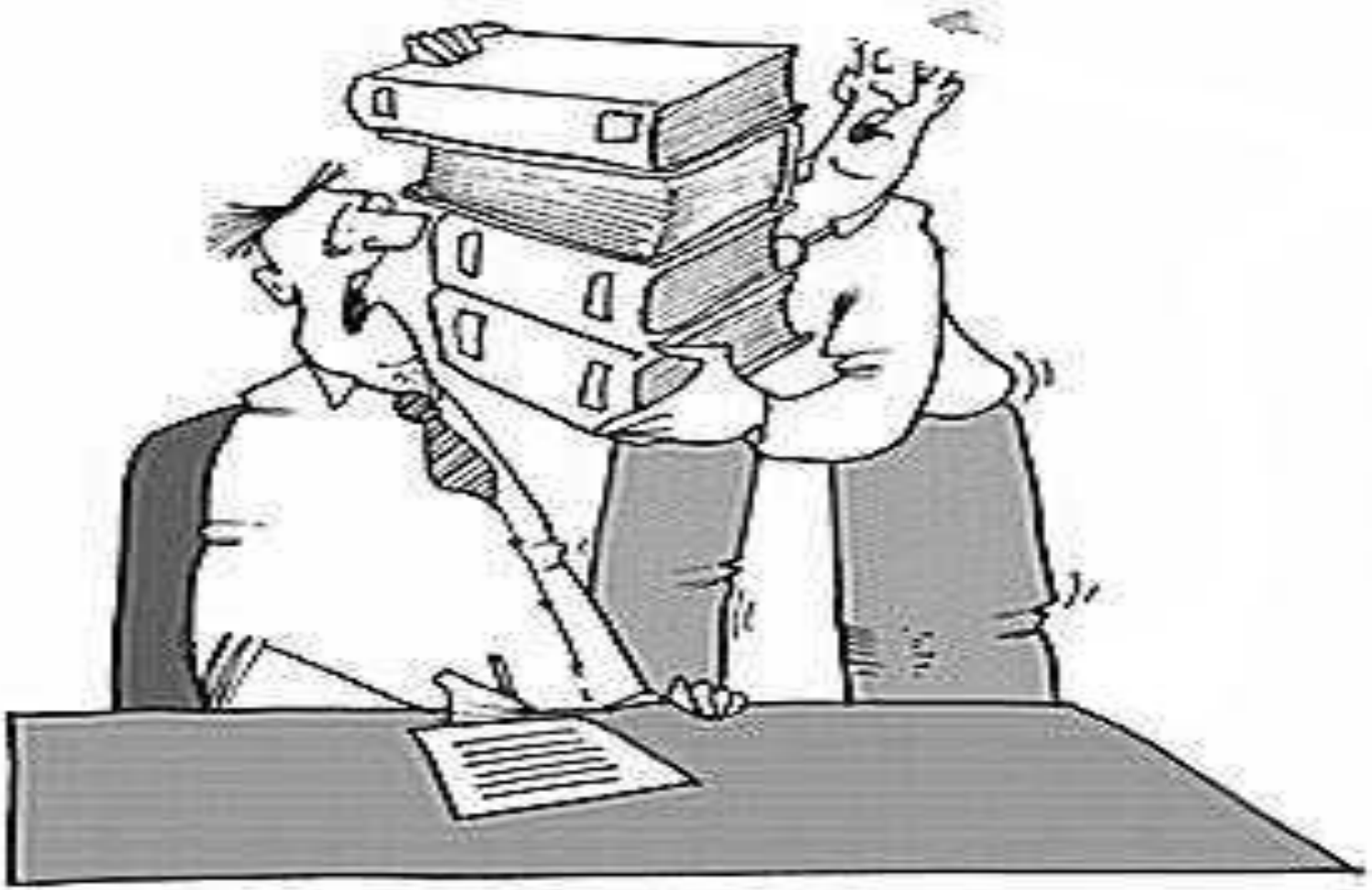

THEY'RE THE DRAFT GUIDELINES ON HOW TO RUN A 'PAPERLESS' OFFICE

How are they produced?

1. A local group or a national body **decides to develop CPGs** in a clinical area in which there is a need for such guidelines (select clinical problem: rank in order of priority, define and refine the problem, frame the clinical problem).
2. **Data is synthesized** from research information and relevant practice patterns by searching the literature (including existing guidelines) and then weighing the strength of the evidence from the resulting trials or studies.
3. **Data is reviewed,** appraised, distilled and collated as guidelines; that is, as recommendations about strategies for investigation and management.
4. The sponsoring organization and other interested organizations then **endorse the guidelines.**
5. **CPGs are disseminated,** usually by traditional means such as mailing them to members or publishing them in recognized professional clinical journals.
6. Various groups or individual practitioners may attempt to **implement the guidelines** more actively, through various and often multiple strategies to assist, convince or otherwise influence physicians, patients and their caregivers.
7. CPGs are subjected to **re-appraisal, evaluation** and **reiteration** of the process.

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Neuroendocrine bronchial and thymic tumours: ESMO Clinical Practice Guidelines for diagnosis, treatment and follow-up

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incidence

The annual incidence of lung neuroendocrine tumour has been reported to be 1.35/100 000/year and the overall age adjusted incidence for thymic carcinoid 0.02/100 000/year. Of all neuroendocrine tumours, ~25% are located in the respiratory tract. Both bronchial and thymic carcinoids may be part of multiple endocrine neoplasia type 1 syndrome (MEN-I) (5%–15%). The median age at diagnosis for lung neuroendocrine tumours is 64 years and for thymic tumours 59 years.

diagnosis

Neuroendocrine tumours of the lung and thymus should be referred to a centre with particular interest in and knowledge of the disease for careful evaluation and treatment.

Neuroendocrine tumours of the lung include the low-grade typical carcinoid (TC), intermediate-grade atypical carcinoid (AC) and the high-grade large cell neuroendocrine carcinoma (LCNEC) and small-cell carcinoma (SCLC). Neuroendocrine tumours of the lung comprise ~20%–25% of all invasive lung malignancies. The most common neuroendocrine lung tumour is the SCLC, which accounts for 15%–20%, followed by LCNEC, at ~3% and the carcinoids, which account for 1%–2% of all lung cancer. About 70% of all carcinoids are located in the major bronchi, and the remainder in the periphery of the lungs. They occur more frequently (61%) in the right than in the left lung, and especially in the middle lobe. Diffuse idiopathic pulmonary neuroendocrine cell hyperplasia (DIPNECH) is a rare preneoplastic condition comprising a generalized proliferation of pulmonary neuroendocrine cells predominantly in women and non-smokers. Up to 92% of patients are symptomatic, presenting with haemoptysis, cough, recurrent pulmonary infection, fever, chest discomfort and unilateral wheezing.

The carcinoid syndrome is very rare in patients with pulmonary and thymic carcinoids, ranging to ~2%, usually caused by serotonin. Nevertheless, a carcinoid crisis may occasionally occur in previously asymptomatic patients following bronchoscopic biopsy or surgical manipulation. In ~2% of patients with Cushing's syndrome it is caused by ectopic ACTH production from these tumours.

Diagnostic work-up includes chest X-rays followed by computed tomography (CT) scan, bronchoscopy, somatostatin receptor scintigraphy in selected cases, particularly those with ectopic hormone production (e.g. Cushing's syndrome, SIADH). Positron emission tomography (PET) scan with fluorodeoxy glucose (FDG) often shows false-negative results but might be positive in more aggressive high-proliferation tumours. The tumour cells from bronchial tumours have certain morphological, ultrastructural, immunohistochemical and molecular characteristics in common, but there are important differences in incidence, clinical epidemiological, survival and molecular characteristics. The diagnosis is made by histological examination of tumour tissue assisted by immunohistochemical detection of neuroendocrine markers. For diagnosis of thymic tumours thoracotomy may be required. For bronchial localizations, in patients with centrally localized carcinoids, tissue samples are taken during bronchoscopic examination. Using the rigid bronchoscope has the advantage of larger and more reliable biopsy samples. Brush or fine-needle cytology is of no or limited value for the diagnosis of

Guideline	Multi disciplinarity	Methodological experts	Patient advocates
ASCO	Yes	Yes	Yes
ESMO	Occasionally	No	No
NICE	Yes, extended	Yes	Yes
SIGN	Yes, extended	Yes	Yes
START	Yes	Yes	No
NHMRC	Yes, extended	Yes	Yes
NCI	No	No	No
NCCN	No	No	Occasionally
CCO	Yes	Yes	Yes

Guideline	Review of evidence	External review of guideline	Comprehensive for tumour type
ASCO	Systematic	Yes	No, focused GL
ESMO	Narrative	Yes	Yes
NICE	Systematic	Yes, extensive	Some
SIGN	Systematic	Yes, extensive	Yes
START	Narrative	Yes	Yes
NHMRC	Systematic	Yes, extensive	Yes
NCI	Narrative	Yes	Yes
NCCN	Narrative	Yes	Yes
CCO	Systematic	Yes, extensive	No, focused GL

Guideline	No of guidelines	Size	Cost data	Update	
ASCO	21	24	Optional	3 years	
ESMO	47	3	No	Yearly	
NICE	13	120	Yes	3-5 years	
SIGN	12	60	Yes	3-5 years	
START	67	20	No	3 years	
NHMRC	12	300	Yes	5 years	
NCI	80	40	No	Monthly	
NCCN	34	80	No	Yearly	
CCO	108	35	No	3 years	

Gaps/Problems

- What is the best methodology? Who are the stakeholders to be involved (healthworkers, authorities, industry, patients)?
- How to involve patient groups? Which ones? To which extent in the decision-making process?
- How to eliminate bias in the development process? What is the best review process?
- How to balance cost-effectiveness considerations vs best available management consideration?
- How to grade and weigh evidence?

More gaps and problems

- Which cancer care outcome parameter to use?
- How to grade patient preference as evidence?

- Multiple CPGs exist: Which one to use? International collaboration? To Develop or to Adopt/Adapt?
- Are CPGs and the recommended practices applicable in real-life setting?

- Frequency of update?

LOE- SOR

Levels of evidence at descending order, used in establishing guidelines [25, 58, 59]

1. High-quality randomized controlled trials or meta-analyses
2. Small randomized controlled trials
3. Non-randomized trials with concurrent controls
4. Non-randomized trials with historical controls
5. Quasi-experimental studies
6. Non-experimental descriptive studies (e.g. comparative, and case-control studies)
7. Expert committee reports or opinions or clinical experience of respected authorities, or both

A	Strong evidence for efficacy with a substantial clinical benefit, strongly recommended
B	Strong or moderate evidence for efficacy but with a limited clinical benefit, generally recommended
C	Insufficient evidence for efficacy or benefit does not outweigh the risk or the disadvantages (adverse events, costs,..), optional
D	Moderate evidence against efficacy or for adverse outcome, generally not recommended
E	Strong evidence against efficacy or for adverse outcome, never recommended

Looking for evidence

- Optimal method for evidence identification?
- Systematic vs Narrative?
- How to weigh Evidence?
- What about CPGs for Rare Diseases, for which low-quality or no evidence is avaible?

"The opinion of experts has been a traditional source of all the errors throughout medical history"

Feinstein AR. Fraud, distortion, delusion, and consensus: the problems of human and natural deception in epidemiologic science. Am J Med 1988;84:475-478.

How to evaluate cancer CPGs: AGREE

Domains

1. Scope and Purpose

- The overall objectives of the guideline are specifically described.
- The clinical questions covered by the guideline are specifically described.
- The patients to whom the guideline is meant to apply are specifically described.

2. Stakeholder Involvement

- The guideline development group includes individuals from all pertinent professional groups.
- Patients' views and preferences have been sought.
- Guideline target users are clearly defined.
- The guideline has been piloted among target users.

3. Rigor of Development

- Systematic methods were used to search for evidence.
- The criteria for selecting the evidence are clearly described.
- The methods for formulating the recommendations are clearly described.
- The health benefits, side-effects and risks have been considered in formulating the recommendations.
- There is an explicit link between the recommendations and the supporting evidence.
- The guideline has been externally reviewed by experts prior to its publication.
- A procedure for updating the guideline is provided.

4. Clarity and Presentation

- The recommendations are specific and unambiguous.
- The different options for condition management are clearly presented.
- Key recommendations are easily identifiable.
- The guideline is supported with tools for application.

5. Applicability

- The potential organizational barriers in applying the recommendations have been discussed.
- The potential cost implications of applying the recommendations have been considered.
- The guidelines present key review criteria for monitoring and/or audit purposes.

6. Editorial Independence

- The guideline is editorially independent from the funding body.
- Conflicts of interest of guideline development members have been recorded.

Cancer CPG scores

High Scores

- *Multidisciplinary development, selecting evidence and formulating recommendations*
- *Health benefits, side-effects, and harms (various options clearly presented)*

Low Scores

- *Applicability, Barriers to Implementations, Cost data*
- *Patient involvement*

Burgers JS,et al. International Assessment of the Quality of Clinical Practice Guidelines in Oncology Using the Appraisal of Guidelines and Research and Evaluation Instrument. J Clin Oncol 2004; 22:2000-2007.

Main reasons for major disagreement in scientific content:

Frequency of CPG update!

Cost-effectiveness considerations, source of funds, rapidity of acceptance of medical breakthroughs.

	ASCO 2003	ESMO 2008	NICE 2005	SIGN 2005 (comparison standard)	START	NHMRC 2004	NCI 2007	NCCN 2008	CCO 2006–2007
Epidemiology, screening and presentation	80–100	80–100	80–100			80–100	60–80	60–80	–
Diagnosis	80–100	80–100	80–100		–	80–100	60–80	60–80	80–100
Staging	80–100	80–100	80–100		–	80–100	80–100	60–80	80–100
Surgery	80–100	80–100	80–100		–	80–100	80–100	80–100	80–100
Radiotherapy	60–80	60–80	60–80		–	80–100	40–60	60–80	80–100
Chemotherapy	60–80	60–80	80–100		–	40–60	60–80	60–80	60–80
Other therapies (biologics)	40–60	40–60	80–100		–	40–60	40–60	40–60	40–60
Palliative and supportive care	80–100	80–100	80–100		–	80–100	60–80	80–100	–
Follow-up	60–80	60–80	80–100		–	80–100	–	40–60	80–100
Implementation and Research	–	–	80–100		–	–	–	–	–
Mean agreement score (%)	89	89	98		–	91	80	80	91

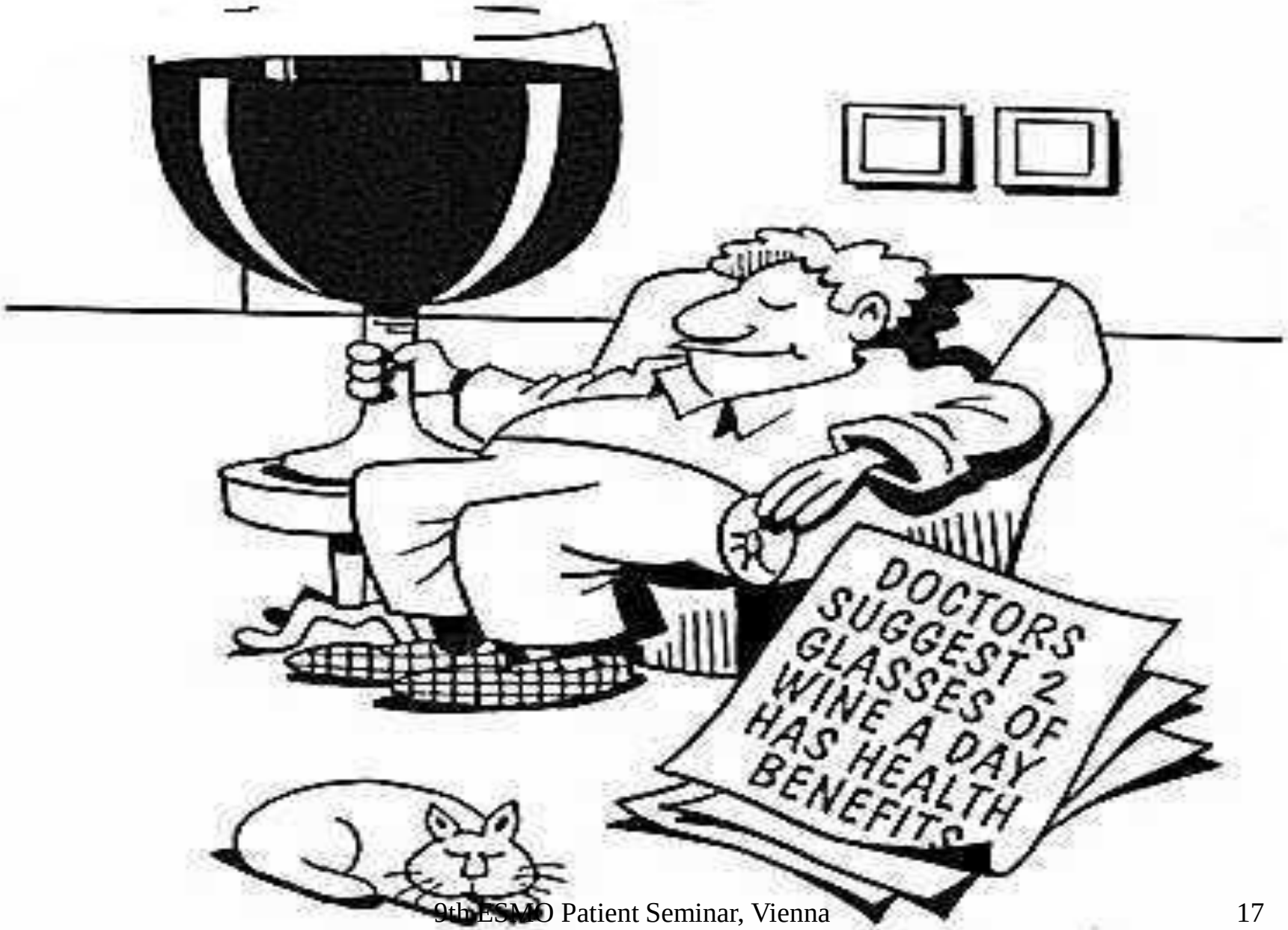
"systematically developed statements to assist practitioner and patient decisions about appropriate health care for specific clinical circumstances"

- *Systematically developed statements:*
- **Even with systematic reviews, the evidence is filtered and synthesized by the expert.**

- *To assist practitioner and patient decisions:*
- **Which practitioner? Which patient decision? (influenced by social, financial and cultural contexts).**

- *About appropriate health care:*
- **Any relatively safe treatment resulting in some survival benefit or only cost-effective therapies yielding substantial patient benefits?**
- **Which outcome matters most? Survival, QoL, Patient Satisfaction, Cost/effectiveness ratio?**

- *In specific clinical circumstances:*
- **Rich or poor country? Privately funded or state-funded health systems?**


DOCTORS SUGGEST 2 GLASSES OF WINE A DAY HAS HEALTH BENEFITS