ANALYTICAL REPORT

LOW-VALUE GRANTS FOR PUBLIC MONITORING OF THE DELIVERY AND AVAILABILITY OF MEDICINES AT LOCAL LEVEL

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Contents

Acronyms and abbreviations

JRA	Juvenile rheumatoid arthritis
MoH	Ministry of Health of Ukraine
MPS	Mucopolysaccharidosis
UNDP	United Nations Development Programme

Executive summary

Among the projects under UNDP Health and Transparency Programme is the project Low-Value Grants for public monitoring of the local delivery and availability of medicines and medical devices procured by UNDP for the Ministry of Health of Ukraine (MoH). Launched in 2017, this project involves working with non-governmental organisations (NGOs) to collect data on the procurement of medicines and medical products and their distribution to local health care facilities in different oblasts. It also aims to understand the overall level of satisfaction of patients and physicians with the volumes and timing of deliveries.

The third round of monitoring, which took place in 2019, included collection of quantitative data from databases and websites, and of qualitative data from surveys and interviews with 1,408 patients, 109 physicians and 13 members of staff of regional health care departments, about the medicines that patients have been prescribed and satisfaction with supplies. It was conducted with the participation of more NGOs than in previous years, and a much expanded list of oblasts, nosologies and medicines than in preceding iterations.

The monitoring showed that both physicians and patients clearly confirmed the gradual improvement in the medicine procurement system between 2015 and 2019: the schedule of medicine supplies was being better planned, and as of mid-2019 it achieved a steady level of provision throughout the year. An important factor in the positive assessment of the procurement system by stakeholders was an increase in the volumes of medicines procured, which was achieved by both increasing the MoH's budget allocations for most of the nosologies and reducing the prices achieved in tenders. At the same time, the monitoring revealed a number of problems in the system of ordering, procurement, distribution and use of medicines which need to be solved to further improve the process and, ultimately, patient outcomes.

These findings from the 2019 round of monitoring suggest a number of actions that could improve the procurement and delivery system.

- The MoH of Ukraine should improve the planning and implementation of procurement by establishing and monitoring annual deadlines for decision-making at every stage of the process for ordering, procurement, distribution and use of medicinal products, ensuring that oblasts have enough time to calculate the correct need for each medicine or medical product for each nosology. It should also ensure unhindered communication and interaction between all stakeholders at each stage of decision-making.

- Treatment protocols should be reviewed and, where necessary, updated to ensure compliance with unified health care standards that following the advanced European ones for each nosology, and a unified methodology for calculating the full need for each nosology and a standardized data collection methodology should be developed and shared with regional experts. Patient registers should also be created and systematically updated to calculate patients' needs, and the National List of Essential Medicines should be analysed and updated as required.

- The supply chain also needs to be optimized – specifically, the timely preparation and issuance of MoH and regional health care departments' distribution orders and the prompt dispatch of medicines from central warehouses to the regions.

- The MoH should also consider the introduction of provision of home treatment for haemophilia and certain orphan diseases, which will significantly improve patients' quality of life. This system should extend to children.

- The National Health Service of Ukraine should develop clear clinical paths for the treatment of patients with nosologies which were previously treated at specialized facilities (viral hepatitis, autism spectrum disorders, orphan diseases, etc.). It should also promote the widespread adoption of home treatment and outpatient care, to reduce the need for hospitalization and lower the cost of treatment. Diagnostic services that are an integral part of the treatment of many socially significant diseases, including viral hepatitis, should be provided free of charge when the need to pay for diagnostic testing prevents patients from receiving treatment, even if free medicines are available.

Introduction

The UNDP Low-Value Grants project for public monitoring of the local delivery and availability of medicines and medical devices procured by UNDP for the Ministry of Health of Ukraine (MoH) has two main goals. These are: 1) to undertake an independent, third-party assessment to provide UNDP with real-life information about the availability and access to treatments that UNDP procures, and 2) to develop the capacity of Ukrainian patients organisations to conduct autonomous, impartial studies, the results of which they can use as an advocacy tool.

Launched in 2017, this project involves working with non-governmental organisations (NGOs) to collect data on the procurement of medicines and medical products and their distribution to local health care facilities in different oblasts. It also aims to understand the overall level of satisfaction of patients and physicians with the volumes and timing of deliveries. The third round of monitoring, which took place in 2019, expands on the work done in 2017 and 2018 by working with more NGOs, assessing substantially more medicines and nosologies in more oblasts, and collecting qualitative data from many more patients and physicians (Table 1).

Table 1. Public monitoring of local delivery and availability of medicines: coverage by year, 2017–2019

Review year	2017	2018	2019
Number of NGOs participating	4	4	6
Number of medicines assessed	17	15	132
Number of nosologies	2	2	12
Number of oblasts	4	4	11 (24 for orphan diseases)
Number of patients surveyed	537	304	1408
Number of physicians surveyed	10	11	109

Six NGOs took part in this round of monitoring:

- Charity Foundation 'Treasury of Hope', Rivne
- Public Association 'Orphan Diseases of Ukraine', Kyiv
- Charity Children Foundation 'Give World to Child', Cherkasy
- All-Ukrainian Charity Organization 'Initiative for Life', Mykolaiv
- Public Organisation 'Creative Association Nivroku', Ternopil
- Charity Foundation 'STOPCANCER', Lutsk.

After consulting with the participating organisations, the list of nosologies and medicines that were monitored was extended to include those that could be considered representative of Ukraine's overall medical procurement and supply system. These were:

- hepatitis B and C;
- autism spectrum disorders;
- paediatric oncology;
- orphan diseases, including mucopolysaccharidosis (MPS), arterial hypertension, paediatric and adult cystic fibrosis, and epidermolysis bullosa;
- childhood haemophilia;
- adult haemophilia;
- juvenile rheumatoid arthritis (JRA); and
- delivery of diagnostic reagents for mass screening of newborns for phenylketonuria, congenital hypothyroidism, cystic fibrosis and adrenogenital syndrome.

This round of monitoring analysed 132 medicines (see the Appendix) and covered 11 oblasts: Cherkasy, Chernihiv, Lviv, Kherson, Khmelnytskyi, Mykolaiv, Rivne, Ternopil, Vinnytsia, Volyn and Zhytomyr. Analyses of medicines for orphan diseases were undertaken in 24 oblasts and Kyiv.

Methodology

This research was conducted in two parts: 1) collecting quantitative data on the supply of medicines from databases and websites; and 2) capturing qualitative data from surveys and interviews about what medicines patients have been prescribed and satisfaction with supplies. Supply data came from the websites of the MoH, databases of health care departments and facilities (https://eliky.in.ua/ and https://liky.ua/), and responses to official written requests sent to the MoH, Regional State Administrations (RSAs), health care departments and facilities, and the state enterprises Ukrmedpostach and Ukrvactsina. Qualitative data came from responses to requests sent to regional health care departments and interviews with specialist physicians and patients with the relevant diseases or their parents/caregivers. The study surveyed 1,408 patients, 109 physicians and 13 members of staff of regional health care departments. The response rate was more than 90 per cent. This was a convenience sample with no preliminary calculations of target p-values. The inclusion approach was 'as many as possible', to ensure a comprehensive and multifaceted picture of the availability of medicines in the oblasts studied. The geographical selection of oblasts was based on epidemiological data for different nosologies, and an attempt was made to have broad geographical coverage. The diseases that were included were based on the areas of work of the participating NGOs, as well as on complaints that UNDP received in 2019 about medicines shortages.

Results

Children with haemophilia type A or B or von Willebrand disease

According to the World Federation of Hemophilia, there were almost 300,000 people worldwide with haemophilia or other blood clotting disorders in 2018. Over the past 15 years, the number of patients with various forms of coagulopathy has almost doubled, and more recently the incidence has been increasing on average by 6 per cent per year.[1] The constant increase in incidence of haemophilia is due both to natural causes and to improvements in the quality of diagnostics.

In 2016, according to the MoH, 2,569 people were diagnosed with 'haemophilia' in Ukraine, including 667 children.[2] The prevalence of this nosology is significantly lower than global trends, which may suggest that there is an inadequate coverage of screening and specialized diagnostics for bleeding disorders in Ukraine.

For this round of research, 5 physicians and 118 parents/caregivers of patients were surveyed in 5 oblasts (Cherkasy, Chernihiv, Rivne, Vinnytsia and Volyn).

[1] World Federation of Hemophilia, 'Report on the WFH Annual Global Survey 2018', Montreal, 2018, https://www.wfh.org/en/our-work-research-data/annual-global-survey.
[2] State Expert Centre of the Ministry of Health, 'Hemophilia. Evidence-based clinical guidelines', Kyiv, 2016, https://dec.gov.ua/wp-content/uploads/images/dodatki/KN/KN_Gemof.pdf

Table 2. Summary of research into medicines supplies for paediatric haemophilia

Oblast	Health care facility for inpatient treatment	Number of other health care facilities	Number of medicines for which full supply achieved	Total number of patients registered	Total population of the oblast[3]	Number of patients as a percentage of the total population	Number of parents/ caregivers interviewed	Respondents as a percentage of all patients	Number of doctors interviewed
Cherkasy	Cherkasy Regional Centre for Paediatric Oncology and Haematology			18	1,191,093	0.0015	11	61	1
Chernihiv	Chernihiv Regional Children's Hospital	26	0/6	23	990,201	0.0021	23	100	1
Rivne	Rivne Regional Children's Hospital	36	4/5	26	1,152,704	0.0023	22	85	1
Vinnytsia	Vinnytsia Regional Children's Hospital	49	10/10	46	1,544,049	0.0030	38	83	1
Volyn	Volyn Regional Children's Territorial Medical Association	27	6/8	24	1,031,205	0.0023	24	100	1
Total				137	5,909,252	0.0023	118	86	5

Inpatient treatment of paediatric patients with haemophilia is generally only available at regional children's hospitals, and usually only in the case of injury or other causes of bleeding. Primary care physicians are also involved in the treatment of patients with haemophilia, as medicines are distributed to the primary health care centre at patients' place of residence, and the physician dispenses medicines directly to the patients' parents or caregivers.

A typical procedure for ordering medicines is that the regional hospital applies to the MoH for medicines to treat children with type A or B haemophilia or von Willebrand disease, purchased from the state budget, and the medicines are delivered from the central warehouse to regional warehouses for redistribution to other health care institutions.

Desk research suggests that most of the requests were only partially completed, as the delivery of medicines under the MoH procedures entails several stages. In most cases, the requested quantity did not meet 100 per cent of need, as the volume of medicines is restricted by the financial resources allocated to the nosology in each oblast. The actual availability of free medicines for children met about 50 per cent of the actual need calculated according to international standards,[4] and varied between 20 per cent and 55 per cent for certain items in the nomenclature.

[3] Source: State Statistics Service of Ukraine, http://database.ukrcensus.gov.ua/PXWEB2007/ukr/news/op_popul.asp

[4] Council of Europe, 'Resolution CM/Res(2017)43 on principles concerning haemophilia therapies (replacing Resolution CM/Res(2015)3)', Brussels, 2017, https://www.edqm.eu/sites/default/files/resolution_cm_res_2017_43_on_principles_concerning_haemophilia_therapies.pdf

Significant differences were found in the nomenclatures ordered by paediatric haematologists in different oblasts, with 19 different medicines used (see Figure 11 in the Appendix). Certain medicines that were commonly used in one oblast were not used at all in others. There was a lack of timely deliveries. It took between 6 and 50 days to deliver medicines from the central warehouse to regional warehouses and hospitals, with an average of 35.2 days. There was considerable variability in the time taken from the issuance of the MoH order to the receipt of medicines at regional warehouses, which reflects the non-systematic nature of the process and its dependence on subjective factors. Also, neither the MoH, Ukrmedpostach or Ukrvactsina announce the dates of medicine deliveries to the regions.

Physicians acknowledge that 100 per cent supply of medicines for treatment of children with haemophilia has not been achieved. However, they confirm significant progress in the quantity of medicines delivered in 2017–2019. They identified the following problems with the delivery system:

- the lack of an officially approved algorithm for calculating the need for medicines;
- the lack of diagnostics (3 physicians);
- insufficient financial resources allocated to purchase medicines to meet 100 per cent of demand (5);
- irregular and unpredictable schedule of medicine deliveries during the year (5);
- periodic stock-outs of medicines for prevention, and no possibility of planning treatment for 2–3 years (5); and
- communication problems with the MoH/health care department (1).

Their average level of satisfaction (on a 10-point scale) with the volume of medicines purchased was 7.2 in 2019, and with the stability of supply 6.0. They also noted as an achievement that Ukraine had recently created a complete register of children with bleeding disorders, which enables the supply of medicines to be individualized.

All of the **patients** surveyed received free medicines purchased from the state budget. The main problems they identified are shown in Figure 1:

- delays in deliveries of free medicines (82 per cent of patients);
- interruptions to their treatment (72 per cent); and
- medicines are not available at pharmacies (67 per cent).

In addition, 4 per cent of patients had to purchase additional medicines for treatment at their own expense.

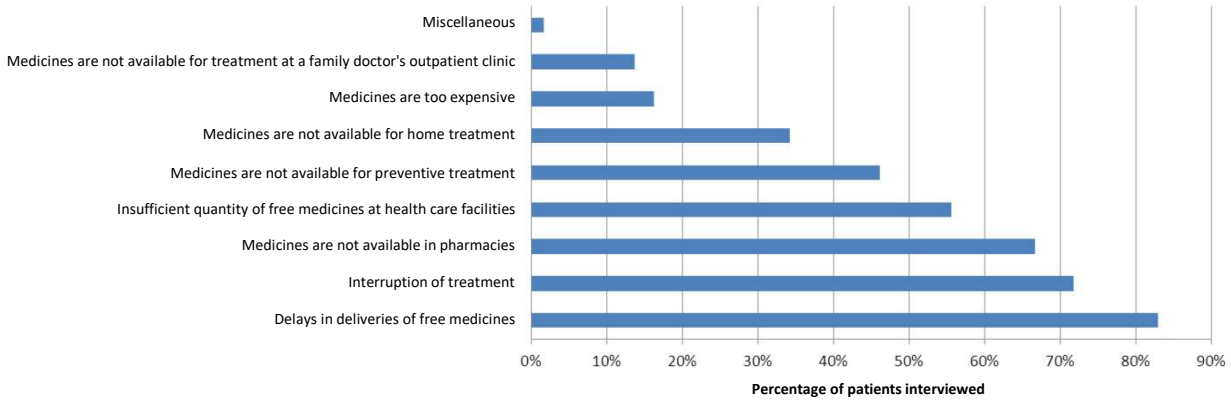

Figure 1. The main problems related to supplies of medicines for paediatric haemophilia patients

All of the oblasts that were studied offer home treatment and prophylaxis, which has greatly improved access to treatment and prevented the development of complications. Patients' satisfaction with the volume and stability of medicine supplies in 2019 varied from 4.1 in Chernihiv to 8.7 in Vinnytsia (based on a 10-point scale), which suggests the presence of local factors in a particular oblast that affect the quality of health care but are not directly related to the medicine delivery system.

Adult haemophilia

The research into the supply of medicines for adult haemophilia patients covered one doctor, and 28 (85 per cent) of the 33 adult haemophilia patients at the Cherkasy Regional Medical Diagnostic Haematology Centre.

Table 3. Summary of research into medicines supplies for adult haemophilia

Oblast	Health care facility for inpatient treatment	Total number of patients registered	Total population of the oblast	As a percentage of the general population	Number of patients interviewed	As a percentage of all patients	Number of doctors interviewed
Cherkasy	Cherkasy Regional Medical Diagnostic Haematology Centre	33	1,191,093	0.0028	28	85	1

According to the one doctor interviewed, the quantity of medicines received only covers 40 per cent of the full need, but has increased compared to 2015 or 2016. The main reason is the insufficient allocation of funding for this nosology. The doctor complained about the lack of an officially approved algorithm and a way to calculate the need for medicines; insufficient financial allocations to meet 100 per cent of need; a lack of medicines for prophylactic treatment; the absence of a patient register; a lack of proper diagnostics; and restrictions on the National List of Essential Medicines. Delays in the delivery of free medicines from the MoH warehouse to hospital warehouses were between 14 and 23 days.

Nearly three quarters (71 per cent) of **patients** reported receiving medicines free of charge. One respondent indicated that he had received preventive treatment as a participant in clinical trials for new medicines, and one patient reported that he had been asked to pay a charitable contribution. Figure 2 shows the main problems identified by patients regarding the supply of medicines. All patients identified the fact that medicines are not available in pharmacies, and that medicines are too expensive. This is of particular significance given that 96 per cent of patients had to buy additional medicines – the highest rate of all studied nosologies. In addition, 96 per cent of patients mentioned delays in supplies of medicines, although more detailed interviews revealed that those delays were related to the period 2015–2017, when procurement was being transitioned away from the MoH to the international organisations. In 2018–2019, the supply of medicines had stabilized and was occurring systematically.

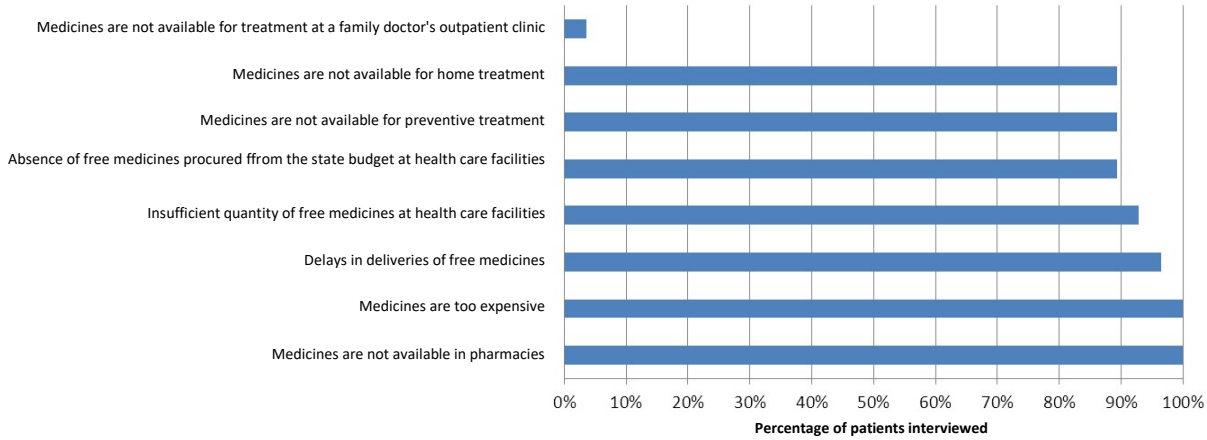

Figure 2. The main problems related to supplies of medicines for adult haemophilia patients

Thus, the treatment of haemophilia, especially for adult patients, is characterized by numerous problems that have accumulated over years and are the result of an outdated treatment system. At the same time, gradual positive changes can be seen, primarily due to the increase in the quantity of medicines procured by the State between 2017 and 2019.

Children with oncology and oncohaematology diseases

The treatment of children with oncology and oncohaematology diseases is carried out according to approved treatment protocols and includes a wide range of medicines such as chemotherapeutics, antibiotics, antifungal medicines and others. It has been established that the incidence of malignant neoplasms among children is steadily increasing, with a moderate decrease in mortality. The highest incidence is recorded in children in the first year of life. There is a slight decrease in incidence in children aged 1–14 years, but an increase at age 15–19 years. The incidence of malignant neoplasms among children is primarily due to leukemia, lymphoma, tumours of the central nervous system, epithelial tumours, malignant bone tumours and soft tissue sarcomas.

The research was conducted in 5 oblasts, through interviews with a total of 188 parents/caregivers of patients and 5 physicians.

Table 4. Summary of research into medicines supplies for treatment of children with oncology and oncohaematology diseases

Oblast	Health care facility for inpatient treatment	Total number of patients registered	Total population of the oblast	Number of patients as a percentage of the total population	Budget for paediatric oncology in 2018 (UAH millions)	Number of parents/ caregivers interviewed	As a percentage of all patients	Number of doctors interviewed
Cherkasy	Cherkasy Regional Centre for Paediatric Oncology and Haematology	291	1,191,093	0.0244		42	24	1
Chernihiv	Chernihiv Regional Children's Hospital	148	990,201	0.0149	10.025	37	25	1
Rivne	Rivne Regional Children's Hospital	58	1,152,704	0.0050	21.085	34	59	1
Vinnytsia	Vinnytsia Regional Children's Hospital	274	1,544,049	0.0177	20.721	39	14	1
Volyn	Volyn Regional Children's Territorial Medical Association	172	1,031,205	0.0167	14.263	36	21	1
Total		943	5,909,252	0.0160		188	20	5

Deliveries of medicines are made directly from the central warehouses of Ukrmedpostach and Ukrvactsina to the warehouses of regional medical institutions. They were found to take between 13 and 62 days from issuing the MoH order to arrival at health care facilities' warehouses. The considerable variability in the delivery times indicates that the supply procedures are not well defined or systematic.

Four of the five **doctors** interviewed think that 100 per cent of the need for medicines is not being met. The medicines received accounted for only 55 per cent of actual patient need in 2019. Despite these shortcomings, doctors' level of satisfaction was 7.5 (on a 10-point scale).

All five doctors identified the lack of long-term planning of medicine supplies and supply delays as the main problems related to the supply of medicines, while two mentioned that the budget for this nosology was insufficient. They also mentioned a lack of information on delivery timing in 2017–2018 (some critical medical devices have not been received yet) and the inability to purchase additional medicines not included in the National List of Essential Medicines. For example, the absence of first-line medicines at the beginning of treatment caused physicians to use second- and/or third-line medicines, contrary to protocols and at a higher cost.

Doctors choose the types and quantities of medicines and medical products to be ordered, and this is evident in the significant differences found between the oblasts: medicines that were commonly used in some oblasts were not used at all in others (see Figure 12 in the Appendix).

Nearly all (99 per cent) of the **patients** surveyed received medicines for free, although one indicated that they were asked to make charitable contributions in return for free medicines, and 83 per cent purchased additional drugs. Although most parents/caregivers made no observations on the quality of medicines that were given to their children in health care facilities, 11 per cent indicated that they had refused free medicines at least once due to a lack of trust in the

manufacturer (generic medicines) or due to side effects. In such cases, they purchased medicines from pharmacies.

Among the most common challenges identified by patients (see Figure 3) were: insufficient quantity of medicines (42 per cent); delays in deliveries of free medicines (34 per cent); high prices for medicines in pharmacies (30 per cent); and the lack of home treatment (25 per cent) and preventive treatment (22 per cent).

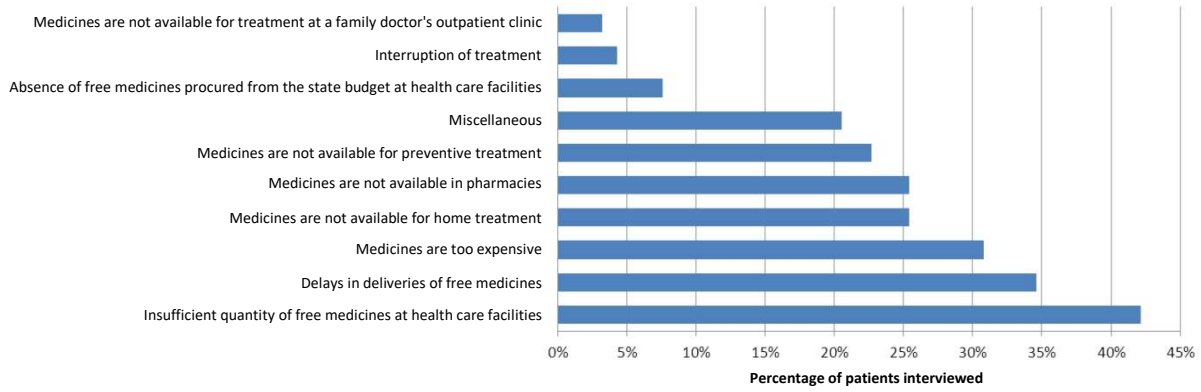

Figure 3. The main challenges identified for treatment of children with oncology and oncohaematology diseases

Patients considered that the procurement of medicines and medical products had improved between 2015 and 2019. Their level of satisfaction with the delivery of medicines was 8.0 (out of 10) for the period 2017–2019.

Children with mental and behaviour disorders of the autism spectrum, with schizophrenia, affective or hyperkinetic disorders

According to the MoH, as of 1 January 2017, 1,673,328 residents of Ukraine were registered as having mental and behavioural disorders, including 694,928 persons with disorders resulting from alcohol and drug use (or 3.9 per cent of the population). In general, the Ukrainian mental health care system has inherited the organisational structure, strategies and practices of the Soviet system. However, a number of positive changes have occurred in this area. In particular, the Law of Ukraine 'On Psychiatric Assistance' has been adopted, associations of experts have been created, and care protocols for certain mental and behavioural disorders have been developed.

Between 4 and 26 cases of autism are diagnosed for every 10,000 children in Ukraine, and incidence has increased by 273 per cent over the last 10 years. The prevalence for European countries is: 1 case of autism per 150–155 newborns, or 40–45 cases of autism per 10,000 thousand, and 60–70 cases of autism spectrum disorders per 10,000 population.[5]

The research on child mental and behavioural disorders was conducted in 3 oblasts, through interviews with 143 parents/caregivers and 11 doctors.

[5] A.L. Horb and A. Martynenko, 'Prevalence of Autism Spectrum Disorders in Ukraine: A Look at the Problem with the Eyes of a Pediatric Neurologist', Association of Pediatric Neurologists of Ukraine, Kyiv, https://neuronews.com.ua/ua/archive/2012/6-2/article-689/poshirenist-rozladiv-zi-spektru-autizmu-v-ukrayini-poglyad-na-problemu-ochima-dityachogo-nevrologa#gsc.tab=0.

Table 4. Summary of research into medicines supplies for treatment of children with mental and behaviour disorders

Oblast	Health care facility for inpatient treatment	Total number of patients registered	Total population of the oblast	Number of patients as a percentage of the total population	Number of parents/ caregivers interviewed	As a percentage of all patients	Number of doctors interviewed
Cherkasy	Cherkasy Regional Psychoneurological Dispensary or regional hospitals	373	1,191,093	0.0313	40	11	3
Kherson	Kherson Regional Psychiatric Hospital	320	1,027,013	0.0312	51	16	4
Mykolaiv	Mykolaiv Regional Psychiatric Hospital No. 1	347	1,119,124	0.0310	52	15	4
Total		1,040	3,337,230	0.0311	143	14	11

Significant differences were found in the treatment systems in the different oblasts that were studied (see Figure 13 in the Appendix). The majority of respondents emphasized the need for up-to-date diagnostics, non-drug treatment and rehabilitation approaches in the treatment process.

Deliveries of medicines took between 10 and 49 days from the issuing of the orders by the MoH to arrival at health care facilities. Delivery of medicines by Ukrvactsina to local warehouses took between 6 and 28 days, while onward distribution across the oblasts took a further 3–20 days. These medicines are used for outpatient and home treatment of patients.

In all three oblasts studied, **doctors** noted that there were no problems receiving the quantity of medicines ordered, but it did not cover the full need of patients. Two thirds (64 per cent) of the doctors said that the existing budget only covered about 80 per cent of the need for free medicines for children. They identified the absence of an officially approved algorithm and a way to calculate the need for medicines as a problem. In addition, two thirds of the doctors also highlighted communication problems between the MoH, oblast health care departments and health care facilities, which was the highest indicator among all the nosologies investigated. A quarter of the doctors complained about the short expiration dates of the medicines delivered. Despite a number of problems identified, they noted a gradual improvement in the medicine procurement system between 2017 and 2019.

Three quarters (77 per cent) of **patients** received free medicines, although a similar number also bought medicines. Most of those who did not receive free medicines were in Kherson oblast. Two patients from Cherkasy oblast and two from Kherson oblast indicated that they were asked to make a charitable contribution to receive the medicines.

It was found that free medicines procured from the state budget were available only to patients with autism spectrum mental disorders. Patients with other mental disorders only started to receive free medicines in 2018-2019 and previously had to buy them out of pocket. At the same time, 26 per cent of patients refused the medicines they were offered for free, which is the highest rate among all the nosologies studied. They indicated that they were treated without medication (through dietary supplements, diet), so the medicines available were not received or consumed.

Among the main problems identified by patients (see Figure 4) are an insufficient quantity of medicines (59 per cent), delays in deliveries (41 per cent) and the high cost of medicines in pharmacies (41 per cent).

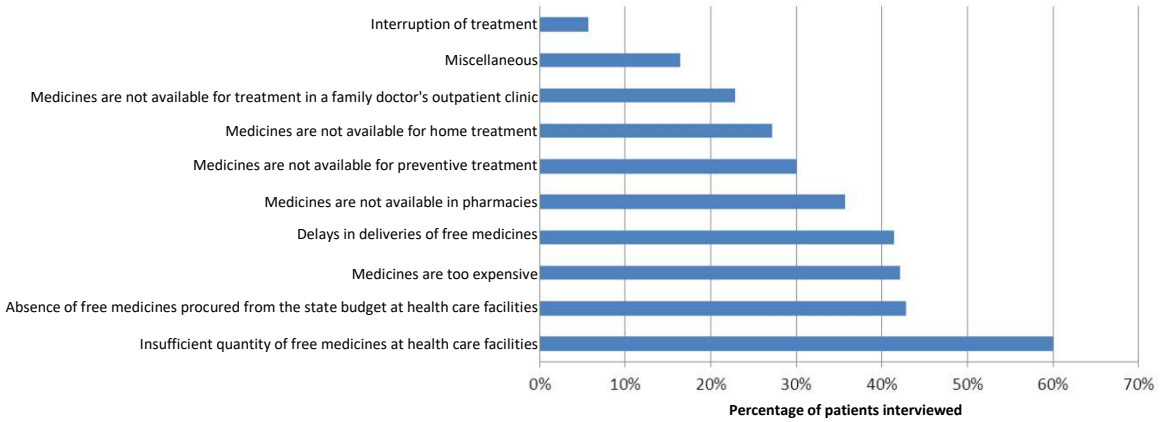

Figure 4. Main problems for patients with autism spectrum disorders in the oblasts studied

Improvements in the medicine procurement system between 2015 and 2019 were reflected in increased patient satisfaction with the system, although this varied considerably by oblast: 7.2 (on a 10-point scale) in Cherkasy oblast, 6.9 in Mykolaiv oblast and only 2.9 in Kherson oblast.

Viral hepatitis B and C

Hepatitis B, which is caused by the HBV virus, is a serious global medical and social problem. The World Health Organization estimates that approximately 887,000 people die each year from HBV infection, due to liver cirrhosis, hepatocellular carcinoma and other adverse effects[6]. Hepatitis C is one of the most dangerous diseases of the liver of viral etiology, and its prevalence is increasing each year. Most people infected with HCV develop liver cirrhosis or hepatocellular carcinoma, and every year about 399,000 people die from HCV-related liver diseases[7]. The situation regarding hepatitis B and C in Ukraine is also quite critical. The highest incidence of hepatitis B was observed in Mykolaiv, Ivano-Frankivsk and Sumy oblasts.[8]

Monitoring was conducted in 5 oblasts, through interviews with a total of 369 patients and 34 physicians.

[6] World Health Organization, https://www.who.int/en/news-room/fact-sheets/detail/hepatitis-b
[7] World Health Organization, https://www.who.int/news-room/fact-sheets/detail/hepatitis-c
[8] Public Health Centre of Ukraine, 'Hepatitis B in Ukraine: Epidemiological characteristics and burden', Kyiv, 2018, https://phc.org.ua/sites/default/files/uploads/files/VGV-2018.pdf.

Table 4. Summary of research into medicines supplies for treatment of hepatitis B and C

Oblast	Main health care facility where treatment is delivered	Total number of patients registered with hepatitis B and C	Total population of the oblast	Number of patients as a percentage of the total population	Number of patients interviewed	As a percentage of all patients	Number of doctors interviewed
Kherson	Kherson Regional Infectious Diseases Hospital G. Gorbachevsky	2,540	1,027,013	0.25	50	2.0	1
Khmelnytskyi	Khmelnytskyi City Infectious Diseases Hospital	1,168	1,253,930	0.09	64	5.5	9
Mykolaiv	Mykolaiv Regional Adult Infectious Hospital	4,347	1,119,124	0.39	51	1.2	4
Rivne	Central City Hospital	5,535	1,152,704	0.48	60	1.1	11
Ternopil	Ternopil Municipal Ambulance Hospital and Ternopil Regional Medical Centre	1,876	1,038,183	0.18	144	7.7	9
Total		15,466	5,590,954	0.28	369	2.4	34

In Europe, eight medicines used to treat hepatitis C are recommended by the European Association for the Study of the Liver (EASL),[9] and five of these eight medicines are procured and used in Ukraine. Treatment is regulated by unified clinical protocols for primary, secondary (specialized) and tertiary (highly specialized) medical care and rehabilitation. Typically, patients with hepatitis B or C from all over an oblast are treated at a specialist hospital. Subject to indications and the availability of medicines, they can take medicines at home. However, a wide range in the quantity and nomenclature of medicines used was found (as shown in Figure 14 in the Appendix).

Deliveries of medicines were found to take between 2 and 34 days from the issuing of an MoH order to arrival at local warehouses. Orders were issued by regional health care departments in a timely manner.

Three quarters (76 per cent) of the **doctors** surveyed confirmed that the quantity of medicines received does not match the amounts requested or the actual needs of hospitals based on the number of patients. According to the doctors, the level of provision of hepatitis medicines was 57 per cent of the quantity need.

Among other problems identified, 71 per cent of doctors noted irregular supplies of medicines during the year, while 66 per cent mentioned significant delays and interruptions in the flow of medicines, 31 per cent mentioned the incorrect sequence of medicine deliveries, and 28 per cent mentioned occasional stock-outs of medicines at health care facility warehouses.

In addition, 41 per cent of doctors mentioned that certain medicines were missing from the National List of Essential Medicines, while 29 per cent stated that it was impossible to undertake long-term planning (2–3 years) of supplies, 27 per cent noted communication problems between the MoH and health care facilities, and a similar number highlighted insufficient availability of

[9] Public Health Centre of Ukraine, 'Recommendations of the European Association for the Study of the Liver on Treatment of Hepatitis C', Kyiv, 2018, https://phc.org.ua/sites/default/files/users/user90/%D0%A3%D0%9A%D0%A0%20EASL%20%D0%93%D0%B5%D0%BF%D0%B0%D1%82%D0%B8%D1%82%20%D0%A1%202018.pdf.

diagnostic tests to detect the disease. If patients are unable to pay the full cost of diagnostic tests, they cannot be registered to receive free treatment.

The doctors noted an increase in supplies of free medicine for the treatment of viral hepatitis since 2018. Until then, supplies of direct-acting antivirals were rare, which affected the treatment available to patients with hepatitis C. A decrease in the purchase price for these medicines in Ukraine contributed significantly to this effect.

Three quarters (78 per cent) of the **patients** interviewed received free medicines procured from the central budget. The main problems patients faced in receiving medicines for their treatment are shown in Figure 5. Delays in the supply of free medicines were the most common problem, identified by 38 per cent of respondents, followed by the insufficient quantity of free medicines at health care facilities (15 per cent) and the prohibitive price of the medicines (14 per cent).

There were no complaints about the lack of availability of home treatment, since treatment of viral hepatitis involves dispensing medicines to patients once a month. However, they have to attend a regional hospital for this; therefore, a small number of patients wish to receive medicines from a family doctor instead. Patients enrolled in the free treatment programme were generally satisfied with the quantity of medicines delivered and the consistency and reliability of their delivery.

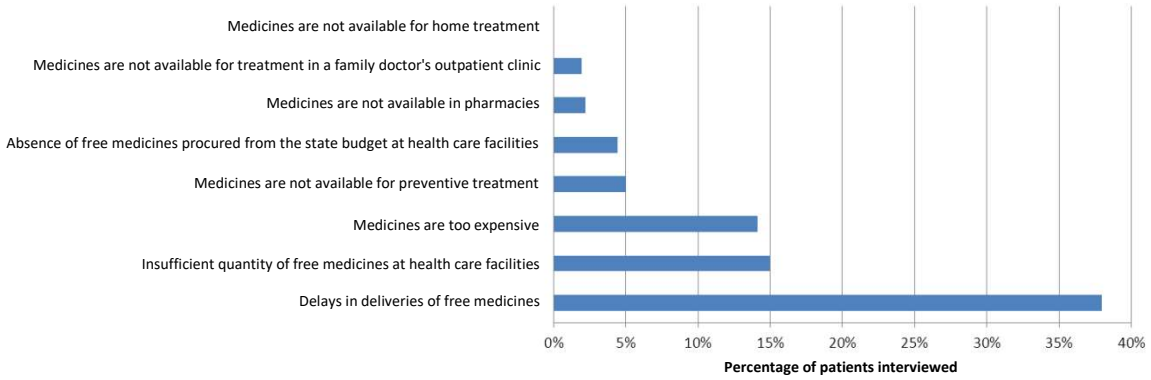

Figure 5. Main problems for patients with viral hepatitis

Patients receiving hepatitis C treatment with modern direct-acting antivirals have to undergo a single course of treatment with a high probability of cure. Therefore, not all the patients interviewed could assess the effectiveness of delivery.

At the same time, significant differences in the level of patients' satisfaction with their treatment in different oblasts were revealed, which indicates the presence of factors specific to each oblast. The highest levels of satisfaction were in Mykolaiv oblast, and the lowest in Khmelnytskyi oblast.

The medicines procured for treatment of viral hepatitis in 2018 had a significantly higher proportion of direct-acting antiviral medicines compared to the monitoring of procurement in 2016, due to a significant decrease in their procurement price and changes in the clinical management of the patients paradigm. This is a significant achievement because it enables hepatitis C to be treated more efficiently. Nevertheless, significant problems remain, such as with the regular delivery of medicines procured and the inability to plan long-term treatment courses for patients with viral hepatitis diagnosed between deliveries of medicines. Another major problem for the mass treatment of hepatitis is the limited availability of free diagnostic tests, which is necessary for the patient to be registered and receive free medicines.

Resistant juvenile rheumatoid arthritis

Juvenile rheumatoid arthritis (JRA) is the most common chronic rheumatic joint disease in childhood. It is a chronic disease accompanied by continuous inflammation of one or more joints, with unknown cause, which lasts for more than six weeks. The global incidence of this nosology is hard to establish – in particular, because of the lack of unified and accurate nomenclature and classification of the condition, which is increasingly frequently called 'juvenile idiopathic arthritis' in world practice.

In Ukraine, the prevalence of JRA is 0.2–0.4 per 1,000 children, and the incidence is 0.09 per 1,000 children.[10]

The main goals of the treatment of patients with JRA are to achieve remission of the disease and to preserve the quality of life by reducing the symptoms of arthritis and preventing joint replacements. Current JRA treatment is based on the use of immunobiological basic medicines – cytokine blockers responsible for development of the inflammatory process. The national unified clinical protocol for medical care for children with juvenile arthritis was approved by MoH Order No. 832 of 22 October 2012.

The research was conducted in 5 oblasts, through interviews with 4 doctors and 83 patients.

Table 5. Summary of research into medicines supplies for treatment of children suffering from resistant JRA

Oblast	Health care facility where treatment is provided	Total number of patients registered	Total population of the oblast	Number of patients as a percentage of the total population	Number of parents/ caregivers interviewed	As a percentage of all patients	Number of doctors interviewed
Khmelnytskyi	Khmelnytskyi Regional Children's Hospital	18	1,253,930	0.0014	13	72	1
Lviv	Western Ukrainian Specialized Children's Medical Centre	54	2,510,988	0.0022	25	46	1
Rivne	Rivne Regional Children's Hospital	21	1,152,704	0.0018	16	76	1
Volyn	Volyn Regional Children's Territorial Medical Association	83	1,031,205	0.0080	11	13	1
Zhytomyr	Zhytomyr Regional Children's Clinical Hospital	28	1,207,270	0.0023	18	64	0
Total		204	7,156,097	0.0028	83	41	4

Treatment takes place at one specialist children's hospital in each oblast, although two respondents from Zhytomyr oblast indicated that the medicines were also available from the family doctor's outpatient clinic.

Logistical delays occurred periodically between the issuing of the MoH order and the dispatch of medicines from the central warehouse to the regions (up to 15 days). Thereafter, delivery by Ukrvactsina and then Ukrmedpostach from the central warehouse occurs within one day.

[10] V.V. Berejniy, T.V. Marushko and S.V. Marushko, 'Peculiarities of the clinical course of rheumatoid arthritis in adolescent children', Kyiv, 2006, http://www.mif-ua.com/archive/article/220.

The delivery schedule is not effective, since there is no clear mechanism for timely distribution of medicines. This can (and does, as evidenced by doctors and patients) lead to interruptions in treatment, which reduce its effectiveness. In 2018–2019, the frequency of dispatches to the regions increased. In the first half of 2019, they also became more regular, although the problem has not been fully resolved. Indeed, at the time of the survey, there had been no supplies of medicines at all since the beginning of September 2019. This was confirmed by the data provided by Ukrmedpostach, and is also noted in patient questionnaires.

Three of the four **doctors** interviewed think the full need for medicines is satisfied. Two of them noted the problem of insufficient funding for this nosology and the absence of Etanercept/Enbrel from the National List of Essential Medicines.

Three of the four doctors reported delays, interruptions and irregular deliveries of medicines. Sometimes this lead to an interruption in treatment (2 answers). Two of the doctors mentioned that it was impossible to undertake long-term planning (2–3 years) of medicine supplies. If these problems are not overcome, they can counteract the effect of the medicines being purchased, since patients do not receive a full course of treatment.

Regarding the quantity and stability of the delivery system for medicines for JRA, the doctors in Lviv oblast consistently scored both indicators at 10 out of 10 for all time periods. Doctors in Khmelnytskyi, Rivne and Volyn oblasts noted improvements in the system in 2014–2016 compared to 2013, but without any significant further improvement in 2017–2019.

There is significant variation between oblasts in the quantity and nomenclature of medicines ordered (see Figure 15 in the Appendix). These medicines are ordered by a specialist in each oblast at his/her own discretion; as a result, patients in different oblasts receive different medicines.

Almost all **patients** receive treatment at regional hospitals. Only two respondents in Zhytomyr oblast replied that they received outpatient treatment from a family doctor in addition to the regional hospital. Nearly all (99 per cent) of the respondents said they were receiving medicines for free. Two respondents from Zhytomyr oblast indicated that they partially paid for medicines, while four respondents reported they refused free medicines. Two-thirds (66 per cent) of respondents reported no out-of-pocket purchases of medicines, although the highest proportion of parents/caregivers who indicated that they purchased medicines at their own expense were in Rivne oblast.

The problems faced by respondents during their treatment are shown in Figure 6. The most commonly mentioned are insufficient quantity of free medicines at health care facilities (mentioned by 35 per cent of respondents), the absence of free medicines procured from the state budget at health care facilities (33 per cent) and delays in deliveries of free medicines (32 per cent).

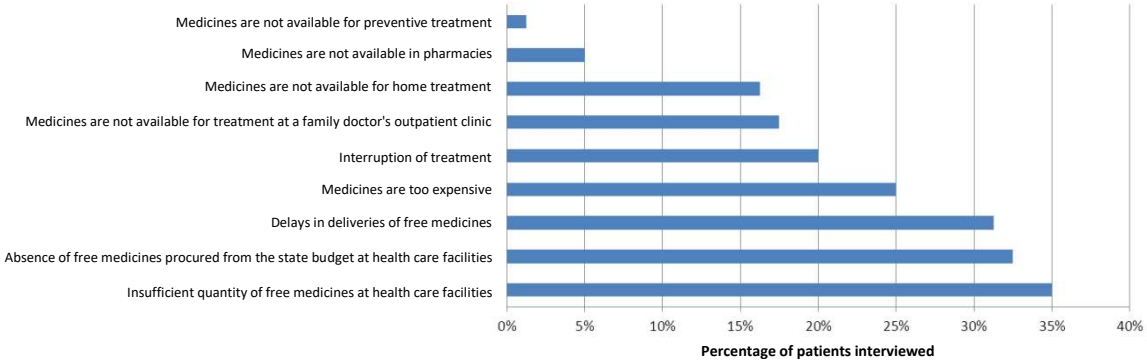

Figure 6. Problems with treatment of patients with JRA in all oblasts studied

However, the problems identified differ significantly by oblast, as does the respondents' level of satisfaction with the quantity of medicines purchased from the state budget, although this has generally been increasing over time. Patient satisfaction with the stability of supplies in Khmelnytskyi and Volyn oblasts has decreased, due to additional delays in deliveries of medicines at the time of monitoring – in the second half of 2019. Nevertheless, it must be understood that the answers to these questions are completely subjective: they are not based on an objective assessment of the provision of appropriate treatment, but on the relevance of the situation to their perception of high-quality treatment (which may be understated or inaccurate).

Lviv oblast receives the most free medicines and has a powerful civil society organisation of parents of children with JRA. In Rivne and Zhytomyr oblasts, most people wanted to be treated in district hospitals, rather than in regional centres, and on an outpatient basis. Also, in Zhytomyr oblast, many respondents complained about the process for obtaining medical documents for free medicines being too long.

Therefore, the system for procuring, distributing and delivering medicines to treat children with resistant JRA does not yet ensure the provision of high-quality care for all patients. An important factor restricting patients' quality of life and their satisfaction with treatment is the lack of home and outpatient treatment. Doctors and patients noted an insufficient quantity of medicines that are provided centrally, while parents/caregivers of patients considered the lack of a stable supply, which leads to interruptions in treatment, an even more significant problem. The absence of deliveries of medicines to the regions from September 2019 shows that this process depends on political will. Also, the availability of public information on the delivery and use of medicines differs by health care facility.

Reagents for mass screening of newborns for phenylketonuria, congenital hypothyroidism, cystic fibrosis and adrenogenital syndrome

Neonatal screening is a mass examination of newborns to identify a number of hereditary diseases. It is carried out for all newborns without exception.

The monitoring for this programme was performed in Cherkasy oblast, where 8,523 newborns were registered as of 31 December 2018. All babies were screened for rare orphan and genetic diseases, except for three cases when the parent refused to allow it. In Cherkasy oblast, 2 maternity hospitals, a regional perinatal centre, 20 central district hospitals and a district hospital have maternity departments. Blood samples from newborns for mass screening for phenylketonuria, congenital hypothyroidism, cystic fibrosis and adrenogenital syndrome are collected and are centrally dispatched to the laboratory of the medical and genetics centre of the

Cherkasy Regional Centre for Family Planning and Human Reproduction. Its director and staff were interviewed for the study.

There were shortfalls in deliveries of six of the seven reagents ordered in 2018–2019, ranging from 13 per cent to 28 per cent (see Figure 7). Deliveries of only one reagent achieved 100 per cent of the actual need. Deliveries were delayed for up to 10 months, but the need for the current year was covered by the medicines delivered the previous year.

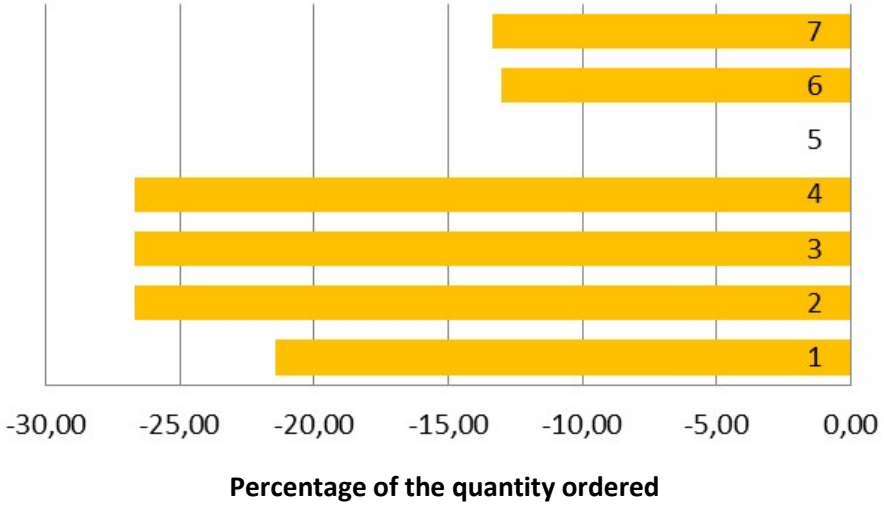

Figure 7. Shortfalls in deliveries of reagents ordered for screening (percentage)

Notes: 1 – Test kit for screening newborns for phenylketonuria in dried blood spots on filter paper; 2 – Test kit for screening newborns for congenital hypothyroidism in dried blood spots on filter paper; 3 – Test kit for screening newborns for cystic fibrosis in dried blood spots on filter paper; 4 – Test kit for screening newborns for adrenogenital syndrome in dried blood spots on filter paper; 5 – Kit for detecting the most common mutations in the CFTR gene by the LIPA method; 6 – Paper test forms for blood sampling of newborns; 7 – Plates with U-shaped wells for immunology testing.

The **doctor** interviewed noted the erratic timing of deliveries, and the inability to predict the exact number of births and to calculate the exact need for reagents. Deliveries of reagents were not optimally distributed over time, and some reagents had a short expiration date due to delayed delivery. However, he rated his satisfaction with the number of reagents in 2019 at 10/10, and the stability of supply 9/10. He proposed submitting an application for reagents no later than November for the following year. Reagents should be delivered twice a year. A centralized reserve of reagents should also be created to avoid stock-outs in the oblasts. It is also necessary to expand the list of nosologies which are subject to screening, including congenital deafness.

Orphan diseases

Four orphan diseases were the subject of monitoring: epidermolysis bullosa, pulmonary hypertension, mucopolysaccharidosis (MPS) and cystic fibrosis.

The **design** of this study was different from other nosologies. The monitoring was carried out in 24 oblasts of Ukraine and Kyiv, including the National Specialized Children's Hospital (NSCH) Okhmatdyt in Kyiv (treatment of EB and MPS). Comparative analysis of different oblasts was not carried out, due to the small number of patients with orphan diseases.

An online survey involved 47 doctors treating patients with orphan nosologies, as well as 13 health care departments of regional state administrations. The health care departments of Kyiv, Luhansk, Lviv and Odesa oblasts did not provide any of the information requested in the survey.

A total of 479 patients from all oblasts of Ukraine were also interviewed, representing 29.4 per cent of the 1,628 patients with orphan nosologies receiving treatment in the country (see Table 6). The majority (306 or 64 per cent) of patients were aged 1–17 years; 90 (19 per cent) were 18–29; 49 (10 per cent) were 30–39; and 34 (7 per cent) were aged 40 or older.

Table 6. Patients with orphan diseases interviewed in the study

Disease	Number of patients registered	Number of patients interviewed	As a percentage of the total number of patients
Cystic fibrosis	870	272	31
Epidermolysis bullosa	89	76	85
Mucopolysaccharidosis	627	95	15
Pulmonary hypertension	42	36	86
Total	1,628	479	29

Epidermolysis bullosa

Epidermolysis bullosa is a rare (orphan) hereditary disease that occurs with a frequency of 1:20,000–30,000. To reduce pain, prevent and treat infections and prevent complications, patients with epidermolysis bullosa require constant and life-long use of special **medical devices** for wound care, such as non-adhesive dressings, soft absorbent wipes, polyamide grids, soft tubular bandages and elastic fixation bandages.

Pulmonary hypertension

Pulmonary arterial hypertension is a threatening pathological condition, with a frequency of 0.03:2,000, caused by persisting high blood pressure in the pulmonary vascular bed with the gradual constriction of medium and small vessels of the lungs. Patients with pulmonary arterial hypertension need life-long usage of medicines. The survival of untreated patients is 2–2.5 years from the time of diagnosis.

Mucopolysaccharidosis

MPS occurs with a frequency of 1:100,000 or less. It is characterized by a shortage of the lysosomal enzymes that cleave glycosaminoglycans. All diagnostic tests for the four types of MPS that are treated by under the MoH of Ukraine are carried out at the Centre of Orphan Metabolic Diseases at NSCH Okhmatdyt in Kyiv.

Cystic fibrosis

Cystic fibrosis is a lethal hereditary disease most often affecting Caucasians (on average 1:2,500–3,500 newborns, ranging from 1:1,700 to 1:4,000).

Distribution of medicines

Following approval of the relevant order by the MoH, medicines and medical products are shipped by Ukrmedpostach and Ukrvactsina to the regions, where they are delivered to the the recipient organisation's distribution warehouse. As a rule, the logistics process from the date of an order issued by the MoH to the delivery of medicines to a hospital in a region takes approximately 32–68 days. The MoH generally approves orders within 30 days, which thus

increases the lead times for deliveries to 62–98 days. It then takes approximately 1–20 days from the time medicines are received by medical institutions until they are dispensed to patients.

Availability and use of medicines and medical products

Around 60 per cent of the doctors and health care department officials interviewed reported that the volume of medicines did not meet the full clinical need. However, in practice, when they refer to the need or supply, they often mean the quantity available from the budget allocated to the nosology, rather than patients' actual need.

For pulmonary hypertension, there is no approved methodology to calculate the full need for the treatment for each patient; therefore it is calculated based on the number of prescriptions issued by doctors guided by treatment protocols. It was found that supplies of the nine medical products/devices used in treatment satisfied between 19 per cent (Iloprostum) and 68 per cent (Bosentanum) of the total need. Supplies of medicines ranged from 54 per cent (Sildenafilum) to 100 per cent (Iloprostum, Bosentanum) of the quantities ordered, except for Ambrisentan (5 and 10 mg), which was not delivered at all.

For MPS, it was found that supplies of the four medical products/devices used in treatment satisfied between 52 per cent (Elosulfase alpha) and 82 per cent (Galsulfasum) of the total need. At the time of monitoring, 100 per cent of all medicines ordered were received.

For cystic fibrosis, there was no approved calculation methodology as of 2018. Need was assessed individually for each patient, taking into account the severity of the condition and their age and weight. It was found that supplies of the four medical products/devices used to treat children satisfied from 25 per cent (Pancreatin) to 57 per cent (Dornasum alpha) of the total need. In most cases, at the time of monitoring, 100 per cent of all medicines ordered had been received. Regarding medicines for cystic fibrosis in adults, it was found that supplies of the two medical products/devices used in treatment (Pancreatin and Dornasum alpha) satisfied 29 per cent of the total need. At the time of monitoring, 100 per cent of the Pancreatin and 36 per cent of the Dornasum alpha ordered had been received.

For epidermolysis bullosa, the MoH approved a methodology in 2019 to calculate the individual needs of each patient, based on their age and the degree of skin damage. It was found that supplies of the 14 medical products/devices used for treatment satisfied between 16 per cent (Medicomp wipes) and 23 per cent (Mepilex® dressings) of total need. In most cases, at the time of monitoring, 100 per cent of the medicines ordered had been received, although less than 25 per cent of the Medicomp wipes ordered had been delivered.

The main issue encountered in ordering medicines and medical products/devices (see Figure 8) was insufficient funding allocated to the nosology, mentioned by 34 of the respondents, followed by the impossibility of undertaking long-term planning (17 respondents) and certain medicines not being available on the National List of Essential Medicines (14).

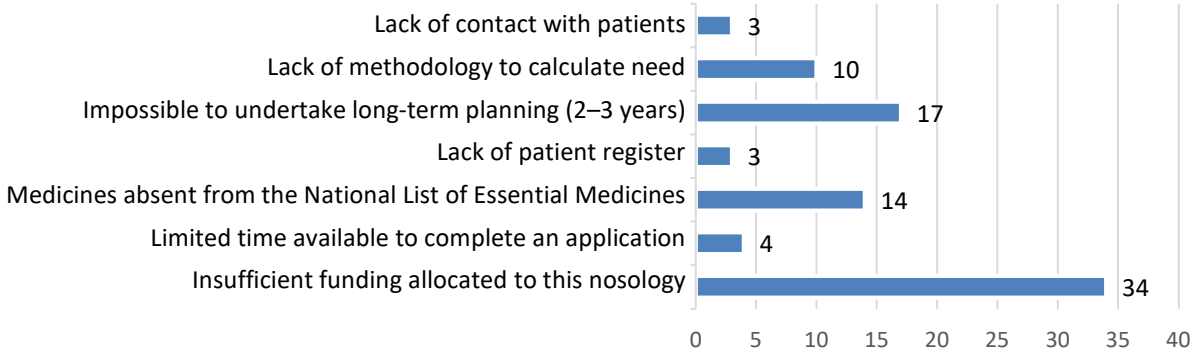

Figure 8. Problems with ordering medicines for orphan diseases

The respondents mentioned the same three reasons as the main ones for why supplies of medicines fail to meet the full need (see Figure 9).

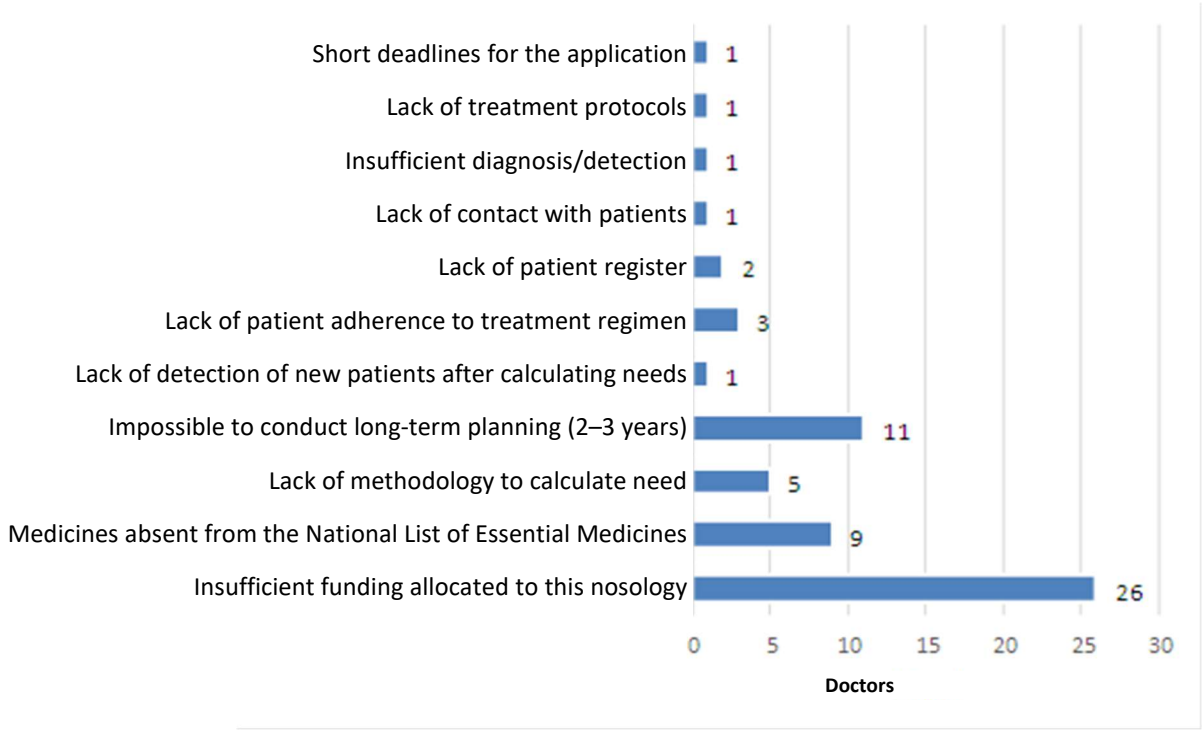

Figure 9. Reasons for medicines supplies failing to meet full need

Problems mentioned by doctors regarding the receipt of medicines procured by the MoH were interruptions in treatment courses due to breaks in deliveries of medicines (mentioned by 23 respondents), lack of patient adherence to treatment (7), expired shelf life of medicines (2) and the impossibility to redistribute medicines to other health care facilities (2). According to health care department officials, the main problems were significant delays and interruptions of MoH deliveries of medicines (23) and the MoH's failure to inform them in a timely manner about medicines delivery schedules during the year (17). The main problems identified by hospitals were significant delays and interruptions in the delivery of medicines and irregular deliveries of medicines throughout the year (each mentioned by 26 respondents) and periodic stock-outs of medicines at health care facility warehouses (11 respondents).

As can be seen, one of the main issues is that delays in the delivery of medicines causes treatment interruptions, and only 59 per cent of the health care experts surveyed deemed that medicines were distributed on time. Communication issues between the MoH, health care departments and health care facilities were highlighted by 19 per cent of the doctors and 13 per cent of the health care department officials interviewed. The absence of information on the volume of medicines and timing of deliveries is the main issue for health care departments.

Although there was much criticism of the procurement process, the level of satisfaction with both the quantity and stability of the delivery of medicines procured from the state budget for orphan nosologies indicates a clear upward tendency from around 3.5 in 2014–2016 to around 6.2 in 2017–2019. This may be partly because three of the nosologies studied started to receive medicines in 2017.

The main issues that **patients** faced during treatment are shown in Figure 10. The most commonly mentioned issue was that medicines are too expensive, followed by delays in deliveries of free medicines, and a lack of free medical products/devices at health care facilities.

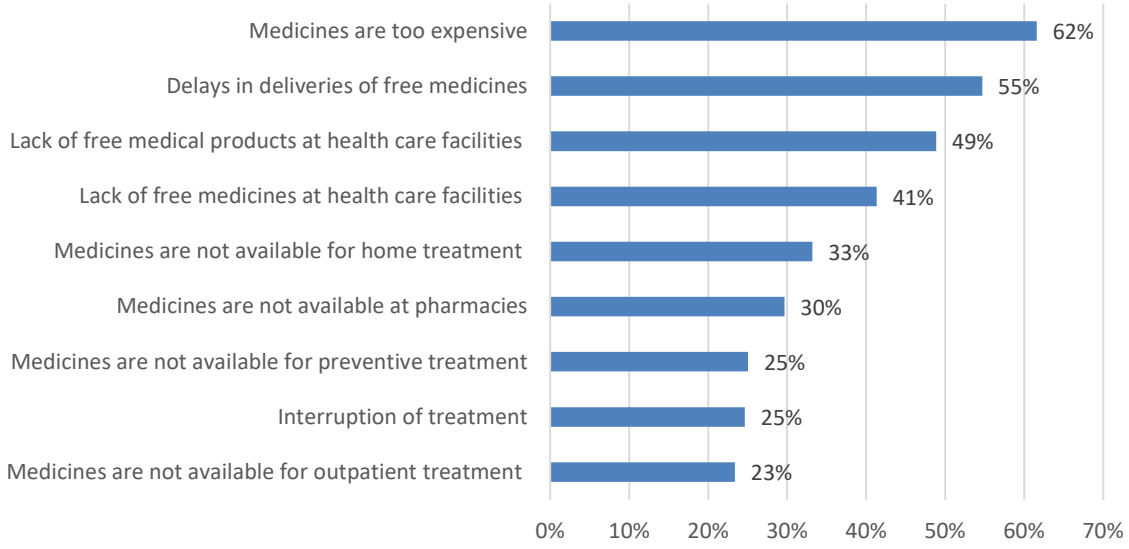

Figure 10. The main issues reported by patients with orphan diseases

The timing of deliveries for the 2018 fiscal year was not significantly affected by the changes that occurred in 2016–2017 (delegation of procurement powers from the MoH to international organizations). However, the delivery of medicines for 2018 was delayed by 7–12 months, which was in line with the general tendency in 2016–2018. Patients' satisfaction with the **quantity** of medicines received averaged 5.4 on a 10-point scale (ranging from 3.7 for adults with cystic fibrosis to 6.7 for epidermolysis bullosa). Satisfaction with the **stability** of medicine delivery was averaged 5.2 (ranging from 3.6 for adults with cystic fibrosis to 6.3 for epidermolysis bullosa).

Coverage of free medicines ranges from 23 per cent of the needs of epidermolysis bullosa patients to 86 per cent of those of children with cystic fibrosis. Only an average of 30 per cent of patients with orphan diseases were aware of their right to affordable medicines. Medicines for all of the conditions analysed are expensive and subject to special accounting. Patients, doctors and health care department officials did not report any corrupt practices or cases of opacity in the delivery or distribution of medicines, and the study did not identify any either.

Thus, the monitoring found that medicines and medical products/devices funded from the state budget failed to meet the full need of any of the orphan nosologies studied. The additional provision of medicines funded from local budgets is limited by the National List of Essential Medicines. For all nosologies, interruptions in deliveries of medical products were identified, caused by unjustified delays in deliveries from logistics operators to patients (up to 3–4 months from the time the order is issued by the MoH to the day they are received by the patient). The absence of patient registers makes it impossible to predict the need for medicines and observe their movement at all stages of delivery. Communication gaps between the MoH and the regions regarding expenditures for orphan nosologies, as well as between the regional health departments and specialized orphan disease centres, have been identified.

Conclusions

- The main factors restricting the provision of medicines and medical products were found to be insufficient funding allocated to each of the diseases, and the overall lack of efficiency of the procurement system in Ukraine. This was identified by 77 per cent of the medical professionals surveyed. In addition, 40 per cent of patients complained about the insufficient quantity of free medical products, while 24 per cent complained that they were not available at health care facilities. However, both physicians and patients confirmed that the volumes of medicines and medical products procured had increased between 2015 and 2019.
- Delays in supplies of medicines and medical products to hospital warehouses (and thus to patients) were identified as a problem by 70 per cent of medical professionals and 47 per cent of patients. The main reason for this was delays in issuing orders by the MoH and regional health care departments, and the lack of effective management of the stages from preparation of the order to the dispatch of products to the regions. This stage is a bottleneck in the procurement process and could take between 7 and 55 days. In addition, 37 per cent of doctors complained about the unpredictable frequency of deliveries throughout the year, and not being able to undertake long-term planning of the treatment process. However, the physicians' and patients' level of satisfaction with the organisation of the procurement process and the stability of deliveries suggest that the delivery process improved steadily from 2015 to 2019 for each of the nosologies studied.
- A comparative analysis of the situation in different oblasts made it possible to identify differences for each nosology at the regional level in: 1) timing of actual deliveries; 2) volumes and nomenclature of medicines ordered; and 3) doctors' and patients' satisfaction with the procurement process.
- Significant differences were identified in the ways to calculate an oblast's need for medicines, as well as the nomenclature of medicines ordered – in particular, taking into account the volume of medical products for preventive or urgent care, the use of originator or generic medicines, interferons or direct-acting antiviral medicines to treat hepatitis, plasma-derived or recombinant medicines for haemophilia, the latest or traditional cancer medicines, etc. These differences were especially notable for nosologies with long lists of medicines in the nomenclature (haemophilia, oncological diseases). Thus, medicines that are commonly used in some oblasts may not be used at all by others, which indicates a significant degree of subjectivity in decision-making by regional experts – in particular, their preference for a certain producer.
- As one of the main issues, doctors and regional health care department officials highlighted the lack of complete national patient registers as a planning and decision-making tool. This makes it impossible to obtain complete information about the need for medicines for each patient, to plan deliveries on time, to individualize treatment and adjust it quickly when the effectiveness of treatment changes. This problem particularly concerns patients with chronic and orphan conditions receiving life-long treatment.
- Another problem identified during the monitoring, which was confirmed by 25 per cent of doctors, was communication: 1) between experts at the same level across Ukraine (the lack of a professional environment); 2) between doctors and regional health care departments; and 3) between health care departments and the MoH when planning an oblast's needs (tight deadlines for the preparation of nomenclature within the funding allocated), as well as in implementing the delivery process (the failure to inform doctors about the timing of deliveries of certain categories of medicines). This problem is particularly acute for rare orphan nosologies, where the number of specialized doctors is limited, and the expertise of family doctors is insufficient. In addition, medical professionals expressed concerns about the lack of continuous training about modern trends in clinical management of patients and quantification of medicines needs.

- The study found that the MoH had published information about the delivery of medicines to Ukraine and the regions less regularly in 2019 than in 2018. In 2018, the MoH website regularly updated information on the distribution of medical products across Ukraine, their volumes and delivery schedules. In 2019, the majority of respondents noted a lack of up-to-date information on the website at the time of monitoring (October–November 2019). It was noted that, in such circumstances, the website of UNDP in Ukraine – as a procurement organisation – was the only source of the latest information on the medicines procured.
- The majority of patients surveyed (88 per cent) received at least one medicine procured from the state budget free of charge. Only 1.3 per cent of patients reported the need to make a charitable contribution or other informal payment as a condition of receiving free medicines. However, 34 per cent of patients bought additional medicines not covered by government programmes.
- This monitoring identified examples of the effective use by patient organisations and doctors of the national platforms that contain information on the availability of free medicines in hospitals: https://eliky.in.ua/ and https://liky.ua/. All health care facilities publish information about available stocks of medicines, but they use different methods. Usually they prepare printouts of the hospital's warehouse database, which are updated with varying frequency. At the same time, the monitoring showed insufficient utilization of the capacities of these national platforms. The health care facilities explain that regularly updating the databases takes up too much staff time. Nevertheless, the possibility to remotely check the remaining amounts of medicines and medical products at health care facilities across Ukraine is extremely valuable, not only for patients but also for doctors, as it allows certain medicines to be quickly redistributed to another facility.
- The monitoring was not limited to the processes of delivering medicines procured centrally from the state budget, but also covered data on a number of issues related to the organisation of the delivery of medicines and medical products at the local level. In particular, 34 per cent of doctors mentioned as a problem that it was impossible to procure additional medicines not included in the National List of Essential Medicines from local budgets. Yet such local purchases are important to ensure a steady supply of medicines throughout the year, which greatly increases the satisfaction of both patients and physicians with the supply system. A notable example is the regional procurement of medicines for JRA in Lviv oblast, which resulted in almost 100 per cent satisfaction among both doctors and patients with the medicine delivery process in 2018–2019.
- One of the main factors that significantly affect patients' perception of the procurement process, and the provision of health care in general, are the particularities of the treatment process, namely: inpatient, outpatient and home treatment. Nearly a quarter (23 per cent) of patients complained about the lack of home treatment. Comparative analysis between the oblasts and nosologies identified a consistent pattern: patient satisfaction with the medicine delivery system was higher when medicines were more available for home/outpatient use, the process of dispensing them at the health care facility was well planned, and when they could receive treatment promptly. This is illustrated by comparing patient satisfaction rates between paediatric haemophilia (with home and preventive treatment) and adult haemophilia (without home treatment): an average of 7.1 for children and only 3.2 for adults (on a 10-point scale). Specialized doctors and patients with JRA and orphan diseases also claimed that it was necessary to introduce home treatment.
- In general, the monitoring showed that both physicians and patients clearly confirmed the gradual improvement in the medicine procurement system between 2015 and 2019: the schedule of medicine supplies was being better planned, and as of mid-2019 it achieved a steady level of provision throughout the year. An important factor in the positive assessment of the procurement system by stakeholders was an increase in volumes of medicines procured, which was achieved by both increasing the MoH's budget allocations for most of

the nosologies and reducing the prices achieved in tenders. At the same time, the monitoring revealed a number of problems in the system of ordering, procurement, distribution and use of medicines which need to be solved to further improve the process and, ultimately, patient outcomes.

Limitations

- The study was carried out by six different NGOs, with different levels of research expertise.
- The study design stipulated that, for some nosologies, data were collected and analysed by two or more organisations. This could potentially lead to discrepancies in the data analysis.
- Researchers were unable to ensure representative samples for each nosology (by age, gender, severity of disease and other factors).
- The participating organisations had a certain expertise in dealing with specific categories of patients, but the diseases monitored might not be relevant to the organisations' previous experience.
- The study of orphan diseases was designed differently from the other nosologies due to the specificity of those diseases (e.g., a small number of patients, life-long dependence on medicines, insufficient awareness of the diseases among general practicioners). Therefore the results are not comparable to the results related to other nosologies.
- Finally, the participating organisations collected a considerable volume of material, which could not be included in the final report in its entirety.

Recommendations

For the Ministry of Health of Ukraine

- Improve the planning and implementation of procurement by establishing and monitoring annual deadlines for decision-making at every stage of the process for ordering, procurement, distribution and use of medicinal products.
- Ensure unhindered communication and interaction between all stakeholders at each stage of decision-making regarding the ordering and procurement of medicines: between the MoH, regional health care facilities, experts and procurement organisations.
- Develop and make regional experts aware of a unified methodology for calculating the full need for each nosology as well as a standardized data collection methodology.
- Ensure that oblasts have enough time to calculate the correct need for each medicine or medical product for each nosology, taking into account the available medicine stocks. In certain cases where medicines have an intrinsic short shelf life or in case of sudden epidemiological outbreak, a more regular (twice or three times a year or *ad hoc*) recalculation of needs may be necessary.
- Ensure the collective nature of decision-making by regional experts so that the applications for the delivery of medicines are unbiased, impartial and optimized.
- Review and, where necessary, update protocols to ensure compliance with unified health care standards for each nosology. This is particularly important for settings that use substandard treatments and clinical management of patients.
- Create patient registers with all relevant safety measures to avoid disclosure of diagnosis for all nosologies, and ensure that they are systematically updated to calculate patients' needs. This should initially be done for chronic and orphan diseases, given the need for effective life-long planning and monitoring of the use of expensive medicines for those patients.
- Analyse the need for changes to the National List of Essential Medicines based on the applications from the regions, which will improve supplies of medicines procured from local budgets.
- Optimize the supply chain – specifically, the timely preparation and issuance of MoH and regional health care departments' distribution orders and the prompt dispatch of medicines from central warehouses to the regions.
- Consider the introduction of provision of home treatment for haemophilia and certain orphan diseases. This will give patients the opportunity to take a medicine to stop bleeding in an emergency at home, which will significantly improve their quality of life. This system should extend to children.

For the National Health Service of Ukraine

- Develop clear algorithms for family physicians to obtain consultations from specialists regarding the treatment and referral of patients (clinical paths) with nosologies which were previously treated at specialized facilities (viral hepatitis, autism spectrum disorders, orphan diseases, etc.).
- Promote the widespread adoption of home treatment and outpatient care, with appropriate billing of services, which will reduce the need for hospitalization and lower the cost of providing effective medical services to patients, in particular those in need of life-long medical care, such as for chronic and orphan diseases.

- Provide free diagnostic services that are an integral part of the treatment of many socially significant diseases, including viral hepatitis, when the need to pay for diagnostic testing prevents patients from receiving treatment, even if free medicines are available.

Authors

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All-Ukrainian Charity Organization 'Initiative for Life'
Charity Children Foundation 'Give World to Child'
Charity Foundation 'STOPCANCER'
Charity Foundation 'Treasury of Hope'
Public Association 'Orphan Diseases of Ukraine'
Public Organization 'Creative Association Nivroku'

List of reports prepared by programme participants[11]

- Analytical Report by Charity Children Foundation 'Give World to Child' (Cherkasy): 'Public monitoring of the delivery, availability and use of medicines in Cherkasy oblast (paediatric haemophilia; paediatric oncology and haematology; mental and behavioural disorders of autism spectrum, schizophrenia, affective disorders, hyperkinetic disorders in children; procurement of reagents for mass screening of newborns for phenylketonuria, congenital hypothyroidism, cystic fibrosis and adrenogenital syndrome)', 69 pp.
- Analytical Report by Charity Foundation 'Treasury of Hope' (Rivne): 'Monitoring the availability of essential medicines in Rivne, Zhytomyr, Khmelnytskyi, Volyn and Lviv oblasts (juvenile rheumatoid arthritis)', 40 pp.
- Analytical Report by Charity Foundation 'STOPCANCER' (Lutsk): 'Public monitoring of the delivery, availability and use of medicines in Volyn, Rivne, Vinnytsia and Chernihiv oblasts (paediatric haemophilia; paediatric oncology and haematology)', 26 pp.
- Analytical Report by All-Ukrainian Charity Organisation 'Initiative for Life' (Mykolaiv): 'Public monitoring of the delivery, availability and use of medicines in Mykolaiv and Kherson oblasts (hepatitis B and C; mental and behavioural disorders of autism spectrum, schizophrenia, affective disorders, hyperkinetic disorders in children)', 16 pp.
- Analytical Report by Public Organisation 'Creative Association Nivroku' (Ternopil): 'Public monitoring of the availability, use and timeliness of delivery of medicines procured by UNDP for the budget funds of the Ministry of Health of Ukraine for patients with hepatitis B and C to warehouses and health care facilities of Ternopil, Rivne and Khmelnytskyi oblasts', 15 pp.
- Analytical Report by Public Association 'Orphan Diseases of Ukraine' (Kyiv): 'Public monitoring of the delivery, availability and use of medicines in 24 oblasts of Ukraine, Kyiv and National Specialized Children's Hospital (NSCH) Okhmatdyt (epidermolysis bullosa, pulmonary hypertension, cystic fibrosis in children and adults, mucopolysaccharidosis)', 61 pp.

[11] All reports are available in Ukrainian only.

Appendix

Medicines and medical products investigated in this monitoring

Children with type A or B haemophilia or von Willebrand disease

Blood coagulation factor VIII (recombinant)	250 IU	ReFacto AF
Blood coagulation factor VIII (recombinant)	500 IU	ReFacto AF
Blood coagulation factor VIII (recombinant)	1,000 IU	ReFacto AF
Blood coagulation factor VIII (recombinant)	1,500 IU	NovoEight
Human blood coagulation factor VIII (plasma)	250 IU	Octanate
Human blood coagulation factor VIII (plasma)	500 IU	Emoclot
Human blood coagulation factor VIII (plasma)	1,000 IU	Emoclot
Human blood coagulation factor IX (recombinant)	500 IU	Rixubis
Human blood coagulation factor IX (plasma)	500 IU and/or 600 IU	Aimafix
Human blood coagulation factor VIII and Von Willebrand factor	500 IU	Immunate 500 IU FVIII/ 375 IU VWF
Human blood coagulation factor VIII and Von Willebrand factor	500 IU	Wilate 500 Human coagulation factor VIII and human von Willebrand factor
Human blood coagulation factor VIII and Von Willebrand factor	1000 IU	Immunate 1000 IU FVIII/ 750 IU VWF
Human blood coagulation factor VIII and Von Willebrand factor	1000 IU	Wilate 1000 Human coagulation factor VIII and human von Willebrand factor
Human blood coagulation factor VIII (plasma)	1000 IU	Emoclot
Eptacog alpha (recombinant blood coagulation factor VIIa)	2 mg (100 KIU)	NovoSeven
Eptacog alpha (recombinant blood coagulation factor VIIa)	5 mg (250 KIU)	NovoSeven
Anti-inhibitor coagulant complex	500 IU	Feiba NF 500 IU
Anti-inhibitor coagulant complex	1000 IU	Feiba NF 1000 IU
Desmopressin	15 µg/ml, 1 ml	Octostim
Desmopressin	15 µg/ml, 1 ml	Octostim

Adult haemophilia patients

Human coagulation factor VIII (plasma)	1000 IU	Emoclot 1000 I.U./10 ml Human coagulation factor VIII
Human coagulation factor VIII (plasma)	500 IU	Emoclot, Human coagulation factor VIII (plasma), ampule, vial, syringe, 500 IU
Human coagulation factor VIII (recombinant)	3000 IU	Kogenate Bayer 3000 IU
Human coagulation factor VIII (recombinant)	2000 IU	Kogenate Bayer 2000 IU
Human coagulation factor VIII (recombinant)	1500 IU	NovoEight
Human coagulation factor VIII (recombinant)	1000 IU	ReFacto AF
Human coagulation factor VIII (recombinant)	500 IU	ReFacto AF
Human coagulation factor IX (plasma)	500 IU and/or 600 IU	Aimafix 500 I.U./10 ml

Human coagulation factor IX (plasma)	500 IU and/or 600 IU	Aimafix 500 I.U./10 ml
Human coagulation factor IX (plasma)	1000 IU and/or 1200 IU	Aimafix 1000 I.U./10 ml
Human coagulation factor IX (plasma)	1000 IU and/or 1200 IU	Aimafix 1000 I.U./10 ml
Human coagulation factor IX (recombinant)	500 IU	Rixubis
Human coagulation factor IX (recombinant)	1000 IU	Rixubis
Human coagulation factor VIII and Willebrand factor (factors quotient 1 to 0,75 and more)	1000 IU	Fanhdi® 100 IU/ml
Human coagulation factor VIII and Willebrand factor (factors quotient 1 to 0,75 and more)	500 IU	Fanhdi® 50 IU/ml
Eptacog alfa (recombinant coagulation factor VIIa)	2 mg (100 KIU)	NovoSeven
Eptacog alfa (recombinant coagulation factor VIIa)	5 mg (250 KIU)	NovoSeven
Anti-inhibitor coagulant complex	1000 IU	Feiba NF 1000 IU
Anti-inhibitor coagulant complex	500 IU	Feiba NF 500 IU
Desmopressin	15 micrograms/mL, 1 mL	Octostim

Children with cancer and haematological malignancies

Vincristine	1 mg	Vincristine Teva
Vinorelbine	10 mg	Vinorelbine Vista
Dactinomycin	0.5 mg	Cosmegen Liovak
Doxorubicin	50 mg	Doxorubicin Teva
Etoposide	200 mg	Etoposide Teva
Ifosfamide	1000 mg	Holoxan
Carboplatin	50 mg	Carboplatin
Methotrexate	1000 mg	Methotrexate-Teva
Methotrexate	5000 mg	Methotrexate Ebeve
Rituximab	100 mg	Rixaton
Temozolomide	100 mg	Temodal
Filgrastim	30 million IU	Neutromax
Cyclophosphamide	50 mg	Endoxan
Cytarabine	1000 mg	Cytosar
Cytarabine	100 mg	Cytosar
Asparaginase	10,000 IU	Asparaginase
Mercaptopurine	50 mg	Puri-Netol

Children with mental and behaviour disorders of the autism spectrum, with schizophrenia, affective disorders, hyperkinetic disorders

Risperidone	1 mg/mL	Risset
Risperidone	1 mg	Rispetril
Risperidone	2 mg	Rispetril
Olanzapine	5 mg	Zolafren
Atomoxetine	10 mg	Monsetin 10
Atomoxetine	18 mg	Monsetin 18
Atomoxetine	25 mg	Monsetin 25
Atomoxetine	40 mg	Monsetin 40
Atomoxetine	60 mg	Monsetin 60
Valproic acid salts	1 ml/57.64 mg	Depakine
Valproic acid salts	300 mg	Valprocom 300 Chrono
Valproic acid salts	500 mg	Valprocom 500 Chrono
Levetiracetam	1 ml/100 mg	Levetiracetam Grindeks
Levetiracetam	250 mg	Levetiracetam Grindeks
Levetiracetam	500 mg	Levetiracetam Grindeks
Lamotrigine	50 mg	Lamictal
Lamotrigine	100 mg	Lamictal

Patients with viral hepatitis B and C

PEG- interferon α-2a	180 µg	Pegferon
Tenofovir	300 mg	Tenofovir Disoproxil Fumarate
Lamivudine	100 mg	Zeffix
Ribavirin	200 mg	Copegus
Sofosbuvir	400 mg	Myhep
Ombitasvir/ Paritaprevir/ Ritonavir	12.5 mg/75 mg/50 mg	Vylvio
Dasabuvir	250 mg	Vyrelakir
Sofosbuvir/Ledipasvir	400 mg/90 mg	Ledvir
Daclatasvir	60 mg	My Decla
Sofosbuvir/Velpatasvir	400 mg/100 mg	Myhep All

Children suffering from resistant form of juvenile rheumatoid arthritis

Adalimumab	40 mg of adalimumab in 0.8 ml solution	Humira
Adalimumab	40 mg of adalimumab in 0.8 ml solution	Humira
Tocilizumab	80 mg/4 ml	Aktemra
Tocilizumab	80 mg/4 ml	Aktemra
Tocilizumab	200 mg/10 ml	Aktemra
Tocilizumab	200 mg/10 ml	Aktemra
Etanercept	50 mg / ml in pre-filled 0.5 ml syringes (25 mg)	Enbrel®
Etanercept	50 mg / ml in pre-filled 0.5 ml syringes (25 mg)	Enbrel®
Etanercept	50 mg / ml in pre-filled 1 ml syringes (50 mg)	Enbrel®
Etanercept	50 mg / ml in pre-filled 1 ml syringes (50 mg)	Enbrel®

Reagents for mass screening of newborns for phenylketonuria, congenital hypothyroidism, cystic fibrosis and adrenogenital syndrome

Test set for newborn screening for phenylketonuria from blood spots dried on filter paper	Test kit for screening newborns for phenylketonuria in samples of blood dried on filter paper Neonatal Phenylalanine, 960 tests Labsystems, Diagnostics
Test set for newborn screening for phenylketonuria from blood spots dried on filter paper	Test kit for screening newborns for phenylketonuria in samples of blood dried on filter paper Neonatal Phenylalanine, 960 tests Labsystems, Diagnostics
Test set for newborn screening for phenylketonuria from blood spots dried on filter paper	Test kit for screening newborns for phenylketonuria in samples of blood dried on filter paper Neonatal Phenylalanine, 960 tests Labsystems, Diagnostics
Test set for newborn screening for congenital hypothyroidism from blood spots dried on filter paper	Set for newborn screening for congenital hypothyroidism Neonatal hTSH FEIA Plus, 960 tests, Labsystems, Diagnostics
Test set for newborn screening for phenylketonuria from blood spots dried on filter paper	Test kit for screening newborns for phenylketonuria in samples of blood dried on filter paper Neonatal Phenylalanine, 960 tests Labsystems, Diagnostics
Test set for newborn screening for congenital hypothyroidism from blood spots dried on filter paper	Set for newborn screening for congenital hypothyroidism Neonatal hTSH FEIA Plus, 960 tests, Labsystems, Diagnostics
Test set for newborn screening for congenital hypothyroidism from blood spots dried on filter paper	Set for newborn screening for congenital hypothyroidism Neonatal hTSH FEIA Plus, 960 tests, Labsystems, Diagnostics
Test set for newborn screening for congenital hypothyroidism from blood spots dried on filter paper	Set for newborn screening for congenital hypothyroidism Neonatal hTSH FEIA Plus, 960 tests, Labsystems, Diagnostics
Test set for newborn screening for cystic fibrosis from blood spots dried on filter paper	Test kit for newborn screening for cystic fibrosis in samples of blood dried on filter paper, Neonatal IRT FEIA 960 tests, Labsystems, Diagnostics
Test set for newborn screening for cystic fibrosis from blood spots dried on filter paper	Test kit for newborn screening for cystic fibrosis in samples of blood dried on filter paper, Neonatal IRT FEIA 960 tests, Labsystems, Diagnostics
Test set for newborn screening for cystic fibrosis from blood spots dried on filter paper	Test kit for newborn screening for cystic fibrosis in samples of blood dried on filter paper, Neonatal IRT FEIA 960 tests, Labsystems, Diagnostics
Test set for newborn screening for cystic fibrosis from blood spots dried on filter paper	Test kit for newborn screening for cystic fibrosis in samples of blood dried on filter paper, Neonatal IRT FEIA 960 tests, Labsystems, Diagnostics
Test set for newborn screening for adrenogenital syndrome from blood spots dried on filter paper	Test kit for newborn screening for adrenogenital syndrome in samples of blood dried on filter paper DELFIA® Neonatal 17α-OH-progesterone kit 960 tests,Wallac
Test set for newborn screening for adrenogenital syndrome from blood spots dried on filter paper	Test kit for newborn screening for adrenogenital syndrome in samples of blood dried on filter paper DELFIA® Neonatal 17α-OH-progesterone kit 960 tests,Wallac
Test set for newborn screening for adrenogenital syndrome from blood spots dried on filter paper	Test kit for newborn screening for adrenogenital syndrome in samples of blood dried on filter paper DELFIA® Neonatal 17α-OH-progesterone kit 960 tests,Wallac
Test set for newborn screening for adrenogenital syndrome from blood spots dried on filter paper	Test kit for newborn screening for adrenogenital syndrome in samples of blood dried on filter paper DELFIA® Neonatal 17α-OH-progesterone kit 960 tests,Wallac

Kit to identify the most common mutations in the CFTR gene by the LIPA method	Kit to identify the most common mutations in the CFTR gene by the LIPA method 4-410 CF StripAssay by ViennaLab Diagnostics GmbH
Kit to identify the most common mutations in the CFTR gene by the LIPA method	Kit to identify the most common mutations in the CFTR gene by the LIPA method 4-410 CF StripAssay by ViennaLab Diagnostics GmbH
Paper test blanks for blood collection from newborns	Paper test-blanks for blood sampling from newborns 903 Ukraine Neonatal Card виробництва EBF, Inc.
Immunological plates with U-form bottom	Immunoassay plate with U-type bottom Microtest Plate 96 Well, R, Sarstedt AG & Co.

Orphan diseases

Epidermolysis bullosa

Elastic fixing bandage Batist FIXA-CREP 12 sm *4 m or equivalent	1 bandage	FIXA - CREP 12cm x 4m
Mepilex Lite 20 x 50 cm (dressing for open wounds, sterile) or equivalent	1 bandage	Mepilex® Lite 20 x 50 cm
Mepilex Transfer 20 x 50 cm (dressing for open wounds, sterile) or equivalent	1 bandage	Mepilex® Transfer 20 x 50 cm
Mepitel 10 x 18 cm (dressing for open wounds, sterile) or equivalent	1 dressing	Mepitel® 10 x 18 cm
Sterile dressing Tubifast Red Line 10m or equivalent	1 bandage	Tubifast® Red line 10 m
Sterile dressing Tubifast Green Line 10m or equivalent	1 bandage	Tubifast® Green line 10 m
Sterile dressing Tubifast Blue Line 10m or equivalent	1 bandage	Tubifast® Blue line 10 m
Sterile dressing Tubifast Yellow Line 10m or equivalent	1 bandage	Tubifast® Yellow line 10 m
Sterile dressing Tubifast Purple Line 10m or equivalent	1 bandage	Tubifast® Purple line 10 m
Nonwoven wipe, sterile Mesoft 10x10 sm (2 pcs) #150 or equivalent	1 pack (150 pcs)	Medicomp® 10 x 10 cm
Elastic fixing bandage Batist FIXA-CREP 4 sm *4 m or equivalent	1 bandage	FIXA - CREP 4cm x 4m
Elastic fixing bandage Batist FIXA-CREP 4 sm *4 m or equivalent	1 bandage	FIXA - CREP 4cm x 4m
Elastic fixing bandage Batist FIXA-CREP 6 sm *4 m or equivalent	1 bandage	FIXA - CREP 6cm x 4m
Elastic fixing bandage Batist FIXA-CREP 8 sm *4 m or equivalent	1 bandage	FIXA - CREP 8cm x 4m
Elastic fixing bandage Batist FIXA-CREP 10 sm *4 m or equivalent	1 bandage	FIXA - CREP 10cm x 4m

Pulmonary arterial hypertension

Iloprost	10 µg / ml, 2 ml	Ventavis
Sildenafil	20 mg	Revatio®
Bosentan	62.5 mg	Bosentan-Sandoz
Bosentan	125 mg	Bosentan-Sandoz
Riociguat	1 mg	Adempas
Riociguat	2 mg	Adempas
Riociguat	2.5 mg	Adempas
Ambrisentan	5 mg	Volibris
Ambrisentan	10 mg	Volibris

Cystic fibrosis – Children

Dornase alpha	2.5 mg/2.5 mL in ampule	Pulmozyme®
Pancreatin	10,000 Units in one capsule	Creon 10,000
Pancreatin	25,000 Units in one capsule	Creon 25,000
Colistimethate Sodium	2 million IU	Colomycin injection

Cystic fibrosis – Adults

Dornase alpha	2.5 mg/2.5 ml, in ampules	Pulmozyme
Pancreatine	25,000 units per capsule	Kreon® 25,000

Mucopolysaccharidosis

Laronidase	100 Unit/mL	Aldurazyme
Laronidase	100 Unit/mL	Aldurazyme
Laronidase	100 Unit/mL	Aldurazyme
Laronidase	100 Unit/mL	Aldurazyme
Idursulfase	2 mg/mL	Elaprase
Idursulfase	2 mg/mL	Elaprase
Idursulfase	2 mg/mL	Elaprase
Galsulfase	1 mg/mL	Naglazyme
Galsulfase	1 mg/mL	Naglazyme
Elosulfase alpha	1 mg/mL	Vimizim
Elosulfase alpha	1 mg/mL	Vimizim

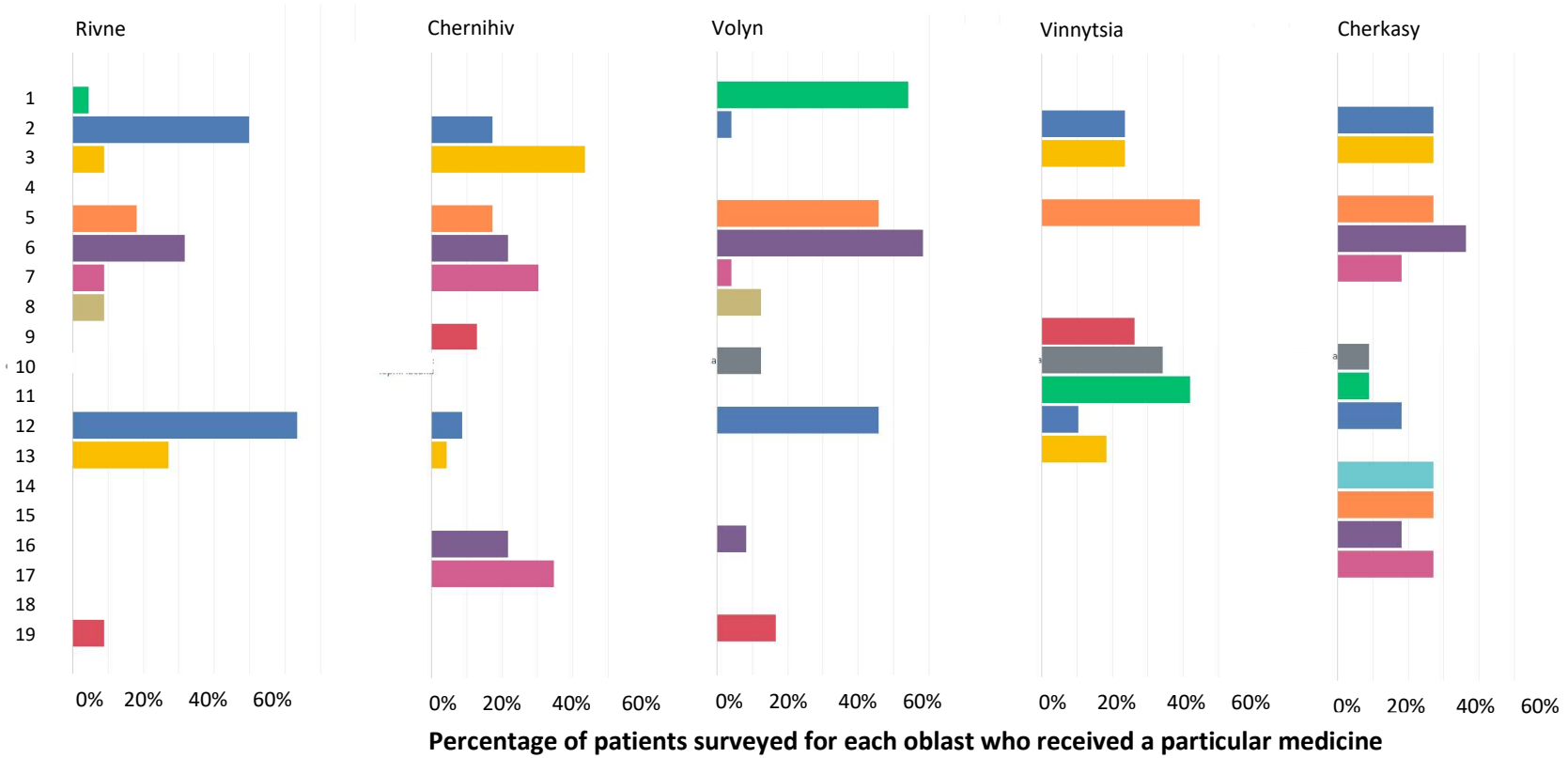

Figure 11. Nomenclature and relative quantity of medicines used to treat haemophilia in children in the oblasts studied

1 – Blood coagulation factor VIII (recombinant) 250 IU, 2 – Blood coagulation factor VIII (recombinant) 500 IU, 3 – Blood coagulation factor VIII (recombinant) 1000 IU, 4 – Blood coagulation factor VIII (recombinant) 1500 IU, 5 – Human blood coagulation factor VIII (plasma) 250 IU, 6 – Human blood coagulation factor VIII (plasma) 500 IU, 7 – Human blood coagulation factor VIII (plasma) 1000 IU, 8 – Human blood coagulation factor XI (recombinant) 500 IU 9 – Factor IX human blood coagulation (plasma) 500 IU and/or 600 IU, 10 – Human blood coagulation factor VIII and human von Willebrand factor 500 IU, 11 – Human blood coagulation factor VIII and human von Willebrand factor 500 IU, 12 – Human blood coagulation factor VIII and human von Willebrand factor 1000 IU, 13 – Human blood coagulation factor VIII and human von Willebrand factor 1000 IU, 14 – Eptacog alpha (recombinant blood coagulation factor VIIa) 2 mg (100 KMO), 15 – Eptacog alpha (recombinant coagulation factor VIIa) 5 mg (250 KMO), 16 – Anti-inhibitory coagulant complex 500 IU, 17 – Anti-inhibitory coagulant complex 1000 IU FEIBA, 18 – 15 µg/ml, 1 ml, 19 – other.

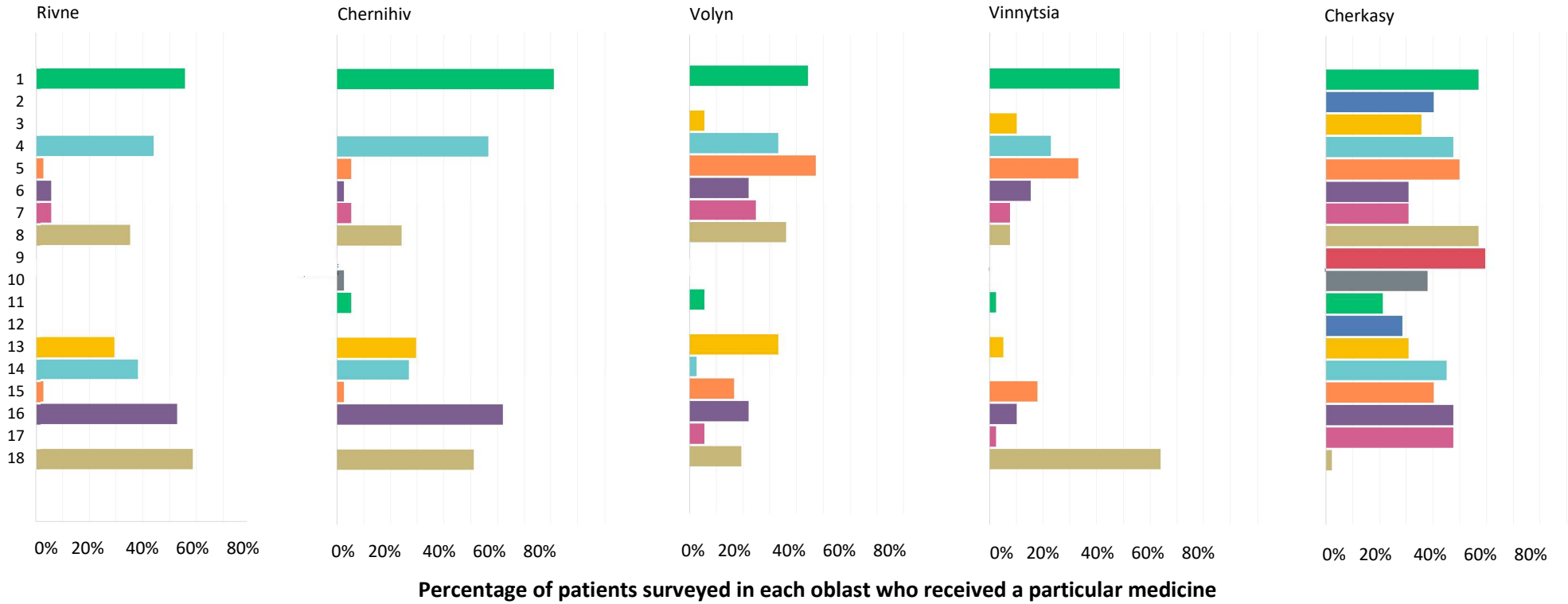

Figure 12. Nomenclature and relative quantity of medicines used to treat cancer in children in the oblasts studied

1 – vincristine, 2 – vinorelbine, 3 – dactinomycin, 4 – doxorubicin, 5 – etoposide, 6 – ifosfamide, 7 – carboplatin,
8 – methotrexate 1000, 9 – methotrexate 5000, 10 – rituximab, 11 – temozolomide 100, 12 – filerastim ,
13 – cyclophosphamide, 14 – cytarabine 1000, 15 – cytarabine 100, 16 – asparaginase, 17 – mercaptopurine, 18 – other

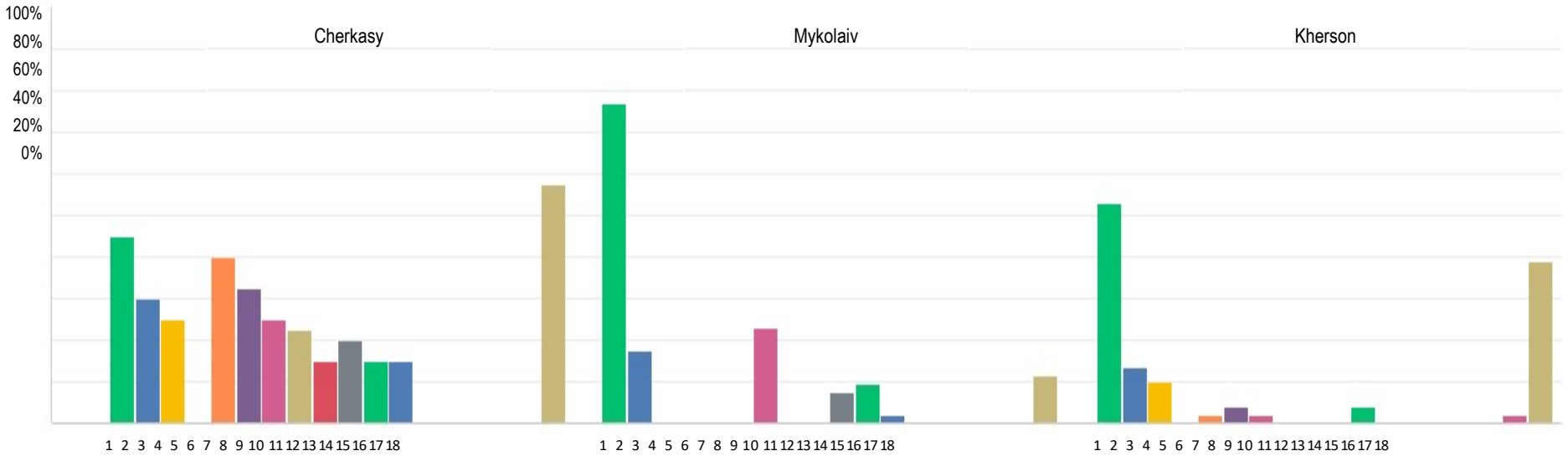

Figure 13. Nomenclature and relative quantity of medicines used for treatment of mental and behavioural disorders in children in the oblasts studied

1 – Risperidone, oral solution, 1 mg/ml, 2 – Risperidone, tablets, 1 mg, 3 – Risperidone, tablets, 2 mg, 4 – Olanzapine, tablets, 5 mg, 5 – Atomoxetine, capsules, 10 mg, 6 – Atomoxetine, capsules, 18 mg, 7 – Atomoxetine, capsules, 25 mg, 8 – Atomoxetine, capsules, 40 mg, 9 – Atomoxetine, capsules, 60 mg, 10 – Valproic acid salts, syrup, 1 ml/57,64 mg, 11 – Valproic acid salts, tablets, 300 mg, 12 – Valproic acid salts, tablets, 500 mg, 13 – Levetiracetam, oral solution, 1 ml/100 mg, 14 – Levetiracetam, tablets, 250 mg, 15 – Levetiracetam, tablets, 500 mg, 16 – Lamotrigine, dispersible tablets, 50 mg, 17 – Lamotrigine, dispersible tablets, 100 mg, 18 – other.
Note: The vertical axis indicates the percentage of patients interviewed for each area who received a particular medicine.

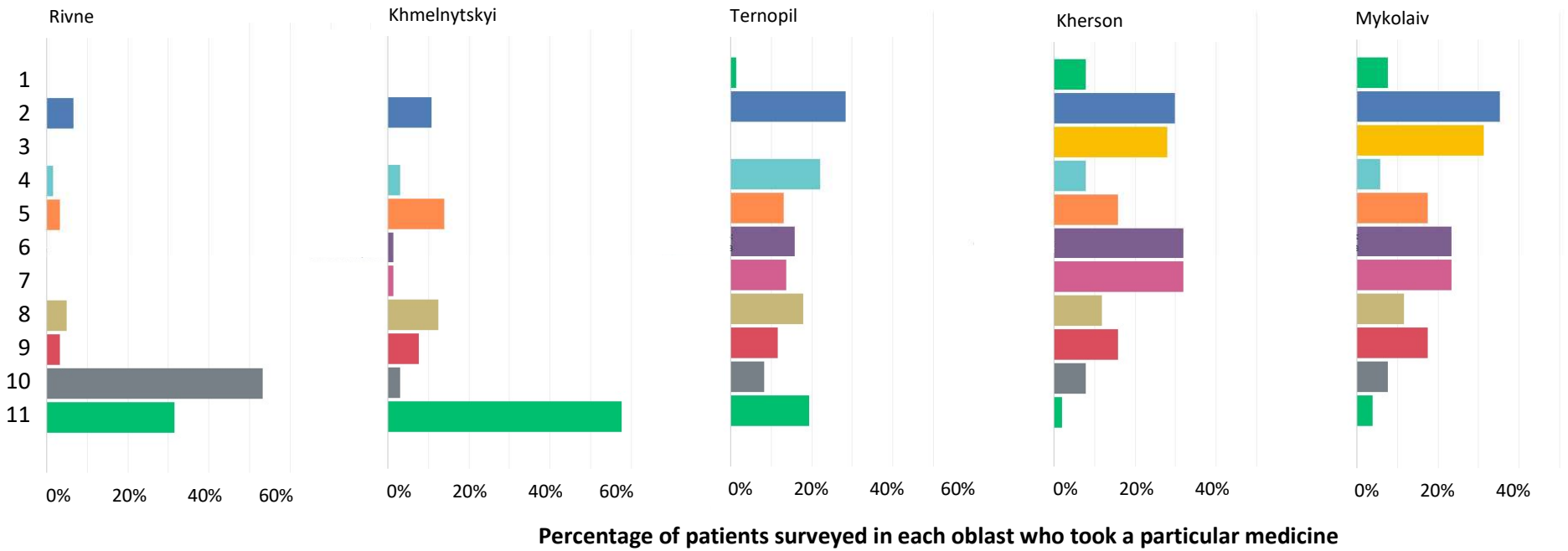

Figure 14. Nomenclature and relative quantity of medicines used to treat viral hepatitis in the oblasts studied

1 – Peginterferon α – 2a, 2 – Tenofovir, 3 – Lamivudine, 4 – Ribavirin, 5 – Sophosbuvir, 6 – Ombitasvir/Paritaprevir/Ritonavir, 7 – Dasabuvir, 8 – Sophosbuvir/Ledipasvir, 9 – Daclatasvir, 10 – Sophosbuvir/Velpatasvir, 11 – other

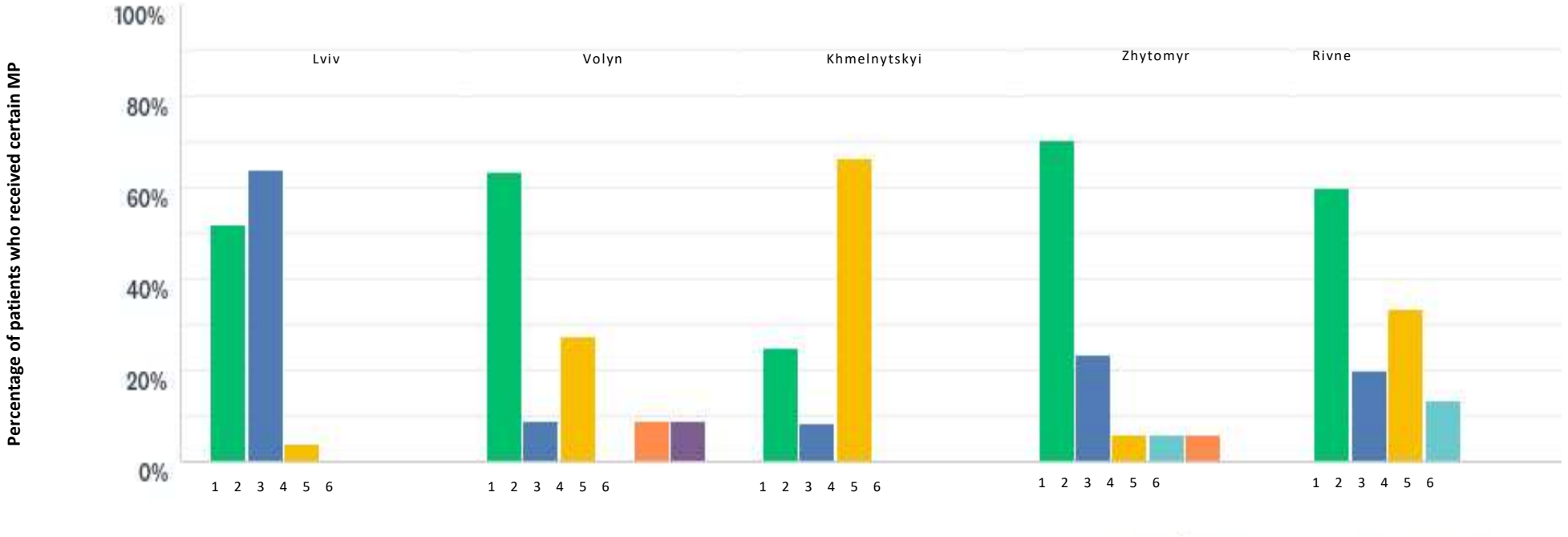

Figure 15. Nomenclature and relative number of medicines ordered for treatment of JRA in the oblasts studied

1 – Adalimumab, 2 – Tocilizumab, 80 mg, 3 – Tocilizumab, 200 mg, 4 – Etanercept, 25 mg, 5 – Etanercept, 50 mg, 6 – other.