



Building cancer registries in a lower resource setting: The 10-year experience of Golestan, Northern Iran

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ABSTRACT

Introduction: The Golestan population-based cancer registry (GPCR) was established in Golestan province, Northern Iran, within the Asian belt with predominance of upper-gastrointestinal cancers. We aimed to present the experiences of the registry in a resource-limited setting over the 10 years since its inception (2004–2013). **Methods:** The GPCR was established as a research project to enable sustainable funding. A clear plan was developed for use of the GPCR data. New primary cancers were registered based on international standards, indices of data quality were routinely assessed and age-standardized incidence rates (ASR) per 100,000 person-years calculated using IARC's CanReg-5 software.

Results: Overall, 19807 new cancer cases were registered during the study period, an average of 1981 cases per annum, with overall ASR of 175.0 and 142.4 in males and females, respectively. The GPCR data suggested gastrointestinal and breast cancers as the most common malignancies in Golestan province. We observed increasing incidence rates of breast and colorectal cancers but declining trends of esophageal cancer. Overall, indices of data quality were within acceptable ranges.

Conclusions: The GPCR data have been included in IARC's *Cancer Incidence in Five Continents* series, were used in 21 research projects, and published as 30 research papers. The key ingredients for the successful establishment and maintenance of the GPCR included sustainable sources of funding, a clear action plan for the use of data as well as stakeholder cooperation across all areas of the registration. The GPCR may be considered as a model for planning population-based cancer registries in lesser-resourced settings.

1. Background

According to worldwide data available in the GLOBOCAN series of

the International Agency for Research on Cancer (IARC), 14.1 million new cases of cancers and 8.2 million cancer-related deaths occurred in 2012 [1]. During the last decades, the number of cancer cases have

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certainly increased, in part due to population ageing and growth, increasing the priority for operational national cancer control programs. Access to epidemiological data from population based cancer registries on the scale and profile of new cancer cases and deaths is a cornerstone in cancer control planning.

The first population-based cancer registries were initiated in the 1920s in Europe and the U.S. some years later [2]. The formal relations developed between the International Agency for Research on Cancer (IARC) and the International Association of Cancer Registries (IACR) in the early-1970s, meant cancer registration activities were advocated according to internationally accepted protocols and standards. According to the *Cancer in Five Continents* (CI5) Volume X, there were more than 290 population-based cancer registries considered of high quality in 68 countries worldwide, but most of these registries are from developed countries [3].

The Golestan province of Northern Iran has been known as a high risk area for upper gastrointestinal cancers since the 1970s [4,5]. Determining the underlying risk factors of these cancers has historically been a major challenge for health authorities in this high risk region during recent decades. To address this, the “Gastric and Esophageal Malignancies in Northern Iran” (GEMINI) project was conducted by the Digestive Diseases Research Institute (DDRI) in collaboration with the IARC, the National Cancer Institute (NCI) and Golestan University of Medical Sciences (GOUMS) [6]. The GEMINI project consisted of a series of studies including case-control studies, ecological studies, screening studies and the Golestan Cohort Study (GCS). Establishment of cancer registry was considered as a prerequisite condition to conduct these studies, especially the GCS. To meet this requirement and as a first step to cancer control in this high-risk population, the Golestan Population-Based Cancer Registry (GPCR) was established to provide reliable cancer statistics to GEMINI research group as well as to local and national health policy makers. The GPCR data were published in the CI5 and the registry was accepted as a voting member by the IACR in 2007 [3]. Early results of the GPCR have published previously [7,8]; in this paper we describe the process of establishing and maintaining the GPCR. By sharing the 10-year experience of the GPCR, we hope to provide a practical example on how a population-based cancer registry can flourish in a low resource setting.

2. Methods

2.1. Registration area

The GPCR covers the population of Golestan province, located in the northeast of Iran. The total land area of the province is 20438 km², about 1.3% of total land area of Iran and about half of the population lives in urban areas. Almost all cancer-related diagnostic and therapeutic services including cancer surgery (open and laparoscopic surgeries), radiotherapy, chemotherapy, CT-scan, MRI, upper endoscopy, colonoscopy, sonography, mammography and pathological examinations are provided within the province. There are seven referral hospitals in covering the Western and Eastern parts of the province.

2.2. Population data

National population censuses are officially undertaken every five years by the Iranian Statistical Center, with the last census done in 2016. In addition, provincial population census is officially done every year by the Deputy of Health of GOUMS. There are only minor differences between the national population census data and those for the provincial population; we therefore used the latter in our registry, given the data were consistently available for all individual years.

2.3. Source of funding

Access to permanent and stable financial support was an important

challenge in the establishment and maintenance of the GPCR. We assessed different scenarios and were able to attain research grants as a means of sustainably funding the GPCR; we conducted the GPCR as a research project that was later approved by the GOUMS review board.

Another key aspect of the registry’s development was to ensure comprehensive cooperation of the stakeholders involved the registration process. We invited motivated healthcare professionals, in both the public and private sectors, as well as staff from the health, research, treatment, information technology and food/drug domains within the GOUMS to join as GPCR collaborators; as a stakeholders’ group, the GPCR collaborators were given priority access to the GPCR data.

2.4. Organization of the GPCR

The GPCR was established by the Golestan Research Center of Gastroenterology and Hepatology (GRCGH), affiliated to GOUMS, under the supervision of DDRI affiliated to Tehran University of Medical Sciences (TUMS). The GPCR included a steering committee comprising the principal investigators (PIs) of the GPCR research project and the Chancellor of GOUMS. A Secretariat consisted of representatives from GRCGH, the stakeholders listed above, as well as a consultant pathologist and an epidemiologist.

2.5. Study design

The GPCR included two phases with different designs for data collection. During the first phase (in 2001), data on cancer patients diagnosed between 1996 and 2000 were retrospectively collected and the results published [8]. After a few years where the registry ceased to function, a second (prospective) phase of GPCR data collection began in 2004, as a population-based cancer registry. In the present paper, we focus on a 10-year prospective phase of the GPCR: from 2004 to 2013.

2.6. Definitions, rules and standards

The GPCR registered only primary cancers, with all definitions and protocols of data collection were defined according to standards and rules developed by the IARC and IACR, including multiple primary rules [9–11]. We aimed to register tumors with malignant or in situ behaviors. In other words, the GPCR did not register tumors with benign or uncertain behaviors. Based on IARC and IACR guidelines, certain patient and tumor characteristics were considered as necessary items for data collection. These included patient’s registration number, first name, last name, sex, age and address as well as topography of tumor, morphology and behavior of tumor, method of diagnosis, date of diagnosis and source of data. The GPCR also collected available data on optional items including patients’ national identification number, father’s name, ethnicity, marital status and phone number as well as grade of tumor, modalities of treatment, vital status and date of death. The GPCR data collection form was developed to ensure the collection of the above-mentioned variables.

2.7. Sources of data

We determined all potential sources of data including health care centers throughout the province. This information was obtained from the deputy of treatment affairs of the GOUMS and the list was updated annually. All public and private diagnostic and therapeutic centers (hospitals, pathology/laboratory centers, imaging centers and selected specialist physician’s offices) as well as primary health centers throughout the Golestan province were considered as potential sources of data.

The Death registry unit was another source of the data; the GPCR regularly received information on cancer-related deaths from this unit housed within the health department of GOUMS. We matched this data against the incident cancer case file using linkage methods to identify

unreported cases; these were then registered as death certificate only (DCO) cases. We also collected information on cancer patients referred to healthcare centers outside the registration area. The GPCR regularly received data from sources in neighboring provinces, particularly in Tehran, Khorasan Razavi and Mazandaran to minimize under-ascertainment.

2.8. Data collection methods

The next step was to ensure dedicated cancer registry collaborators were available to support collection from each source. We aimed to find interested personnel from healthcare centers and invite them to collaborate with the GPCR as abstractors; we were able to assign abstractors in 65% of GPCR sources. Among these sources, data were collected passively, i.e., notifications of newly-diagnosed cancer cases were sent to the GPCR office on a routine, and continuing basis. In the remaining 35% of sources for which we could not find an abstractor, active data collection methods were required. GPCR staff regularly visited these sources to directly collect information on cancer cases. All abstractors and GPCR staff were trained in dedicated cancer registry workshops. After training GPCR abstractors and staff, the process of data collection commenced using the GPCR data collection forms.

2.9. Coding systems, data entry and analysis

Data on patients' place of resident was collected as a necessary item. At the time of data entry, addresses were coded using an official list of divisions and subdivisions of Iran (including the name of all provinces, cities, towns and villages). We obtained this list from the Statistical Center of Iran (SCI). At the time of analysis, all cases with address codes within the registration area of Golestan province were entered into the analysis and subjects with address codes outside this area excluded.

The third edition of the International Classification of Diseases for Oncology (ICD-O-3) was used for coding tumor characteristics, including topography, morphology, behavior and grade [12]. Data were entered into CanReg-4, a free software created and published by the IARC [13]; the system is being upgraded to the newer CanReg-5; the data were analyzed using the latter software [14]. The GPCR routinely reports indices of the quality of data, as well as the number of cases, age-specific rates, crude rates and age-standardized incidence rates (ASR) using the Segi-Doll world population [15]. In the present paper, as with international projects including CI5, only tumors with malignant behavior were included in the analysis to ensure comparability of the results.

2.10. Quality of data

We routinely calculated and controlled different indices of quality of data including the proportion of cases with microscopic verification (MV%), cases diagnosed only by death certificate (DCO%), cases with unknown age, and cases with unknown primary site. In addition, 10% of the collected data were re-checked and compared with original documents in selected sources to verify the completeness and accuracy of the abstraction process.

2.11. Use of the data

As is central to all cancer registries, the main aim of the GPCR is to provide accurate data on cancer patients to health policy makers. Therefore, the GPCR data were annually analyzed and annual reports provided to GOUMS authorities as well as to all stakeholders. The GPCR data were also used to conduct research projects; most of these were resulted in national and international collaborations between GRCGH and GOUMS with different universities, institutes and organizations. We developed a clear plan for use of the GPCR data by external users. Briefly, applicants were asked to provide a short research proposal to

the research council of the GRCGH. After a peer-review and approval process undertaken by the GRCGH research council, data on requested variables were provided to the principal investigator of the study. The study plan and general information on the available data were announced to researchers and all other potential stakeholders inside and outside the GOUMS.

2.12. Ethical considerations

The protocol of all GPCR research projects were approved by the ethics committee of GOUMS. All GPCR staff were trained to appropriately consider confidentiality in all stages of the registration process, including data collection, transmission, access to and storage of data, data usage and record linkage. Confidentiality measures were used to ensure the preservation of anonymity of cancer cases, as well as the optimal quality and use of the registry data. On receipt of a research proposal requesting use of the GPCR data, if the protocol involved analysis of available data, there was no need for ethical approval; if however, investigators aimed to collect additional data on cancer patients, they had to apply for new approval from GOUMS ethics committee in addition to scientific approval by the GRCGH research council.

3. Results

3.1. New cases and incidence rates

The total number of new cancer cases registered at the GPCR 2004–2013 was 19807, 10577 diagnoses (53.4%) in males and 9230 (46.6%) in females. The median (inter-quartile range) age of cancer patients was 58 (44–70) years. The ASR of cancers were 175.0 and 142.4 in males and female, respectively, with cancers of the stomach, esophagus, colorectum, lung as well as leukemia, the most common cancers in men. In women, cancers of the breast, esophagus, colorectum, stomach and leukemia were the top five malignancies. Table 1 shows incident cases, age-specific rates and ASRs (per 100,000 persons-year) for the 10 most common cancers in Golestan province during the study period. Figs. 1 and 2 show the temporal variations of the ASR of the five highest ranking cancers in the province between 2004 and 2013.

3.2. Quality of data

Table 2 shows the temporal variations in indices of quality of GPCR data during the study period. The DCO and MV proportions were 7.4% and 73.2% of cases, respectively. The MV% increased from 62.5% in 2004 to 77.5% in 2013. In contrast a decreasing trend was observed for the DCO%, from 21.2% in 2004 to 4.7% in 2013.

3.3. Use of the data

The GPCR data were used to conduct 21 research projects including 13 student thesis (MSc, MD and PhD) and eight collaborative research papers. The results of these projects as well as other related works were published in more than 30 research articles, mostly in international journals. In addition, the GPCR data were used in different international collaborative projects. Our data were compiled in recent CI5 Volumes [3], as well as the third Volume of the International Incidence for Childhood Cancer (IICC-3) [16].

4. Discussion

Population-based cancer registries are a cornerstone of cancer control planning, yet their development remains a major challenge in LMIC. The aim of this paper was to demonstrate how the GPCR as a subnational PBCR was established with the appropriate degree of

Table 1

Incident cases, age-specific and age standardized incidence rates (ASRs) (per 100,000 persons-year) for the 10 most common cancers in Golestan province 2004–2013 by sex (Source: GPCR).

Gender	Organ	Number	%	Age specific rate						Crude rate	ASR	
				0-14 years	15–24 years	25–34 years	35–44 years	45–54 years	55–64 years			> =65 years
Male	Stomach	1576	15.8	0.0	0.4	3.3	16.0	59.4	188.2	1289.6	18.4	27.4
	Esophagus	1221	12.3	0.0	0.6	1.5	12.9	50.6	151.5	962.2	14.2	21.6
	Colorectal	911	9.2	0.0	1.5	6.8	23.1	57.7	104.9	487.3	10.6	14.9
	Lung	907	9.1	0.1	0.8	2.8	12.9	39.9	130.0	590.9	10.6	16.0
	Leukemia	817	8.2	14.9	7.9	7.5	15.8	33.9	65.4	327.4	9.5	12.3
	Prostate	690	6.9	0.1	0.1	0.3	0.9	11.4	52.9	931.3	8.0	12.0
	Skin	661	6.6	0.8	1.0	2.8	9.3	25.2	86.9	537.6	7.7	11.4
	Lymphoma	567	5.7	4.2	7.5	9.1	12.7	28.8	44.4	170.2	6.6	8.0
	Bladder	529	5.3	0.0	0.8	1.8	5.1	25.3	69.0	428.6	6.2	9.2
	Nervous system	475	4.8	5.0	4.9	7.9	13.6	22.5	42.0	112.1	5.5	6.9
Female	Breast	2121	24.0	0.0	5.3	36.4	116.8	179.5	140.6	274.3	25.1	29.3
	Esophagus	930	10.5	0.0	0.4	1.6	7.3	39.2	122.0	720.2	11.0	16.8
	Colorectal	715	8.1	0.0	1.6	7.5	15.2	53.1	80.8	322.1	8.5	11.6
	Stomach	686	7.8	0.0	0.3	3.1	10.1	28.1	75.9	532.7	8.1	12.0
	Leukemia	599	6.7	10.3	4.7	6.3	12.3	29.8	48.9	216.7	7.1	9.1
	Skin	416	4.7	0.2	0.4	2.5	8.1	22.7	47.2	270.5	4.9	7.1
	Ovary	400	4.5	0.6	2.7	5.7	16.6	26.2	38.5	78.7	4.7	5.7
	Nervous system	369	4.2	3.7	3.1	6.7	10.7	18.7	30.6	104.1	4.4	5.3
	Lung	362	4.1	0.4	0.8	2.3	5.4	14.4	39.8	260.4	4.3	6.2
	Lymphoma	333	3.8	2.1	5.5	7.6	8.8	11.6	25.8	84.2	3.9	4.5

financing and human resources, present summary results over the first decade, and to review the specific determinants that have ensured the sustainability of the GPCR during the first 10 years. This hopefully aids health planners in other LMIC in developing such institutions to develop the necessary data to inform cancer policy.

Similar to previous reports from this region of Iran [7,8], we found declining trends in the incidence of esophageal cancer (Figs. 1 and 2). But, despite this declining trend, cancers of the esophagus and stomach remained the leading malignancies in this population, especially among males (Table 1). These cancer statistics were useful in designing the GCS, a large-scale prospective cohort study of more than 50,000 participants [17,18]. Findings from the GCS revealed an array of different risk factors for these cancers in this high-risk population including hot tea [19], smoking and opium consumption [20,21], obesity [22], poor oral hygiene [23], socioeconomic status [24], diet-related habits and behaviors [25,26]. The results of the GPCR and GCS were provided to GOUMS officials and other stakeholders to be considered in designing specific cancer control program in this population.

Malignancies of the colorectum, breast (in female) and lung (in male) were also among the most common cancers observed in the Golestan province (Table 1), with increasing incidence rates of these cancers during the study period (Figs. 1 and 2). Similar temporal patterns have been reported in other populations [27]. The increasing prevalence of well-known modifiable lifestyle-related risk factors

including obesity, dietary habits, low physical activity and smoking are among the most probable explanatory factors for these trends [27,28]. With such patterns and trends brought to light using the GPCR data, the need to design effective primary prevention programs aimed at reducing or an elimination of the candidate risk factors, as well as suitable secondary prevention programs should be considered a priority in instigating cancer control policies in the region.

Our findings suggested relatively poor quality for the GPCR data during earlier years of its activity. As shown in Table 2 however, data quality indices have improved and reached desirable levels in the later part of the study period. The proportions of cases with unknown primary site were within acceptable ranges [3] during the study period. The highest proportion was found in first year (2004). Then, after a declining trend during 2005–2009, there was a second peak in the years 2010–2011. Although we could not find evidence to clearly explain these trends, the addition of new sources of data as well as recruitment of additional registrars may be considered possible explanations. Irrespectively, the differences were not considerable (about 2–3 percent) and are not likely to have negative effects on the quality of the GPCR data. According to a quality evaluation, the GPCR can be considered as a high quality population-based cancer registry. Comparing data quality indicators at the GPCR relative to those from other high-quality cancer registries in the region [3], the MV% and DCO% were within acceptable ranges. In addition, as part of the GPCR's quality control

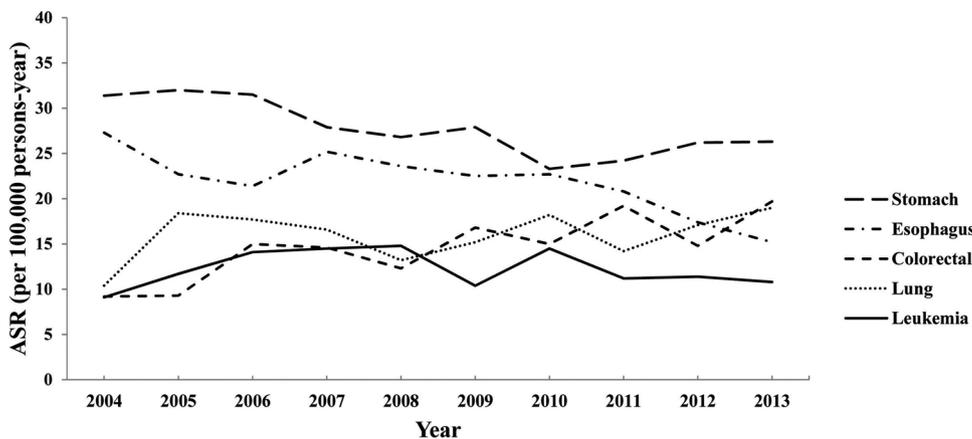


Fig. 1. Temporal variations in age standardized incidence rates (ASR) of five common cancers in Golestan province during 2004 and 2013-Males.

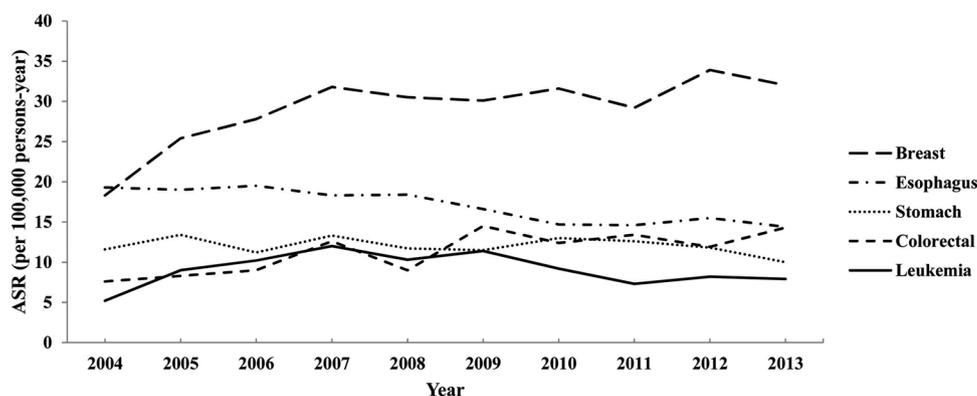


Fig. 2. Temporal variations in age standardized incidence rates (ASR) of five common cancers in Golestan province during 2004 and 2013-Females.

program, research projects with different methodologies including capture-recapture were conducted [29], resulting in encouraging findings with regards the completeness of the GPCR data. Finally, inclusion of the GPCR data in the CI5 series [3] is a broad indicator of the quality of the GPCR data.

We routinely used the GPCR data to prepare annual reports for health policy makers in GOUMS, as well as other stakeholders. In addition, the data were used for conducting international research projects with different designs, including case-control, cross-sectional, survival analysis and diagnostic accuracy studies. The results of these studies were published in different local and international journals [7,8,29–57]. The GPCR data were also used in GEMINI studies, especially in the GCS. Close collaboration between the GPCR with the GEMINI was a great opportunity for the GPCR progress and it was mutually supported by the GEMINI. These processes should collectively result in an improvement of the GPCR data.

A clear operational plan for the use of registry data role is essential in the sustained development of cancer registries. We defined a specific strategy that ensured the GPCR data and reports were made available to all stakeholders, including the research community. Other determinants supporting the continuity of the GPCR included safeguarding sustainable sources of funding and comprehensive collaborations across all sections of the GOUMS. To achieve this, the GPCR was conducted as a research project; the GPCR research proposal allowed access to appropriate funding in the form of research grants. In addition, the privilege of being a collaborator in the GPCR research project was a strong incentive for the GOUMS authorities, physicians and other healthcare professionals alike, ensuring the GPCR had good cooperation with all relevant stakeholders.

In conclusion, the GPCR data informed planners of the importance of cancers of the gastrointestinal tract as well as breast cancer, as the most common malignancies in the Golestan province between 2004 and 2013. We also found that declining trends in esophageal cancer incidence rates were offset by increasing trends in the breast and colorectal cancer incidence rates, during the study period. Our results showed generally improving trends in indices of data quality, with the GPCR data quality reaching acceptable levels of quality in the latter years. The main indicators for the successful establishment and

maintenance of the GPCR included sustainable sources of funding, a transparent plan for the use of data that ensures the comprehensive cooperation of all institutional authorities and healthcare professionals working with the GPCR. The GPCR may be considered as one model in the sustainable planning of population-based cancer registries in LMIC.

Authorship contribution

GR: conceptualized and designed the study; performed statistical analysis; wrote the manuscript; RM: conceptualized and designed the study; interpreted data; edited, and critically reviewed manuscript; ShS, AF, NA: initiated, conceptualized and designed the study; interpreted data; critically reviewed manuscript; MH, MT, SeS, SM: collaborated in collection of cancer incidence data; edited and critically reviewed manuscript; SB, AM, NJ, NS: collaborated in collection of cancer incidence data; collaborated in data processing; HM, FS, FGK: collaborated in data processing; collaborated in quality control; MA, AJ, SeH: collaborated in data processing; interpreted data; SuH: collaborated in data processing; collaborated in quality control; wrote the manuscript; AS, HP: performed statistical analysis; interpreted results; critically reviewed manuscript; MP, MG: collaborated in collection of cancer mortality data; collaborated in quality control; FB: edited and critically reviewed manuscript; collaborated in quality control; All authors read and approved the final manuscript.

Conflict of interest statement

The authors declare no conflicts of interest.

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Table 2

Temporal changes in the indices of quality of data in Golestan population-based cancer registry (GPCR) 2004–2013.

	2004	2005	2006	2007	2008	2009	2010	2011	2012	2013
Microscopic verification (%)	62.5	70.3	71.0	73.6	74.8	74.8	74.6	75.4	77.0	77.5
Death certificate only (%)	21.2	11.3	8.3	5.6	4.6	4.7	5.0	3.8	4.7	4.7
Unknown primary site (%)	5.9	2.2	1.2	1.5	2.4	2.3	4.9	5.1	2.6	1.5
Unknown method of diagnosis (%)	0	0	0	0	0	0	0	0	0	0
Unknown age (%)	0	0	0	0	0	0	0	0	0	0
Unknown sex (%)	0	0	0	0	0	0	0	0	0	0

ASR: Age standardized incidence rates (per 100,000 person-years).

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