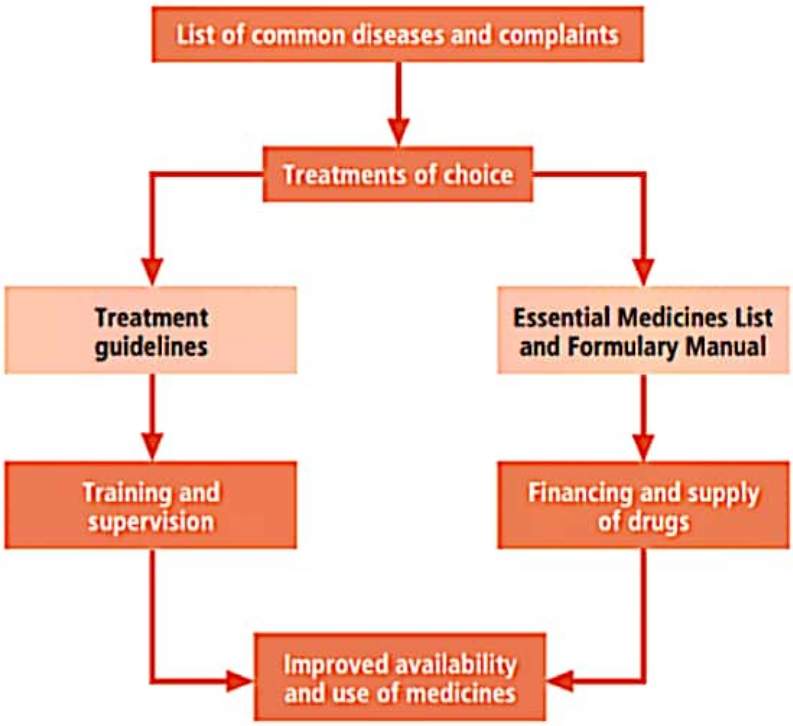
Figure 3.1 How STGs and EMLs lead to better prevention and care



3.2 The formulary list (essential medicines list)

> Essential medicines are those that satisfy the priority health care needs of the population. They are selected with due regard to disease prevalence, evidence of efficacy, safety and comparative cost-effectiveness. Essential medicines are intended to be available within the context of functioning health systems at all times in adequate amounts, in the appropriate dosage forms, with assured quality and adequate information, and at a price the individual and the community can afford. The implementation of the concept of essential medicines is intended to be flexible and adaptable to many different situations; exactly which medicines are regarded as essential remains a national responsibility (WHO 2002a).

It is difficult to achieve efficiency in the hospital pharmaceutical system if there are too many medicines. All aspects of drug management, including procurement, storage, distribution and use, are easier if fewer items must be dealt with. Appropriate selection of drugs can achieve the following results:

- **Cost containment and enhanced equity in access to essential medicines:** Procuring fewer items in larger quantities results in more price competition and economies of scale with regard to quality assurance, procurement, storage and distribution. Such economies can lead to improved drug availability at lower costs, so benefiting those who are in most need.
- **Improved quality of care:** Patients will be treated with fewer but more cost-effective medicines for which information can be better provided and prescribers better trained. Prescribers gain more experience with fewer drugs and recognize drug interactions and adverse reactions better. Quality of care will be further improved if medicine selection is based on evidence-based treatment guidelines.

3.2.1 Criteria in medicine selection

Which drugs are selected depends on many factors, such as the pattern of prevalent diseases, the treatment facilities, the training and experience of available personnel, the financial resources, and genetic, demographic and environmental factors. WHO (1999) has developed the following selection criteria:

- Only those medicines should be selected for which sound and adequate data on efficacy and safety are available from clinical studies, and for which evidence of performance in general use in a variety of medical settings has been obtained.
- Each selected medicine must be available in a form in which adequate quality, including bioavailability, can be assured; its stability under the anticipated conditions of storage and use must be established.
- When two or more medicines appear to be similar in the above respects, the choice between them should be made on the basis of a careful evaluation of their relative efficacy, safety, quality, price and availability.
- In cost comparison between medicines, the cost of the total treatment, and not only the unit cost of the medicine, must be considered. Where drugs are not entirely similar, selection should be made on the basis of a cost-effectiveness analysis.
- In some cases, the choice may also be influenced by other factors, such as pharmacokinetic properties, or by local considerations such as the availability of facilities for storage or manufacturers.
- Most essential medicines should be formulated as single compounds. Fixed-ratio combination products are acceptable only when the dosage of each ingredient meets the requirements of a defined population and when the combination has a proven advantage over single compounds administered separately in therapeutic effect, safety or compliance.
- Drugs are specified by the international nonproprietary name (INN) or generic name without reference to brand names or specific manufacturers.

All DTCs should agree an explicit set of criteria, based upon the WHO criteria, for selecting medicines, so that the selection process can be objective and evidence-based. Without an evidence-based approach, decisions may be taken according to the doctors who 'shout loudest', and it may be difficult to persuade other prescribers to abide by the list. The criteria for drug selection and the procedure for proposing a drug to be added to the formulary list should be published (see section 3.2.3). Not all evidence is equally strong. For example, randomized controlled trials are less subject to bias than expert opinion and are therefore thought to constitute a higher level of evidence. The level of evidence should be acknowledged when publishing selection criteria and decisions. One classification scheme for levels of evidence is that used by the Scottish Intercollegiate Guideline Network (SIGN), as shown in Table 3.1.

3.2.2 Developing and implementing a formulary list

The hospital formulary list should be consistent with the national essential medicines list (EML), if the latter is available. It is very important that an explicit and previously agreed process and selection criteria be followed at each step in order to increase prescriber confidence in the validity and usefulness of the list.

Table 3.1 **SIGN levels of evidence**

1++	**High-quality** meta analyses; systematic reviews of randomized controlled trials (RCTs); or RCTs with a **very low risk of bias**
1+	**Well conducted** meta analyses; systematic reviews of RCTs; or RCTs with a **low risk of bias**
1–	Meta analyses; systematic reviews of RCTs; or RCTs with a **high risk of bias**
2++	**High quality** systematic reviews of case-control or cohort studies; or high quality case-control or cohort studies with a **very low** risk of confounding, bias, or chance and a **high probability** that the relationship is causal.
2+	Well conducted case-control or cohort studies with a **low risk** of confounding, bias, or chance and a **moderate probability** that the relationship is causal
2–	Case-control or cohort studies with a **high risk** of confounding, bias, or chance and a **significant risk** that the relationship is not causal
3	Non-analytic studies, e.g. case reports
4	Expert opinion.

STEP 1 Prioritize a list of common problems/diseases being treated in the hospital and determine the first choice of treatment for each problem

The diseases may be ranked to identify the most common diseases being treated in the hospital by consulting all medical departments and reviewing the previous hospital mortality and morbidity records. For each disease, an appropriate first-choice of treatment should be identified using STGs – either nationally or locally developed. If there are no published STGs endorsed by the health ministry, publications by WHO, unbiased professional organizations and academia can be used. Alternatively, an expert committee can be brought together to identify the appropriate treatment for each of the common health problems. A commonly used alternative method of developing a formulary list – easier, but not recommended – consists of reviewing the existing formulary list of the hospital concerned or any other hospitals in the country. In such circumstances, the *WHO model list of essential medicines* (WHO 2002a) may also be used as a starting point. The capability of the hospital and its staff to handle specific drugs should not be forgotten during the selection process. For example, warfarin is not suitable for use unless the hospital has a facility to monitor prothrombin time (blood clotting time).

STEP 2 Draft, circulate for comment, and finalize the formulary list

A draft of the list must be prepared. It is useful to identify:

- the most important medicines (which are absolutely essential) and those that are less essential
- the most expensive medicines
- whether all the medicines that are prescribed in large volumes, or are expensive, are essential (see ABC analysis and VEN analysis in chapter 6).

Each department, whether clinical or involved in non-clinical drug management, must be given the chance to comment on the list. The DTC must deliberate on their comments and provide feedback. All information to be discussed and deliberated upon, such as disease profile and STGs, must be available during the discussions, together with evidence-based reviews where possible. Finally, the DTC must agree and disseminate the formulary list and the reasons for its choices.

STEP 3 Develop policies and guidelines for implementation

The formulary list will never be useful unless there are documented policies and guidelines on how it should be used. These should include:

- who should use the list (prescribers and the procurement department should both abide by the list)
- how the list should be reviewed and updated
- a clear mechanism for adding and deleting medicines from the list (section 3.2.3)
- how medical staff can request medicines that are not included on the list in exceptional or emergency situations (for example, certain non-formulary drugs may be prescribed by authorized senior doctors for specified less common conditions on a named patient basis).

STEP 4 Educate staff about the formulary list and monitor implementation

All the staff in the hospital must be educated about the list. A common problem is that prescribers continue to request and use medicines not on the list. This results in patients having to buy their medicines from pharmacies outside the hospital, or the procurement group buying non-formulary medicines, without the approval of the DTC. There should be a clear system of implementation, accountability and enforcement including reprimands and sanctions. End users and opinion leaders can be involved in evaluating and enforcing the implementation.

3.2.3 Managing a formulary list (EML): adding and deleting drugs

All applications to add medicines to the list must be made on an official application form (see annex 3.1). Individual doctors making an application must get the endorsement of their head of department. The application should include the following information:

- the pharmacological actions of the medicine and its proposed indication
- why the medicine is superior to those already on the formulary list
- evidence from the literature to support inclusion on the formulary list
- declaration of interest as to whether the applicant has received any financial support from the supplier, i.e. the manufacturing company or wholesaler.

The request should be sent to the DTC secretary who will arrange for the request to be formally evaluated by the responsible person – either him/herself, or a drug information pharmacist, or drug information centre staff.

Evaluations of applications to add new medicines to the list

These should be conducted using explicit documented criteria, preferably evidence-based, as previously agreed by the DTC and covering the following areas:

- **Criteria for consideration of new treatments for conditions not amenable to existing drug therapy, or treatments representing major improvements in survival and quality of life:**
  - — the efficacy, effectiveness and safety of the medicine, as assessed by locally available literature (see section 4.1)
  - — the quality of the drug (which may be considered adequate if registered by the national regulatory body) and a supply chain of acceptable quality (with regard to manufacture, storage and transport)

— whether the hospital has the necessary clinical expertise and laboratory services to use the medicine, and what role specialists should play to regulate therapy

— an estimation of the cost (and potential savings) to the hospital should the drug be introduced – this should include costs of the medicine itself, hospitalization and investigation (see section 4.5)

— availability of the drug on the market.

- **Criteria for treatments representing minor improvements in therapy compared to existing listed medicines. The committee should consider all of the above and in addition:**

  — whether the new drug is really superior to existing ones in terms of efficacy, safety, or convenience of dosing/administration; claimed minor improvements are often proved to be unimportant

  — how the total cost for a course of treatment with the new drug compares with already listed drugs (see section 4.5).

- **Criteria for treatments that are therapeutically equivalent to existing listed medicines. The committee should consider all of the above and in addition:**

  — whether the new drug is really therapeutically equivalent, and not inferior, to existing drugs in terms of efficacy, safety, or convenience of dosing/administration

  — whether the total cost for a course of treatment with new medicine is less than with the already listed medicines (see section 4.5.3).

- **Criteria for use of non-formulary medicines. If the use of non-listed drugs is allowed in certain circumstances, then these drugs need not be included in the list. Such circumstances may include:**

  — non-response or contraindications to available medicines

  — whether to continue therapy for a patient who had been stabilized on a non-listed medicine before admission to hospital and where changing to another drug is considered detrimental.

- **Criteria for restricting the use of certain drugs to specified specialist prescribers only. Such circumstances may include:**

  — the danger of unnecessarily increasing antimicrobial resistance with inappropriate use of third- or fourth-generation antimicrobials; thus they should be limited to prescription by infectious disease or clinical microbiology specialists

  — the danger of serious side-effects that could occur unnecessarily with inappropriate use, for example chemotherapeutic or cytotoxic agents; thus they should be limited to prescription by specialized physicians with knowledge of these medicines.

Written report of the drug evaluation

A written report should be compiled by the person who conducted the evaluation, and discussed at a scheduled DTC meeting. This report should contain the following information:

- the drug monograph, including pharmacology, pharmacokinetics, efficacy as compared to placebo and other medicines, clinical trial analysis (from the literature – see chapter 4), adverse drug reactions, drug interactions, cost comparison
- recommendations based on the evidence-based information

- expert opinions and recommendations from knowledgeable and respected physicians and pharmacists
- how much the new medicine would cost the hospital
- whether the new drug belongs to the national EML and whether it is reimbursable by health insurance schemes.

Discussion and voting procedures

The report should be discussed by the DTC members and a vote taken on the recommendations presented by the person who compiled the drug evaluation report. The final decision should then be disseminated to all health-care staff in the form of minutes, in newsletters and at departmental meetings.

Non-listed requests

A register of all non-listed medicine requests should be kept by the pharmacy and the name of the requesting doctor, the name and quantity of the medicine and the indication for which the medicine was requested should be recorded. When compiled at the end of the year, this information can tell the DTC about prescriber adherence to the formulary list and can also help in deciding whether or not to add drugs onto the list.

Pruning the list

If a new medicine is added to the list for reasons of improved efficacy, safety or lower price, serious consideration should be given to deleting the medicine which was previously on the formulary list for the same indication, for two reasons:

- if the 'new' medicine is better, why continue to have a less good 'old' medicine on the list?
- if no effort is made to consider deleting medicines, none will be deleted and the list will grow in size.

3.2.4 Maintaining a formulary

Routine review of different therapeutic categories is an important part of formulary management. An efficient formulary management process will not passively wait for applications to add new medicines to the formulary. New drugs and treatments are emerging all the time, and without evaluation the formulary may become a collection of older, less effective drugs. Therefore, the entire formulary should be reviewed every 2–3 years. This can be done by evaluating all the formulary medicines within each therapeutic class in a systematic way on a regular basis and comparing them to other new non-formulary medicines within that class. Thus, in order to efficiently maintain a formulary, a DTC should meet regularly to discuss and decide upon:

- requests for the addition of new medicines and deletion of old medicines
- systematic review of a therapeutic class of medicines
- review of programmes to identify and resolve medicine use problems.

All decisions of the DTC should be documented (minuted).

BOX 3.1 PRINCIPLES OF FORMULARY LIST MANAGEMENT

- Select drugs according to the needs of patients
- Select drugs of choice for the conditions identified
- Avoid duplications, both therapeutic and pharmaceutical (dosage forms)
- Use explicit selection criteria, based on proven efficacy, safety, quality and cost
- Use evidence-based information whenever possible
- Be consistent with national EMLs and STGs
- Consider requests for the addition of new drugs only when made by health-care staff, not by the pharmaceutical industry
- Require that requests for the addition of new drugs are justified using documented evidence on efficacy, relative efficacy, safety and comparative cost-effectiveness and that the person requesting any new drug declare any conflict of interest
- Carry out annual systematic reviews of all therapeutic classes to avoid duplication.

3.2.5 Improving adherence to a formulary

The existence of a well-maintained formulary does not mean that prescribers will adhere to it. Methods to promote formulary adherence include the following (see also chapter 7 and MSH 1997, chapter 10 'Managing Drug Selection', chapter 11, 'Treatment Guidelines and Formulary Manuals' and chapter 38 'Hospital Drug Services'):

- reviewing and taking action on all non-formulary medicine use; action may include adding the medicine to the formulary, educating the prescriber about the non-formulary status of the medicines or banning use of the medicine within the hospital
- prohibiting the use of non-formulary drug samples in the hospital
- establishing procedures and approved drug product lists for therapeutic interchange or substitution (see section 7.3.3)
- providing easy access to the formulary list, with copies at each drug ordering location and in pocket manuals for staff
- involving medical staff in all formulary decisions
- advertising and promoting all formulary changes
- establishing agreed procedures for clinical trials with non-formulary medicines.

3.3 Formulary manual

The formulary manual is the publication that brings all the important summary information on medicines in the formulary list together in a manual. There is no set standard on how this document is arranged or what is in the manual. Normally it would contain an alphabetically and therapeutically arranged listing of all the formulary drugs, and a section on drug usage including doses, contraindications, side-effects, drug interactions and price. Ideally the manual should include a section on the medicines of choice and alternates for treating the medical conditions of the region. Annex 3.2 shows a list of the information that should be available in a comprehensive formulary. The DTC may be selective in what information is presented for each item, depending on what has been approved for use locally; for example, including only some but not all dosage forms, strength, indications