DRUG INFORMATION BULLETIN

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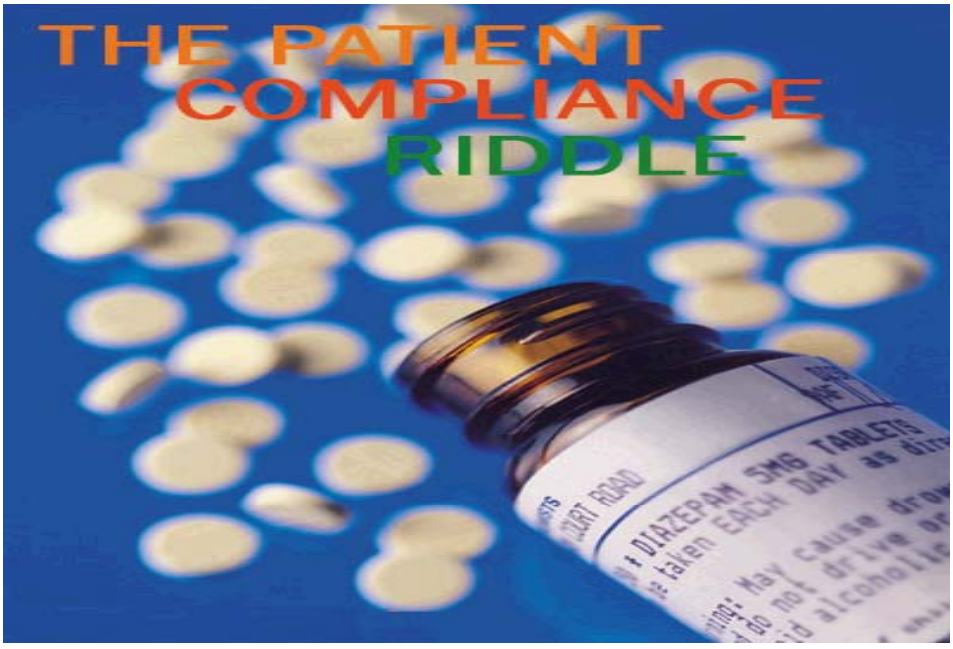

Contents

Special points of interest:

* Do you know that Ethiopia Radio is transmitting Drug Information and activities of DACA every Wednesday night (21:45)?
* DACA's website is under development
* Drug Information centers will be established.

New Publications

In line with the mandates entrusted to it, DACA in collaboration with professionals in the country developed **Standard Treatment Guidelines** (for Zonal Hospital, District Hospital, Health Center and Health Station), **Formularies** (for District Hospital and Health Center) and **Standard prescription paper**, which are available free of charge. Please note that we are unable to supply copies of the publications to individual professionals themselves. Requests should be addressed direct to the regions concerned.

Familiarization workshop was conducted

Continuing its effort of promoting rational drug use in the country, DACA has popularized the prepared STGs, Formularies and Standard Prescription Paper on a National workshops which were held at different towns of the country.

Editorial

In this Issue, more emphasis is given to the strategies and interventions that are implemented currently to promote rational drug use nationally. This article is presented in the current issue and News column of the bulletin.

As you all aware that ART has been commenced nationally a year before. And good adherence is a decisive factor for success Antiretroviral treatment. However, because of its life long treatment, costly, complicated treatment regimens, and accompanied with unpleasant adverse effects, poor adherence to a regimen could be a great challenge. This and related topics are presented in the scientific information up date column.

Under the Regulatory tips column, newly published treatment Guidelines and Formularies are described.

The tutorial part of this issue provides answers for seven self-test questions which have been asked in the previous issue (vol.1 Issue 3). We couldn't include new questions because the allocated space for this column is already covered by the answers of previous questions.

Unlike the previous issue, the "Readers' view" column is not included for the reason that we didn't receive letters from our readers. We encourage our readers to send us their views and other drug related articles, with genuine sources. Besides, we will acknowledge and support participants' effort and contribution for the attainment of our objectives.

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Promoting Rational Use of Drugs (PRUD)

Definition of Rational Use of Drugs

The conference of experts on the rational use of Drugs, convened by the World Health Organization (WHO) in Nairobi in 1985, defined rational as follows:

the rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their own individual requirements, for an adequate period of time, and at the lowest cost to them and their community.

The Problem Of Irrational Use Of Drugs

Irrational or non-rational use is the use of medicines in a way that is not compliant with rational use as defined above. World wide more than 50 % of all medicines are prescribed, dispensed, or sold inappropriately, while 50 % of patients fail to take them correctly. Moreover, about one-third of the world's population lacks access to essential medicines, common types of irrational drugs use are:

- The use of too many drugs per patient (poly pharmacy);
- Inappropriate use of antimicrobials, often in inadequate dosage, for non-bacterial infections;
- Over-use of injections when oral formulations would be more appropriate;
- Failure to prescribe in accordance with clinical guidelines;
- Inappropriate self-medication, often of prescription only drugs. .

Lack of access to drugs and inappropriate doses result in serious morbidity and mortality, particularly for childhood infections and chronic diseases, such as hypertension, diabetes, epilepsy and mental disorders.

Inappropriate use and over-use of drugs waste resources often out-of pocket payments by patients and result in significant patient harm in terms of poor patient out comes and adverse drug reactions.

Furthermore, over-use of antimicrobials is leading to increased anti-microbial resistance and non-sterile injections to the transmission of hepatitis, HIV/AIDS and other blood, borne diseases. Finally, irrational over-use of drugs can stimulate inappropriate patient demand, and lead to reduced access and attendance rates due to medicine stock-outs and loss of patient confidence in the health system.

Assessing the problem of irrational use:

To address irrational use of medicines, prescribing, dispensing and patient use should be regularly monitored in terms of:

- **The types** of irrational use, so that strategies can be targeted towards changing specific problems;

- **The amount** of irrational use. So that the size of the problem is known and the impact of the strategies can be monitored;

- **The reasons** why medicines are used irrationally. So that appropriate, effective and feasible strategies can be chosen. People often have very rational reasons for using medicines irrationally. Causes of irrational use include lack of knowledge, skills or independent information. Unrestricted availability of medicines, overwork of health personnel, inappropriate promotion of

medicines and profit motives from selling medicines.

In general, two broad types of data, *quantitative and qualitative*, are useful for identifying problems of inappropriate drug use and for learning about their underlying causes.

Quantitative Methods

Quantitative data are very useful for finding out what behaviors are happening in a given situation, and how often they are happening. These data can therefore be used to identify specific problems or to measure the success of interventions to change these problems. .

Table 1 lists some of the wide range of quantitative data sources that may be useful in different situations for learning about drug use practices. It is clear that there are many possible ways to measure different aspects of drug use.

LOCATION OF DATA	DATA SOURCES	USEFUL FOR STUDYING
Public Sector Administrative Offices, Medical Stores	RETROSPECTIVE: - drug supply orders - stock cards - shipping and delivery receipts	- aggregate patterns of drug use and expenditures - comparative use of drugs within therapeutic classes - comparative use by different facilities or areas
Health Facility Clinical Treatment Areas and Medical Record Departments	RETROSPECTIVE: - patient registers - health worker logs - pharmacy receipts - medical records PROSPECTIVE: - patient observations - patient exit surveys - inpatient surveys	- aggregate patterns of drug use and expenditures - drug use per case, overall & by group (age, sex, health problem, etc.) - provider-specific prescribing patterns - features of patient-prescriber interaction
Health Facility Pharmacies	RETROSPECTIVE: - pharmacy logs - prescriptions retained in pharmacies PROSPECTIVE: - patient exit surveys - patient observations	- aggregate patterns of drug use and expenditures - dispensing practices - features of patient-dispenser interaction
Pharmacies and Retail Drug Outlets	RETROSPECTIVE: - prescriptions retained in pharmacies PROSPECTIVE: - customer exit surveys - customer observations - "simulated visits"	- private sector prescribing practices drug sales without prescription - self-medication practices - features of customer-sales attendant interaction
Households	RETROSPECTIVE: - family medical records - household surveys PROSPECTIVE: - household drug audits - family medical records	- total community drug use - care-seeking behavior - self-medication practices - family drug use - patient compliance

Table 1: Sources of quantitative Date on drug use

Qualitative methods

Quantitative methods describe drug use patterns, or pinpoint specific problems that need attention. However, quantitative methods are usually not good for understanding *why* these patterns or problems exist. Qualitative techniques are better suited to examine underlying feelings, beliefs, attitudes, and motivations.

In order to change problems effectively, we often need to find out more about why they are happening. For this purpose, it is helpful to collect qualitative data about the problem in the form of descriptions, ratings, observations, or some other less easily quantifiable form.

Qualitative methods are based on talking to people, or observing their behavior.

Some common methods to collect qualitative data on drug use include; in-depth interviews, focus groups, structured observations, structured questionnaires, and simulated patient visits.

Experience from many countries has encouraged the development of a standard method of measuring drug use practices, based on drug use indicators.

WHO/INRUD have designed drug use indicator that can be used to identify general prescribing and quality of care problems at health care facilities since 1993.

Selected WHO/INRUD drug use indicators (WHO, 1993)

Prescribing indicators:

- % Medicines prescribed by generic name
- % Encounters with an antibiotic prescribed
- % Encounters with an injection prescribed
- % Medicines prescribed from essential medicines list or formulary

Patient care indicators:

- Average consultation time
- Average dispensing time
- % Medicines actually dispensed
- % Medicines adequately labeled
- % Patients with knowledge of correct doses

Facility indicators:

- Availability of essential drugs list or formulary to practitioners
- Availability of clinical guidelines
- % Key drugs available

Complementary Drug Use Indicators:

- Average drug cost per encounter
- % Prescriptions in accordance with clinical guidelines

Framework For Changing Drug Use Practices

A wide range of factors causes problems in drug use.
These factors differ in importance from problem to problem and from setting to setting. Before trying to correct any problem in drug use, it is helpful to identify which factors are most important in causing the problem at hand. These can be identified using the methods mentioned

under the title assessing the problem of irrational use.

Overview of intervention strategies

Different strategies can improve drug use. These strategies can be grouped into three broad categories.

Educational: Seeking to inform or persuade prescribers, dispensers, or patients to use drugs in a different way.

Managerial: Structuring or guiding decisions through the use of specific processes, forms, packages, or monetary incentives.

Regulatory: restricting allowable decisions by placing absolute limits on availability of drugs.

WHO/INRUD recommends *twelve core interventions* to promote more rational use of Drugs

1. A mandate multi-disciplinary national body to coordinate medicine use policies
2. Clinical guidelines
3. Essential drugs list based on treatments of choice
4. Drugs and Therapeutics Committees districts and hospitals
5. Problem-based pharmacotherapy training in undergraduate curricula
6. Continuing in-service medical education as a licensure requirement
7. Supervision, audit and feedback
8. Independent information on drugs
9. Public education about drugs
10. Avoidance of perverse financial incentives
11. Appropriate and enforced regulation
12. Sufficient government expenditure to ensure availability of drugs and staff.

As you consider each intervention think about the settings and types of problem for which it may be appropriate. Which of the possible underlying factors influencing drug use does each intervention target? What would the potential strengths and weaknesses of such a strategy be in your institution?

When thinking about interventions, remember that it is usually more effective to combine several different strategies to improve a single problem in drug use.

For example, in-service training programs for prescribers about malaria treatment can be combined with supportive community education through the media. Or regulations that limit access to anti-diarrhea drugs can be combined with the dissemination of standard diarrhea treatment guidelines.

1. A mandated multi-disciplinary national body to coordinate medicine use policies.

Many Societal and health system factors, as well as professionals and many others, contribute to how drugs are used. Therefore, a multi-disciplinary approach is needed to develop, implement and evaluate interventions to promote more rational use of medicines.

A national regulatory authority is important in materializing these activities. In case of our country, the Drug Administration and Control Authority (DACA) is the agency that develops and

implements most of the legislation and regulation on pharmaceuticals. Ensuring rational use will require many additional activities, which will need coordination with many stakeholders.

Thus a national body is needed to coordinate policy and strategies at National level, in both the public and private sectors.

2. Clinical guidelines

Clinical Guidelines (Standard treatment guidelines, prescribing policies) consists of systematically developed statements to help prescribers make decisions about appropriate treatments for specific clinical conditions. Evidence - based clinical guidelines are critical to promoting rational use of drugs. Firstly they provide a benchmark of satisfactory diagnosis and treatment against which comparison of actual treatments can be made. Secondly, they are a proven way to promote more rational use of drugs provided they are: (1) developed in a participatory way involving end-users, (2) easy to read; (3) introduced with an official launch, training and wide dissemination; and (4) reinforced by prescription audit and feedback. Guidelines should be developed for each level of care (ranging from paramedical staff in primary health care clinics to specialist doctors in tertiary referral hospitals), based on prevalent clinical conditions and the skills of available prescribers. Evidence-based treatment recommendations and regular updating help to ensure credibility and acceptance of the guidelines by practitioners. Sufficient resources are needed to reimburse all those who contribute to the guidelines, and to cover the costs of printing, dissemination and training.

Currently, Drug Administration and Control Authority (DACA) of Ethiopia has developed standard treatment guidelines for different health facilities including for zonal and District Hospitals, Health Centers and for Health stations. These guidelines are supposed to be disseminated in the near future to all health institutions in the country.

3. Essential Drugs list based on treatments of choice

Essential drugs are those that satisfy the priority health care needs of the population.

Using an essential Drugs list (EDL) makes drugs management easier in all respects; procurement, storage and distribution are easier with fewer items; and prescribing and is dispensing are easier for professionals if they have to know about fewer items. A national EDL should be based upon national clinical guidelines. Drug selection should be done by a Central committee with an agreed membership and using explicit, previously agreed criteria, based on efficacy, safety, quality, cost (which will vary locally) and cost-effectiveness. EDLs should be regularly updated and their introduction accompanied by an official launch, training and dissemination. Public sector procurement and distribution of medicines should be limited primarily to those medicines on the EDL, and it must be ensured that only those health workers approved to use certain drugs are actually supplied with them. Government activities

in the pharmaceutical sector (e.g. quality assurance, and training), should focus on the EDL. The Drug Administration and Control Authority (DACA) is currently developing EDL for Ethiopia using the WHO model list of Essential drugs as a starting point.

4. Drugs and therapeutics committees in Hospitals

A Drugs and therapeutic committee (DTC), also called a pharmacy and therapeutics committee, is a committee designated to ensure the safe and effective use of medicines in the facility or area under its Jurisdiction. Such committees are well established in industrial countries as a successful way of promoting more rational, cost-effective hospitals to have DTCs by making it an accreditation requirement to various professional societies. DTC members should represent all the major specialities and the administration; they should also be independent and declare any Conflict of interest. A senior doctor would usually be the chairperson and the chief pharmacist, the secretary. Factors critical to success include: clear objectives a firm mandate, support by the senior hospital management; transparency, wide representation; technical competence; a multidisciplinary approach; and sufficient resources to implement the DTC's decisions.

Results of one study conducted a year before in Ethiopia revealed that only 44 % of the study group has already established DTC in their institutions but out of which less than 7 % were actively functional at study period.

The main functions of DTC are

- Evaluating and selecting drugs for the formulary and providing for its periodic revision. This includes developing rigorous evidence - based criteria for selection of drugs, taking into account efficacy, safety, quality and cost;
- Assessing drug use to identify potential problems.
- Promoting and conducting effective interventions to improve drug use (including educational, managerial and regulatory methods).

In addition Committees may;

- Manage adverse drug reactions
- Manage medication errors
- Promote infection control practices

5. Problem-based training in pharmacotherapy in undergraduate curricula.

The quality of basic training in pharmacotherapy for undergraduate medical and paramedical students can significantly influence future prescribing. Rational pharmacotherapy training, linked to clinical guidelines and essential drugs lists, can help to establish good prescribing habits. Training is more successful if it is problem-based, concentrates on common clinical conditions, takes into account students' knowledge, attitudes and skills, and is targeted to the students' future prescribing requirements.

The guide to Good Prescribing describes the problem-based approach, which has been adopted in a number of medical schools.

6. Continuing in-service medical education

Continuing in-service medical education (CME) is a requirement for licensure of health professionals in many industrialized countries. CME is likely to be more effective if it is problem based, targeted, involves professional societies, universities and the Ministry of Health, and is face- to -face. Printed materials that are unaccompanied by face-to-face interventions, have been found to be ineffective in changing prescribing or dispensing behavior. CME need not be limited only to professional medical or paramedical personnel, but may also include people in the informal sector such as medicine retailers often CME activities are heavily dependent on the support of pharmaceutical companies, as public funds are insufficient. This type of CME may not unbiased. Governments should therefore support efforts by University departments and national professional associations to give independent CME.

7. Supervision, audit and feed back0

Supervision is essential to ensure good quality of care. Supervision that is supportive, educational and face-to-face, will be more effective and better accepted by prescribers than simple inspection and punishment. Effective forms of supervision include prescription audit and feedback, peer review and group processes. Prescription audit and feedback consists of analyzing prescription appropriateness and then giving feedback. Prescribers may be told how their prescribing compares with accepted guidelines or with that of their peers. Involving peers in audit and feedback (peer review) is particularly effective. In hospitals, such audit and feedback is known as drug use evaluation.

Group process approaches amongst prescribers consists of health professionals themselves identifying a medicine use problem and developing, implementing and evaluating a strategy to correct the problem. This process needs facilitation by a moderator or supervisor.

8. Independent Drug Information

Often, the only information about medicines that practitioners receive is provided by the Pharmaceutical industry and may be biased. Provision of independent (unbiased) information is therefore essential. Drug information centers (DICs) and drug bulletins are two useful ways to disseminate such information. Both may be run by government or a University teaching hospital or a non-governmental organization, under the supervision of a trained health professional. Whoever runs the DIC or bulletin must (1) be independent of outside influences and disclose any financial or other conflict of interest, and (2) use evidence-based medicine and transparent deduction for all recommendations made.

In our country the Drug Information Division of Drug Administration and control Authority run this activity. The division produce and cascade current awareness drug information bulletin

quarterly and currently the division has published Drugs formulary that provides independent information on drugs available at District Hospital and Health Center level.

9. Public Education about medicines

Without sufficient knowledge about the risks and benefits of using medicines and when and how to use them, people will often not get the expected clinical outcomes and may suffer adverse effects. This is true for prescribed medicines, as well as medicines used without the advice by health professionals. Governments have a responsibility to ensure both the quality of medicines and the quality of the information about medicines available to consumers. This will require medicines available to consumers. This will require.

- Ensuring the over-the-counter drugs are sold with adequate labeling and instructions that are accurate, legible, and easily understood by lay persons. The information should include the medicine name, indications, contraindications, dosage, drug interactions and warnings concerning unsafe use or storage.
- Monitoring and regulating advertising, which may adversely influence consumers as well as prescribers, and which may occur through television, radio, newspapers and the internet.
- Running targeted Public education campaigns, which take into account cultural beliefs and the influence of social factors. Education about the use of medicines may be introduced into the health education component of school curricula or into adult education programs, such literacy courses.

10. Avoidance of perverse financial incentives

Financial incentives may strongly promote rational or irrational use. For example, prescribers who earn money from the sale of medicines (e.g. dispensing doctors) prescribe more medicines, and more expensive medicines, than prescribers who don't; therefore the health system should be organized so that prescribers do not dispense or sell medicines.

11. Appropriate and enforced Regulation

Regulation of the activities of all actors involved in the use of medicines is critical to ensuring rational use. If regulations are to have any effect, they must be enforced and the regulatory authority must be sufficiently funded and backed up by the judiciary.

Regulatory measures to support rational use

- Registration of medicines to ensure that only safe efficacious medicines of good quality are available in the market and those unsafe non-efficacious drugs are banned.
- Limiting prescription of drugs by level of prescriber, that includes limiting certain drugs to being available only with a prescription and not available over-the-counter.
- Setting educational standards for health professionals and developing and enforcing codes of conduct; this requires the cooperation of the professional societies and universities.
- Licensing of health professionals - doctors, nurses, paramedics
  - to ensure that all practitioners have the necessary competence with regard to diagnosis, prescribing and dispensing.
- Licensing of drug out lets - retails shops, wholesalers - to ensure that oil supply outlets maintain the necessary stocking and dispensing standards.

- Monitoring and regulating medicine promotion to ensure that it is ethical and unbiased. All promotional claims should be reliable, accurate, truthful, informative, balanced, up-to-date, capable of substantiation and in good taste.

12. **Sufficient Government expenditure to ensure availability of drugs and staff.**

Back of essential medicines leads to the use of non-essential drugs, and lack of appropriately trained personnel leads to irrational prescribing by untrained personnel. Furthermore, without sufficient competent personnel and finances, it is impossible to carry out any of the core components of a national program to promote rational use of drugs. Poor clinical out come, needless suffering and economic waste are sufficient reasons for large government investment.

Governments are responsible for investing the necessary funds to ensure that all public health facilities have sufficient, appropriately trained health professionals and enough essential drugs at affordable prices for all the population, with specific provisions for the poor and disadvantaged. Achieving this will require limiting government procurement and supply to essential medicines only, and investing in adequate training, supervision and health staff salaries.

≡Summary

Rational use of drugs requires that patients receive medications appropriate to their clinical needs, in doses that meet their individual requirements, for an adequate period of time, and at the lowest cost to them and their community.

Irrational drug use occurs with polypharmacy, with the use of wrong or ineffective drugs, or with under use or incorrect use of effective drugs. These actions have an adverse impact on the quality of drug therapy and cost and may cause adverse reactions or negative psychosocial impacts.

A prescriber's lack of knowledge and experience is only one factor in irrational drug use. Other underlying factors can be found in the dispensing process, the patient or community, and the health system itself.

Strategies to address irrational drug use can be characterized as educational, managerial, or regulatory. Whichever method to change drug use is selected, the intervention is likely to contain the elements of focusing on key factors, targeting facilities with the worst practices, and using credible sources and communication channels. Personal contact (face-to-face meetings, for example) can sometimes be used to convey a limited number of key messages; these can be repeated and clarified using different media.

When implementing a strategy, the logical steps are to

- identify the problem
- understand the underlying causes;
- list possible interventions;
- asses available resources;
- choose an intervention;
- monitor and restructure the activity, as necessary

Interventions should be based on an understanding of the cause of the problem and on active strategies to change behavior. Experience indicates that the most effective interventions are those that

- identify key influence factors;
- target individuals or groups with the worst practices;
- use credible communication channels;
- use personal contact whenever possible;
- limit the number of messages;
- repeat key messages using different methods;
- provide better drug use alternatives.

Adapted From: PRDU training session guide document, 2004 (unpublished book)

Optimizing analgesic response when pain is uncontrolled by oral opioids

When pain is not controlled by opioids administered by mouth, other options must be considered. This issue of *Cancer Pain Release* reviews the options, considers the benefits and the risks associated with alternative methods of administration and presents recent evidence about their effectiveness in providing relief and comfort to the patient.

The Facts

When managing moderate to severe cancer pain, morphine continues to be the standard against which other opioids are compared. Oral administration of opioids is preferred as recommended since 1986 by the World Health Organization, because it is simple, convenient and effective.

Opioids can also be administered in a wide variety of formulations other than oral tablets, including liquid solutions, capsules, transmucosal lozenges, suppositories, skin patches and subcutaneous, intravenous and spinal injections.

The Choice of an alternative route is influenced by a consideration of the benefits, risks, effectiveness and costs for each individual patient; the choice is also limited by what drugs and delivery options are available in the country or care setting.

Q/Is the administration of opioids by mouth always preferred to manage cancer pain?
A/Yes, oral administration is recommended in most patients because it is convenient, well-tolerated, and usually the least expensive method. We try to keep patients on oral analgesics as long as possible. In fact, oral opioids can be successfully administered until death.

Q/Under what circumstances is it necessary to consider alternatives to oral opioids?
A/When the patient develops an inability to absorb oral opioids and is very uncomfortable. In the case of severe vomiting, bowel obstruction, inability to swallow tablets or capsules, or when the patient is confused, and alternative route must be used. Since oral opioids take at least an hour to reach their peak effect, the oral route may not be optimal to achieve rapid relief when this is necessary.

Q/Are there side effects that might provoke a change from the oral route?
A/ In a survey of strategies used by physicians to select opioids and route of administration, the route was changed in 61 % of cases. We know that up to 70 % of patients benefit from a change in route for opioid administration. Ultimately many patients - if not most will require at least one route conversion during the course of their disease.

Q/Before switching route, should other steps be taken?
A/it is best to observe a patient's response to several different opioid administered one by one before switching from the oral to another route. Patients who experience poor analgesia or cannot tolerate one opioid may tolerate another opioid well. There is great variability in response to different opioids.

Q/How complex is conversion to a different route? What skills are required?
A/Clinicians should be highly skilled in pain assessment and have appropriate knowledge of equianalgesic opioid dosing. Conversion doses are approximate and doses must be individualized. When changing from the oral to another route of opioid administration, the clinician should first compare the relative potency of the opioid between routes. Then,

dosing and volume for different routes and different opioids should be addressed. Another consideration is either adding or adjusting a nonopioid adjuvant medication is indicated. Finally, the feasibility of combining the opioid and an adjuvant in a single route should be examined.

Q/are there other drug-related factors to consider?
A/The degree of absorption and the onset of action of the drug are important factors. Opioids are well absorbed by the oral or rectal route. However, when the drug is delivered directly into the system intravenously or subcutaneously, the drug does not go through the liver and is absorbed even faster. Opioids absorbed from the gut must be given in higher doses than when given intravenously or subcutaneous. When changing the route, one must convert the dose according to known potency ratios. Thereafter, it is the response of the patient and there need for pain control that must guide the dose and the frequency of the opioid.

Q/Besides drug and dose-related factors, what other factors should be considered when changing from the oral route of administration?
A/The clinician also needs to take into account whether the pain is stable and continuous, or whether the patient is experiencing incident or breakthrough pain. The financial resources of the patient and the availability of support at home are other important factors to take into consideration.

Q/What are some of known benefits of changing the route of administration of an opioid?
A/Changing the route of administration or the opioid formulation can bring faster pain relief and/or a longer duration of relief, and possibly reduce side effects.

Q/are there side effects associated with particular routes of opioid administration?
A/There is very limited evidence to suggest differences inside effects associated with specific routes of administration. We know from small studies that a few patients experience less nausea and vomiting with rectal and subcutaneous administration than with oral morphine. In another study, switching from oral to subcutaneous morphine produced significantly less drowsiness in some patients. We also know that patients receiving transdermal fentanyl may experience less constipation that with oral morphine. It is not clear whether this is route or drug related effect.

Q/What is the most common indication for administration of morphine other than by mouth?
A/Inability to swallow is common to many patients in the last hours or days of life. When patients present with very severe pain, it is often appropriate to initially control the pain with a parenteral opioid formulation and --after some relief of achieved -- switch the patient to an oral formulation.

Q/What alternative method is appropriate for a patient unable to swallow?
A/Transdermal delivery of fentanyl is effective as long acting morphine and oxycodone. However it is formulated as a long acting preparation with 72 hours duration, and is therefore of limited usefulness for a patient with rapidly changing pain. Transmucosal fentanyl citrate is a formulation that provides rapid pain relief during break through episodes.

Q/If the patient can swallow, but oral morphine causes intolerable or unmanageable side effects, should the opioid or the route be changed?
A/This question remains unresolved in clinical practice. Although in some patients a change of opioids at the same level of analgesia can

reduce side effects, there are no definitive data on which to base practice guidelines. Physicians who are able to change the route of administration do so, while those who cannot change the drug.

Q/In resource-limited settings, physicians and nurses may not have the possibility to switching the route of administration or may not have another opioid available. What to do then?
A/When changing drugs, comparisons must be made at equianalgesic doses. By contrast, when changing the route of administration and not the drug, the dose of the drug must be adjusted, particularly if the opioid undergoes extensive first pass metabolism. In practice, there is a great deal of variability among clinicians, based on personal experience.

Q/Would you say personal experience is paramount in selecting an opioid formulation?
A/Yes, a health worker will tend to choose the drug delivery option with which he or she is most familiar. However, it may not be the best option for the patient and clinicians should strive to be comfortable using all the opioids available in their country. In addition, clinicians must know how to calculate doses when switching between different opioids and between routes of opioid administration.

Q/If a patient's Pain is insensitive to opioids, or if a patient experiences movement-related pain, is a change of drug or a change of route with the same drug indicated?
A/These are challenging cases to diagnose and manage and the issue remains controversial. The same drug by a different route is likely to act on the same receptors. The issue is whether changing the route allows to increase the dose and produce effective analgesia without an increase in side effects.

Q/Is there a rule of thumb for pain assessment in relation to drug delivery?
A/A careful review of the way pain fluctuates with time is essential: continuous pain needs continuous analgesia. White a sustained-release oral opioid is the option of choice, a transdermal formulation, or a continuous subcutaneous infusion is indicated if oral formulations are not tolerated.

Q/Do many cancer patients benefit from spinal delivery?
A/A minority of cancer patients are candidates for spinal analgesia. These patients have somatic or neuropathic pain that is not responding to oral morphine. Or they develop morphine side effects which prevent any further escalation of the dose.

Q/Why is intrathecal delivery favored over epidural delivery?
A/An external intrathecal catheter is easier to place and use at home in very ill patients late in the course of their disease. The intrathecal administration has a lower incidence of catheter occlusion, lower malfunctioning rate, lower dose requirement, and provides more effective pain control. Intrathecal treatment is more suitable for treatment at home by continuous infusion than the epidural treatment, because of lower daily doses and volumes.

Q/How important is it to reduce the invasiveness of therapy?
A/Because of other large number of cancer patients outside of medical facilities, physicians, nurses and other health workers must often transfer care responsibilities to patients and their families. Simple, safe and effective routes of opioid delivery are essential for these patients to experience pain relief in the home setting.

Q/To what extent is cost a factor ?
A/ In our country economic settings, cost will determine the choice of the opioid formulation.

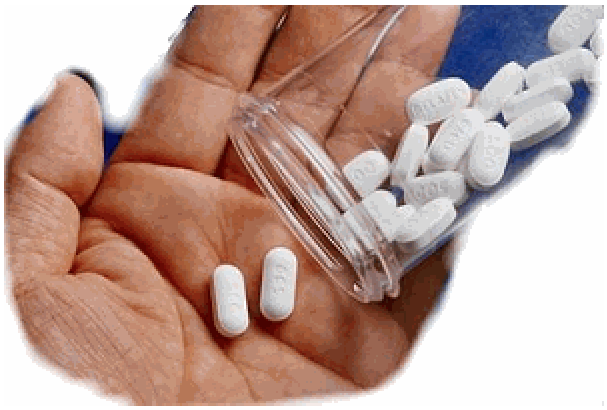
Q/Is there a role for patient preference?
A/In some situations, Patients may have a strong preference for a medication or for a certain mode of delivery. Therapeutic options should be presented to the patient, and patient preferences should weigh into final decision-making. Patients and caregivers must find the alternative route acdeptable.

Q/Do you have any further comments?
A/The ability to deliver opioids for sever pain via alternative routes increases the options for caregivers and patients. Switching route provides a therapeutic alternative for clinicians who need to improve analgesia and minimize side effects.

Adapted From: WHO, Cancer Pain Release, vol 16, Nos. 1 & 2--2003.

ADHERENCE TO ANTIRETROVIRAL TREATMENT

1. **Types of non-adherence**
2. **Challenges in assessing adherence**
3. **Predictors of adherence**
4. **A framework for interventions to increase adherence**
5. **Conclusions**



Of those patients suffering from HIV/AIDS, approximately one-third take their medication as prescribed. Even when patients fully comprehend the consequences of non-adherence to medications, adherence rates are suboptimal. Good adherence is a decisive factor in treatment success.

Unlike other chronic diseases, the rapid replication and mutation rate of HIV means that very high levels of adherence (e.g.≥95%) are required to achieve durable suppression of viral load. Recent studies of patients with HIV/AIDS have reported low adherence rates, similar to those seen for other chronic diseases. Suboptimal adherence may rapidly lead to resistance, which can then be transmitted to other people. The potent and effective new combination of antiretroviral agents, known as highly active antiretroviral therapy (HAART), have proven efficacious in reducing viral load and improving clinical outcomes. However, the large number of medications involved, the complicated dosing requirements and the suboptimal tolerability make adherence difficult. Because of the great importance of adherence to antiretroviral treatment of HIV, good strategies for maximizing adherence are essential.

There is no doubt that HAART is one of the most celebrated treatment advances in recent medical history. Nucleoside reverse transcriptase inhibitors (usually two) when combined with non-nucleoside reverse trancriptase inhibitors, protease inhibitors, or both, are highly effective in reducing viral replication and improving clinical outcomes. In patients with HIV/AIDS, these multi drug regimens, although remarkably efficacious, result in HIV treatment having the most complicated regimens that have ever been

prescribed for conditions requiring continuous open-ended treatment.

Many researchers believed initially that HAART would completely eradicate the virus from the host. However, low levels of viral replication persist in small reservoirs even when viral loads are undetectable. Resting memory T -cells, which harbour proviral DNA, survive for far longer than originally thought. Therefore adherence to HAART must be almost perfect to achieve lasting viral suppression. Paterson and colleagues found that adherence at levels less than 95 % independently predicted viral resistance, hospital admissions and opportunistic infections. Even among patients who reported adherence rates of ≥95 %, 22 % experience virologic failure during the study period. In another study, Bangsburg and colleagues found that none of the individuals with adherence greater than 90 % progressed to AIDS, whereas 38 % and 8 % of those with adherence rates ≥50 % and 51 - 89 % respectively progressed to AIDS. Missing even a single dose in a 28 day reporting period has been shown to predict treatment failure.

Non-adherence to HAART can have important public health implications. Drug resistance can be transmitted to other persons during high-risk activity, which can then limit therapeutic options. Some studies have reported that as many as 80 % of isolates from newly infected people are resistant to at least one class of currently approved antiretroviral medications, and that 26 % of isolates are resistant to several classes of medication. Although these estimates are at the higher end of the spectrum, they nonetheless suggest that transmission of drug-resistant strains is increasing.

Because adherence of patients with HIV to antiretroviral medications is essential for both clinical effectiveness and public health, research in this area has burgeoned over the past few years.

1. Types of non-adherence

Non-adherence can take many different forms. The patient may simply fail to fill the prescription. If the prescription is filled, the patient may incorrectly time the medication or take the wrong dose because he or she misunderstood, or forgot, the health professional's instructions. Patients may also forget a dose completely or prematurely terminate the medication. Moreover, patients may self-adjust their regimen because of side effects and toxicity or personal beliefs.

2. Challenges in assessing adherence

It is easy for health professionals to miss adherence problems because patient self-reports of adherence tend to be exaggerated due perhaps both to a recall bias and desire to please the provider and avoid criticism. Some patients have been known to dispose of their medication before a scheduled check on their adherence to it so as to appear to have adhered. Inadequate adherence coupled with biased reporting is ubiquitous across medicine. Conversely, patients who report problems with adherence are rarely trying to mislead their providers.

In addition to the misreporting of adherence by patients, estimates of adherence made by health care providers are also usually over-optimistic. Moreover, providers of health care are not able to predict very accurately which patients will adhere. Many providers believe that factors associated with socioeconomic status such as lack of education and poverty is good predictors of non-adherence. However, predictors of adherence vary greatly across populations and settings and no one factor has been consistently associated with non-adherence across all studies.

3. Predictors of adherence

Four types of factor have generally been found to predict problems with adherence to medication: regimen characteristics, various patient factors, the relationship between

provider and patient and the system of care. The following section focuses on the first three factors; a discussion of factors associated with the system of care is beyond the scope of this topic.

A. Regimen-related factors

Complexity of regimen. Adherence to HIV medications is an extremely complicated process that includes both the drugs themselves and adjustment to daily life necessary to provide the prerequisite conditions for effective drug therapy. Some regimens require several doses of medication per day together with various requirements or restrictions on food intake and other activities. These complexities, in addition to the problems of toxicity and side effects, can greatly influence an individual's willingness and ability to adhere to the therapy.

Many health professionals believe that pill burden strongly influences adherence. However, the effect of pill burden on adherence is closely associated with disease stage. Symptomatic individuals perceive a higher risk for complications of non-adherence to medication, than do asymptomatic patients. Dosing schedules and food restrictions or requirements appear to have a more pervasive influence on adherence than pill burden. In the treatment of many diseases, once-daily or twice-daily doses are preferred. For instance, Eldred and colleagues found that patients on twice-daily doses or less reported better adherence (>80%) and were more likely to take their medications when away from home. Paterson and colleagues also found that a twice-daily dose was associated with better adherence than a three-times daily dose. However, other studies have failed to confirm this association, including the large Health Care Services Utilization Study with more than 1900 participants. Wenger and colleagues demonstrated that the "fit" of the regimen to an individual's lifestyle and schedule, and the individual's attitude towards treatment were better predictors of adherence than dosing schedule. It is likely, however, that fewer doses do allow for easier "fitting" of medications into an individual's schedule.

Regimens that involve close monitoring and severe lifestyle alterations together with side effects may lead not only to frustration and treatment fatigue, but also ultimately to noncompliance. Regimens requiring fewer alterations in lifestyle patters (e.g. fewer pills per day and fewer dietary restrictions) are likely to have a positive influence on adherence to medication.

To the extent possible, regimens should be simplified by reducing the number of pills and frequency of therapy and by minimizing drug interactions and side effects. This is particularly important for patients with strong biases against many pills and frequent dosing. There is evidence that simplified regimens that require fewer pills and lower dose frequencies improve adherence. When choosing appropriate regimens, the patient's eating habits should be review and the specific food requirements of the regimen discussed so that the patient understands what is required before his or her agreements to such restrictions is sought. Regimens requiring an empty stomach several times per day may be difficult for patients suffering from wasting, just as regimens requiring a high fat intake may be difficult for patient with lactose intolerance or fat aversion.

Side-effects. Side effects have also been consistently associated with decreased adherence and patients who experience more than two aversive reactions are less likely to continue their treatment. HAART regimens usually have temporary side effects including transient reactions (diarrhea and nausea) as well as longer-lasting effects (i.e. lipodystrophy and neuropathy). The extent to which side effects alter a patient's motivation to adhere to a treatment regimen depends greatly on the specific on textual issues surrounding the individual. The literature on side effects clearly

shows that optimal adherence occurs with medications that remove symptoms, whereas adherence is reduced by medications that produce side effects. Although HAART may greatly increase quality of life in symptomatic individuals, it probably has a negative effect on quality of life in asymptomatic individuals.

Patients quickly discontinue therapy or request changes of medication if they experience side effects. Whether real or perceived, side effects account for more regimen changes than does treatment failure. One large study of more than 860 HIV-positive patients in Italy reported that more than 25 % of treatment-naive patients discontinued their treatment within the first year because of toxicity and other side effects. Another study in France found that patients subjective experience of side-effects within the first 4 months of treatment predicted non-adherence more than any other predictors, including socio demographic variables, number of medications or doses per day. The symptoms that cause the most distress are fatigue, diarrhea, nausea and stomach pain, most of which can be successfully treated.

One serious side effect that may affect adherence to HIV medications is lipodystrophy. Kasper and colleagues found that 37 % of their respondents either stopped or changed their medications because they developed lipodystrophy. Of those who were adherent 57 % stated that they had seriously considered discontinuation of therapy while 46 % stated that they would change medications if symptoms worsened.

Lipodystrophy affects between 30 % and 60 % of persons on HAART. Physical manifestation vary greatly but can include fat accumulation on the upper back and neck under the muscles of the abdomen (crix belly or protease paunch), lipomas and breast enlargement; it may also cause peripheral wasting of fat in the face, legs, arms, and buttocks. Physiologically, these physical deformities are usually preceded by hyperglycaemia, insulin resistance, hypercholesterlaemia and hypertriglyceridaemia. The exact relationship of these physiological changes to lipodystrophy is unclear. Nonetheless, lipid abnormalities must be treated and this can increase the complexity and side effects of already complex regimens. Selecting regimens that do not contribute to dyslipidaemia or lipodystrophy may allay fears of disfigurement and support adherence.
In the light of these findings, simplified regimens with fewer pills and fewer doses, and that minimize side effects, are desirable for achieving maximum adherence.

B. Patient-related factors

A patient's behavior is the critical link between a prescribed regimen and treatment outcome. The most effective regimen will fail if the patient does not take the medication as prescribed or refuses to take it. Consequently, all things being equal, the most important factors influencing adherence are patient-related.

Psychosocial issues. Perhaps more than anything else, life stress can interfere with proper dosing of protease medication regimens, and such stress is experienced more often and to a greater degree by individuals of low socioeconomic status. Although studies of most demographic characteristics of patients have generally failed to establish consistent links with adherence to medication, some recent studies have described several variables that have a possible association. Adherence is apparently more difficult for patients with lower levels of education and literacy, and a few studies have reported lower adherence among blacks and women, although this finding has not been consistent. Women have cited the stress of childcare as being related to missed doses. The abuse of alcohol and intravenous drugs and the

presence of depressive symptoms have also been linked with poor adherence to medications

Although some studies have demonstrated that a history of substance abuse is unrelated to adherence, active substance abuse is one of the stronger predictors of non-adherence. Nevertheless, even active substance abusers can achieve good adherence if the provider takes the time to address the patient's concerns about the medications, including anticipation of, and management of, side effects. Mocroft and colleagues demonstrated that intravenous drug abusers were significantly less likely to begin antiretroviral therapy but among those who did, the response to therapy was similar to that of other exposed groups.

Psychological distress has also been shown to affect adherence. Depression stress, and the manner in which individuals manage stress are among the most significant predictors of adherence but correlations with other psychiatric comorbidities are weaker. Hopelessness and negative feelings can reduce motivation to care for oneself and may also influence a patient's ability to follow complex instructions. Adolescents with HIV who reported high levels of depression demonstrated lower adherence than did their peers who were not depressed. These finding are similar to those of studies on other chronic conditions that have demonstrated a relationship between adherence and depression.

Just as social support acts as a buffer for many psychosocial problems, it also affects adherence behavior. Patients with supportive friends and families tend to adhere to HAART better than those without these supports. In addition to the support that can be provided by clinic staff in the form of a good relationship between provider and patients, recommendations for improving adherence often include providing a telephone counseling line were messages can be left for nurses, and enlisting the support of pharmacists. It is important to encourage patients to involve family and friends in their care and to follow up on referrals to support groups, peer-counseling and community based organization.

Several psychosocial predictors of acceptable levels of adherence to HIV medications have been identified in a large scale, multisite investigation of HAART. These include:

- Availability of emotional and practical life support;
- The ability of patients to fit the medications into their daily routines.
- The understanding that poor adherence leads to resistance
- The recognition that taking every dose of the medications is important, and
- Feeling comfortable taking medications in front of other people.

Such psychosocial aspects of treatment may be easily overlooked yet have been documented as being crucial to consistent adherence to HIV medications regimens.

Patient-belief system. A patient's knowledge and beliefs about disease and medicine can influence adherence. Understanding the relationship between adherence and viral load and between viral load and disease progression is integral to good adherence behaviour. Wenger and colleagues found better adherence in patients who believed antiretroviral medication to be effective. Negative beliefs regarding the efficacy of HAART may also affect adherence behavior. For example many African Americans were found to be reluctant to take zidovudine because they believed that it was toxic. Siegel and colleges showed that African American men were more likely those Caucasian men to report scepticism about medications and their ability to adhere to those medications. Other beliefs such as those regarding interference with the actions of

HAART by alcohol and drugs can also affect adherence.

The list below explains additional patient and medication related strategies too improve adherence.

- Inform patient, anticipate, and treat side - effects
- Simplify food requirements.
- Avoid adverse drug interactions.
- If possible reduce dose frequency and number of pills.
- Negotiate a treatment plan, which the patient understands and to which he or she is committed
- Take time, and use several encounters, to educate the patient and explain the goals of therapy and the need for adherence.
- Establish the patient's readiness to take medication before the first prescriptions is written.
- Recruit family and friends to support the treatment plan.
- Develop a concrete plan for a specific regimen including dealing with side effects and relate it to meals and the patient' daily schedule.
- Provide a written schedule with pictures of medications, daily or weekly pillboxes, alarm clocks, pagers or other mechanical aids to adherence.
- Set up adherence support groups or add adherence issues to the regular agenda of support groups.
- Develop links with local community-based organizations to help explain the need for adherence using educational session and practical strategies.
- Consider' pill trials' with jellybeans.

Confusion and forgetfulness are major obstacles in achieving adherence to HIV medication regimen. Difficulty in understanding instructions has also been reported to affect adherence. Requirements and/or restrictions on the intake of food and water, or the temporal sequences of dosing can be confusing. Misunderstandings may arise as a result of a complex regimen, and /or from poor instructions from the healthcare provider. In the AIDS Clinical Trial Group, 25 % of the participants failed to understand how their medications were to be taken. In another study, less adherent individuals reported significantly greater confusion than did adherent individuals over how many pills to take and how to take them.

The most commonly cited reason for non-adherence is forgetfulness; for example, Cheney and colleagues reported that 66 % of their respondents gave this as the main reason for non-adherence. Ostrop and colleagues demonstrated that not only is forgetfulness the most common reason for non-adherence, but also that the middle dose in a three times a day regimen is the most commonly forgotten. Although other studies have not confirmed this finding doses are more commonly missed in three times daily regimens than in once daily or twice daily regimens.

Patient-provider relationship.A meaningful and supportive relationship between the patient and health care provider can help to overcome significant barriers to adherence, but few providers routinely ask about adherence or offer counseling. Factors that strengthen the relationship between patient and provider include perceptions of provider competence, quality and clarity of communication, compassion, involving the patients as an active participant in treatment decisions and convenience of the regimen. Conversely patients become frustrated with health care providers when misunderstandings occur, treatment becomes complex the patient is blamed for being a "bad patient" or side effects go unmanaged. These frustrations may lead to poor adherence. Specific strategies for clinicians and health teams are listed below:

- Establish trust
- Serve as educator, source of information, continuous support and monitoring
- Provide access between visits for questions or problems by giving the patient a pager number, and arranging for coverage during vacation periods and conferences.
- Monitor adherence; intensify management during periods of low adherence (e.g. by means more frequent visits, recruitment of family and friends, deployment of other team members, referral for mental health or chemical-dependency services).
- Utilize health team for all patients, for difficult patients and for those with special needs (e.g. peer educators for adolescents or for intravenous drug users).
- Consider the impact of new diagnoses (e.g. depression, liver disease wasting recurrent chemical dependency), on adherence and include adherence intervention in their management.
- Enlist nurses, pharmacists, peer educator volunteers, case managers, drug counselors, physician's assistants, nurse practitioners and research nurses to reinforce the message of adherence.
- Provide training on antiretroviral therapy and adherence to the support team.
- Add adherence interventions to the job descriptions of HIV support-team members; add continuity of-care role to improve patient access.

4. A framework for interventions to increase adherence

Experiences with HAART suggest that adherence is arguably the most important issue in successfully managing HIV/AIDS. A multifaceted approach to improve adherence is the most likely to be beneficial, particularly a combination of actively involving patients in their own health care decisions, provision of appropriate supports, multidimensional educational programs that teach behavioral skills to the patient to enhance his or her adherence, and tailoring of the regimen to fit the patient.

The provider must accurately assess both the patient's willingness to adhere in the context of possible side effects, and his or her willingness to overcome potential barriers to taking the medications as prescribed. Furthermore, it is essential that the patient adequately understands the importance of adherence and the serious consequences of non-adherence (i.e. treatment failure, or in some cases, disease progression, drug-resistance or death).

Especially for a condition such as HIV, where poor adherence can cause resistance, it may prove wise to delay active treatment until the patient understands the demands of the regimen and feels truly committed to it. One way in which to gauge a person's readiness to adhere to a regimen, identify specific barriers to adherence, and to simultaneously strengthen the patient-provider relationship is to ask the patient an idea of a trial run of the regimen. This may be done using vitamin pills or jellybeans, with different tablets or different colored beans representing the various medications. Such a trial can give patients a perspective on how dosing schedules and other complexities, such as food restrictions or requirements will fit into their daily routine. A trial lasting a few weeks is usually sufficient for assessing a patient's ability to stick to the regimen and overcome the barriers. However, such a trial run is unable to mimic possible side effects

For children who rely on the support of caregivers to maintain their adherence, the caregivers must believe the rationale for the regimen and assume responsibility for maintaining it. Moreover, every attempt should be made too involve the children in the decision-making process to the extent of their capability. Although infants may have little influence on adherence, older children can have more influence on whether or not they take their medications as prescribed.

Whether developed or acquired, resistance complicates treatment decisions. As a variant becomes progressively resistant to current medications, the therapeutic options become limited. Then the only solution is to select medications from a new treatment class or prescribe medications from existing classes that have demonstrated efficacy against variants resistant to current medications. However, forced selection limits the ability to fit a regimen to patients' lifestyles and schedules.

Ideally, the health practitioner should work together with the patient to select a regimen that will fit with his or her lifestyle. If more than one regimen may be appropriate for a given patient, providers may want to discuss the regimen, the number of pills, the dosing schedule, instructions and potential side effects with patient. This discussion will foster a more collaborative and positive relationship between the practitioner and the patient, which is likely to enhance adherence. Once the regimen is decided upon, practitioners must make certain that patients fully understand the dosing schedules and instructions.

Rather than associating doses of medication with times of the day, fitting the regimen to the patient's lifestyle calls for working with the patient to associate medication doses with routine activities performed at the times that the medications should be taken. For example, morning doses can be associated with morning rituals (e.g. brushing teeth or reading the newspaper), an evening doses can be associated with evening routines (e.g. children's homework or watching television news programs). In general it is likely that accomplishing this "fit" will be easier with regimens that require infrequent dosing (i.e. once or twice a day). However, the principle of associating medications with daily activities can also accommodate more frequent and complex regimens.

The most simple, effective and potent regimen will fail if patients experience side effects that they perceive as problematic and terminate their medications. At the time that the regimen is prescribed health professionals should be proactive and provide strategies to help patients manage any side effects that may occur. Given that experiencing side effects is associated with non-adherence, providers and their team members should remain in close contact with the patient during early treatment with a new regimen to allow for the timely identification and management of all side effects and toxicities. A further advantage of this approach is that it provides an opportunity for reinforcing adherence behavior. A powerful reinforcer of adherence behavior is positive feedback regarding medication efficacy. Consequently, laboratory and other tests should be conducted soon after the initiation of treatment to show the extent to which it has been effective.

Health care providers and their teams should address the patient related factors and psychosocial issues associated with non-adherence. While these may vary across conditions screening for active substance abuse and depressed mood would be appropriate in many patient groups. Finally, enlisting the support of family members and "significant others", or employing "treatment buddies" to administer medications can greatly enhance adherence.

Preliminary reports have suggested that adherence rates are almost 100 %, 85 % of patient's have non-detectable virus in peripheral blood. Clinical outcomes have been excellent in all patients receiving DOT-HAART, enabling up to 90 % of them to resume normal daily activities within 3 months of initiation of treatment. Also, hospitalization rates have decreased by more than half since the start of the program and a sharp decline in mortality has been observed.

The implementation of demonstration projects of good HIV/AIDS care practice using targeted research or evidence based quality improvement

processes, is urgently needed for effectively fighting against the disease. As Pabblos-Mendez stated "research need not hold back care, we should learn by doing".

Table 2: Factors affecting adherence to therapy for HIV/AIDS and interventions for improving it, listed by the five dimensions and the interventions used to improve adherence

HIV/AIDS	Factors affecting adherence	Interventions to improve adherence
Socioeconomic-related factors	(-)Women: stress of childcare; low income; African American men; lack of social support (+)Support of family and friends; Caucasian men.	Family preparedness; mobilization of community-based organizations; intensive education on use of medicines for patients with low levels of literacy; assessment of social needs
Health Care Team/health System-related Factors	(-)Lack of clear instructions from health professionals; poor implementation of educational interventions (+)Good relationship between patient and physician; support of nurses and pharmacists.	Good patient-physician relationship multidisciplinary care; training health professionals on adherence; training of health professionals on adherence education; training in monitoring adherence; training caregivers; identification of the treatment goals and development of strategies to meet them; management of disease and treatment in conjunction with the patients; uninterrupted readily availability of information; regular consultations with nurses/physicians; non judgmental attitude and assistance; rational selection of medications.
Condition-related Factors	(-)Asymptomatic patients (+)Symptomatic patients; understanding the relationship between adherence and viral load.	Education on use of medicine; supportive medical consultation; screening for comorbidities, attention to mental illness, as well as abuse of alcohol and other drugs.
Therapy-related Factors	(-)Complex treatment regimens; close monitoring severe lifestyle alterations; adverse events; adverse effects of treatment; lack of clear instructions about how to take the medications. (+)Less frequent dose fewer pills per day; fewer dietary restrictions; fitting medication to individuals lifestyle; belief that medication is effective.	Simplification of regimens; education on use of medicines; assessment and management of side-effects patient-tailored prescriptions; medications for symptoms; education or adherence continuous monitoring and reassessment of treatment, management of side-effects.
Patient-related Factors	(-)Forgetfulness; life-stress; alcohol use; drug use; depression; hopelessness and negative feelings, beliefs that alcohol and drug use interfere with medications (+)Positive beliefs regarding the efficacy of antiretroviral medications.	Monitoring drug and/or alcohol use psychiatric consultation behavioral and motivational intervention; counseling, psychotherapy; telephone counseling memory aids and reminders, self-management of disease and treatment.

Conclusions: -

The problems of adherence are ubiquitous across medicine. Because adherence is a complex process, attempts to improve it need to be multifaceted. Factors such as the complexity of the treatment regimen, patient-related factors and the relationship between the patient and the provider of care, all affect adherence.

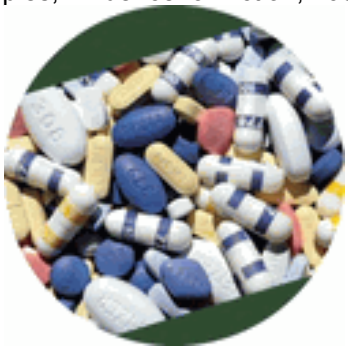
Health care providers should work to establish a collaborative treatment relationship with their patients. This can be fostered by involving the patients in selecting regimens with dosing schedules, pill burdens and side-effects that they believe are tolerable and will "fit" into their daily lives. Pharmaceutical companies are currently working diligently to develop once daily and twice-daily regimens with fewer side effects and higher tolerability that will better achieve this fit. Providers should openly discuss with patients their readiness to follow treatment, the potential barriers to adherence and possible solutions to problems. While the provider and his or her team can be a source of support, other possible sources (including family, friends and formal support services) should also be discussed with patients.

Clinicians should also be aware of the prevalence of mental health disorders and disorders related to psychoactive substance abuse in certain HIV-infected populations, as inadequate mental health treatment services may jeopardize the ability of affected individuals to adhere to their medical treatment. Appropriate attention to mental illness, as well as to abuse of alcohol and other drugs could greatly enhance adherence to medical treatment of HIV. Social and living conditions, fit of regimen to lifestyle availability and nature of social support and treatment expectations can also affect adherence.

No patient should be excluded from consideration for antiretroviral therapy simply because he or she exhibits a behavior, characteristic or risk factor that might be judged as predictive of non-adherence. The health care team should make all possible efforts to ensure that patients adhere to therapies. Awareness of patients' risk factors for non-adherence can help to guide clinicians in tailoring regimens to maximize adherence.

Poor adherence to a regimen is only one of several possible reasons for its failure. Others that must be assessed include initial resistance to one or more of the therapeutic agents, altered absorption or metabolism, and multi-drug pharmacokinetics that adversely affect levels of therapeutic drugs. It is therefore important to assess patient adherence carefully before changing antiretroviral therapy. Case managers, social workers and other health care providers involved in the care of the patient may assist in this evaluation.

Adapted From: WHO 2003, Adherence to Long-Term Therapies; Evidence for Action, 2003.



Eight Health Professionals Attended An International Training Course On Promoting Rational Use of Drugs (PRUD)

An International training Course on **Promoting Rational Use Of Drugs** was organized by Management Sciences for Health (MSH)/International Network For Rational Drug Use (INRUD), WHO/EDM, and INRUD/Kenya held from February 1-14, 2004, at the Fairview Hotel, Nairobi, Kenya.

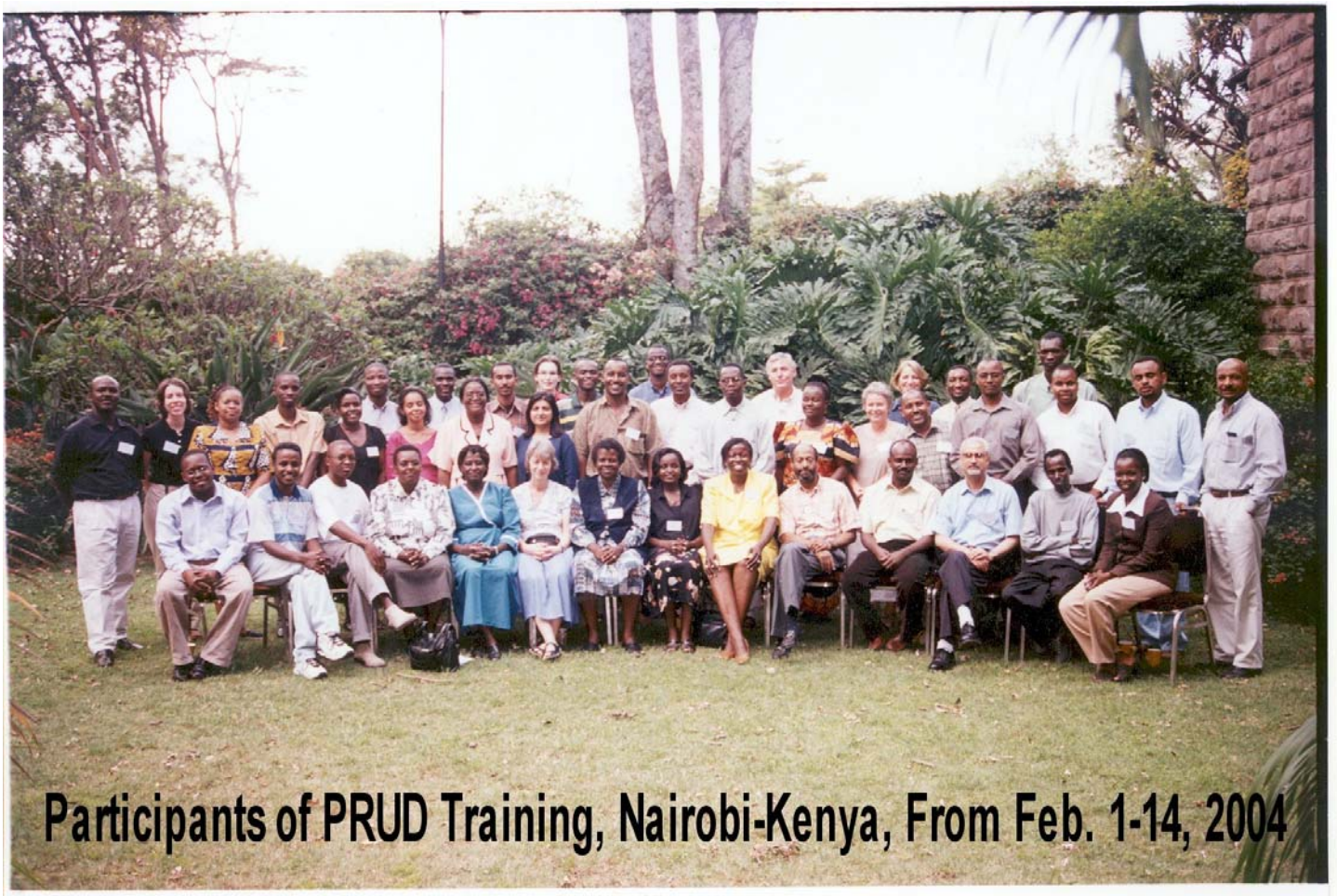
The two-week course was intended for Physicians, Pharmacists, health program managers, policy makers, researchers, and representatives of organizations interested in improving the use of drugs. The course focused on methods of studying and remedying inappropriate drug use, including problems with the ways in which drugs are prescribed, dispensed, and consumed.

Participants were from eight countries including Ethiopia, Kenya, Sudan, Zambia, Uganda, Ghana, Namibia and Tanzania. And totally 39 participants attended the training course. Most of participants are Pharmacists working in drug regulatory authorities, hospitals, non-governmental health facilities and so on. In the training, Participants learned practical approaches for applying key concepts such as Essential drugs lists, indicators of drug use, and methods for changing inappropriate drug use behavior.

The training was more of participatory and each participant has got a chance to share his/her experience for others.

In the training Ethiopia has sent **eight** health professionals who are from Drug Administration and Control Authority (DACA) (2), PASS/Ministry of Health (1), AAU/School of Pharmacy(1), Tigray regional Health bureau (1), Oromiya regional Health bureau (1), Amhara regional Health bureau (1), and Southern Nations, Nationalities and People (SNNP) Health bureau (1).

Like any others national drug policy, Drug Policy of the transitional Government of Ethiopia emphasized the importance of promoting rational use of drugs as its main objectives. This, giving chance for health professionals working in the field from different regions and institutions to attend an international training course, is as part of promoting rational use of drug in the country.



Participants of PRUD Training, Nairobi-Kenya, From Feb. 1-14, 2004

National Workshop on Familiarization of Standard Treatment Guideline (STG), Formulary and EDL.

Continuing its effort of promoting rational drug use in the country, DACA has popularized the prepared STGs, Formularies and Standard Prescription Paper on a continuous four round National workshops starting from May 5, 2004.

Irrational prescribing, dispensing and patient use of drugs is not only a National problem but also a global threat. Studies conducted in Ethiopia describe a pattern that includes polypharmacy, use of drugs that are not related to diagnosis, unnecessarily costly drugs, inappropriate use of antibiotics, indiscriminate use of injections, irrational self medication with under- and overdosing, use of drugs with unproven efficacy and safety, incorrect administration, dosage, duration e.t.c. Irrational drug use leads to reduce quality of therapy and waste of resources.

To contain the irrational drug use practice, the Drug Administration and Control Authority (DACA) of Ethiopia has made significant efforts. Among the efforts has been done so far, preparing & distributing revised national drug list, list of drugs for different levels of health facilities and retail out lets; produce and cascade current awareness drug information bulletin quarterly; prescribing control of NPS and banning of unsafe and doubtful drugs.

Continuing implementing various strategies and interventions to promote better drug use, the Authority has prepared:

- STANDARD TREATMENT GUIDELINES for different levels of health facilities including for Zonal hospital, District Hospital, Health Center and Health Station,
- DRUG FORMULARIES for District hospital and Health center, and
- STANDARD PRESCRIPTION PAPER

And to effect the widely use and acceptance of these documents among professionals, DACA has convened continuous four round three-days national familiarization workshops at different towns of the country to health professionals drawn from all regions.

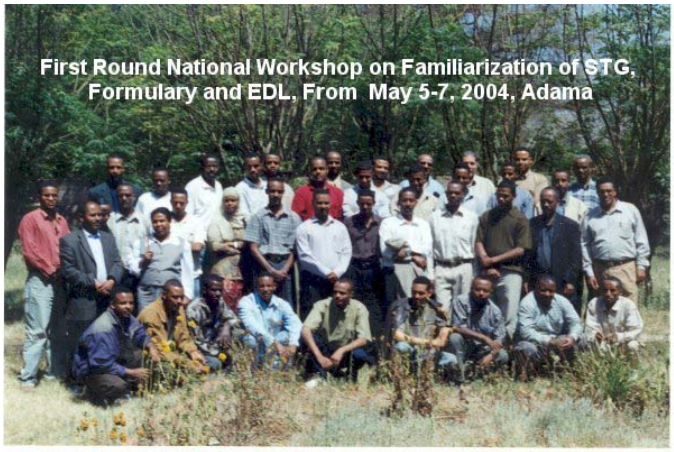
At the beginning of each workshops, representatives of invited regions has presented regional drug use situation. Following, Ato Wondie Alemu presented problem of irrational drug use in general. These two sessions initiated the participants to think about the importance of the above documents to tackle or intervene the problem. Topics on good prescribing, dispensing practice and patient compliance was also presented consecutively as these are the final target to be achieved after implementing the interventions. Assessing drug use problems and Framework for changing drug use problems were another two topics presented in the workshops. These sessions have given participants some insight on how to assess drug use situation or to see the effect of the interventions that is going to be introduced and to design other more interventions specific to the problems identified.

Then, the prepared *Standard Treatment Guidelines*, *Formularies* and *Standard Prescription Paper* were popularized by members of task forces of the respected documents.

On the final session of the first round workshop which was held at Adama Ras Hotel hall, Nazareth, from May 5-7, 2004, draft of Essential drug list of Ethiopia prepared by the Authority was evaluated by participants. The document had been distributed a month before for participants to come with their comments and at this session important comments and suggestions for finalizing the document was gathered from the discussion of the participants.

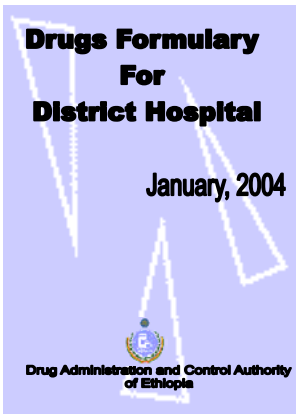
Participants were given the published STG and Formulary documents.

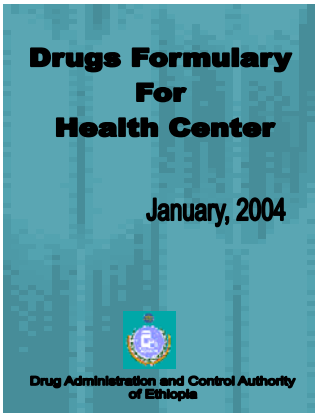
Generally, the workshops generated a great deal of discussion on challenges and potential solutions to implementing rational drug use activities.



Publications

In its efforts to promote safe and cost-effective use of drugs, DACA has recently released the first edition of FORMULARY for Health Centers and District Hospitals.





The Formularies are the first national publication to give comprehensive information on 253 & 400 Drugs contained in the drugs lists for Health Centers and District Hospital, respectively. It presents information on the recommended Use, Caution/warnings, Drug-interactions, Contraindications, Side effects, Dose and Administration of these drugs. Correct use of this tool will improve patient safety and limit superfluous medical spending.

As research continues to confirm the value of STANDARD TREATMENT GUIDELINE (STG) as an important element of good medical decision-making, the **Drug Administration And Control Authority (DACA)** Of Ethiopia has published the first edition of the Guidelines in different versions for different level of health facilities including Zonal Hospital, District Hospital, Health Centers and Health Station.

The present STG contains guides to general and special prescribing, specific treatment guidelines for a large number of common health conditions in Ethiopia, and relevant annexes that are useful for treatment and prevention. Diseases are classified into sections: infectious, non-infectious, common pediatric problems, common obstetric/ gynecological problems, common skin conditions and acute/emergency problems. Every disease has a brief description on the disease pattern, including ways of diagnosis and treatment. Both non-drug and drug treatment, both first line and alternatives drugs are listed for the treatment of a given disease. Under drug treatment, information on doses, course of therapy, dosage forms, side effects, contraindications and drug interactions are given for first line and alternative drugs.

These standard treatment guidelines are designed to be used as a guide to treatment choices and as a reference book to help in the overall management of patients. It is emphasized that the choices described here have the weight of scientific evidences to support them, together with the collective opinion of a wide group of recognized national experts.

The content of these treatment guidelines will undergo a process of continuous review comments or suggestions for improvement are welcome. Those comments or suggestions for addition of disease should include evidence of prevalence as well as a draft treatment guideline using the format set one in these guidelines. In the cases of a request for a new drug or replacing a listed product with another product, the evidence base must be clearly defined and included with the request.

These comments or suggestions should be sent to
The Drug Administration and control Authority (DACA) of Ethiopia
P.O. Box 5681
Addis Ababa, Ethiopia