

LIVER CIRRHOSIS: IT IS TIME TO ACT!

MOLDOVA CASE

Master of Public Health Thesis Project Utilizing Problem Solving Framework

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Executive Summary

Liver Cirrhosis is known as a disease causing irreversible scarring of the liver, however treatment of the underlying liver disease and determination of its possible causes can slow or stop the progression of cirrhosis.

The number of patients with chronic liver diseases, such as viral hepatitis and cirrhosis has increased over time all over the world. Liver cirrhosis is a major clinical problem worldwide and is associated with high morbidity and mortality, and often affects persons during the most productive years of life.

According to WHO and available statistical data there is a disastrous situation with respect to liver cirrhosis in the Republic of Moldova. For the majority of the main causes of death in the Republic of Moldova, mortality due to diseases of the digestive system, with a leading role being played by chronic liver diseases and cirrhosis has been one of the highest in the WHO European Region as a whole. Although chronic liver diseases and cirrhosis are the main cause of death in the Republic of Moldova, and have a significant impact on quality of life of these patients, there has been relative paucity of data with respect to the real situation, and as a result no strategic plan and actions for diseases prevention. The goal of this thesis is to elaborate strong strategies for public health policy-makers in order to make possible to prevent chronic liver diseases, especially liver cirrhosis in the Republic of Moldova, and to decrease the impact of liver cirrhosis on the society.

In order to reduce the public health impact of cirrhosis in the Republic of Moldova, primary prevention programs that focus on encouraging alcohol abstinence, reducing high-risk behaviors for hepatitis virus infection and vaccinating for Hepatitis B, and enforcing the law with respect to pesticide use are urgently needed. Action plan should include four main strategies: 1. National Alcohol Harm Reduction Strategy; 2. Promoting vaccination (HBV) program; 3. Reducing high-risk behaviors for VH; 4. Law enforcement with respect to pesticides use.

Implementation of this action plan should be in close collaboration with the Government of the Republic of Moldova, Ministry of Health and Social Protection, Ministry of Ecology and Environment Protection, non-governmental organizations, social programs, and International representatives working in this field. This plan is a long-term one.

In conclusion, it is very important to implement the action plan on a national level and governmental support is of considerable importance. The challenges are significant and so are the efforts and resources required to meet them for the best outcome.

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List of Abbreviations

(In alphabetic order)

CH – chronic hepatitis

GAVI – Global Alliance for Vaccination and Immunization

DU – drug users

HBV – Viral Hepatitis B

HCV – Viral Hepatitis C

HDV – Viral Hepatitis D

HGV – Viral Hepatitis G

LC – liver cirrhosis

NGO – Non-Governmental Organization

OCPs – persistent organochlorinated compounds

POPs – persistent organic pollutants

VH – Viral hepatitis

WHO – World Health Organization

I. Statement of problem

Definition of problem

Liver Cirrhosis (LC) is known as a disease causing irreversible scarring of the liver (1). Cirrhosis of the liver is a chronic, diffuse (widely spread throughout the organ), degenerative disease in which the parenchyma (the functional organ tissue) deteriorates; the lobules are infiltrated with fat and structurally altered; dense perilobular connective tissue forms; and often areas of regeneration develop (1). Approximately one-third of cirrhosis cases are "compensated," meaning there are no clinical symptoms (2). Compensated cases are usually discovered during routine tests for other problems or during surgery or autopsy. Early diagnosis is critical in cirrhosis to establish the cause of the disease and to determine the amount of existing liver damage. A positive diagnosis of liver cirrhosis requires the use of several laboratory tests; imaging procedures (computerized axial tomography scans, radioisotope liver scans, and ultrasound); physical examination; liver biopsy; and observation of the patient's symptoms (2).

Cirrhosis of the liver is an irreversible process, but treatment of the underlying liver disease and determination of its possible causes can slow or stop the progression of cirrhosis (2). One causal factor is alcohol: stopping the intake of alcohol will stop progression of alcoholic cirrhosis. Ending the use of hepatotoxic drugs and removing sources of environmental toxins will also stop progression. The possible presence of metabolic diseases (hemochromatosis, Wilson's disease) should be investigated (2). Identifying the presence of hepatitis viruses is essential. Chronic Viral Hepatitis B and C may respond to treatment with interferon, but it is very individually. Unfortunately, there are no commonly accepted, effective, conventional drug therapy regimes to reverse liver damage that has been caused by cirrhosis, chronic hepatitis (CH), and alcoholic liver disease (1).

The number of patients with chronic liver diseases, such as viral hepatitis (VH) and cirrhosis has increased over time all over the world (1, 2). According to WHO, annual country reports and available statistical data there is a disastrous situation with respect to LC in the Republic of Moldova (3). For the majority of the main causes of death in the Republic of Moldova, mortality due to diseases of the digestive system, with a leading role being played by chronic liver diseases and cirrhosis has been one of the highest in the WHO European Region as a whole (3). Although chronic liver diseases, including cirrhosis are the main causes of death in the Republic of Moldova and have a significant impact on quality of life of these patients, there has been relative paucity of data with respect to the real situation, and as a result no strategic plan and actions for diseases prevention.

The Scientific Center of Public Health and Sanitary Management collects medical statistical data from the whole Republic. The Center has changed the methodology of data collection several times (in 1996, 1998, and 2000). Consequently, validity of data is questionable. Nevertheless, there is a great and urgent necessity to illuminate the problem with respect to LC in the Republic of Moldova, to present the trends of the disease over last 14 years, and to identify the “red zones” with the highest prevalence of LC comparative to other Moldovan regions.

II. Magnitude of the problem

LC is a major clinical problem worldwide and is associated with high morbidity and mortality, and often affects persons during the most productive years of life (4).

1. Comparative trends of liver cirrhosis

Mortality from liver cirrhosis rose by 75% from 1950 to 1973 (from 8.5 to 14.9 deaths per 100,000 population) in the United States, accounting for 33,350 deaths in the peak year of

1973 (5). An estimated 25,000 persons in the United States died of liver disease in 1998, making it the 10th leading cause of death (5).

The major morbidity and mortality from Hepatitis B is seen in chronic carriers, according to Canadian experts (6). Up to 25% of Canadian men infected in childhood can be expected to die from hepatitis B-related complications such as LC in the fourth and fifth decade (6).

According to WHO, mortality due to LC has been continuous by increasing during last 20 years all over the world (3). Over the years, mortality due to LC has increased more significantly in comparison with other diseases in United States (7). In the developing countries, liver cirrhosis is one of the six main causes of death (7). In the Republic of Moldova, the situation with LC is getting worse over the years. In rural areas, mortality due to LC is situated in third place in the placement of deaths (7).

If in the early 80s in Moldova, mortality due to liver cirrhosis accounted about 60-65 deaths per 100,000 of population, in present this figure accounts for about 82-84 deaths per 100,000 of population (7). These figures are higher by more than twice in comparison with similar countries from European Union and ex-Soviet countries (3, 7). This tragic situation is based on multiple factors, with leading roles played by alcohol consumption (Appendix 2) and a large spread of viral hepatic infection.

Notable is the fact, that all non-viral causes, such as: alcohol (11%), toxins, drugs, pesticides, etc, are more frequent in LC development (77.6%). Only 22.4% of patients with liver cirrhosis have viral cause: HBV-10%, HCV-5% (7).

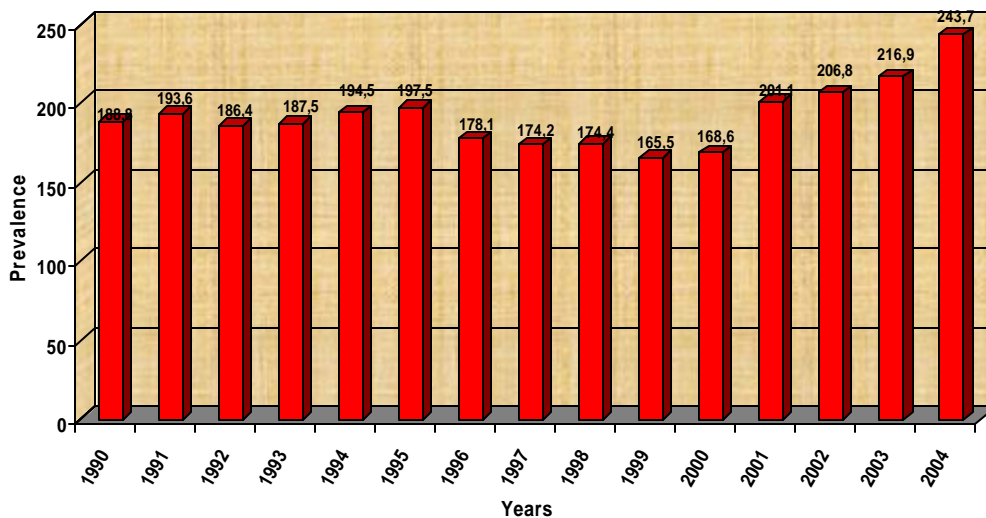
2. Statistical justification of the problem in the RM

Statistical data (2002) presents that from 10,000 adult populations about 290 people have LC (8). According to the report, presented by the Scientific Center of Public Health and Sanitary Management, from the main causes of death in the Republic of Moldova in 2003, mortality due to diseases of the digestive system has been placed on the first place (8). Mortality rate in 2003 (100,000 population) due to diseases of digestive system constituted in total in the Republic – 114 (including chronic hepatitis), from which only LC represents 90.9 (that means 79.7% from total) (7).

3. Prevalence

During the period 1990-2004, the prevalence of liver cirrhosis increased by 29.1% in the Republic of Moldova. From the Figure 1, several slight decreases in 1992 and during the period 1995-1999 can be observed. However, a significant increase during the period 2000-2004 by 44.5% was detected. The greatest increases in prevalence of liver cirrhosis during one year were monitored in the period 2000-2001 by 19.3% and in 2003-2004 by 12.4%.

Figure 1 Prevalence of LC in the Republic of Moldovaduring the period 1990-2004 (per 100,000 population)

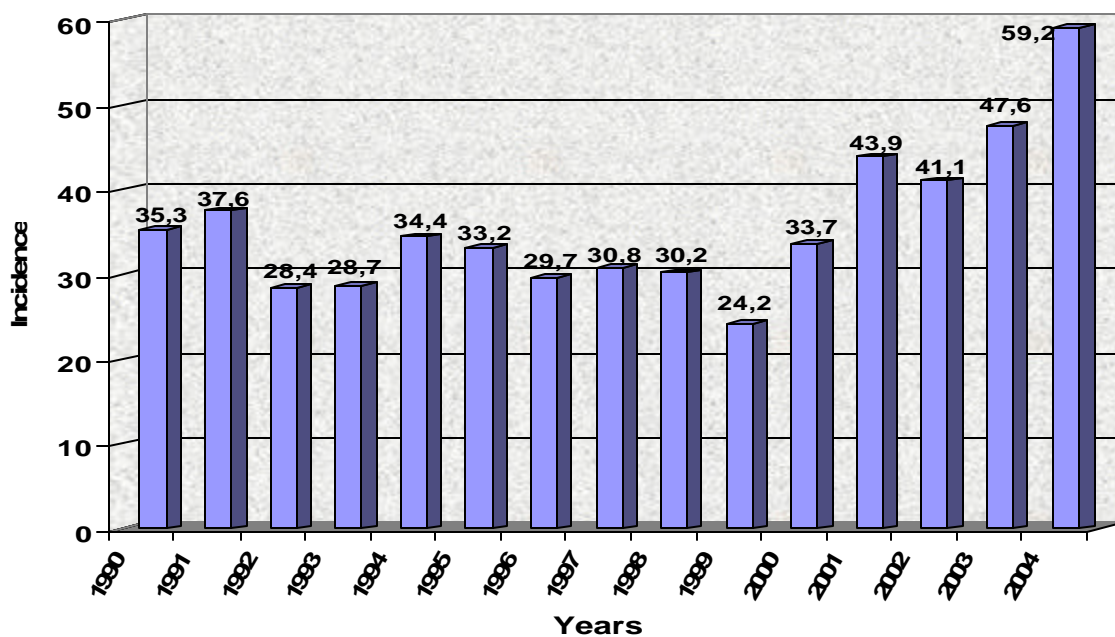


Source: Scientific Center of Public Health and Sanitary Management

4. Incidence

Over the last 14 years the incidence of LC increased by 67.7% in the Republic of Moldova. On the Figure 2, several slight decreases in 1992, 1996, 1999 are observable, however, an impressive increases from 2000 to 2001 by 30.1% (it is the greatest increase in incidence during one year), and from 2003 to 2004 by 24.3% were identified.

Figure 2 Incidence of LC in the Republic of Moldova during the pe riod 1990-2004 (per 100,000 population)



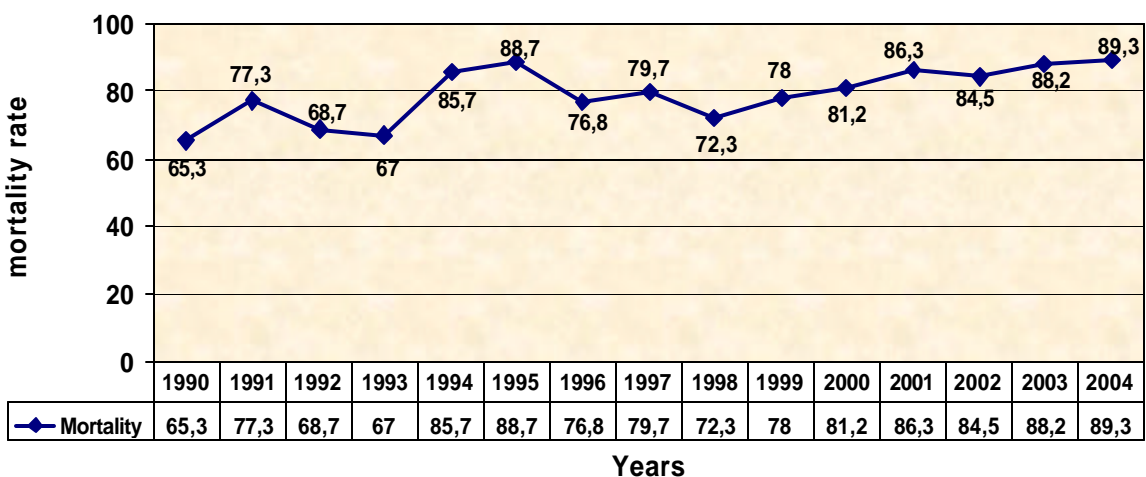
Source: Scientific Center of Public Health and Sanitary Management

5. Mortality

Mortality due to diseases of digestive system in the Republic of Moldova, especially due to liver cirrhosis is one of the highest in the Eur opean region. On the Figure 3, an increase in mortality rate over the last 14 years by 36.7% can be observe d. The figure shows several increases followed by several decreases from 1990 to 1998. The greatest decrease during this period was observed from 1991 to 1993 by 13.32%, which was followed by the greatest increase from 1993 to 1995 by 32.3%. From 1998 until 2004, can be monitored a

continual increase by 23.51%. Over this period was detected only one slow decrease by 2% in 2002.

Figure 3 Mortality due to LC in the Republic of Moldova during the period 1990-2004 (per 100,000 population)



Source: Scientific Center of Public Health and Sanitary Management

Notable is the fact that, on these three figures can be observed a decrease during the same period of time 1996 - 2000. There is no any information that could explain this fact. However, there are some facts that may enlighten these decreases. Firstly, the Scientific Center of Public Health and Sanitary Management has changed the methodology of data collection several times in 1996, 1998 and 2000. Secondly, the Center did not get any statistical data from Transnistria region due to political issue for 4 years (from 1996 until 2000).

Taking into consideration above-mentioned details, an assumptions that the decreases in prevalence, incidence and mortality from 1996 until 2000 are the consequences of these changes could be made.

Nevertheless, available data provides us with undoubtedly evidence that the situation with LC in the republic is dramatic.

6. Distribution of the prevalence and mortality by the region, 2003 and 2004 (Health Mapping approach)

The Republic of Moldova has 32 administrative districts, which are called “rayons”. Health Mapper software was chosen for better visualization of the problem with respect to LC in the republic. Applying such computer program was possible to detect the regions with the highest prevalence of LC comparative to others, which were called “red zones” (See Maps 4 and 5). In 2003 was detected only one red zone - **Calarasi rayon** where the prevalence of LC is higher than in other rayons (See Map 4). In 2004 were detected three red zones - **Calarasi rayon, Hincesti rayon, and Edinet rayon** (See Map 5). However, Calarasi has the highest prevalence of LC in comparison to other red zones in 2004.

Calarasi is known as rayon that is very rich in vineyard. More than a half of population from this rayon makes wine. In early 80s was built a big Wine Factory in Calarasi. In Calarasi, as in a whole country were used a huge amount of pesticides from 1950 until 1990, that led to disastrous soil pollution. In addition, Moldova is well known as endemic region with respect to Viral Hepatitis B (18).

In view of these facts, it is clear why Calarasi rayon is the red zone with the highest prevalence of LC in the Republic of Moldova.

7. Economic Impact

Cirrhosis is an irreversible disease (9). For some people, the only chance for a long-term cure is a liver transplant, which is very expensive and extremely difficult to perform. Most patients die from cirrhosis in the fifth or sixth decade of life (10). Morbidity and mortality due to liver cirrhosis have a dramatic impact on the society from the socio-economic perspective of view.

8. Human Impact

Patients with cirrhosis are at high risk for poor nutritional status (either obesity or weight loss); poor response to bacterial and viral infections; stomach ulcers, kidney disorders, and gallstones; liver cancer; and diabetes mellitus (1, 10). Poor nutritional status often includes deficiencies in proteins, vitamins, trace elements, or methionine (1). Additionally, these patients may also exhibit enhanced or even severe reactions to prescription or "recreational" drugs. Often persons who have liver cirrhosis are poor surgical candidates (10). General anesthesia during surgery reduces cardiac output, causes pooling of blood in the blood vessels in the stomach cavity, and reduces hepatic blood flow, putting the patient's liver at even greater risk for additional damage from reduced blood flow (9, 10). Persons with well-compensated cirrhosis (few or mild clinical symptoms) have an increased but acceptable risk when surgery is required, but surgery should be avoided in cirrhotic patients unless absolutely necessary (10).

9. Importance

Over the years, it has become more and more apparent that LC is a major public health concern, and has a dramatic impact on quality of life of patients, and on the whole society. It adversely affects many persons in the most productive years of their life.

It is apparent that LC is a major public health problem in the Republic of Moldova. Taking into consideration that many of causes that lead to this specific disease's development reflect life style, habits, and behaviors such as alcohol consumption, that becomes a burden in the Republic [(11) appendix 2]; inject drug uses; unprotected sex; poor situation with POPs, it is evident that all these causes could be prevented. More than a half of all LC could be prevented just if we will **ACT** basing on the knowledge we have (12).

In order to reduce the impact of LC on the society it is necessary to introduce special prevention programs focusing on alcohol abstinence and viral hepatitis prevention and law enforcement of pesticide use. All these issues are the components of public health policy.

10. Goal and Objectives

The goal of this thesis is to elaborate strong strategies for public health policy-makers in order to make it possible to prevent chronic liver diseases, especially liver cirrhosis in the Republic of Moldova, and to decrease the impact of liver cirrhosis on the society.

Objectives:

1. to review literature, both national and international; bibliography, with respect to the problem of LC worldwide and in the Republic of Moldova;
2. to analyze a available statistical data, trends of LC over last 14 years, and to apply mapping approach for better visualization of the problem in the Republic of Moldova;
3. to formulate policy recommendation and possible action plan for further proceedings for public policy-makers and public health stakeholders.

This thesis is aimed to acquaint public health policy decision-makers with the problem in the Republic of Moldova and to identify and formulate strategies to reduce the public health impact of liver cirrhosis.

III. Key determinants

Convincing epidemiological data suggest a strong association between alcohol consumption, chronic hepatitis (Hepatitis B, C, D, and G) and cirrhosis mortality (5). A large fraction of cirrhosis mortality has long been associated in both medical and popular thinking

with heavy drinking. According to some data from 60% to 90% of cirrhosis is caused by excessive alcohol consumption (13). While alcohol affects many organs in the body, it is especially harmful to the liver. Alcohol is metabolized in the body, and the liver performs most of that work, potentially incurring serious damage in the process. Not only does alcohol destroy liver cells, it also destroys their ability to regenerate, leading to a syndrome of progressive inflammatory injury to the liver (14).

Although alcohol consumption and viral hepatitis are the most common causes of LC, there are other causes, which include: alpha₁-antitrypsin deficiency, Wilson's disease, hemochromatosis, primary biliary cirrhosis, primary sclerosing cholangitis, drugs and chemicals, pesticides, metabolic and inherited disorders (10, 13, 14).

All causes could be included into four major groups: VH, alcohol, chemical substances and other causes (Appendix 1). The first group includes VH such as HBV, HCV, HGV, and HDV. All these viruses are transmitted from men to men through blood, and human tissue liquid (saliva, sperms, etc). Besides this transmission, there is a vertical transmission from mother to child, which is called perinatal transmission. Most infections acquired at time of birth (15). Less than 5% of infections occur in uterus (15).

According to some authors, it is necessary about 5 years for chronic hepatitis development, and at least 5 years after that for LC development (7). The most dangerous is presence of HCV in association with HBV (15). HDV needs presence of HBV; otherwise, HDV could not develop and virus could not survive in the human body. HGV was discovered recently and the information provided about this virus is almost about the ways of transmission. The second group takes in alcohol products. The third group includes chemical substances such as toxins, hazardous products, some drugs (medication), and pesticides. The fourth group comprises specific diseases that lead to LC development:

primary biliary cirrhosis; primary sclerosing cholangitis; alpha₁-antitrypsin deficiency; Wilson's disease; hemochromatosis; metabolic and inherited disorders.

According to Canadian experts, newborns that are infected with HBV have a greater than 90% chance of becoming chronic carriers. In adults, the rate of chronicity after infection is controversial. Older literature suggests that about 5% to 10% of HBV-infected adults become carriers (16). Newer literature suggests that the figure may be lower than that, perhaps as low as less than 1% (15). The corollary is that the majority of carriers worldwide probably come from the pool of infected infants and children (16).

IV. Prevention / Intervention Strategies

Fortunately, since the major causes of cirrhosis are related to lifestyle behaviors such as alcohol consumption, injecting drug use, and unprotected sex, most cases of cirrhosis are preventable. More than half of all liver disease could be prevented if only we simply acted on the knowledge we already have (12).

Currently, in the Republic of Moldova has been implementing the National Immunization Program of newborns against Viral Hepatitis B. This program was introduced in 1995 and the Ministry of Health, Epidemiology Branch, with financial support of the Government of the Republic of Moldova, Government of Japan/JICA, and Global Alliance for Vaccines and Immunization (GAVI), conduct and control this program (17). The proportion of children under 7 years have received vaccination against Hepatitis B increased steadily from 16.8 percent in 1995 to 98.9 percent in 2003 (17). Rapid achievement and maintenance of high immunization coverage in the subsequent birth cohorts resulted in a reduction of acute clinical HBV cases in children under seven years of age by more than 98% (17). This program was planned to run until 2007. From 2005 was decided to cover also age

group from 7 to 16 years (18). This will make possible to prevent and control HBV in childhood.

This is the sole strategy to prevent development of chronic liver disease in the Republic of Moldova.

Based on the key determinants and risk factors that lead to LC development, it is reasonable to assume that in order to reduce the public health impact of cirrhosis, primary prevention programs that focus on: encouraging alcohol abstinence; reducing high-risk behaviors for hepatitis virus infection; vaccinating for Hepatitis B; enforcing the law with respect to pesticide use are urgently needed in the Republic of Moldova.

If cirrhosis is made an urgent public health priority nationally, a dramatic impact can be made on its prevention with these efforts.

Additional options for intervention/prevention:

1. Promoting vaccination (HBV) program

The Republic of Moldova is an endemic region with respect to Viral Hepatitis B. The National Infant Immunization against Hepatitis B Program is an excellent start in Hepatitis B prevention.

The ideal vaccination policy is to screen pregnant women, provide hepatitis B immunoglobulin to their offspring, and vaccinate all newborns, as well as to institute a catch-up program for the rest of the population below about age 35 to 40 years (16, 17). In addition to neonatal vaccination, should be introduced universal preadolescent vaccination.

2. National Alcohol Harm Reduction Strategy

Avoiding or limiting the use of alcoholic beverages is an excellent place to start, because it is well documented that alcohol destroys liver cells. The Government and other

stakeholders should work together on this strategy, to ensure that the strategy is developed and implemented in a coherent and effective way. There are several control knobs should be used by the specialists as an intermediate goal - alcohol harm reduction: prices, age restriction, centralized marketing, producing for export, through them to achieve the final goal. There is a clear association between price, availability, and consumption.

Main points of this prevention strategy are:

- **Price:** Higher prices of alcohol brought about by increases in tax will significantly reduce alcohol-related problems. *The prices could be equalized on beer, wine, and distilled spirits based on their alcohol content.*
- **Age restriction:** Minimum Legal Drinking Age should be raised to 21 years. This restriction to all alcohol drinks, with no exception for beer.
- **Warning labels:** Every alcohol contains bottle must have attach warning label, ex. “dangerous for your life”
- **Centralized Marketing:** The alcohol products should be marketing in the specialized shop centers. This will solve several points, such as restrict availability and falsification of alcohol drinks.
- **Producing for export:** This particular policy is directly related to the Government. It is well known the fact that Moldova is an agrarian country and reaches in vineyards. Winemaking is a part of our tradition. Collecting wine from population and adjusting the wine’ export system, establishing new partnership relations with EU, not only with Russia, could potentially reduce the morbidity from alcohol and will contribute to the development of socio-economic status of the population. Taking into account that 1/3 of population

makes wine could significantly improve socio-economic status of Moldavian people.

- **Educational campaign on Radio and TV:** Educational programs on TV and radio with comprehensible explanation to the population about the harm of alcohol consumption are extremely necessary.
- **Advertising of alcohol production on TV and Radio:** To ban advertising of alcohol production, including beer, on radio and TV.

3. Reducing high-risk behaviors for VH

- **Medical equipment** (single use syringes, licensing of the private medical centers, continual control of dentists and beauty centers, blood transfusion system/equipment, etc)
- **Medical staff** (annual control for Hbs-Ag)
- **Drug uses** (educational programs, leaflets, promoting the single use syringes distribution programs, Collaboration with NGO and programs working with DU and HIV/AIDS)
- **Protected sex** (educational programs, leaflets, promoting condom's distribution programs among sex-workers)

4. Law enforcement with respect to pesticides use

In the 1950-1990s an estimated total amount of 560,000 tons of pesticides were used in Moldova including 22,000 tons of persistent organochlorinated compounds (OCPs) (19). Starting with land reform in the mid 1990s, the number of large pesticides users (agricultural farms) was in a continuous decline, consequently the number of people professionally exposed to pesticides at the work place also dropped from 34,700 persons in 1993 to 8,800 in

2002 (19). However, this does not mean that the total number of exposed people decreased in the same proportion since many people continue to apply pesticides on the individual plots under less controlled conditions. The contamination frequency decreased during the last decade but data from 2000 indicated that pesticide residuals are still present in the soil and underground water (19).

Poor enforcement of specific rules and working instructions related to pesticides storage, transportation, preparation, use, as well as insufficient awareness of the population on the health risk associated with pesticides led to pollution of the soil by inadequate and uncontrolled pesticides use on the individual plots of farmers.

This becomes the responsibility of the Government of the Republic of Moldova, public health policy makers, policy makers, and Moldovan population to identify, formulate, and implement strategies in order to reduce the public health impact of liver cirrhosis on the society.

V. Policy and Priority Settings

Table 1 Intervention strategies/ Priority Settings

Eligibility criteria	Promoting vaccination program	National alcohol harm reduction	Reducing high-risk behaviors for VH	Law enforcement with respect to pesticides use
<i>Effectiveness</i>	++++	++++	+++	+++
<i>Feasibility</i>	++++	++	+++	++
<i>Cost</i>	+++	++++	++	+
<i>Political Acceptability</i>	++++	+	+++	++
<i>Priority Settings</i>	++++	++++	+++	+++
<i>Advantages</i>	<ul style="list-style-type: none"> ▪ Rapid achievement and maintenance of high immunization of 	<ul style="list-style-type: none"> ▪ Increasing alcohol produces regulation and policy 	<ul style="list-style-type: none"> ▪ Decreasing contamination and transmission of VH 	<ul style="list-style-type: none"> ▪ Increasing population awareness ▪ Increasing POPs

	<ul style="list-style-type: none"> ▪ the population ▪ Cost-effective ▪ Medium term for implementation 	<ul style="list-style-type: none"> ▪ Contribute to decreasing morbidity from alcohol ▪ Increasing population awareness ▪ Contribute to increasing of SES of the population 	<ul style="list-style-type: none"> ▪ Short term for implementation 	regulation/policy
Disadvantages	<ul style="list-style-type: none"> ▪ Financial dependence from outside donors 	<ul style="list-style-type: none"> ▪ Long term ▪ Low political acceptability <i>(Influenced stakeholders have a profit from alcohol business)</i> ▪ Difficult to implement on national level 	<ul style="list-style-type: none"> ▪ Bureaucracy ▪ Corruption 	<ul style="list-style-type: none"> ▪ Long term (suggestion of law amendments and their adoption)
Priority rating	High	High	Medium	Medium

***Coding:**

+	very low
++	Low
+++	medium
++++	High

Table I provides information of the listed implementation strategies in accordance with eligibility criteria. Each strategy is scored within criterion, and based on that a priority rating is given to each strategy.

1. Promoting vaccination (HBV) program

Such strategy is supported by the Canadian Pediatric Society and has been instituted in other endemic regions and countries where Hepatitis B is highly prevalent, such as Taiwan. It showed sharp decrease in incidence of Hepatitis B among children in Canada and Taiwan, and proved its costs-effectiveness (6). This strategy allows achieving and maintaining a high immunization of the population in a medium term. Based on the

experience of Moldovan medical community during last 10 years implementing the National Infant Immunization against Hepatitis B Program and excellent results - a reduction of acute clinical VHB cases in children under seven years of age by more than 98%, this strategy has a high priority rating.

2. National Alcohol Harm Reduction Strategy

Using the experience reported in Great Britain, Canada in programs focused on alcohol harm reduction, and adapting to the Republic of Moldova the National Alcohol Harm Reduction Strategy, which comprises several key points, could be suggested.

In the Republic of Moldova, the prices on alcohol production are very accessible for most of the people. Implementing regulation policy in UK, Canada, researches found that higher prices for beer were associated with a lower frequency of beer consumption among youth and that the difference was more pronounced for heavier consumers (one to seven drinks per week) than for lighter consumers (less than one drink per week) (20). These findings are significant for policy development, because they provide scientific data for evaluating the effect of a policy option.

There is an obvious association between price, availability, and consumption. Therefore, it is necessary to introduce policy regulation on the following key points: price, age restriction, warning labels, centralized marketing, producing for export, educational campaign on Radio and TV, and advertising of alcohol production on TV and Radio.

The impact of introducing specific policies depends on social and political contexts of these strategies. This strategy does not aim to cut alcohol consumption by the whole population. Instead, it focuses on the prevention, minimization, and management of the harms caused by alcohol misuse. The National Alcohol Harm Reduction Strategy is a long

prospective one. In spite of several disadvantages as low political acceptability, because influenced stakeholders have a profit from alcohol business, and difficulty to implement on national level, this strategy has a high priority rating.

3. Reducing high-risk behaviors for VH

Continual control of medical equipment in medical centers, beauty centers; using single use syringes will contribute to decreasing of transmission of viral hepatitis. It is necessary to establish a system that will supervise and monitor all these process and significantly contribute to decreasing of contamination and transmission of VH. This strategy has two main disadvantages: bureaucracy and corruption. Thus, this strategy has medium feasibility and priority.

4. Law enforcement with respect to pesticides use

Besides alcohol consumption, the environment situation, particularly using of pesticides in agriculture also should be taking into consideration by the Government. Law enforcement of specific rules and working instructions related to pesticides storage, transportation, preparation, use, as well as increasing of public awareness on the health risk associated with pesticides is the major advantage of this strategy. The adoption of new amendments is a long-lasting process and time is needed to make a new law work. A medium priority rating is given to this strategy.

Each of the above mentioned strategies has its advantages and disadvantages. A combination of proposed strategies including in one action plan should be used to achieve the best results. However, they cannot be implemented all at once. Regularly implementation of strategies (from high to medium priority) is more feasible and appropriate.

Barriers for implementation

There are several barriers to implement suggested strategies. Firstly, it is a complicity to reach influenced stakeholders from the Government and the Ministry of Health in order to put forward action plan due to the reason that the Government and Ministries are closed zones for outside. Secondly, political problems with Transnistria region could throw obstacles in action plan implementation in this region; consequently, it would be difficult to implement this plan on national level.

In addition, bureaucracy could potentially pose obstacles in process of plan implementation.

VI. Specific recommendations

Specific recommendations are the following. At the beginning to take into consideration all proposed strategies, implementing new ones and strengthening others. These potential strategies are linked in one chain. Dropping out one ring from this chain will minimize all efforts; as a result, the proposed action plan will have no effect. Therefore, it is necessary to implement the whole plan of actions for maximum effect. A positive effects reported by Great Britain and Canada from alcohol harm reduction campaign is a plus for recommending it.

It is recommended to encourage the implementation of healthy life style in wide range of the population. Individuals and organizations, along with policymakers, reviewing this policy paper or participating in the tool development and testing process are strongly encouraged to become involved in this important effort at some level.

In addition, several inter-related action steps are recommended:

- get a place at the policy-making table;

- get professional statistical data analysis related to the issue;
- increase public awareness of alcohol potential to inflict damage;
- promote and strengthen national immunization program;
- assess the expected impacts of policy changes prior to decisions to implement them;
- direct resources and attention to the most effective prevention strategies

The practical solution to this policy problem is a strategy, and thus no single recommendation will provide a complete solution. Therefore, the recommendations are divided into separate strategies with each addressing one aspect of the problem and solution. Nevertheless, no one of recommended proposal should be missed; otherwise, it will be difficult to achieve the final goal.

VII. Implementation and Evaluation

The Action Plan should be implemented on a national level. It is clear that the plan implementation requires strong government commitment; active involvement of authorities from different sectors as Ministry of Health and Social Protection, Ministry of Ecology and Environment Protection, inter-sectorial cooperation; close collaboration among involved sectors, and technical and financial support by international organizations. Besides governmental institutions, in the development and implementation should be involved non-governmental organizations, social programs, and International representatives working in this field. This problem is connected not only to health but also to jurisprudence and social issues.

Monitoring

A coordinate committee will be created for plan monitoring, which will include representatives from the Government, lawyers, physicians, social workers, journalists, ecologists and psychologists. This committee will monitor strategies implementation every six months during three years. According to their findings, it will be possible to make some changes in policy strategies on different level and direct resources, and attention to the most effective prevention strategies. Therefore, it is very important that the proposed strategies have the flexibility to be changed or allowed for improvements.

Evaluation

Evaluation will be based on health indicators such as incidence rates and mortality rates. A three years is needed to asses the impact of plan evaluation, that is a process evaluation. For outcome evaluation, it is necessary at least 5 years to asses the success of the plan, bearing in mind that LC is a chronic disease, which requires time for development. This action plan is a long-term one.

Conclusion

In conclusion, it is very important to implement the action plan on a national level and it is obvious that governmental support is of considerable importance.

The challenges are significant and so are the efforts and resources required to meet them for the best outcome.

Reference List

1. Galambos JT. Cirrhosis. Philadelphia: Saunders, 1979:1-2.

2. Boyer, J.L., Blum, H.E., Maier, K.P. Liver Cirrhosis and its Development
Yale Univ., New Haven, CT. Proceedings of the Falk Symposium 115 held in Basel,
Switzerland, on October 22-24, 1999 (Part II of the Basel Liver Week 1999; XI International
Congress of Liver Diseases).

3. Highlights on Health in the Republic of Moldova, WHO Report 2001.
Available from URL: http://www.euro.who.int/healthinfo/highlights/20011012_6.

4. Karsan, H. A., Rojter, S. E., & Saab, S. (2004). Primary prevention of cirrhosis.
Public health strategies that can make a difference. *Postgrad.Med.*, 115, 25-30.

5. Corrao, G., Arico, S., Carle, F., Russo, R., Galatola, G., Tabone, M. et al. (1991). A
case-control study on alcohol consumption and the risk of chronic liver disease.
Rev.Epidemiol.Sante Publique, 39, 333-343.

6. Hepatitis B Vaccination Program
Available from URL: http://www.pulsus.com/Gastro/11_05/casl_ed.htm#Chronic

7. Dumbrava T-V. et al (2004). Liver Cirrhosis: etiology, pathogenesis, clinics and
treatment, 82-89

8. The Scientific Center of Public Health and Sanitary Management, Annual
Statistical Reports 2002, 2003.

9. Gines P, Quintero E, Arroyo V, et al. Compensated cirrhosis: natural history and
prognostic factors. *Hepatology* 1987;7 (1):122-8

10. Liver Cirrhosis: etiology, clinics, prognosis: <http://www.lef.org/protocols/prtcl-068d.shtml>
11. World Health Organization Regional Office for Europe, HFA database, Alcohol consumption and harm, Annual pure alcohol consumption, in liters per person, Report 2003, update 2004, Available from URL <http://www.euro.who.int/eprise/main/who/countryInformation/Country?AreaCode=MDA>
12. Rothenberg RB, Koplan JP. Chronic disease in the 1990s. *Ann Rev Public Health* 1990;11:267-96
13. Kamper-Jorgensen, M., Gronbaek, M., Tolstrup, J., & Becker, U. (2004). Alcohol and cirrhosis: dose-response or threshold effect? *J.Hepatol.*, 41, 25-30.
14. Arthur MJ. Mechanisms of progression and regression of liver fibrosis. In: Okita K, ed. *Liver cirrhosis*. Tokyo: Springer, 2001:1-9
15. National Network of STD/HIV Prevention Training Centers. *Viral Hepatitis*, July 2005. Available PDF format.
16. Chronic Hepatitis B in Children. Available from URL: http://www.pulsus.com/Gastro/11_05/casl_ed.htm#Chronic
17. The National Infant Immunization Program Report to the Global Alliance for Vaccine and Immunization (GAVI), Ministry of Health of the Republic of Moldova, 2003
18. Medical Program on National TV channel, Ministry's of Health Report on Viral Hepatitis B in the Republic of Moldova, March 2005
19. The National Implementation Plan for Persistent Organic Pollutants (POPs), draft proposal, Moldova, 2004

20. Annual Report of the Chief Medical Officer 2002

Available from URL: <http://www.dh.gov.uk/PublicationsAndStatistics>

[/Publications/AnnualReports/AnnualReportsBrowsableDocument/fs/en?CONTENT_ID=4094860&MULTIPAGE_ID=4873344&chk=bZj9Jd](http://www.dh.gov.uk/PublicationsAndStatistics/Publications/AnnualReports/AnnualReportsBrowsableDocument/fs/en?CONTENT_ID=4094860&MULTIPAGE_ID=4873344&chk=bZj9Jd)

21. Corrao, G., Zambon, A., Torchio, P., Arico, S., La Vecchia, C., & di Orio, F.

(1998). Attributable risk for symptomatic liver cirrhosis in Italy. Collaborative Groups for the Study of Liver Diseases in Italy. *J.Hepatol.*, 28, 608-614.

22. Propst A, Propst T, Zangerl G, Ofner D, Judmaier G, Vogel W. Prognosis and life expectancy in chronic liver disease. *Dig Dis Sci* 1995;40:1805-15.

23. Davies, P. (1985). The effectiveness of alcohol control policies in Europe.

Eff.Health Care, 2, 137-149.

24. Futatsuka, M., et al. An epidemiological study with risk analysis of liver diseases

in the general population living in a methyl mercury polluted area. Department of Public Health, Kumamoto University Medical School, Japan. *Journal of Epidemiology and Community Health*, Vol 46, 237-240

25. Gaeta, G. B., Stornaiuolo, G., Precone, D. F., Lobello, S., Chiaramonte, M.,

Stroffolini, T. et al. (2003). Epidemiological and clinical burden of chronic hepatitis B virus/hepatitis C virus infection. A multicenter Italian study. *J.Hepatol.*, 39, 1036-1041.

26. Gual, A. & Colom, J. (1997). Why has alcohol consumption declined in countries

of southern Europe? *Addiction*, 92 Suppl 1, S21-S31.

27. Herd, D. (1992). Ideology, history and changing models of liver cirrhosis

epidemiology. *Br.J.Addict.*, 87, 1113-1126.

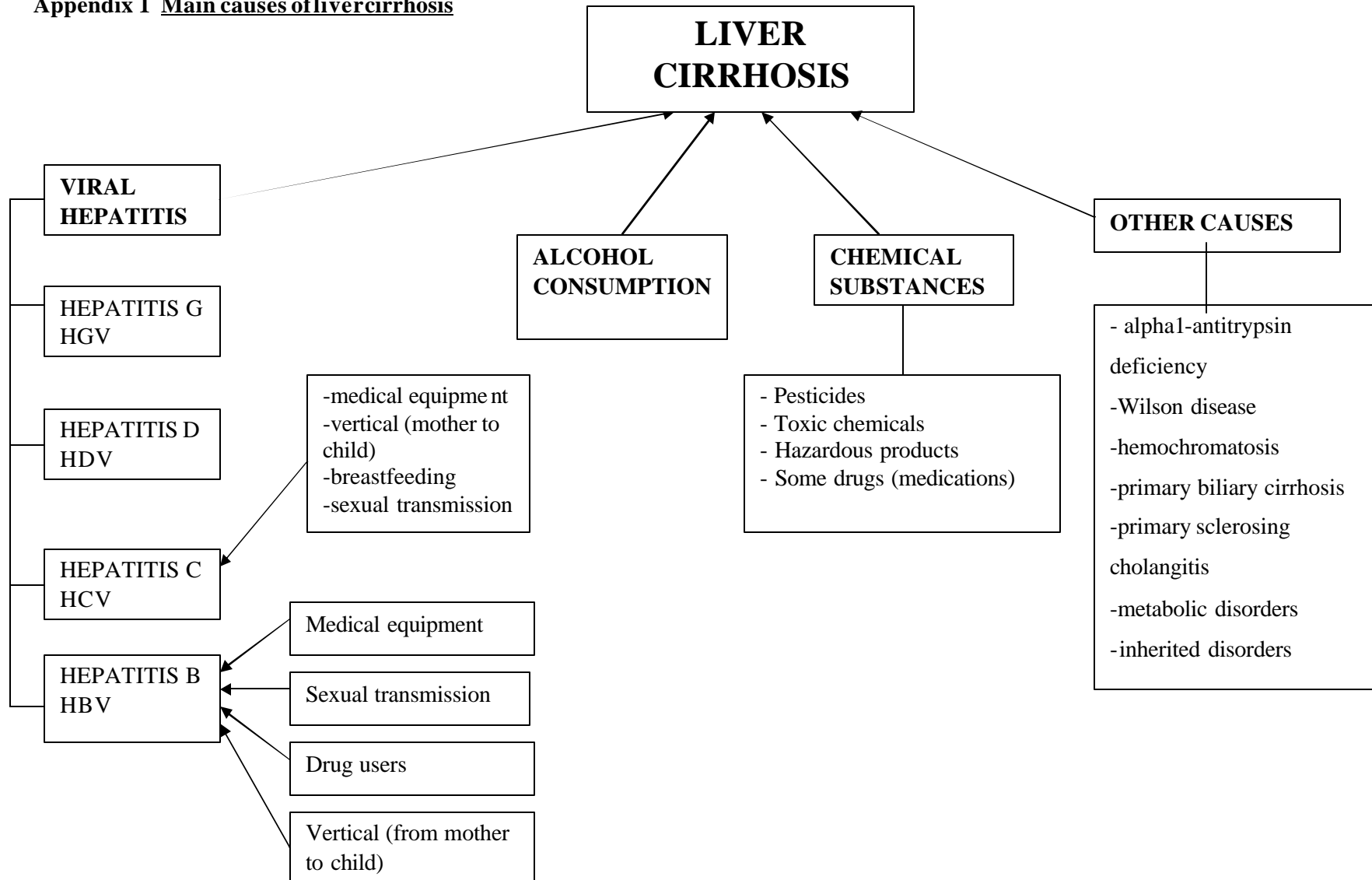
28. Roizen,R., Kerr, W., Fillmore M. C irrhosis mortality and per capita consumption distilled spirtis, US, 1949-94; trend analysis, BMJ 1999; 319;666-670

29. Serra, I., Araneda, J., & Decinti, E. (1995). [Epidemiological profile of liver cirrhosis in Chile 1970-1992]. *Rev.Med.Chil.*, 123, 1425-1431.

30. Yu, M.W., Hsu, F.C., Sheen, I.S., Chu, C.M., Lin, D.Y., Chen C.J., and Liaw Y.F. (1997)Prospective study of hepatocellular carcinoma and liver cirrhosis in asymptomatic chronic hepatitis B virus carriers American Journal of Epidemiology, Vol 145, Issue 11 1039-1047,

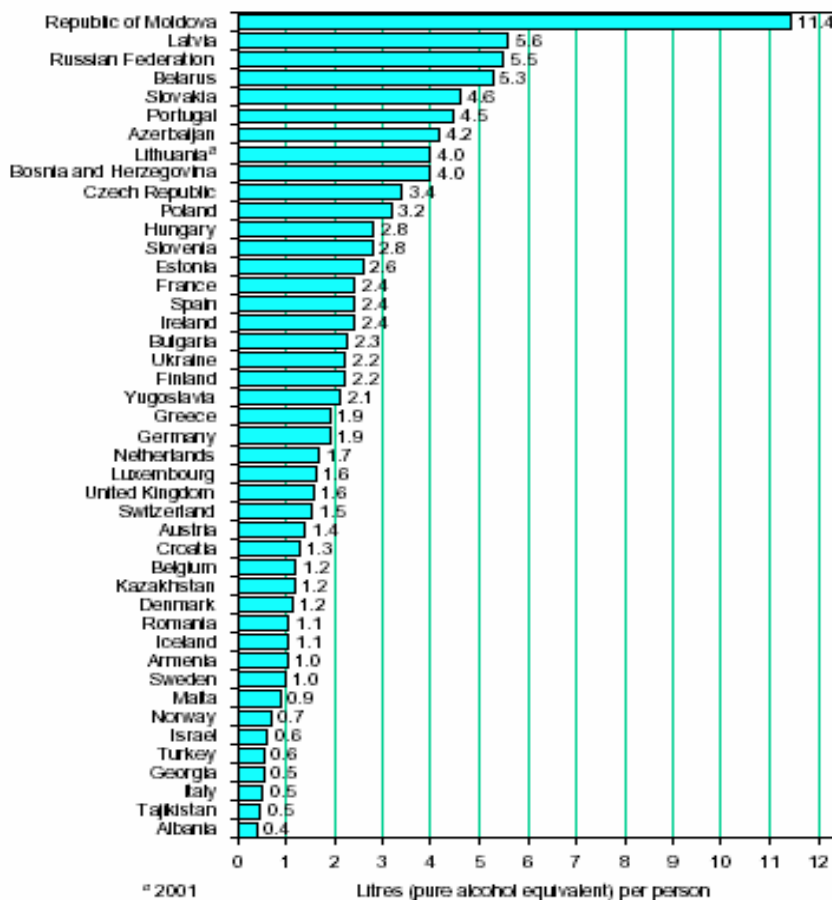
31. A Prescription for Public Health Action in South Eastern Europe, Report 2003, Available from URL: [http:// www.soros.org/.../health/articles_publications/publications/healingthecrisis_20030626/healing_the_crisis.pdf](http://www.soros.org/.../health/articles_publications/publications/healingthecrisis_20030626/healing_the_crisis.pdf)

Appendix 1 Main causes of liver cirrhosis

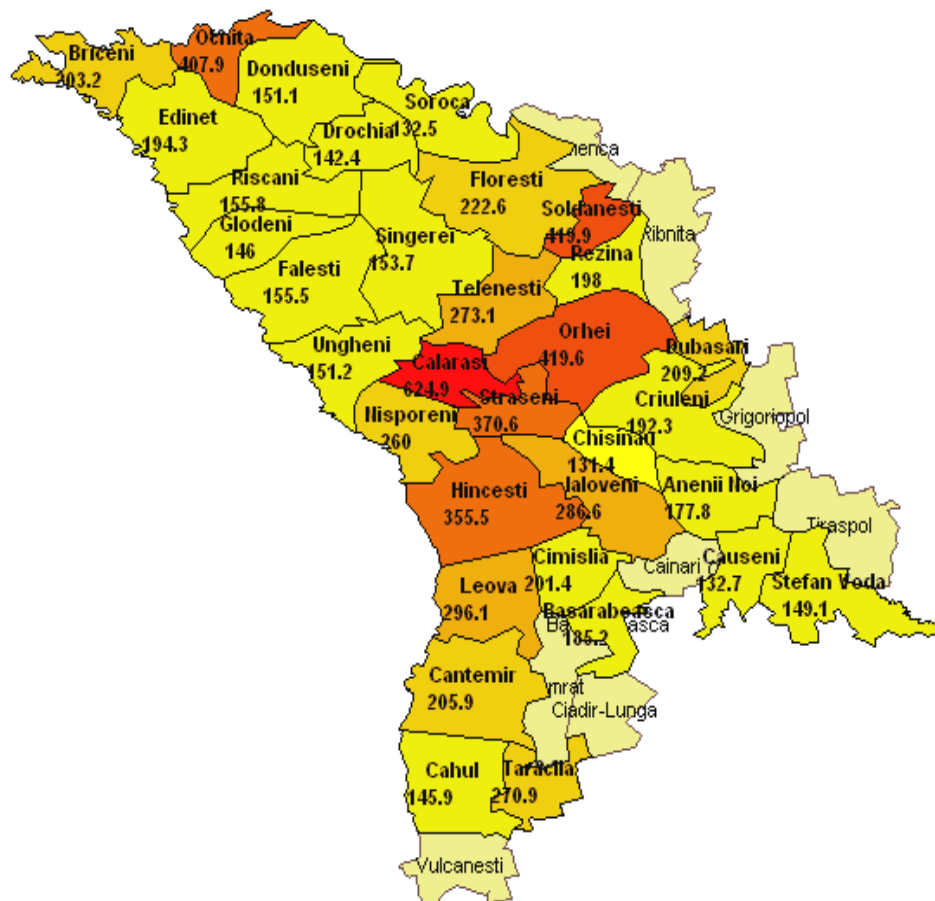


Alcohol

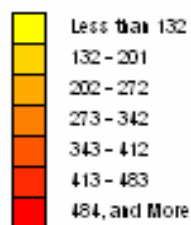
Consumption of spirits, 2000



Map 1 Distribution of the prevalence by the region, 2003

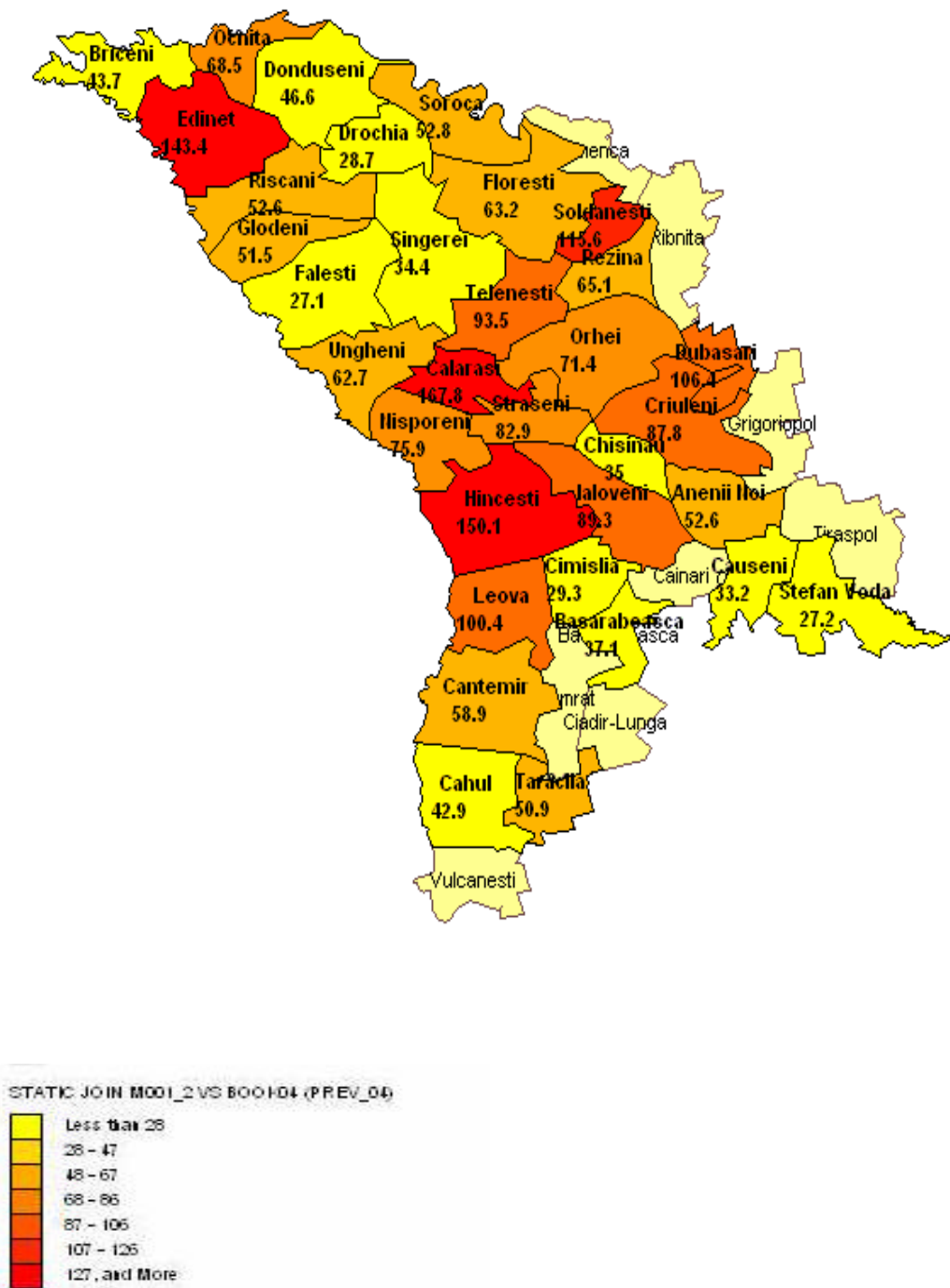


STATIC JOIN M004_A_2 VS NEWBOOK (PREV_03)



Source: Scientific Center of Public Health and Sanitary Management

Map 2 Distribution of the prevalence by the region, 2004



Source: Scientific Center of Public Health and Sanitary Management