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Arts

HISTORICAL IMPORTANCE AND TEACHING OF MUGAM ART

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MUGAM SANATININ TARİHSEL ÖNEMİ VE ÖĞRETİMİ

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Abstract

The presented article is devoted to the study of the historical significance and teaching of mugham art. The historical and theoretical study of mughams is one of the issues of great importance in mugham studies. In the mugham heritage, each mugham has its own place and significance, development history, and path of improvement. The study of all this allows us to shed light on the evolutionary path of mugham art and actualizes research in this direction. The study of performance variants is very important in the study of mughams. Mugham performance variants mature in living experience, opening the way to considering the process of its transmission and change from generation to generation. Along with the experience of live performance, the preserved versions of mughams in sound recordings and musical notations are also of great importance, and their involvement in research is one of the urgent issues. The teaching of mugham art is not only about teaching music, but also about preserving national and spiritual identity, and passing on deep-meaning poetry and musical philosophy to future generations. For this reason, the teaching and promotion of mugham should be a priority area for both musicians and cultural politicians. A separate field has emerged in musicology - mugham studies, and the works of local and foreign music researchers from the Middle Ages to the modern era have enriched this field.

Özet

Sunulan makale muğam sanatının tarihsel önemi ve öğretiminin incelenmesine adanmıştır. Muğamların tarihsel ve teorik incelenmesi muğam çalışmalarında büyük öneme sahip konulardan biridir. Muğam mirasında her muğamın kendine özgü bir yeri ve önemi, gelişim tarihi ve gelişme yolu vardır. Tüm bunların incelenmesi muğam sanatının evrimsel yoluna ışık tutmamızı ve bu yönde araştırmaları hayata geçirmemizi sağlar. Muğamların incelenmesinde icra varyantlarının incelenmesi çok önemlidir. Muğam icra varyantları yaşam deneyiminde olgunlaşır ve nesilden nesile aktarım ve değişim sürecini ele almanın yolunu açar. Canlı performans deneyiminin yanı sıra, muğamların ses kayıtları ve müzik notalarında korunan versiyonları da büyük önem taşır ve bunların araştırmaya dahil edilmesi acil konulardan biridir. Muğam sanatının öğretilmesi yalnızca müzik öğretmekle ilgili değildir, aynı zamanda ulusal ve manevi kimliği korumak ve derin anlamlı şiir ve müzik felsefesini gelecek nesillere aktarmakla ilgilidir. Bu nedenle, muğamın öğretilmesi ve tanıtılması hem müzisyenler hem de kültür politikacıları için öncelikli bir alan olmalıdır. Müzikolojide ayrı bir alan ortaya çıkmıştır - muğam çalışmaları ve Orta Çağ'dan modern çağa kadar yerli ve yabancı müzik araştırmacılarının çalışmaları bu alanı zenginleştirmiştir.

Keywords: Mugham, teaching methods, performance traditions, composer, future generations, improvisation, Eastern countries.

Anahtar kelimeler: Mugham, öğretim yöntemleri, icra gelenekleri, besteci, gelecek nesiller, doğaçlama, Doğu ülkeleri.

GİRİŞ: Muğamların tarihsel ve teorik çalışması, mugham çalışmalarındaki en önemli konulardan biridir. Mugham mirasındaki her mughamın kendine özgü bir yeri ve önemi, gelişim tarihi ve iyileşme yolu vardır. Tüm bunları incelemek, mugham sanatının evrim yolunu aydınlatmamızı sağlar ve bu yöndeki araştırmaları önemli hale getirir. Muğamların incelenmesinde icra varyantlarının incelenmesi çok önemlidir.

Mugham icra varyantları canlı deneyimde olgunlaşır ve nesilden nesile aktarım ve değişim sürecini ele almanın yolunu açar. Canlı performans deneyiminin yanı sıra, ses kayıtlarında ve müzik notalarında korunan mugham varyantları da büyük önem taşır ve bunların araştırmaya dahil edilmesi güncel konulardan biridir.

Muğam, Azerbaycan kültürünün en eski ve en değerli incilerinden biridir, muğam sadece müzik değil, aynı zamanda halkın tarihini, felsefesini, duygularını ve yaşam tarzını yansıtan bir sanat biçimidir. Muğamın nesilden nesile öğretilmesi ve aktarılması, Azerbaycan'ın kültürel mirasını korumak ve geliştirmek açısından büyük önem taşımaktadır. Bu makale, muğam sanatının öğretim yöntemlerini, eğitim sistemindeki yerini ve modern zamanlardaki önemini inceleyecektir.

ANA METİN: 20. yüzyılda Azerbaycan müzik kültürünün tarihi gelişiminde yeni bir aşama dikkat çekicidir. Bu dönemde Azerbaycan profesyonel bestecilik okulu parlak besteci ve müzikolog Üzeyir Hacıbeyli tarafından kurulmuş ve Azerbaycan'da profesyonel müzik yaratıcılığı ve müzikolojinin oluşum dönemi yaşanmıştır. Azerbaycan müziğinin kurucusu, ölümsüz bestecimiz Üzeyir Hacıbeyli'nin derlediği muğam programı günümüze kadar güncelliğini korumuştur. Hatırlayalım ki Üzeyir Bey'den önce bile muğam destgahlarımız vardı ve bunlar icra ediliyordu. Ancak o dönemde icra edilen muğamlar çok uzundu ve doğaçlama açısından oldukça kapsamlıydı. Üzeyir Hacıbeyli muğamları daha kompakt ve özlü hale getirerek dinleyiciler için daha sevilen ve kolay anlaşılabilir bir forma kavuşturmuştur.

Üzeyir Bey'den bu yana birçok besteci eserlerinde muğam motiflerini kullanmıştır. Üzeyir Hacıbeyli'nin "Leyli ve Mecnun" operası hanende sanatına, yani muğam icrasına dayanmaktadır ve halk tarafından sevilmektedir. Operada "Mahur-Hindi", "Çahargah", "Şur", "Rast", "Segah", "Şahnaz" muğamları kullanılmıştır. Sonraki yıllarda muğamlarımız "Aslı ve Kerem", "Şeyh Sanan", "Şah Abbas ve Hurşud Banu", "Rüstem ve Sohrab", "Aşık Garib", "Şah İsmail", "Gelin Kayası", "Ksandan'ın Taleyi" gibi muğam temelli operalarda yaygın olarak kullanılmıştır. "Ksandan'ın Taleyi" operasının ünlü hanende Seyid Mirbabayev'in acı kaderine adandığını belirtmek gerekir.

Muğam, Azerbaycan halk müziğinin en eski ve en zengin türlerinden biridir ve ulusal müzik kültürünün temel direklerinden biri olarak kabul edilir. Müzik, şiir ve felsefi düşüncenin birleşimi olarak oluşan bu sanat, nesilden nesile aktarılmış ve UNESCO tarafından somut olmayan kültürel mirasın bir örneği olarak tanınmıştır. Bu bağlamda, muğamın öğretilmesi ve genç nesillere doğru bir şekilde aktarılması, ulusal ve manevi kimliğin korunması açısından büyük önem taşımaktadır. Muğam, ulusal ve kültürel hafızanın taşıyıcısıdır ve öğretilmesi, insanların kökleriyle olan bağlarını güçlendirir. Muğam öğretimi, profesyonel şarkıcıların ve enstrüman sanatçılarının yetişmesinin temel dayanağıdır. Muğam icrası sadece öğretilmekle kalmaz, aynı zamanda usta-çırak geleneği yoluyla da yapılır. Ülkemizde faaliyet gösteren çocuk müzik okullarında ve kolejlerinde muğam, avaz ve makamın temelleri öğretilmektedir.

Yüksek müzik eğitim kurumlarında muğamın bilimsel-analitik analizi, icra teknikleri ve doğaçlama yöntemleri öğretilir.

Usta-çırak geleneği en etkili öğretim biçimidir ve ünlü şarkıcıların okulları bu konuda özel bir öneme sahiptir. Muğam sanatı teknolojiyle bütünleştirilir ve muğam dersleri, video materyalleri ve notalar dijital platformlarda öğretilir.

Muğamı uluslararası sunumda yabancı müzik okullarında tanıtmak için müfredata muğamın dahil edilmesi ve ortaokullardaki müzik derslerinde muğam hakkında bilgi verilmesi modern çağımızda olmazsa olmaz konulardır. Peki muğam öğretmenin toplum için önemi nedir?! Muğam gençlerde milli gurur duygusu oluşturur ve muğamı dinlemek ve icra etmek insanların estetik zevkini geliştirir. Muğamın şiirsel ve felsefi değeri onu dinleyen ve inceleyen kişinin ruhunu etkiler ve manevi zenginlik kazandırır.

Muğam sanatının kökleri çok eski zamanlara dayanır. Orta Asya, Orta Doğu ve Kafkas kültürlerinin etkisi altında oluşan bu sanat, Azerbaycan halkının müzik geleneklerini birleştirir. Muğam, insan hayatının çeşitli anlarını, neşeyi, hüznü, aşkı, itaati ve mistik duyguları ifade eder. Muğam, Azerbaycan'ın ulusal kimliğinin ayrılmaz bir parçasıdır ve öğrenilmesi uzun ve karmaşık bir süreçtir. Bu sanat esas olarak sözlü gelenek yoluyla aktarıldı, ancak modern zamanlarda eğitim kurumlarında sistematik olarak öğretilir. Tarihsel olarak, muğam sanatçıları (khanandes ve sazandes) bilgilerini öğrencilere bizzat öğretirlerdi. Bu yöntemle öğrenci, ustasıyla uzun yıllar deneyim kazanır ve muğamın inceliklerini öğrenir.

Mugam icracıları genellikle halka açık toplantılarda, düğünlerde ve törenlerde performans sergileme deneyimi kazanmış ve bu da sanatçıların sahne becerilerini geliştirmelerine yardımcı olan canlı bir performans ortamı yaratmıştır. Mugham öğretimi modern çağda bir dizi zorlukla karşı karşıyadır ve bunun için geleneksel ve modern eğitim arasında bir denge sağlanmalıdır. Bazı uzmanlar geleneksel yöntemlerin unutulduğunu ve modern yöntemlerin yeterince etkili olmadığını belirtmektedir. Pop ve elektronik müziğin yaygınlaşması gençlerin mughama olan ilgisini bir nebze azaltmıştır.

Muğam notasyonunun standartlaştırılması ve eğitim programları üzerinde çalışmalar devam ediyor. Muğam sanatının hayatta kalmasını ve gelişmesini sağlamak için bir dizi önlem alınıyor: Kültür Bakanlığı ve UNESCO ile ortak projeler, muğamı küresel düzeyde tanıtmak için festivaller ve konserler düzenleniyor. Medya ve sosyal ağlarda tanıtım ve muğam performanslarının televizyon ve internet platformlarında dağıtılması gençlerin ilgisini çekiyor. Ortaokullarda muğam derslerinin sayısının artırılması planlanıyor.

İmruz Efendiyeva şunları belirtiyor: "Azerbaycan muğamının bir diğer büyük başarısı da 2008 yılında UNESCO Somut Olmayan Kültürel Miras Temsili Listesi'ne dahil edilmesidir. Azerbaycan muğamı, insanlığın evrendeki yalnızlık duygusunu ve evrende gelişmiş bir medeniyet arayışını somutlaştırmak amacıyla uzaya gönderilen "Voyager" uzay aracına yerleştirilen "Altın Disk'e de dahil edilmiştir. Bu örnekler, muğamın sadece klasik icra çerçevesinde kalmadığını, operadan uzaya kadar geniş bir alanda yansımaları bulduğunu göstermektedir. Küresel tanınırlığı Azerbaycan kültürünün prestijini daha da artırmaktadır." [4, s. 161-166].

Muğam, Azerbaycan halkının kadim ve zengin kültürel mirasının yaşayan bir örneğidir. Öğretilmesi ve korunması sadece geçmişin korunması değil, aynı zamanda gelecek nesiller için değerli bir mirastır. Geleneksel öğretim yöntemlerini modern eğitimle birleştirmek, gençleri bu sanata çekmek ve uluslararası alanda tanıtmak, muğamın sonsuzluğunu koruyacak en önemli adımlardır. Doğu kültürünün genel sisteminde önemli bir rolü olan Azerbaycan muğam sanatı, profesyonel icracıların yaratıcı bir ürünü olarak gelişmiş, nesilden nesile aktarılmış ve müzik hazinesinde eşsiz ve değerli bir yer edinmiştir.

Üstün usta icracılarımız sayesinde dünyayı fetheden muğam sanatı, günümüzde renkli yorumlarıyla zengin bir müzik mirası yaratmıştır. Muğam yaratıcıları ve icracıları, şarkıcılar ve halk çalgısı çalgıcıları - sazenciler, yüzyıllardır büyük bir kültürel zenginliği cıalamış ve ustalığın sırlarını günümüze taşımıştır.

Muğam sanatı birçok ülkede var olmasına rağmen: Türkiye, Özbekistan, Hindistan, İran, vb., Azerbaycan muğamı her zaman benzersizliği, gizemli tazeliliği ve en önemlisi usta şarkıcılarıyla tüm ülkelerin muğamlarından farklılaşmıştır. Doğal olarak, bu sanatçılar uzun yıllardır Ulusal Liderimiz Haydar Aliyev'in büyük ilgisi ve desteğiyle devletimiz tarafından büyük ilgi ve destekle çevrelenmiştir. Büyük liderimiz Haydar Aliyev'in vefatından sonra, Azerbaycan Devlet Başkanı Sayın İlham Aliyev ve Birinci Başkan Yardımcısı Mehriban Aliyeva'nın sayısız çabaları sonucunda, bu gelenek layıkıyla sürdürülmüş ve Azerbaycan muğam sanatı sadece Azerbaycan'da değil, aynı zamanda dünya çapında tanınmış ve UNESCO kültür mirası listesine dahil edilmiştir.

Muğamı tür gruplarına göre incelemenin yanı sıra, müzikolojide her muğamı ayrı bir sanat eseri olarak analiz etmeye büyük ihtiyaç vardır. Bu nedenle muğamın tarihi ve teorik temellerinin incelenmesi her zaman müzikologlarımızın ilgi odağı olmuştur. Dünya müzikolojisinde ve Doğu ve özellikle Azerbaycan müzikolojisinde muğam sanatının incelenmesi alanında çok sayıda yüksek kaliteli çalışma yapıldığı belirtilmelidir. Muğam, Doğu ülkelerinin klasik halk müziğinin ana türüdür ve "muğam" kelimesi İran-Arap-Türk dillerindeki "makam" kelimesinden türemiştir. "Makam" kelimesi telli çalgılarda perde (perde) anlamına gelir. Her muğam, ana (kök) notanın enstrümanın bir perdesinde yer alması nedeniyle bu şekilde adlandırılmıştır.

Yaklaşık 14. yüzyıla kadar Orta Doğu halklarının tek bir müzik türü olmasına rağmen, daha sonra meydana gelen sosyo-politik değişimler sonucunda bu tek müzik türü halklar arasında farklılık göstermeye başladı. Klasik Doğu muğamı 12 ana muğam ve 6 avazdan oluşuyordu, ana muğamlar şunlardı: Uşşak, Nevâ, Busalik, Rast, Araz, İsfahan, Zirafkend, Buzurk, Zangula, Rahavi, Hüseyin Hicaz [6, s.27].

Azerbaycan muğamları şu anda 7 ana ve 3 yardımcı muğamdan oluşmakta olup, ana muğamlar şunlardır: Rast, Şur, Segah, Çahargah, Bayati-Şiraz, Şuştar, Humayun. Yardımcı muğamlar: Şehnaz, Saranj, Çahargah (2. tip). Ancak bahsettiğimiz ana muğamlar aynı zamanda birçok muğamı da kompozisyonlarında birleştirir. Örneğin: "Segah" muğamı, "Mirza Hüseyin segahi", "Zabul segahi", "Haric segahi" gibi destgahları içerir. "Rast" muğamı "Katar", "Mahur-Hintçe", "Orta Mahur", "Bayat-Kacar" ve diğer muğamları içerir.

Muğam sanatının en karakteristik özelliği, her sanatçının bu zengin mirası özümsemiş, şekillendirmiş, kendi yaratıcı üsluplarını bu sanat formuna katmış ve onu daha da derinleştirmiş olmasıdır.

Modern şarkıcılar da bu sanata katkıda bulunarak muğam sanatını geliştirip canlı tutuyorlar. Elbette her şarkıcının muğam icrası farklı duyuluyor. Her icracının kendine özgü bir ses tınısı ve icra tarzı olduğu gibi, muğam söyleme biçimleri de kendine özgüdür. Ancak tüm bu farklılıklara rağmen muğam destgahları biçim ve yapı açısından tekdüze ve standarttır.

"Tekdüzelik" dediğimizde, her muğam destgahının özel bölümleri ve köşeleri ile icra sırasında değişmeden kalması gereken "giriş" ve "ayak" kısımlarını kastediyoruz. Bir şarkıcı "Rast" destgahını söyler

ve sonunda "Mahur-Hindi" muğamının ayağını verirse, bu, icracının muğamı tam olarak kavramadığını ve bu sanata gereken düzeyde hakim olmadığını gösterir. "Rast", "Mahur-Hindi", "Qatar", "Bayatı-Qajar" muğamları "Rast" ailesine dahil olsa da her birinin kendine özgü bir girişi ve ayak kısmı vardır. Bunları karıştırmak bir hata olarak kabul edilir.

Muğam icrasında geleneksel kurallara uymak ve her destgahın kendine özgü yapısı ve mantığı içinde hareket etmek önemlidir. Bu, muğam sanatının saflığını ve derinliğini korumak için temel bir koşuldur. Diğer muğamlar da örnek olarak gösterilebilir. Ancak her bir şarkıcının bu kısımlara, yani giriş ve gelişme bölümlerine, melismalar ve gırtlak nüanslarıyla kendi tarzında doğal olarak yeni renk ve güzellik katabileceği unutulmamalıdır. Muğam icrasında en önemli etkenlerden biri, icra edilen muğamın karakterine uyan bir gazelin doğru seçilmesidir. Bu seçimin, muğamın doğru icrasını belirlediği neredeyse söylenebilir. Bir şarkıcı, majör karakterli bir muğamı minör bir tarzda, yani karamsar, hüznü bir gazelle söylerse, bu dinleyicide hoş bir izlenim bırakmayacaktır, aksi takdirde muğama olan tutkusu sorgulanacaktır. Bu açıdan bakıldığında, muğamda bir gazelin doğru seçilmesi bir zorunluluktur.

Mugam icrasında bir diğer önemli nokta ise gırtlaklı açarken sesli harflerin doğru kullanılmasıdır, bu da icrayı daha hafif, daha akıcı hale getirir ve ağız yapısı daha düzenli görünür. Birçok şarkıcı gırtlaklı açarken ses telleri yerine çenesini gerer, bu da profesyonel olmayan ve kabul edilemez bir icra tarzıdır.

Her şarkıcı, ister icra sırasında ister sahnede otururken olsun, performansı, yüz ifadeleri, sahne hareketleri ve söylediği mughama verdiği karakterle seyirciyi maksimum düzeyde tatmin etmelidir. Kısacası, her icracının yüksek oyunculuk becerisine sahip olması gerekir.

Profesör R.İmrani şöyle yazıyor: "Mugam sadece bir ses değil, ruhun bir ifadesidir. Onu doğru bir şekilde öğrenmek ve canlı tutmak her birimizin görevidir! Çünkü mugham sanatı sözlü geleneğe dayanarak yıllarca ağızdan ağıza aktarılmış ve günümüze güzel, eksiksiz, anlamlı ve uyumlu bir biçimde ulaşmıştır. Bu harika sanat biçimini gelecek nesillerimize daha güzel, modern ve renkli bir biçimde aktarmak için çabalamalıyız" [5, s. 32].

Şarkı söyleme sanatında ustalaşmak isteyen her öğrenci muğam sanatının ciddiyetini ve sorumluluğunu anlamalıdır. Bu sanatı olduğu gibi, doğru ve kurallara uygun bir şekilde öğrenmeli ve gelecek nesillere bozulmadan veya zarar görmeden aktarılacağını anlamalıdır.

SONUÇ: Listelenen tüm bu faktörler bir kez daha Azerbaycan muğamının yüzyıllardır sevildiğini ve seilmeye devam ettiğini kanıtlıyor. Sadece kendi doğal ortamından değil, aynı zamanda küresel ölçekte aklından geçenlerden de bahsediyor. Bundan, muğamlarımızı öğrenmek ve icra etmek isteyen her genç şarkıcının öncelikle muğamımızın köklerini bilmesi, bununla ilgili kapsamlı bilgi edinmesi gerektiği ve bunun da performansına kesinlikle olumlu bir etkisi olacağı sonucuna varabiliriz.

Çünkü muğam sözlü geleneklere dayansa da bilimsel, akademik, doğru ve inceliklere gereken dikkat gösterilerek icra edilmelidir. Muğam o kadar gizemli bir sanat biçimidir ki, dinleyicilerin onu sevmesini veya yabancılaştırmasını sağlayan, icracının kendisidir. Bu nedenle, her şarkıcı bu sanatın ciddiyetini anlamalı ve bunu körü körüne değil, bilinçli bir şekilde icra etmelidir.

Muğam sanatının öğretilmesi, yalnızca müziği öğretme misyonunu değil, aynı zamanda ulusal ve manevi kimliği korumayı ve derin anlamlı şiir ve müzik felsefesini gelecek nesillere aktarmayı da taşır. Bu nedenle, muğamın öğretilmesi ve tanıtılması hem müzisyenler hem de kültür politikacıları için öncelikli bir alan olmalıdır. Müzikolojide ayrı bir alan ortaya çıkmıştır - muğam çalışmaları bilimi ve Orta Çağ'dan modern döneme kadar yerli ve yabancı müzik araştırmacılarının çalışmaları bu alanı zenginleştirmiştir.

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Economic sciences

METHODOLOGICAL INSIGHTS INTO LEGALIZING THE SHADOW ECONOMY VIA FISCAL POLICY

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Abstract

The shadow economy weakens fiscal capacity and undermines public trust. This paper analyzes how fiscal instruments tax simplification, digitalization, and incentive-based policies can be employed to legalize informal activity. Drawing on international experiences and institutional perspectives, the study proposes a framework that integrates fiscal reforms with governance improvements to promote sustainable formalization.

Keywords: shadow economy, fiscal instruments, tax simplification, digitalization, governance, formalization.

The shadow economy, though often associated with illicit activity, in most cases represents economic behavior that is legal in substance but hidden from authorities to avoid taxation, regulation, or social security contributions. It includes unregistered employment, cash-based transactions, underreporting of revenues, and informal self-employment. While such activities can provide short-term livelihood support, particularly in economies with limited labor market opportunities, their long-term effects are detrimental. They weaken fiscal sustainability, undermine fair competition, and erode the state's ability to deliver public goods.

The size of the shadow economy varies significantly across regions. In advanced OECD economies, it is typically estimated between 10–15% of GDP, while in many developing and transition economies it often exceeds 30–40% (Schneider & Medina, 2018). These figures underscore not only the scale of informality but also the need for innovative strategies to integrate these activities into the formal economy. For countries in Central Asia, Eastern Europe, and Latin America, the problem is particularly acute due to institutional weaknesses, complex tax regimes, and low trust in fiscal authorities.

Historically, attempts to reduce the shadow economy have focused on punitive enforcement: strengthening tax audits, increasing penalties, and enhancing surveillance. While these approaches can yield short-term improvements, they often fail to address the root causes of informality, such as excessive compliance costs, insufficient access to credit, and perceived unfairness in the fiscal system. In fact, harsh enforcement can even push small businesses further underground, creating a vicious cycle of distrust and avoidance.

In recent decades, scholars and policymakers have increasingly shifted toward fiscal instruments as a methodology of legalization. Rather than relying solely on coercion, governments can use fiscal policy tools tax simplification, incentives, subsidies, and digital transparency to change the cost–benefit calculus for informal actors. From the perspective of behavioral economics, compliance is not only a function of deterrence but also of perceived fairness and reciprocity: taxpayers are more willing to formalize when they see tangible benefits from taxation, such as improved infrastructure, public services, or targeted subsidies.

Global experiences highlight this shift. In Estonia, e-taxation and digital reporting reduced compliance costs and created trust between taxpayers and the state. In Brazil, the adoption of electronic invoicing (Nota Fiscal Eletrônica) drastically reduced VAT evasion. In Eastern Europe, simplified tax regimes for small businesses provided legal entry points into formal markets. For countries such as Uzbekistan, where informality remains substantial, these lessons point to the importance of embedding fiscal instruments within broader institutional reforms.

The academic literature on the shadow economy is diverse and interdisciplinary, drawing from economics, political science, sociology, and public administration. At the heart of these debates lies the question of how fiscal policy, as both a tool of revenue collection and behavioral regulation, can be strategically applied to legalize informal activities.

Early studies by Feige (1990) and Tanzi (1999) conceptualized the shadow economy as a rational response to excessive taxation and regulation. Schneider (2005) advanced this work by providing cross-country estimates through econometric modeling, demonstrating that tax burden, unemployment, and institutional weaknesses strongly correlate with informality. These studies largely framed the issue in terms of enforcement and compliance costs, laying the groundwork for fiscal instruments as corrective mechanisms.

Bird and Zolt (2015) argue that fiscal systems should be seen not merely as revenue extraction tools but as social contracts between the state and citizens. Tax simplification, broadened tax bases, and reduced distortions create incentives for voluntary compliance. Alm and Torgler (2006) provide empirical evidence that "tax morale" the intrinsic motivation to pay taxes plays as significant a role as deterrence. Their work aligns with Feld and Frey (2007), who develop a psychological model of tax compliance emphasizing fairness, trust, and reciprocity.

The application of behavioral economics has deepened the analysis of shadow economy dynamics. According to Kirchler (2007), taxpayer behavior is shaped by both deterrence and legitimacy: while penalties may influence short-term compliance, long-term formalization requires institutional trust and perceived justice in fiscal systems. La Porta and Shleifer (2014) further highlight that informality persists in contexts where states fail to deliver reliable public services, undermining the fiscal contract.

Institutional quality is therefore central. Kaufmann, Kraay, and Zoido-Lobaton (1999) demonstrate that governance indicators such as rule of law and control of corruption are strongly correlated with lower informality. North's (1990) institutional economics framework situates the shadow economy as an outcome of weak formal institutions, suggesting that fiscal instruments must be embedded in governance reform.

Recent scholarship emphasizes digital transformation as a breakthrough methodology. Pomeranz (2015) shows that third-party reporting through electronic invoicing in Chile dramatically reduced VAT evasion. Naritomi (2019) confirms that consumers, when empowered with digital receipts, act as *de facto* tax auditors. OECD (2018) highlights e-government platforms, e-filing, and blockchain technologies as vital for reducing compliance costs and limiting evasion opportunities.

Comparative studies provide important lessons. In Estonia, digital fiscal administration reduced both evasion and compliance costs (Martinez-Vazquez & Vulovic, 2014). In Brazil, the *Nota Fiscal Eletrônica* became a global benchmark for VAT modernization (de Paula & Scheinkman, 2010). In Eastern Europe, Pashev (2005) demonstrates that tax amnesties and simplified regimes had mixed results: while they provided short-term incentives for formalization, sustainability required broader institutional trust.

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SCIENTIFIC AND THEORETICAL FOUNDATIONS OF GLOBAL FREIGHT TRANSPORT AND EXPORT-ORIENTED INDUSTRY

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Abstract

When we look at the theoretical aspect of international freight transport, the Customs Convention on International Freight Transport with the application of the International Freight Transport (IFT) Handbook occupies an important place among the conventions to which our Republic has acceded. The State Customs Committee is considered the competent body of the convention in the country. According to the order of the Cabinet of Ministers, the Azerbaijan International Road Transport Association (AADBA) is considered the guarantee body implementing the convention.

Export potential, being part of the country's economic potential, is the ability to produce and export various types of material goods and services in quantities and quality corresponding to the requirements of foreign market consumers as a result of the full use of the means of production of the national economy and its individual sectors.

In accordance with the provisions of the Main Multilateral Agreement, it was decided to locate the Permanent Secretariat of the TRACECA Intergovernmental Commission in Baku, and its official opening took place on February 21, 2001. Thus, Azerbaijan has played an important role in determining the main development trajectories, contributing to the restoration of the historical Silk Road.

Currently, Azerbaijan is a participant in the "Silk Road Economic Belt" project, implemented at the initiative of China. In December 2015, within the framework of the state visit of President Ilham Aliyev to China, a memorandum of understanding was signed between the Government of the Republic of Azerbaijan and the Government of the People's Republic of China on the joint promotion of the creation of the "Silk Road Economic Belt".

Keywords: International freight transport, Export potential, Silk Road, Industry, International market, Transit countries

When looking at the theoretical aspect of international cargo transportation, the Customs Convention on International Carriage of Goods (ICG) with the application of the International Carriage of Goods (ICG) Booklet occupies an important place among the conventions to which our Republic has acceded. The State Customs Committee is considered the competent body of the convention in the country. According to the order of the Cabinet of Ministers, the Azerbaijan International Road Transport Association (AADBA) is considered the guarantee body implementing the convention. The Azerbaijan International Road Transport Association (AADBA), a public organization, teaches subjects carrying out cargo transportation by road how to work with documents, conveys innovations related to cargo transportation, and conducts seminars. Most importantly, the Azerbaijan International Road Transport Association (AADBA) provides carriers with an important document - the International Carriage of Goods (ICG) Booklet - in order to avoid difficulties when passing through transit countries. The International Carriage of Goods (ICG) Booklet must be purchased for each flight, and the booklet provides a number of discounts in international cargo transportation. Borders are unobstructed, there is no need to open and check the cargo every time. It is simply checked that the seals and seals of the cargo are intact and recorded in the booklet. After filling out the International Cargo Transport (ICT) booklet, no declaration is needed. The booklet clearly states the names of the goods, their weight, the number of cargo places, recipients, carriers, etc.

Vehicles provide the movement of goods and services from the supplier to the consumer in the international market. Transport creates a connection between the two separate economic sectors of the country - agriculture and industry - and brings together the country's economy as a single complex. Transportation activity means that the production process continues in the circulation process. The

peculiarity of the term transport - formed from the Latin word *transporto*, means *I bring, I carry, I change its place*. These transport services differ depending on the following:

1. Type of transport: water (sea and river), land (railway and road), air (aviation), pipeline, mixed
 2. Subject of transport operations (cargo, passenger, luggage)
 3. Transport characteristics of goods; dry (coal, ore), spreadable (grain, cement, phosphate), filterable (oil and its refining products, vegetable oils)
 4. Periodicity of transportation (permanent and non-permanent)
 5. Procedure for crossing the border (container, ferry, etc.)
 6. Type of transmission (direct, indirect, etc.)
- International transport services are bought and sold as specific goods in international transport markets and are differentiated depending on the type of transport, the geography of transportation and the type of cargo transported.

Export potential, being part of the country's economic potential, is the ability to produce and export various types of material goods and services in quantities and quality appropriate to the requirements of foreign market consumers as a result of the full use of the means of production of the national economy and its individual sectors.

It should be noted that in order to export, there must first be a demand for them. Given that the amount of products that the country can produce is quite small compared to the amount of products on the world market, it is possible that the country will always have a demand potential for oil products. When analyzing export potential, other factors that should be taken into account are quality, compliance with world market standards and prices. In our opinion, if the price of a product in the domestic market is lower than the price of this product on the international market, then there is export potential. In other words, when assessing the export potential of products, prices should be compared and it should be determined whether the product in question can be sold profitably at international prices.

One of the main goals in the industry in the near future will be the restoration and reconstruction of the activities of existing industrial enterprises in the regions, as well as the creation of new enterprises. Here, special attention will be paid to the restoration of agricultural processing enterprises and increasing export potential. In order to achieve the main goal in the industrial sector, it is planned to determine the development directions of the non-oil sector of the industry, support the production of competitive industrial products and promote the creation of export-oriented production areas, strengthen and privatize state-owned or state-owned industrial enterprises with a controlling stake, support the activities of enterprises after privatization, technological reconstruction of production, training of qualified personnel, etc. The implementation of measures is envisaged.

Restoration of the Great Silk Road On the initiative of the national leader Heydar Aliyev, an international conference dedicated to the restoration of the historical Silk Road was held in Baku on September 7-8, 1998 with the participation of the heads of state of 9 countries (Azerbaijan, Turkey, Georgia, Ukraine, Moldova, Romania, Bulgaria, Uzbekistan, Kyrgyzstan), 13 international organizations and delegations of 32 states. At the end of this conference, the "Basic Multilateral Agreement on International Transport for the Development of the Europe-Caucasus-Asia Corridor" was signed on the basis of the European Union's TRACECA program and the Baku Declaration was adopted.

In accordance with the provisions of the Basic Multilateral Agreement, it was decided to locate the Permanent Secretariat of the TRACECA Intergovernmental Commission in Baku, and its official opening took place on February 21, 2001. Thus, Azerbaijan has played an important role in determining the main development trajectories, contributing to the restoration of the historical Silk Road.

Currently, Azerbaijan is a participant in the "Silk Road Economic Belt" project, implemented at the initiative of China. In December 2015, a Memorandum of Understanding was signed between the Government of the Republic of Azerbaijan and the Government of the People's Republic of China on jointly promoting the creation of the "Silk Road Economic Belt".

The Baku-Tbilisi-Kars transport corridor connecting Europe and Asia. The Baku-Tbilisi-Kars railway, which was put into operation on October 30, 2017, is a restoration of the ancient Silk Road on steel highways, ensuring the connection of the Trans-European and Trans-Asian railway networks. On February 7, 2007, an Agreement on the construction of the Baku-Tbilisi-Kars railway was signed in Tbilisi at the initiative of the President of the Republic of Azerbaijan Ilham Aliyev. In November of the same year, the foundation stone of the railway line was laid in the Marabda district of Georgia. In July 2008, a groundbreaking ceremony for the construction of the Kars-Georgian border section was held in the city of Kars. A 504-kilometer section of the Baku-Tbilisi-Kars railway line, with a total length of approximately 850 kilometers, falls on the territory of Azerbaijan. 263 kilometers of the railway line passes through Georgia and 79 kilometers through Turkey. The Baku-Tbilisi-Kars railway more than halve the time it

takes to deliver goods from China to Europe compared to sea transportation. The Baku-Tbilisi-Kars railway, which serves stability and security, is expected to transport 5 million tons of cargo in the first stage, 17 million tons in the second stage, and then a larger volume of cargo.

The construction of this project on the historical Silk Road increases its attractiveness for the countries of the region and, at the same time, facilitates the access of the Central Asian countries - Turkmenistan, Kazakhstan, Uzbekistan, Kyrgyzstan and Tajikistan, as well as Afghanistan, to European and world markets, and is of great importance in the development and integration of their trade relations, economies.

One of the main advantages of the Baku-Tbilisi-Kars project is that Azerbaijan has a direct railway connection with Turkey through the territory of Georgia, which serves to further strengthen relations between the two states. Another issue is the extension of this project to the Nakhchivan Autonomous Republic. In the future, it is planned to build a separate railway line from Kars to Nakhchivan, which will lead to the removal of the autonomous republic from the blockade of Armenia and ensuring its transport independence. In accordance with the instructions of President Ilham Aliyev, the Free Trade Zone established in the Alat settlement of the Garadagh district of Baku, including the territory of the Baku International Sea Trade Port, will also be of particular importance in transforming Azerbaijan into an international transport hub. In addition to playing a leading role in international freight transportation and Europe-Asia logistics chains, the Free Trade Zone will provide exceptional services in promoting local production and promoting the "Made in Azerbaijan" brand worldwide. The Free Trade Zone is planned to serve a market of 130 million people, including the South Caucasus, Central Asia, Iran, Russia and part of Turkey, on a regional scale.

The North-South transport corridor connecting Northern Europe with South Asia In accordance with the "Strategic Roadmap for the Development of Logistics and Trade in the Republic of Azerbaijan", Azerbaijan plays an active role in the creation of the North-South transport corridor. Thus, the country becomes an important transport and logistics hub at the intersection of both transcontinental corridors, in the center of the Eurasian geography.

The North-South transport corridor will connect India, Pakistan, Iran, Azerbaijan, Russia and the countries of Northern Europe. Azerbaijan is the only country in the world that has a land border with both Russia and Iran, and this geographical location is of great importance for the development of trilateral regional cooperation.

The process of creating the Azerbaijani part of the North-South transport corridor has already entered its final stage. The railway from the Azerbaijan-Russia border to the Azerbaijan-Iranian border, which is an important part of this corridor, has been fully operational. Azerbaijan is also participating in the financing of the construction of the Astara-Rasht-Qazvin railway in Iran. Azerbaijan has planned to allocate a loan of \$500 million to the Iranian side for the construction and equipment of the Astara-Rasht railway.

By increasing the volume of transit trade in the region by 2020 in the strategic roadmaps, Azerbaijan has achieved a share corresponding to the following indicators:

- 40 percent on the Central Asia and Black Sea route;
- 25 percent on the Central Asia and Europe route;
- 3 percent on the China and Europe route;
- 40 percent on the Russia and Iran route;
- 25 percent on the Iran and Black Sea route.

In the future, the integration of the North-South and Baku-Tbilisi-Kars transport corridors is envisaged. Azerbaijan is an active participant in both projects. In addition to Azerbaijan, Georgia, Turkey, European countries, China, Kazakhstan and other Central Asian republics will use this. Currently, the process of transforming Azerbaijan into an international transport hub is underway in the following important directions:

- Development of economic, trade, transport and logistics relations between the regions of Europe, the Black Sea, the Caucasus, the Caspian and Central Asia;
- Development of a multimodal corridor built on the shortest land route between China and the European Union;
- Construction of the North-South transport corridor;
- Attraction of transit cargo within the framework of the Great Silk Road;
- Significant improvement of logistics and trade infrastructure and making Azerbaijan a more attractive hub in this area in the region through regulatory incentives;
- Digitalization of the Great Silk Road through the Azerbaijan Digital Trade Hub and TASIM projects;

- *Coordination of relations between various transport sectors;*
- *a coordinated policy in the field of international and domestic tariffs for freight and passenger transport;*
- *development of a coordinated action program for the organization of multimodal (combined) transport, etc.*

Export-oriented industrialization (EOI), sometimes called export-substituting industrialization (ESI), export-led industrialization (ELI) or export-led growth, is a trade and economic policy that aims to accelerate the industrialization process of a country by exporting goods of the country. has a comparative advantage. Export-led growth involves opening domestic markets to foreign competition in exchange for access to markets in other countries.

However, this may not apply to all domestic markets, as governments may aim to protect specific emerging industries in order to develop and exploit their future comparative advantages, and in practice the opposite may occur. For example, many East Asian countries had strong barriers to imports from the 1960s to the 1980s. Reduced tariff barriers, a fixed exchange rate (often used to facilitate exports by devaluing the national currency), and government support for exporting sectors are examples of policies adopted to promote EOI and, consequently, economic growth. Export-led industrialization was particularly characteristic of the post-World War II East Asian Tigers: Hong Kong, Singapore, South Korea, and Taiwan, which developed their economies.

Conclusion

Export-led growth is an economic strategy used by some developing countries. This strategy seeks to gain a place in the world economy for a particular type of export. Industries that produce these exports may receive government subsidies and better access to domestic markets. By implementing this strategy, countries hope to obtain enough hard currency to import goods produced more cheaply elsewhere.[2] Furthermore, recent mathematical research shows that export-led growth is where wage growth is suppressed and is associated with an increase in the productivity of non-tradable goods in the country with a weaker currency. In such a country, the growth in the productivity of export goods is greater than the proportional growth in wages and the growth in the productivity of non-tradable goods. Thus, in an export-oriented developing country, the price of exports decreases, making it more competitive in international trade.

In Azerbaijan, the commissioning of new international airports in various regions of the country in recent years, the construction of new roads, and the leading role in the implementation of regional projects, as part of Azerbaijan's purposeful policy, both contribute to the development of internal transport infrastructure and turn Azerbaijan into a transport hub of Eurasia.

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Medical sciences

THE ROLE OF INTESTINAL MICROBIOTA IN THE DEVELOPMENT AND TREATMENT OF CHRONIC DISEASES

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Abstract

The article is devoted to a comprehensive analysis of the role of intestinal microbiota in the development and treatment of chronic diseases. The mechanisms of the influence of microbiota on the metabolic, immune, cardiovascular and nervous systems, as well as its importance for the psychoemotional state of a person are considered. Particular attention is paid to dysbiosis as a key factor in the pathogenesis of obesity, type 2 diabetes, atherosclerosis, inflammatory and autoimmune diseases. The author emphasizes the importance of modern molecular sequencing technologies, which have made it possible to reveal the diversity of the intestinal microbial community and its close relationship with the physiology of the body.

The article analyzes therapeutic approaches to microbiota correction, including the use of probiotics, prebiotics, symbiotics, postbiotics, and fecal transplantation. It notes the need for individualization of treatment taking into account the genetic characteristics, lifestyle, and environmental factors of the patient. It is concluded that the study of microbiota goes beyond gastroenterology and becomes an important area of personalized medicine, opening up new prospects in the prevention and treatment of chronic diseases.

Keywords: autoimmune diseases, dysbiosis, intestinal microbiota, prebiotics, probiotics.

Introduction: Over the last century, due to the growth in food consumption and the increased availability of products, there has been a significant increase in the incidence of chronic diseases. Cardiovascular pathologies, obesity, the growth of mental disorders, and inflammatory bowel diseases pose a serious threat to public health and force medical institutions to seek new approaches to solving these problems [10, p. 45]. One of the most promising areas in this area is the study of microbiota - a collection of microorganisms that live in the human digestive tract [9, p. 1824].

Interest in microbiota has increased significantly since the early 2000s due to the development of molecular sequencing technologies, which made it possible to study microorganisms without the need to cultivate them in laboratory conditions [4, p. 60]. These studies have convincingly shown that microbiota is an essential component of the human body: its imbalance disrupts key physiological functions and contributes to the development of diseases [1, p. 20].

Today, it has been proven that the composition and balance of intestinal microbiota directly affect metabolism, the functioning of the immune and nervous systems, as well as the psychoemotional state of a person. Disturbances in this balance, known as dysbiosis, are associated with obesity, diabetes, cardiovascular diseases and a number of neurological disorders [5, p. 14]. Thus, microbiota is considered not only as a risk factor, but also as a potential therapeutic target.

The relevance of the topic is determined by several factors. Firstly, the continuing growth in the number of chronic diseases that affect the duration and quality of life. Secondly, the need to search for new methods of therapy that affect the body's natural regulatory mechanisms. Thirdly, the rapid development of technologies that allow studying the microbiome with unprecedented accuracy and depth [6, p. S2].

The purpose of this article is to analyze the role of intestinal microbiota in the pathogenesis of chronic diseases and to consider modern approaches to its correction. To achieve this goal, the following tasks are set:

1. To characterize the functions of normal intestinal microbiota.
2. To examine the signs of dysbiosis formation and its pathogenetic role.
3. To analyze the relationship between microbiota and metabolic, cardiovascular, inflammatory, nervous and immune diseases.

4. To evaluate the possibilities of microbiota correction through dietary, pharmacological and biotechnological methods of prevention.

Microbiota research methods are opening up new horizons in understanding the pathogenesis of chronic diseases and are forming the basis for personalized prevention and treatment strategies. Over the past decade, research has reached a new level thanks to technologies including 16S rRNA sequencing, which has made it possible to identify a huge number of bacterial species comparable to the number of cells in the human body [4, p. 61].

The main representatives of healthy microbiota are bacteria of the genera *Bacteroides*, *Firmicutes*, *Actinobacteria* and *Proteobacteria*. Their balanced ratio is of crucial importance: if it is disrupted, a wide range of chronic diseases develop [5, p. 15]. Modern research shows that microbiota is involved not only in the digestion and absorption of nutrients, but also in the regulation of systemic inflammation, lipid and carbohydrate metabolism, and in the synthesis of vitamins B and K [1, p. 32].

Metabolic products of microorganisms, such as short-chain fatty acids (butyrate, propionate and acetate), have an anti-inflammatory and trophic effect on the intestinal epithelium, reducing the risk of developing inflammatory and neoplastic diseases [2, p. 1335].

In recent years, a number of reviews have been published confirming the key role of the intestinal microbiota in the pathogenesis of obesity, type 2 diabetes mellitus, non-alcoholic fatty liver disease, as well as cardiovascular and neurological disorders [5, p. 14]. These data substantiate the possibility of using the microbiota as a therapeutic target in the treatment of chronic diseases.

Disruption of normal microbiota, known as dysbiosis, is one of the key factors contributing to the development of chronic pathology. Dysbiosis refers to quantitative and qualitative changes in microflora: a decrease in the number of beneficial bacteria (*Bifidobacterium*, *Lactobacillus*) and an increase in the populations of opportunistic microorganisms such as *Clostridium* and *Enterobacteriaceae* [9, p. 1830].

The causes of dysbiosis are varied and are associated with medical, behavioral and environmental factors. Among the most significant are:

1. Long-term use of antibiotics and other medications, leading to the suppression of beneficial microflora.
2. An unbalanced diet that includes excessive amounts of sugar and saturated fat with extremely low fiber content [1, p. 25].
3. Chronic stress and constant psycho-emotional stress.
4. Infectious lesions of the gastrointestinal tract.
5. A sedentary lifestyle and unfavorable environmental conditions [5, p. 16].

Dysbiosis has a multi-level effect on the body. First of all, the intestinal barrier function is disrupted, which leads to increased permeability of the mucous membrane and the penetration of bacterial endotoxins into the systemic bloodstream [9, p. 1829]. These processes initiate chronic low-intensity inflammation, which is the most important pathogenetic mechanism for the development of obesity, type 2 diabetes, atherosclerosis, and inflammatory bowel diseases.

Secondly, dysbiosis changes the production of microbiota metabolites, including short-chain fatty acids (butyrate, propionate and acetate), which normally provide nutrition to enterocytes, regulate inflammatory processes and control carbohydrate and lipid metabolism [2, p. 1336]. A decrease in their synthesis leads to disruption of metabolic processes, the development of insulin resistance and the formation of metabolic syndrome.

In addition, dysbiosis affects the immune system, causing activation of proinflammatory cascades and weakening of anti-inflammatory reactions. This increases the risk of developing autoimmune diseases and allergic conditions, including rheumatoid arthritis, inflammatory bowel disease, bronchial asthma and food allergies [6, p. 518]. Thus, dysbiosis should be considered as one of the key causes of chronic pathology, and its correction is of great importance in modern therapy.

Changes in the composition of the microbiota have a direct impact on the cardiovascular system. One of the critical factors is the formation of trimethylamine-N-oxide (TMAO), a metabolite formed with the participation of a number of bacteria from food components such as choline and carnitine. TMAO is known to promote the progression of atherosclerosis, increase the risk of thrombosis and negatively affect vascular functions [8, p. 1009].

In addition, dysbiosis is associated with increased blood pressure. Certain bacteria participate in the synthesis of short-chain fatty acids, which have a vasoactive effect. Disruption of their production leads to increased inflammatory processes in the vascular wall, which contributes to the development of hypertension and heart failure [2, p. 1340].

An equally important area of research is the influence of dysbiosis on the formation of the "gut-brain" axis. Microbiota affects the nervous system through humoral, neural and immune pathways. Decreased synthesis of neurotransmitters such as serotonin and gamma-aminobutyric acid is associated with anxiety, depression and cognitive impairment [3, p. 1215]. Moreover, there is evidence of a link between dysbiosis and the progression of neurodegenerative diseases, including Parkinson's disease and Alzheimer's disease. Metabolites of pathogenic bacteria can increase inflammation and have a toxic effect on neurons, accelerating degenerative processes.

Thus, a decrease in the diversity of beneficial bacteria leads to a disruption of immune regulation: pro-inflammatory mechanisms are activated and anti-inflammatory reactions are weakened, which increases the likelihood of developing autoimmune diseases and allergic reactions [6, p. S40].

Weakening of anti-inflammatory mechanisms in dysbiosis increases the risk of developing autoimmune diseases such as rheumatoid arthritis and contributes to the formation of allergic reactions, including bronchial asthma, eczema and food allergies [6, p. S25].

Correction of intestinal microbiota is considered as a promising approach to the prevention and treatment of chronic diseases. Modern methods include drug, dietary and biotechnological strategies aimed at restoring the balance of microflora and normalizing its functions [10, p. 198].

Probiotics are live microorganisms that, when administered in adequate doses, have a positive effect on the health of the host. The most studied strains are *Lactobacillus* and *Bifidobacterium*. Clinical studies confirm their effectiveness in irritable bowel syndrome, inflammatory bowel disease, obesity, and metabolic syndrome. However, the therapeutic effect depends on the specific strain, dosage, duration of use, and the individual characteristics of the patient's microbiota [1, p. 30].

Prebiotics— are food components that stimulate the growth and activity of beneficial bacteria. These include inulin, oligosaccharides, and fructo-oligosaccharides. A diet rich in fruits, vegetables, whole grains, and fiber promotes the growth of beneficial flora and increases the production of short-chain fatty acids, which has a positive effect on metabolism, the immune system, and the intestinal barrier function [6, p. S40].

Symbiotics are a combination of probiotics and prebiotics, providing their synergistic effect.

Postbiotics— these are metabolites of microorganisms (for example, butyrate and acetate) that have anti-inflammatory and trophic properties. Their use allows for a positive effect on cellular metabolism and a reduction in the level of inflammatory processes without the need to introduce live microorganisms [2, p. 1340].

Fecal transplant consists of transplanting microbiota from a healthy donor to a patient. This method has shown high efficiency in *Clostridium difficile* infection and demonstrates promise in the treatment of inflammatory bowel diseases. However, it is associated with the risk of pathogen transmission, which requires strict donor selection and compliance with safety protocols [7, p. 950].

In addition to direct intervention in the microbiota, non-drug approaches are important. Regular physical activity, normalization of sleep patterns, and reduction of stress levels have a beneficial effect on the composition of the microbiota, reduce inflammation, and help maintain metabolic and psychoemotional balance [9, p. 1832].

Conclusion

Modern research convincingly proves that the intestinal microbiota plays a key role in maintaining metabolic and immune homeostasis. Disturbances in its composition are associated with a wide range of chronic diseases - from obesity and diabetes to inflammatory and oncological pathologies.

Of particular importance is the study of the mechanisms of interaction between the microbiota, immune and nervous systems. This "triangle" explains why disturbances in the intestines can affect not only the functioning of internal organs, but also cognitive functions, mood and mental health of a person [3, p. 1215].

A promising direction of modern medicine is microbiota modulation. The use of probiotics, prebiotics, symbiotics, postbiotics, fecal transplantation and personalized diets opens up new horizons in the treatment of chronic diseases. At the same time, these methods require further refinement taking into account genetic differences, individual characteristics and lifestyle of patients.

Thus, the study of intestinal microbiota goes beyond gastroenterology and acquires interdisciplinary significance. In the coming years, this approach may become the basis for personalized medicine, aimed not only at eliminating symptoms, but also at restoring the body's systemic balance [10, p. 210].

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LARYNGEAL CANCER: THE COMPLEXITY OF THE PROBLEM**Arman Khozhayev***Professor of the S.N. Nugmanov Department of Oncology,
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This scientific and analytical work presents modern world and local-regional data on incidence, mortality, lethality and five-year survival rate of such oncological pathology of head and neck tumors as laryngeal cancer. The issues of etiology and pathogenesis, features of distribution, modern approaches and principles of complex diagnostics, prospects for improving treatment results, as well as prognosis are covered in detail. The epidemiological characteristics of this pathology in our republic are given in the context of regions of the country.

Keywords: *oncology, otorhinolaryngology, laryngeal cancer, human papillomavirus, biomarkers, RNA, immune-related genes, autophagy, epidemiology, incidence, mortality, lethality, five-year survival rate, prognosis.*

Laryngeal cancer (LC) is a malignant tumor that develops from elements of the non-keratinizing epithelium of the larynx.

The etiologic factors remain unclear to date. In most cases, the patient's medical history includes untreated inflammatory and precancerous diseases of the larynx (laryngitis, papillomas, papillomatosis, dyskeratosis, leukoplakia, pachydermia, fibroma); a long period of smoking, alcohol consumption, work in dusty conditions (textile production), inhalation of harmful carcinogenic substances (oil, its distillation products, benzene, phenolic resins, asbestos); genetic predisposition (the presence of malignant diseases in relatives), as well as age and gender (males over 55 years of age) [1,2].

The diagnostic criteria are as follows. Complaints and medical history. Complaints: cough; hoarseness; sore throat radiating to the ear; difficulty breathing; choking when taking liquid food; enlarged cervical, supraclavicular, subclavian, submandibular, and submental lymph nodes. History: early symptoms of the disease in LC are: hoarseness and cough, which appear already at stage I of the disease; when, at the initial visit of patients, hoarseness has been observed for six months with the addition of other symptoms, this may indicate later stages (III-IV) of the disease. In this case, complaints of shooting pain in the ear, difficulty breathing, choking when taking liquid food or water, and the appearance of enlarged nodes on the neck are also added [1].

Physical examination: indirect laryngoscopy (tumor, formation of one of the parts of the larynx, limited mobility of the true vocal cord or fixation of the affected half of the larynx, narrowing of the glottis); palpation examination of the lymph nodes of the neck on both sides (the presence of enlarged cervical lymph nodes of a dense consistency, immobile or stiff, slightly painful or possibly not painful, more than 1.0 cm in size).

Laboratory tests: cytological examination (increase in cell size up to giant, change in the shape and number of intracellular elements, increase in the size of the nucleus, its contours, different degrees of maturity of the nucleus and other cell elements, change in the number and shape of nucleoli); histological examination (large polygonal or spiky cells with well-defined cytoplasm, round nuclei with clear nucleoli, with the presence of mitoses, cells are located in the form of cells and cords with or without keratin formation, the presence of tumor emboli in the vessels, the severity of lymphocytic plasmacytic infiltration, mitotic activity of tumor cells).

Instrumental examinations: ultrasound examination of the cervical, submandibular, supraclavicular, subclavian lymph nodes (contours are clear, uneven, echogenicity is reduced, there may be areas of mixed echogenicity, the structure of the node is heterogeneous, increased vascularization is possible); computed tomography of the larynx (a tumor formation of the larynx, occupying the right or left half, spreading to the piriform sinus or the root of the tongue or soft tissues of the anterior surface of the neck, or to the trachea area, conglomerates of lymph nodes of various sizes are possible, compressing or displacing or growing into the vascular-nerve bundle of the neck); biopsy of a laryngeal tumor (cytological examination of the material reveals an increase in the size of the cell up to giant, a change in the shape and number of intracellular elements, an increase in the size of the nucleus, its contours, different degrees of maturity of the nucleus and other elements of the cell, a change in the number and shape of nucleoli; histological examination of the material reveals large polygonal or spiky cells with well-defined cytoplasm, round nuclei with clear nucleoli, with the presence of mitoses, the cells are arranged in the form of cells and cords with or without the formation of keratin, the presence of tumor emboli in the vessels, the severity of lymphocyte-plasmocyte infiltration, mitotic activity of tumor cells); fine-needle aspiration biopsy of enlarged lymph nodes of the neck (during cytological examination of the material - an increase in the size of the cell up to giant, a change in the shape and number of intracellular elements, an increase in the size of the nucleus, its contours, different degrees of maturity of the nucleus and other elements of the cell, a change in the number and shape of nucleoli) [1].

As noted by Huang J. et al. [3] though the LC only has 1% of the total cancer cases and related deaths, it is a type of head and neck cancers with the highest prevalence. Cigarette smoking and alcohol consumption was found to have the strongest relation with LC; other potential risk factors include age (≥ 65), sex (male), family history of cancer, chemical workplace exposure, gastro-esophageal reflux, and exposure to human papillomavirus (HPV).

In their work, the authors emphasize that the global incidence and mortality rates of LC in 2020 was extracted from the Global Cancer Observatory (GLOBOCAN) database, developed by the International Agency for Research on Cancer, World Health Organization (WHO) [4].

The Gross Domestic Products (GDP) and Human Development Index (HDI) for each country were retrieved from World Bank and United Nations. For the categorization of HDI rates, <0.550 , $0.550-0.699$, $0.700-0.700$, and ≥ 0.800 are considered low, medium, high, and very high. Data from 1980 to 2020 were obtained, and the data of the most recent 10 years were used for trend analysis. The WHO mortality database was used for cancer-related death data for each country and region. Cancer mortality data was collected from national civil cancer registries on a local and national level with the registering system logging verified cancer deaths and their causes, which is then reported to WHO annually. To ensure the quality of data, only figures with medium quality or above were published by the WHO mortality database based on the timeliness, completeness and coverage of registration and the proportion of deaths assigned to ill-defined causes. All incidence and mortality figures of LC were transformed - using the Segi-Doll world reference population for various nations - into an age-standardised rate (ASR) per 100 000 individuals. Weighting was allocated in accordance with proportions of people in the standard population's corresponding age groups. This enabled the current study to compare incidence and mortality rates across different countries over time [3].

There were 184 615 newly reported cases of LC in 2020, with an ASR incidence of 2.0 per 100 000 persons. Incidence varied geographically, region with the highest incidence was Caribbean (ASR=4.0) followed by Central and Eastern Europe (ASR=3.6) and Southern Europe (ASR=2.9). Regions with the lowest incidence include Middle Africa (ASR=0.76), Western Africa (ASR=0.79), and Central America (ASR=0.86). There was a remarkable disparity among the two sexes in terms of incidence, as the global

ASR of males (ASR=3.6) was more than seven times higher than that of females (ASR=0.49). The highest incidence was in countries with medium HDI (ASR=2.5), followed by very high HDI (ASR=2.3), high HDI (ASR=1.6), and low HDI (ASR=0.94). In 2020, 99 840 LC-related deaths were reported, which was slightly more than 1% of the total cancer-related deaths. Globally, LC has an ASR of 1.0 per 100 000 persons in mortality. In terms of the geographical distribution, the Caribbean region (ASR=2.1) had the highest mortality rate, doubling the global average, followed by Central and Eastern Europe (ASR=1.9), and South-Central Asia (ASR=1.7). Regions with the lowest mortality were Australia and New Zealand (ASR=0.34), Micronesia (ASR=0.45), and Middle Africa (ASR=0.54). Similar to incidence, the highest mortality was in countries with medium HDI (ASR=1.6), followed by high HDI (ASR=0.92), very high HDI (ASR=0.86), and low HDI (ASR=0.71). Among males LC incidence was associated with a higher HDI ($\beta=0.175$, 95% confidence interval (CI): 0.111-0.239, $P<0.001$), prevalence of smoking ($\beta=0.051$, 95% CI: 0.041-0.061, $P<0.001$), alcohol drinking ($\beta=0.040$, 95% CI: 0.028-0.052, $P<0.001$), unhealthy dietary ($\beta=0.012$, 95% CI: 0.006-0.018, $P<0.001$), obesity ($\beta=0.022$, 95% CI: 0.012-0.031, $P<0.001$), hypertension ($\beta=0.031$, 95% CI: 0.022-0.041, $P<0.001$), diabetes ($\beta=0.032$, 95% CI: 0.014-0.051, $P=0.001$), and lipid disorders ($\beta=0.021$, 95% CI: 0.013-0.029, $P<0.001$). Among females, incidence was associated with a higher HDI ($\beta=0.114$, 95% CI: 0.050-0.178, $P<0.001$), prevalence of smoking ($\beta=0.049$, 95% CI: 0.033-0.065, $P<0.001$), inactivity ($\beta=0.040$, 95% CI: 0.009-0.072, $P=0.011$), obesity ($\beta=0.013$, 95% CI: 0.004-0.022, $P=0.004$), hypertension ($\beta=0.012$, 95% CI: 0.002-0.023, $P=0.024$), diabetes ($\beta=0.051$, 95% CI: 0.031-0.071, $P<0.001$), and lipid disorders ($\beta=0.015$, 95% CI: 0.007-0.023, $P<0.001$). Among males LC mortality was associated with a higher HDI ($\beta=0.094$, 95% CI: 0.025-0.163, $P<0.001$), prevalence of smoking ($\beta=0.044$, 95% CI: 0.033-0.054, $P<0.001$), alcohol drinking ($\beta=0.025$, 95% CI: 0.013-0.038, $P<0.001$), unhealthy dietary ($\beta=0.009$, 95% CI: 0.003-0.015, $P=0.002$), obesity ($\beta=0.016$, 95% CI: 0.006-0.025, $P=0.001$), hypertension ($\beta=0.025$, 95% CI: 0.015-0.034, $P<0.001$), and lipid disorders ($\beta=0.013$, 95% CI: 0.004-0.021, $P=0.003$). Among females, mortality was associated with a lower GDP per capita ($\beta=-0.076$, 95% CI: -0.126-0.027, $P=0.003$), and prevalence of alcohol drinking ($\beta=-0.060$, 95% CI: -0.085-0.035, $P<0.001$) [3].

Overall, more countries were showing decreasing trends than increasing trends in LC while such trends were less evidence among female population, younger subjects, and countries from Europe. The overall incidence for males was decreasing while females reported mixed trends. For males, significant increases were found only in Cyprus [average annual percent change (AAPC)=5.88; 95% CI: 0.52-11.52; $P=0.035$], whilst decreasing trends were reported in 24 countries evenly distributed in different continents, Chile (AAPC=-11.5; 95% CI: -20.99-0.88; $P=0.038$) reported the largest decrease, followed by the Philippines (AAPC=-7.71; 95% CI: -12.15-3.05; $P=0.006$), and Norway (AAPC=-5; 95% CI: -8.71-1.14; $P=0.018$). For females, three countries showed significant increasing trends: Japan (AAPC=6.01; 95% CI: 1.51-10.71; $P=0.015$), Switzerland (AAPC=5.61; 95% CI: 0.05-11.49; $P=0.048$), and Czech Republic (AAPC=3.31; 95% CI: 1.28-5.39; $P=0.005$). Evident decreases were found in six countries, with India (AAPC=-8.35; 95% CI: -13.62-2.75; $P=0.009$), Korea (AAPC=-8.28; 95% CI: -11.68-4.74; $P=0.001$), and Turkey (AAPC=-6.05; 95% CI: -10.21-1.69; $P=0.013$) reporting the largest decreases. Similar to the incidence trends, there was a remarkable difference between the mortality trends of males and females. For males, only Thailand (AAPC=5.41; 95% CI: 3.56-7.30; $P<0.001$) reported significant increases. On the contrary, significant decreases were observed in 30 countries. The largest decreases were found in Korea (AAPC=-7.17; 95% CI: -8.65-5.66; $P<0.001$), Singapore (AAPC=-7.10; 95% CI: -13.59-0.11; $P=0.047$), and France (AAPC=-5.96; 95% CI: -6.76-5.15; $P<0.001$). For females, significant increasing trends were found in Israel (AAPC=12.49; 95% CI: 0.81-25.51; $P=0.038$); while significant decreases were reported in eight countries, with Korea (AAPC=-10.58; 95% CI: -15.61-5.24; $P=0.002$), Belarus (AAPC=-7.93; 95% CI: -13.55-1.95; $P=0.010$), and Colombia (AAPC=-5.68; 95% CI: -8.04-3.27; $P=0.001$) reported the most evident decreases. For the older males aged 50 or above two countries reported significant increases: Cyprus (AAPC=6.87; 95% CI: 1.16-12.91; $P=0.024$), and Belarus (AAPC=1.41; 95% CI: 0.28-2.55; $P=0.021$). In contrast, significant decreases were observed in 21 countries sporadically distributed worldwide. The largest decreases were found in Chile (AAPC=-10.31; 95% CI: -19.44-0.14; $P=0.048$), Philippines (AAPC=-7.57; 95% CI: -11.86-3.08; $P=0.005$), and Norway (AAPC=-5.69; 95% CI: -8.87-2.41; $P=0.004$). For females aged 50 or above, three countries, all European countries, reported significant increases: Spain (AAPC=6.76; 95% CI: 2.03-11.72; $P=0.01$), Switzerland (AAPC=5.38; 95% CI: 0.25-10.78; $P=0.042$), and Czech Republic (AAPC=4.00; 95% CI: 1.73-6.32; $P=0.003$) reported the largest increases. On the other hand, four populations showed significant decreasing trends, Turkey (AAPC=-6.50; 95% CI: -11.64-1.07; $P=0.025$) reported the largest decline, followed by Canada (AAPC=-4.36; 95% CI: -6.94-1.70; $P=0.006$), and the white population in the USA (AAPC=-2.98; 95% CI: -5.13-0.78; $P=0.014$). Similar

distribution but larger increase was found in males aged below 50 Norway (AAPC=18.77; 95% CI: 4.55-34.92; $P=0.014$) and Thailand (AAPC=10.24; 95% CI: 0.36-21.09; $P=0.044$) reported significant increasing trends, whereas evident decreasing trends were observed in 17 countries, predominately Asian and European countries, with Germany (AAPC=-17.17; 95% CI: -26.66-6.44; $P=0.007$), Denmark (AAPC=-9.88; 95% CI: -17.74-1.26; $P=0.030$), and France (AAPC=-9.66; 95% CI: -14.70-4.32; $P=0.004$) showing the greatest decreases. From the raw data, the highly significant increasing trend observed in the younger male population of Norway and Thailand was likely due to the statistical base effect as unusually low ASR was reported in the start of the 10-year interval 2010-2011 (Norway); 2003 (Thailand). For their younger females aged below 50, significant decreases were observed in two countries/regions: Hong Kong, SAR, China (AAPC=-12.44; 95% CI: -21.77-1.99; $P=0.026$) and Korea (AAPC=-11.79; 95% CI: -21.66-0.67; $P=0.041$), while no country reported significant increase [3].

In conclusion, our colleagues point out that the reported incidence for LC has been decreasing remarkably for the past decades, especially for the male population, potentially due to the reduced consumptions of cigarettes and alcohol. Its mortality has also been decreasing, possibly attributable to broader availability and applications of treatments. However, regional disparity in mortality remains due to difference in level of access to surgical care. On the contrary, it is alarming that some evident increases were observed in the female populations and younger subjects from some countries. If no mitigation interventions are implemented, such trends may continue. It is also recommended that governments should continue the implementation of smoking and alcohol reduction campaigns, to minimize further burden on healthcare system.

Nocini R. et al. in their work they say that [5] LC is a form of malignancy originating from the anatomic site called larynx (also commonly known as "voice box"), which is anatomically divided in three regions including the supraglottic larynx (encompassing the epiglottis, false vocal cords, ventricles, aryepiglottic folds and arytenoids), the glottis (encompassing the true vocal cords and the anterior and posterior commissures) and the subglottic region. Among squamous cell carcinomas, the well and moderately differentiated forms slightly prevail over poorly differentiated tumors; the larger number of LC cases originate from the glottic region (i.e., approximately two-third), followed by the supraglottic area (about 30%), whilst transglottic and purely subglottic tumors are generally less frequent. The more important risk factors for LC include tobacco use, excessive alcohol ingestion, gastro-esophageal reflux, Plummer-Vinson syndrome, anatomical malformations, exposure to heat, chemicals, asbestos, nickel or ionizing radiations, along with some viral infections (e.g., HPV). The most frequent symptoms of laryngeal malignancies include hoarseness, sore throat, dysphagia and/or painful swallowing, impairment in voice quality, otalgia, cough and hemoptysis. Despite hoarseness can develop early in patients with laryngeal malignancies, in many cases the cancer has already deeply involved the vocal cords and spreads to regional lymphatics at diagnosis. Primary tumor volume, composite nodal volumes, composite primary tumor and nodal volumes are significant predictors of unfavorable prognosis, along with advanced age, performance status, grade and depth of invasion.

In their work, the researchers note that LC is an important oncologic entity, whose prognosis depends on establishing appropriate preventive and diagnostic measures, especially in populations at higher risk. The current incidence, prevalence and mortality of LC are estimated at 2.76 cases/year per 100,000 inhabitants, 14.33 cases/year per 100,000 inhabitants and 1.66 deaths/year per 100,000 inhabitants, respectively, averaging 3.28 million Disability-Adjusted Life Years each year. Incidence and prevalence have increased by 12% and 24%, respectively during the past 3 decades, whilst mortality has declined by around 5%. The epidemiologic burden of this malignancy is approximately 5-fold higher in males and increases in parallel with ageing, peaking after 65 years of age. Both incidence and mortality rates are higher in Europe and lower in Africa, but the ratio between deaths and incidence is the highest in Africa. Incidence has gradually declined in Europe during the past 3 decades, whilst it has increased in South-East Asia and Western Pacific. Cigarette smoking and alcohol abuse contribute for about 90% of overall worldwide mortality for LC. At the same time, the conclusions state that LC still poses a high clinical and societal burden, with an escalating temporal trend not expected to reverse soon [5].

An interesting work was presented by Li C. et al. [6]. In this study, authors aimed to explore the roles of cuproptosis-related genes in LC and their potential as prognostic markers and therapeutic targets. LC, characterized by high recurrence rates and a lack of effective biomarkers, has been associated with cuproptosis, a regulated cell death process linked to cancer progression. They collected comprehensive data from The Cancer Genome Atlas and Gene Expression Omnibus databases, including gene expression profiles and clinical data of LC patients. Using clustering and gene analysis, researchers identified cuproptosis-related genes with prognostic significance. A risk model was constructed based on these

genes, categorizing patients into high- and low-risk groups for outcome comparison. Univariate and multivariate analyses were conducted to identify independent prognostic factors, which were then incorporated into a nomogram. Gene Set Enrichment Analysis was employed to explore pathways distinguishing high- and low-risk groups. This risk model, based on four genes, including transmembrane 2, dishevelled binding antagonist of β -catenin 1, stathmin 2, and G protein-coupled receptor 173, revealed significant differences in patient outcomes between high- and low-risk groups. Independent prognostic factors were identified and integrated into a nomogram, providing a valuable tool for prognostic prediction. Gene Set Enrichment Analysis uncovered up-regulated pathways specifically associated with high-risk patient samples. The authors point out that this study highlights the potential of cuproptosis-associated genes as valuable prognostic markers and promising therapeutic targets in the context of LC and sheds light on new avenues for understanding and treating this complex disease.

In a study by Ren L. et al. [7], immune signatures of LC were systematically analyzed and their role in tumor progression was assessed. Differentially expressed immune-related genes (IRGs) were screened between LC and normal tissues from The Cancer Genome Atlas (TCGA) dataset. Then, two prognosis-related IRGs aquaporin 9 (AQP9) and zeta chain of T cell receptor associated protein kinase 70 (ZAP70) were analyzed by a series of survival analysis. Based on them, molecular subtypes were constructed by unsupervised cluster analysis. Differences in survival outcomes, human leukocyte antigen (HLA) expression and immune cell infiltrations were assessed between subtypes. Expression of AQP9 and ZAP70 was validated in LC tissues and cells by reverse transcription-quantitative polymerase chain reaction (RT-qPCR) and immunohistochemistry. After silencing and overexpressing AQP9 and ZAP70, cholecystokinin-8 (CCK-8), 5-ethynyl-2'-deoxyuridine (EdU), wound healing and transwell assays were performed in TU212 and LCC cells. Totally, 315 IRGs were abnormally expressed in LC. Among them, AQP9 and ZAP70 were distinctly correlated to patients' prognosis. Two subtypes were developed with distinct survival outcomes, HLA expression and immune microenvironment. Low expression of AQP9 and ZAP70 was confirmed in LC. AQP9 and ZAP70 up-regulation distinctly suppressed proliferation, migration, and invasion of LC cells. The opposite results were investigated when their knockdown.

Our colleagues focus on the fact that the obtained findings revealed the roles of AQP9 and ZAP70 in progression of LC, and suggested that AQP9 and ZAP70 could potentially act as candidate immunotherapeutic targets for LC. Collectively, this study proposed two prognosis-related IRGs AQP9 and ZAP70. Two molecular subtypes based on AQP9 and ZAP70 may reflect immune microenvironment of LC. In vitro, their up-regulation inhibited proliferation, migration and invasion of LC cells. Results obtained demonstrated that AQP9 and ZAP70 might be candidate therapeutic targets and prognostic signatures for LC, which may assist guide clinical therapy in the future [7].

Liu W. et al. [8] in their work they say that LC is one of the most common malignant tumors among head and neck cancers. Accumulating studies have indicated that long noncoding RNAs (lncRNAs) play an important role in LC occurrence and progression, however, the functional roles and relative regulatory mechanisms of lncRNA growth arrest-specific transcript 5 (GAS5) in LC progression remain unclear. The expression of lncRNA GAS5 in both LC tissues and cell lines was evaluated using quantitative RT-qPCR assay.

The relationships between lncRNA GAS5 expression and clinical parameters were also analyzed. To determine the biological function of lncRNA GAS5, a lncRNA GAS5-specific plasmid was first transfected into LC cells using lentiviral technology. Cell counting kit-8 assay, flow cytometry, and Transwell assays were used to detect in vitro cell proliferation, apoptosis, cycle distribution, and metastasis abilities, respectively. Furthermore, in vivo cell growth experiments were also performed using nude mice. Additionally, western blotting was performed to identify the underlying regulatory mechanism. In the current study, lncRNA GAS5 was downregulated in LC tissues and its low expression was closely associated with poor tumor differentiation, advanced TNM stage, lymph node metastasis, and shorter overall survival time. In addition, lncRNA GAS5 upregulation significantly inhibited LC cell proliferation both in vitro and in vivo. Moreover, in response to lncRNA GAS5 overexpression, more LC cells were arrested at the G2/M stage, accompanied by increased cell apoptosis rates and suppressed migration and invasion capacities. Mechanistically, this data showed that the overexpression of lncRNA GAS5 significantly regulated the PI3K/AKT/mTOR signaling pathway. lncRNA GAS5 might act as a suppressor gene during LC development, as it suppressed cell proliferation and metastasis by regulating the PI3K/AKT/mTOR signaling pathway; thus, lncRNA GAS5 is a promising therapeutic biomarker for the treatment of LC. Overall, lncRNA GAS5 could serve as a tumor suppressor gene in LC, which would be a promising therapeutic biomarker for LC treatment.

Liberale C. et al. [9] note that LC is one of the most frequent tumors of the upper aero-digestive

tract. While certain factors such as alcohol consumption and tobacco smoking have been established as risk factors for LC, the correlation of many other risk factors with the mechanism of carcinogenesis remains unclear. The process of laryngeal carcinogenesis has been well described; however, there are still aspects that lack understanding, and the underlying biological mechanisms have not been fully elucidated. Indeed, the emerging role of lncRNAs, miRNAs, and mRNAs is becoming increasingly important in our understanding of cancer development and its clinical and therapeutic implications. These non-coding RNAs have been shown to play critical roles in various aspects of cancer biology, including tumor initiation, progression, metastasis, and response to treatment. Gaining insight into the molecular mechanisms involved in carcinogenesis could enable the prediction of tumor progression and facilitate targeted interventions at various stages of the disease. The ultimate goal is to develop precise and effective therapies through a precision medicine approach. Achieving this objective requires further comprehensive studies on the molecular biology of cancer and the role of different risk factors.

Özdaş T. et al. [10] point out that while LC does not show any obvious early symptoms, it tends to have a poor prognosis in advanced clinical stages. Chromosome region maintenance 1 (CRM1) mediates the nuclear export of some RNAs, major and tumor suppressor proteins and has been associated with the pathogenesis of many tumors. However, the clinicopathological significance of CRM1 gene expression in LC has not been clarified yet. CRM1 expression in matched tumor and normal tissues obtained from 43 LC patients were evaluated intracellular for protein and mRNA levels by immunohistochemical staining (IHC), western-blot, and quantitative real-time qRT-PCR, respectively. IHC, western-blot, and qRT-PCR analyses showed that CRM1 expression was significantly increased in LC tissue compared to normal tissue. Increased expression of CRM1 has been associated with poor prognostic clinicopathological features, including advanced tumor stage, increased tumor invasion, larger tumor size, positive lymph node metastasis, distant metastasis, and invasive histological type by IHC, western-blot, and qRT-PCR. Kaplan–Meier survival analysis showed that patients with high expression of CRM1 exhibited lower overall survival compared to those with low expression (Log-rank = 7.16, $p = 0.007$). According to the TCGA datasets, elevated CRM1 expression in head and neck cancer including cases of squamous cell laryngeal origin is associated with advanced tumor stage and histological grade ($p > 0.05$, for all). Consequently, CRM1 plays an important role in LC and may serve as an indicator and prognostic factor for poor overall survival in LC patients. In conclusion, this study revealed that CRM1 is a predictive biomarker for poor overall survival in LC patients, and that the evaluation of the clinical pTNM staging system of the tumor and CRM1 expression together may provide additional prognostic information. Moreover, inhibition of CRM1 expression may be a new therapeutic strategy for LC. Furthermore, prospective large-scale studies are needed to explore the true prognostic role of elevated CRM1 expression in laryngeal squamous cell carcinoma.

The aim of the study by Luo M.S. et al. [11] was to develop an autophagy-related model to predict the prognosis of patients with LC. Autophagy, a major cause of cancer-related death, is correlated with the pathogenesis of various diseases including cancers. Our colleagues analyzed the correlation between expression profiles of autophagy-related genes (ARGs) and clinical outcomes in 111 LC patients from TCGA. Afterward, gene functional enrichment analyses of gene ontology and Kyoto Encyclopedia of Genes and Genomes were performed to find the major biological attributes. Univariate Cox regression analyses and multivariate Cox regression analyses were performed to screen ARGs whose expression profiles were significantly associated with LC patients overall survival (OS). Furthermore, to provide the doctors and patients with a quantitative method to perform an individualized survival prediction, we constructed a prognostic nomogram. Thirty eight differentially expressed ARGs were screened out in LC patients through the TCGA database. Related functional enrichments may act as tumor-suppressive roles in the tumorigenesis of LC. Subsequently, 4 key prognostic ARGs (IKBKB, ST13, TSC2, and MAP2K7) were identified from all ARGs by the Cox regression model, which significantly correlated with OS in LC. Furthermore, the risk score was constructed, which significantly divided laryngeal cancer patients into high- and low-risk groups. Integrated with clinical characteristics, gender, N and the risk score are very likely associated with patients OS. A prognostic nomogram of ARGs was constructed using the Cox regression model. As the researchers note this study could provide a valuable prognostic model for predicting the prognosis of LC patients and a new understanding of autophagy in LC. A novel autophagy-related model and a predictive nomogram were conducted to robustly estimate LC patients survival.

Now, regarding this pathology in our country at the republican level. The incidence of LC in the Republic of Kazakhstan in 2023 was 2.2 per 100 thousand population with an increase rate of 15.5% compared to the previous year (1.9 in 2022), which in absolute numbers amounted to 436 people (370 cases a year earlier), second only to prostate cancer (16.7%). The proportion of cases diagnosed for the

first time in life, recorded by oncology organizations, was 1.2% (1.1% in 2022). At the same time, 384 men fell ill (the proportion is 2.4%, 13th rank place), women - 52 (the proportion is 0.2%, 22nd rank place), which clearly shows the gender difference in the incidence of this pathology with a pronounced predominance of the male population [12].

The LC level above the national average was established in 9 regions of the country: North Kazakhstan - 5.8 (the maximum indicator); Pavlodar - 3.8; Kostanay - 3.6; East Kazakhstan - 3.4; Abay - 3.3; Karaganda - 3.0; Akmola and Atyrau - 2.9; Mangistau - 2.6. This indicator is below the national average in 11 regions: Turkestan - 0.6 (the lowest level); the city of Astana - 1.0; Kyzylorda - 1.2; the city of Shymkent - 1.5; Ulytau and Almaty - 1.8; West Kazakhstan and Zhambyl - 1.9; Aktobe and Zhetysu regions and the city of Almaty - 2.1 per 100 thousand population. Mortality from this pathology was 0.8 per 100 thousand population, the same as a year earlier. The regions where the mortality rate from LC is above the average in the republic include: Abay - 2.5 (maximum level); North Kazakhstan - 1.9; Pavlodar - 1.6; Mangistau and Karaganda - 1.2; Zhetysu - 1.0; Aktobe - 0.9. Akmola, East Kazakhstan, Kostanay regions and the city of Almaty are on par with the national average. The lowest rates were noted in Ulytau - 0.0; Turkestan - 0.1; West Kazakhstan and the city of Shymkent - 0.3; Kyzylorda - 0.5; Atyrau and the city of Astana - 0.6; Zhambyl and Almaty - 0.7 regions per 100 thousand people [12].

One-year lethality was 19.2%, taking the 13th place among all nosological forms of malignant neoplasms. At the same time, the ratio between one-year lethality and neglect (stage IV) was 1.6. At the same time, we recall that the farthest from "1" is the worst ratio between the indicators of one-year lethality and neglect.

Next, regarding preventive examinations. It should be noted that during large-scale preventive examinations of the population in 2023, significantly more patients with malignant neoplasms were actively identified than in 2022. This is 25,193 patients versus 23,623 patients identified in 2022, i.e. +6.6%. This is due to the further abatement of the epidemiological trouble with coronavirus and the increased availability of preventive care for the population. The proportion of patients identified during routine examinations increased from 62.0% to 62.4% of the total number of patients identified per year. As for LC, the early detection of this pathology during preventive examinations increased significantly - from 50.6 to 60.9%. The number of newly identified patients with LC registered with oncology organizations amounted to 425 patients (365 patients in 2022). At the same time, the absolute number of patients with LC identified during medical examinations was 274 people (231 a year earlier), and the proportion was 64.5% and 63.3%, respectively. 167 people out of 274 are patients with stages I and II (in 2022 - 117 patients out of 231). The proportion of patients with LC detected at early stages, as indicated above, was 60.9% against 50.6% a year earlier.

Of course, when analyzing the epidemiological situation, early diagnosis indicators are very important issues.

The regions where the proportion of patients with early stage I of the pathology in question is above the national average (16.5% - 14th rank) include the following regions: the city of Almaty - 34.8% (the best indicator); Abay and Kyzylorda - 30.0%; West Kazakhstan and the city of Astana - 23.1%; North Kazakhstan - 22.6%; Karaganda - 18.8%; Akmola - 18.2%. The lowest rates of early diagnosis were recorded in the Ulytau region (not a single patient with stage I of the disease - 0.0%). Next come: Mangistau - 5.3%; the city of Shymkent - 5.6%; Kostanay - 6.7%; Pavlodar, Zhetysu and Almaty - 7.1%; Atyrau - 10.0%; Zhambyl - 13.0%; East Kazakhstan - 14.3%; Aktobe - 15.0% and Turkestan - 15.4% of the country's regions [12].

It should be noted that every second patient with LC is detected in the early (I-II) stages of this pathology (51.1%). However, the situation with this indicator is deplorable in the Ulytau region - there is not a single patient detected in the early stages of the disease. The regions where the proportion of patients with LC detected at stages I-II is above the national average include the following regions. The best indicator is in the city of Astana - 76.9%. Then follow: Pavlodar - 75.0%; West Kazakhstan - 69.2%; North Kazakhstan - 67.7%; Zhambyl - 65.2%; Aktobe - 65.0% regions and the city of Almaty - 63.0%. Low rates of early diagnosis were recorded in Ulytau - 0.0% (the worst result in the country); Turkestan - 15.4%; Almaty - 21.4%; the city of Shymkent - 22.2%; Zhetysu - 35.7%; Mangistau - 42.1%; East Kazakhstan - 42.9%; Atyrau - 45.0%; Kostanay - 46.7%; Abay, Akmola, Karaganda and Kyzylorda - 50.0% regions [12].

As is clearly seen from the above data, there is a very large spread in early diagnostics rates across the country, from very good to dismal. Of course, it is necessary to take into account migration processes and other factors that affect early diagnostics rates, but nevertheless, the results obtained give reason not to stop there, both for oncologists and otolaryngologists, general practitioners, since improving early diagnostics rates of malignant tumors, as one of the main postulates and one of the main tasks of

medicine in general, continues to be relevant today. The proportion of stage IV LC was 9.4%. At the same time, as mentioned above, the proportion of patients with this nosological form of malignant neoplasms detected at stages I-II was 51.1% (stage I - 16.5%, stage II - 34.6%), which indicates that the largest number of patients with LC was detected at locally advanced with loco-regional damage - stage III of the disease. This stage was 39.5%, i.e. almost two patients out of every five, and we know what aggressive, often complex treatment is used with such a spread of the oncological process and what a disappointing prognosis is for these patients. As for the average national indicator of the proportion of stage IV (9.4%), against this background, West Kazakhstan, Mangistau, Turkestan regions and three megalopolises - the cities of Astana, Almaty, Shymkent stand out, where not a single patient was detected in the terminal stage - 0.0%. Then come: Almaty - 3.6%; Aktobe - 5.0%; North Kazakhstan - 6.5%; Zhetysay and Pavlodar - 7.1%; Zhambyl - 8.7%; Kyzylorda - 10.0%; Kostanay - 13.3%; East Kazakhstan - 14.3%; Atyrau - 20.0%; Akmola - 22.7% regions. This list is closed by three regions, where every fourth patient was detected in the incurable stage of the disease with the worst indicator of 25.0% - Abay, Karaganda and Ulytau regions [12].

The morphological verification rate of LC in the country was 98.8%, second only to non-melanoma skin cancer (99.6%), breast cancer (99.4%) and lip cancer (99.1%) in the first three positions. At the same time, in the Pavlodar region, the morphological verification rate was 92.9%, in Akmola - 95.5%, in Almaty - 96.4%. In other regions, the disease verification rate was 100%.

The total number of patients with malignant neoplasms registered with specialized oncology organizations of the republic continued to increase and by the end of 2023 amounted to 218,186 people, with an increase of 6.0% compared to the previous year (2022 - 205,822, +5.8%). The overall incidence rate of malignant neoplasms increased by 3.9%, from 1055.3 to 1096.4 per 100 thousand people. The growth of this indicator is due to both the increase in the incidence and detection of pathology, and the increase in the survival of cancer patients. In addition, statistical data on patients diagnosed with malignant neoplasms, who have been under observation for 5 years or more, and continue to be observed in 2023, showed that the number of patients under the observation of oncological organizations in Kazakhstan for over five years continued to grow and at the end of the reporting year amounted to 117,616 people, with an increase of 6.2% (2022 - 110,790 people, + 6.6%) (form No. 7).

It is impossible to ignore such an important clinical aspect as the coverage of patients with a first-time diagnosis of LC in the Republic of Kazakhstan with special treatment.

In 2023, the number of hospitalizations for all nosological forms of malignant tumors in the country's oncology organizations amounted to 108,252 cases (2022 - 101,095), with an increase of 7.1% compared to the previous year, which is associated with a constant increase in the number of cancer patients, improved standardization of oncological care, and the development of palliative and restorative services.

At the end of 2023, the absolute number of LC patients who completed specialized treatment was 247 people, continuing treatment - 135 patients. The following results were obtained in percentage terms by methods and types of treatment. Only 12.6% of patients received surgical treatment, only radiation - 19.4%, only drug treatment - 8.9%, combined - 26.7%, complex - 21.5% and chemo-radiation - 10.1%.

Further, regarding the five-year survival of patients. As for LC, at the end of 2023, 2032 people were registered for dispensary care, or 10.2 per 100 thousand of the population. At the end of 2022 - 1899 patients or 9.7 per 100 thousand of the population, respectively.

At the same time, the mortality rate of the observed contingents in 2023 decreased compared to the previous year and amounted to 7.6% in 2023 (8.6% in 2022).

The five-year survival rate of patients with LC was 52.2% in 2023 and 53.2% in 2022 [12].

Summarizing the above, we can conclude that LC, despite not having the highest place in terms of incidence among all existing malignant tumors of other localizations, deserves close attention from specialized specialists. At the same time, taking into account a number of factors, the indicators of early diagnostics do not allow oncologists to "sleep peacefully", since the locally advanced stage III, which prevails over all stages, in addition to being widespread, gives a large number of complications due to the location of vital centers and tissue structures near the primary focus and locoregional metastases. The veiled and variable symptoms, its similarity with various non-core processes, leads to the neglect of the disease. All this requires both oncologists and, first of all, primary health care workers and, of course, otolaryngologists to increase the level of cancer alertness, inform the population about early symptoms that may indicate this pathology or the onset of proliferative changes and conduct high-tech diagnostic measures, including for the purpose of differential diagnosis and, as a result, timely treatment. People

from the risk group are recommended to visit specialized specialists annually and, if necessary, undergo an examination.

An epidemiological assessment of the situation with LC in our country suggests that there are sometimes significant differences in the regions not only in incidence rates, but also in the state of early diagnosis and mortality from this disease. In connection with the above, this pathology continues to be a serious problem in modern clinical oncology.

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OVARIAN CANCER: THE CURRENT STATE OF THE ISSUE**Arman Khozhayev***Professor of the S.N. Nugmanov Department of Oncology,
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This scientific and analytical work presents modern world and local-regional data on incidence, mortality, lethality and five-year survival rate of such a common oncological pathology as ovarian cancer. The issues of etiology and pathogenesis, modern approaches and principles of complex diagnostics, prospects for improving treatment results, as well as the prognosis are covered in detail. The epidemiological characteristics of this pathology in our republic are given in the context of the regions of the country.

Keywords: *oncology, ovarian cancer, biomarkers, cancer antigen 125, human epididymis protein 4, BRCA1/2 mutation, DNA, RNA, epidemiology, incidence, mortality, lethality, five-year survival rate, prognosis.*

Ovarian cancer (OC) is a malignant tumor that most often develops from the ovarian epithelium. Requirements for the pathomorphological conclusion in OC: 1) macroscopic description of the specimen separately for each ovary [size and weight, color, capsule condition, cross-sectional view, approximate ratio of cystic and solid components (in %), presence of papillary structures (if any, in % approximately), and other involved organs]; 2) tumor [total size (3 dimensions: height, width, length), location, type, invasion depth (in relation to the myometrium/endometrium border), myometrium thickness (mm), endometrium, involvement of the serous membrane of the uterus, involvement of the cervix, appendages)]; 3) other findings (presence of invasion into other organs); 4) lymph nodes (if present: size, location, size of the largest lymph node, number, number of cassettes); 5) microscopic description [primary tumor: histologic type, degree of differentiation, invasion, capsule/surface involvement, lymphovascular invasion, immunohistochemical (IHC) markers, metastases (preferably described separately): location of metastases (lymph nodes involved/number of nodes, size of largest metastasis, extension beyond lymph node)] [1].

The diagnostic criteria are as follows. Complaints and anamnesis: all patients are recommended to have a thorough collection of complaints and anamnesis; in the early stages, OC may be asymptomatic or cause minor discomfort; in the advanced stage, the disease manifests itself with non-specific symptoms: an increase in abdominal volume, dyspeptic symptoms, weight loss, loss of appetite, pain in the abdomen or pelvis, shortness of breath, general weakness. The level of evidence for recommendations is A (the level of evidence is 1). Comment: collecting information about complaints and anamnesis details, including family history, is carried out in order to identify factors that may influence the choice of treatment tactics.

Physical examination: a thorough physical examination is recommended; it includes a recto-vaginal examination, palpation of the abdominal organs and all groups of peripheral lymph nodes, auscultation and percussion of the lungs, palpation of the mammary glands. The level of evidence for recommendations is A (the level of reliability of evidence is 1). Comment: special attention should be paid to assessing the patient's condition according to the WHO/ECOG and/or Karnofsky scale, assessing nutritional status, pain syndrome, body temperature, hemodynamics, enlarged peripheral lymph nodes, and the presence of pleurisy and ascites.

Laboratory diagnostic tests: it is recommended to perform a complete general (clinical) blood test, a general therapeutic biochemical blood test with assessment of liver and kidney function, a complete (clinical) urine test, and a study of the blood coagulation system for all patients with OC in order to assess the patient's condition, determine the patient's treatment tactics and algorithm, and assess the prognosis of the disease. The level of evidence for recommendations is C (the level of reliability of evidence is 4). Comments: A complete blood count is performed (repeated) at least 5 days before the start of the next course of chemotherapy; in a complete general (clinical) blood test, it is advisable to assess the following parameters: hemoglobin, hematocrit, erythrocytes, mean corpuscular volume, erythrocyte distribution by size, mean corpuscular hemoglobin content, mean corpuscular hemoglobin concentration, leukocyte platelets, leukocyte formula, erythrocyte sedimentation rate; in a general therapeutic biochemical blood test with an assessment of liver and kidney function indicators - total protein, glucose, bilirubin, creatinine, urea, iron, alanine aminotransferase, aspartate aminotransferase, total bilirubin, lactate aminotransferase, alkaline phosphatase, plasma electrolytes (potassium, sodium, chlorine), in a general (clinical) urine test - determination of color, transparency of urine, its specific gravity, protein in urine, pH, glucose, ketone bodies, urobilinogen, leukocyte esterase, by hardware microscopy of epithelial cells, erythrocytes, cylinders, salt, mucus, bacteria and fungi; as part of the study of the blood coagulation system, a coagulogram (an indicative study of the hemostasis system) is assessed (fibrinogen, prothrombin (according to Quick), international normalized ratio, prothrombin time, prothrombin index, activated partial thromboplastin time, thrombin time, if indicated, additionally - antithrombin III, D-dimer, plasminogen, % activity); it is recommended that all patients undergo a study of the level of adenogenic cancer antigen CA 125 in the blood in order to identify OC and its recurrence. The level of evidence for recommendations is A (the level of reliability of evidence is 1) [1].

In the absence of morphological verification of the diagnosis, it is recommended that all patients with suspected OC undergo determination of human epididymis protein 4 (HE4) in the blood and determination of the Risk of Ovarian Malignancy Algorithm (ROMA) index in order to assess the probability of OC. The strength of the recommendations is B (the level of evidence is 2). Comment: determination of HE4 in the blood and the ROMA index does not replace the need for morphological verification of the diagnosis, but an elevated HE4 level increases the specificity of OC diagnostics; if mucinous carcinoma is suspected, it is recommended, in addition to testing the level of adenogenic cancer antigen CA 125 in the blood, to test the level of adenogenic cancer antigen CA 19-9 in the blood and test the level of carcinoembryonic antigen (CEA) in the blood serum for the purpose of differential diagnosis. The strength of the recommendations is A (the level of evidence is 2). Comment: CEA and CA 19-9 may increase in mucinous OC, which allows for subsequent monitoring of the effectiveness of the treatment; for women under 40, who have a high probability of non-epithelial tumors, it is recommended to perform a study of the alpha-fetoprotein level in the blood serum, a study of the level of chorionic gonadotropin in the blood, and a study of the level of inhibin B in the blood at the diagnostic stage. The level of evidence for recommendations is C (the level of reliability of evidence is 5). Comment: non-epithelial ovarian tumors predominate at a young age (detailed information is provided in the section on non-epithelial ovarian tumors). All patients with high-grade serous and endometrioid carcinomas are recommended to undergo molecular genetic testing for mutations in the BRCA1 and BRCA2 genes in the blood or by scraping the oral mucosa and/or in biopsy (surgical) material as predictors of the disease outcome and the choice of the patient's treatment algorithm. The level of evidence for recommendations is B (the level of reliability

of evidence is 2). *Comment: the frequency of mutations in the BRCA1 and BRCA 2 genes in the indicated histological types of tumors is about 15%. Information about the presence of a BRCA mutation is useful for determining a higher sensitivity of the tumor to therapy with alkylating agents, platinum derivatives and poly (adenosine diphosphate-ribose) polymerase (PARP) inhibitors [1].*

1. All patients with OC or suspected OC are recommended to undergo computed tomography (CT) of the chest, abdominal cavity, retroperitoneal space, and kidneys at the diagnostic stage, with or without intravenous contrast in order to determine the extent of the tumor process and plan the treatment algorithm. The level of evidence for recommendations is A (the level of reliability of evidence is 1). *Comment: CT allows (a) to visualize the primary tumor, (b) to identify metastases of the disease, (c) to assess the possibility of performing an optimal cytoreductive surgery. If CT is contraindicated or insufficiently informative, magnetic resonance imaging (MRI) with intravenous contrast may be performed. If distant metastasis is suspected, positron emission tomography (PET)/CT may be performed.*

2. All patients with OC or suspected OC are recommended to undergo MRI of the pelvic organs with or without intravenous contrast at the diagnostic stage in order to determine the extent of the tumor process and plan the treatment algorithm. The strength of the recommendations is A (the level of evidence is 1). *Comment: MRI allows (a) to visualize the primary tumor, (b) to identify metastases of the disease, (c) to assess the possibility of performing an optimal cytoreductive surgery. In case of contraindications to MRI examination or its insufficiently informativeness, as well as when it is not possible to perform MRI, CT with or without intravenous contrast is indicated. If distant metastasis is suspected, PET/CT can be performed.*

3. All patients with OC or suspected OC are recommended to undergo chest X-ray at the diagnostic stage if CT of the chest is not possible. The strength of the recommendations is C (the level of evidence is 5). *Comment: CT of the chest organs is more sensitive and specific in detecting metastases in the lungs and mediastinal lymph nodes.*

4. All patients with OC or suspected OC are recommended to undergo ultrasound examination of the lymph nodes in the cervical-supraclavicular region, axillary, inguinal lymph nodes, ultrasound of the abdominal cavity, retroperitoneal space and pelvis at the diagnostic stage if CT/MRI/PET-CT cannot be performed in order to determine the prevalence of the tumor process and plan the treatment algorithm. The level of evidence for recommendations is B (the level of reliability of evidence is 2). *Comment: Ultrasound is the simplest method for visualizing formations in the abdominal cavity, in the pelvic cavity, and secondary lymph node damage. However, this method is significantly inferior to CT/MRI/PET-CT in terms of making a decision on the first stage of treatment. Evaluation of the effect of chemotherapy according to RECIST 1.1 criteria is also impossible based on the results of ultrasound.*

5. All patients with OC or suspected OC at the diagnostic stage are recommended to undergo examination of the mammary glands in order to exclude secondary (metastatic) ovarian lesions or primary multiple malignant neoplasms. The level of evidence for the recommendations is A (the level of reliability of the evidence is 1). *Comments: Women under 40 years of age undergo ultrasound examination of the mammary glands in the first phase of the menstrual cycle, if available; women over 40 years of age are recommended to undergo mammography in the first phase of the menstrual cycle, if available. Examination of the mammary glands is carried out in accordance with the principles set out in the clinical guidelines for malignant neoplasms of the mammary glands.*

6. For patients with OC, diagnostic laparoscopy is recommended to clarify the extent of the process, morphologically verify the diagnosis and assess resectability, as well as in cases where the performance of optimal cytoreduction is questionable for staging or if it was not adequately performed during previous cytoreduction, as well as for morphological verification of the diagnosis if less invasive methods are not effective [1].

As noted by Zhu B. et al. [2] the incidence and mortality of gynaecological cancers (GCs) can significantly impact women's quality of life and increase the health care burden for organisations globally. The objective of study was to evaluate global inequalities in the incidence and mortality of GCs in 2022, based on The Global Cancer Observatory (GLOBOCAN) 2022 estimates. The future burden of GCs in 2050 was also projected. Data regarding to the total cases and deaths related to GCs, as well as cases and deaths pertaining to different subtypes of GCs, gathered from the GLOBOCAN database for the year 2022. Predictions for the number of cases and deaths in the year 2050 were derived from global demographic projections, categorised by world region and Human Development Index (HDI). In 2022, there were 1 473 427 new cases of GCs and 680 372 deaths. The incidence of gynecological cancer reached 30.3 per 100 000, and the mortality rate hit 13.2 per 100 000. The age-standardised incidence of GCs in Eastern Africa is higher than 50 per 100 000, whereas the age-standardised incidence in Northern Africa

is 17.1 per 100 000. The highest mortality rates were found in East Africa (age-standardised mortality rates of 35.3 per 100 000) and the lowest in Australia and New Zealand (age-standardised mortality rates of 8.1 per 100 000). These are related to the endemic areas of HIV and HPV. Very high HDI countries had the highest incidence of GCs, with age-standardised incidence rates of 34.8 per 100 000, and low HDI countries had the second highest incidence rate, with an age-standardised incidence rates of 33.0 per 100 000. Eswatini had the highest incidence and mortality (105.4 per 100 000; 71.1 per 100 000) and Yemen the lowest (5.8 per 100 000; 4.4 per 100 000). If the current trends in incidence and mortality are maintained, number of new cases and deaths from female reproductive tract tumours is projected to increase over the next two decades. In conclusion, the authors point out that in 2022, GCs accounted for 1 473 427 new cases and 680 372 deaths globally, with significant regional disparities in incidence and mortality rates. The highest rates were observed in Eastern Africa and countries with very high and low HDI, with Eswatini recording the most severe statistics. If current trends continue, the number of new cases and deaths from GCs is expected to rise over the next two decades, highlighting the urgent need for effective interventions.

OC is a leading cause of death in women worldwide, with more than 300,000 new cases and nearly 200,000 deaths globally each year [3].

Medina J.E. et al. emphasize in their work that [4], OC is a leading cause of death for women worldwide, in part due to ineffective screening methods. Unfortunately, OC is usually detected in advanced stages (stages III and IV) due to nonspecific clinical symptoms at earlier stages and the lack of an effective screening approach. Consequently, there is a clear unmet clinical need for the development of highly specific and sensitive assays to detect OC in its earliest stages. In their study, the authors used whole-genome cell-free DNA (cfDNA) fragmentome and protein biomarker [cancer antigen 125 (CA-125) and HE4] analyses to evaluate 591 women with OC, with benign adnexal masses, or without ovarian lesions. Using a machine learning model with the combined features, researchers detected OC with specificity >99% and sensitivities of 72%, 69%, 87%, and 100% for stages I to IV, respectively. At the same specificity, CA-125 alone detected 34%, 62%, 63%, and 100%, and HE4 alone detected 28%, 27%, 67%, and 100% of OCs for stages I to IV, respectively. This approach differentiated benign masses from OCs with high accuracy (AUC = 0.88, 95% confidence interval, 0.83-0.92). These results were validated in an independent population. These findings show that integrated cfDNA fragmentome and protein analyses detect OCs with high performance, enabling a new accessible approach for noninvasive OC screening and diagnostic evaluation.

Qian F. et al. [5] in their study note that OC is the fifth leading cause of cancer deaths in US women, due to its typically advanced stage at presentation. Furthermore, unlike breast or colorectal cancer, there is no proven screening method for OC to identify early disease and initiate treatment to improve survival. Family history, oral contraceptive use, parity, body mass index (BMI), and genetic variants are potentially useful in estimating lifetime risk. Along with this, because of differences in age at onset and tumour histology/grade, risk factors for OC might be different for BRCA1/2 mutation carriers than women in the general population. Penetrance of BRCA1/2 mutations is likely modified by other genetic variants and lifestyle or reproductive factors. Investigation of these factors could aid in implementation of strategies to reduce OC risk among mutation carriers. In their work, the authors point out that height and BMI are associated with higher OC risk in the general population, but whether such associations exist among BRCA1/2 mutation carriers is unknown. The researchers applied a Mendelian randomisation approach to examine height/BMI with OC risk using the Consortium of Investigators for the Modifiers of BRCA1/2 data set, comprising 14,676 BRCA1 and 7912 BRCA2 mutation carriers, with 2923 OC cases. They created a height genetic score using 586 height-associated variants and a BMI genetic score using 93 BMI-associated variants. Associations were assessed using weighted Cox models. Observed height was not associated with OC risk (hazard ratio [HR]: 1.07 per 10-cm increase in height, 95% confidence interval [CI]: 0.94-1.23). Height genetic score showed similar results (HR = 1.02, 95% CI: 0.85-1.23). Higher BMI was significantly associated with increased risk in premenopausal women with HR = 1.25 (95% CI: 1.06-1.48) and HR = 1.59 (95% CI: 1.08-2.33) per 5-kg/m² increase in observed and genetically determined BMI, respectively. No association was found for postmenopausal women. Interaction between menopausal status and BMI was significant (pinteraction < 0.05). Our colleagues emphasize that the results of their observation of a positive association between BMI and OC risk in premenopausal BRCA1/2 mutation carriers is consistent with findings in the general population.

Jara-Rosales S. et al. [6] in their work they say that in 2020, OC ranked fourth in incidence among gynecological cancers worldwide, following breast cancer, cervical cancer, and uterine cancer. In terms of mortality, it ranked third, establishing itself as one of the most lethal gynecological cancers. A 2021

study revealed that the variability in the incidence depends on each country and region, but the mortality rate remains similar among the 185 countries included. This behavior is attributed to nonspecific symptoms and the lack of screening programs, leading to diagnoses at advanced stages with unfavorable prognoses for patients [7]. OC constitutes a group of diverse diseases, each characterized by its own morphology and biological behavior. This heterogeneity implies that different subtypes may respond differently to treatments and show variations in their progression rates [8]. It is therefore essential to recognize this diversity to effectively address the different manifestations of OC. The risk factors for OC are divided into two categories: modifiable and non-modifiable. Modifiable factors include smoking, hormone replacement therapy, and dietary elements, among others. Non-modifiable factors include heredity, mutations in the BRCA1 and BRCA2 genes, family history, Lynch syndrome, uninterrupted ovulation cycles, and the presence of endometriosis, among others [7].

Our colleagues conducted an exhaustive search was conducted to identify literature to describe the OC biology and physiopathology for new readers, in particular focused on clinical researchers. In addition, a more stringent search was performed to find studies related to the genetic components, social determinants, and comorbidities associated with OC in South America. The search was performed through PubMed and Google Scholar, using the MeSH descriptors and keywords such as "Hereditary Breast and Ovarian Cancer Syndrome", "Latin America", "BRCA1 Genes", "BRCA2 Genes", and "Ovarian Neoplasms". Additionally, the keywords "Obesity", "chronic disease", "Comorbidity", "poverty", "education", "race", "ethnicity", "menarche", "menopause", "multiparity", "urbanization", "epidemiology", and "risk factors" were utilized to capture relevant studies. Due the reported disparities in clinical trials and other biomedical studies, the Latin American population is greatly underrepresented in most of the cancer and genomic databases, including local investigations. For this reason, the number of identified reports according to the specific topics was very small for further analysis. The revision of the literature was conducted based on original articles, including cohort studies, case-control studies, cross-sectional studies, and experimental research investigating the risk factors for OC in the South American population, and the selected articles were published within the last 10 years, with full-text availability, and were written in English or Spanish. The authors considered studies involving women from 12 South American countries, without age restrictions, focusing particularly on those analyzing genetic components, socio-economic determinants, and comorbidities. Considering the main goal of this work, they excluded studies focused on OC treatment, research validating laboratory tests for detecting OC-related mutations, and non-original content such as reviews, opinions, editorials, letters to the editor, and conference abstracts. Articles that did not clearly specify the region or country of interest, or those centered on education about OC risk factors, were also excluded. [6].

In the conclusions following from the study, the researchers note that based on the revised articles, it can be concluded that although there are reports on the prevalence of mutations in the BRCA1 and BRCA2 genes in South American countries, such as Chile, Colombia, Argentina, Uruguay, and Brazil, including Mexico as Hispanic, the general prevalence is close to 15-20% in women with hereditary risk factors or those diagnosed with ovarian and/or breast cancer. However, it is important to highlight that the available studies are limited. More research is needed to accurately determine the prevalence of the punctual mutation in each country, as well as those mutational signatures that could be unique for the Latin American population. In terms of the social, demographic, and economic factors that influence the incidence of OC, these vary by country, but similarities are observed in age, being more prevalent in women over 50 years old, and in women with poor education and difficulties in accessing healthcare. Similarly, the absence of studies regarding the effect of contraception and hormone replacement therapy in the Latin American population is highlighted, despite being widely studied factors in the international scientific literature. This gap in the research underscores the need to address these aspects in future research in the region. This article has several limitations, starting with the very limited number of studies published and the number of participants in each study. The revised literature covers several years of research conducted in each country; these years may represent disparities in funding for biomedical research, the number and capabilities of each research group and the possibility of enrolling patients, and the access to technological facilities. For now, it is not possible to conduct a more comprehensive analysis; however, this work may promote the interest of other researchers to collaborate in the systematic revision of current and future data. Regarding the need to improve lifestyles as a preventive measure to reduce the possibility of morbidities and the concomitant development of OC, although the literature may not be sufficient to conclusively establish a direct link between obesity and/or diabetes and the development of OC, the indirect association suggests the importance of conducting additional clinical studies. These studies could confirm or dismiss the hypothesis that obesity and diabetes could be related to

the risk of developing OC, thereby providing a more solid basis for future interventions and prevention strategies [6].

Bryant A. et al. [9] provide data showing that OC is the seventh most common cancer among women and a leading cause of death from gynaecological malignancies. Epithelial OC is the most common type, accounting for around 90% of all OCs. This specific type of OC starts in the surface layer covering the ovary or lining of the fallopian tube. Surgery is performed either before chemotherapy [upfront or primary debulking surgery (PDS)] or in the middle of a course of treatment with chemotherapy [neoadjuvant chemotherapy and interval debulking surgery (IDS)], with the aim of removing all visible tumour and achieving no macroscopic residual disease (NMRD). The aim of this study was to investigate the prognostic impact of size of residual disease (RD) nodules in women who received upfront or interval cytoreductive surgery for advanced (stage III and IV) epithelial OC (EOC). To assess the prognostic impact of RD after primary surgery on survival outcomes for advanced (stage III and IV) EOC. In separate analyses, primary surgery included both upfront PDS followed by adjuvant chemotherapy and neoadjuvant chemotherapy followed by IDS. Each RD threshold is considered as a separate prognostic factor. The authors searched CENTRAL (2021, Issue 8), MEDLINE via Ovid (to 30 August 2021) and Embase via Ovid (to 30 August 2021). Our colleagues included survival data from studies of at least 100 women with advanced EOC after primary surgery. RD was assessed as a prognostic factor in multivariate prognostic models. They excluded studies that reported fewer than 100 women, women with concurrent malignancies or studies that only reported unadjusted results. Women were included into two distinct groups: those who received PDS followed by platinum-based chemotherapy and those who received IDS, analysed separately. The researchers included studies that reported all RD thresholds after surgery, but the main thresholds of interest were microscopic RD (labelled NMRD), RD 0.1 cm to 1 cm [small-volume residual disease (SVRD)] and RD > 1 cm [large-volume residual disease (LVRD)]. Two review authors independently abstracted data and assessed risk of bias. Where possible, they synthesised the data in meta-analysis. To assess the adequacy of adjustment factors used in multivariate Cox models, authors used the 'adjustment for other prognostic factors' and 'statistical analysis and reporting' domains of the quality in prognosis studies tool.

Our colleagues also made judgements about the certainty of the evidence for each outcome in the main comparisons, using GRADE. The researchers examined differences between FIGO stages III and IV for different thresholds of RD after primary surgery. They considered factors such as age, grade, length of follow-up, type and experience of surgeon, and type of surgery in the interpretation of any heterogeneity. The authors also performed sensitivity analyses that distinguished between studies that included NMRD in RD categories of < 1 cm and those that did not. This was applicable to comparisons involving RD < 1 cm with the exception of RD < 1 cm versus NMRD. They evaluated women undergoing PDS and IDS in separate analyses. The researchers found 46 studies reporting multivariate prognostic analyses, including RD as a prognostic factor, which met inclusion criteria: 22,376 women who underwent PDS and 3697 who underwent IDS, all with varying levels of RD. While we identified a range of different RD thresholds, authors of the work mainly report on comparisons that are the focus of a key area of clinical uncertainty (involving NMRD, SVRD and LVRD). The comparison involving any visible disease (RD > 0 cm) and NMRD was also important. SVRD versus NMRD in a PDS setting In PDS studies, most showed an increased risk of death in all RD groups when those with macroscopic RD (MRD) were compared to NMRD. Women who had SVRD after PDS had more than twice the risk of death compared to women with NMRD (HR 2.03, 95% CI 1.80 to 2.29; I² = 50%; 17 studies; 9404 participants; moderate-certainty). The analysis of progression-free survival found that women who had SVRD after PDS had nearly twice the risk of death compared to women with NMRD (HR 1.88, 95% CI 1.63 to 2.16; I² = 63%; 10 studies; 6596 participants; moderate-certainty). LVRD versus SVRD in a PDS setting. When authors compared LVRD versus SVRD following surgery, the estimates were attenuated compared to NMRD comparisons. All analyses showed an overall survival benefit in women who had RD < 1 cm after surgery (HR 1.22, 95% CI 1.13 to 1.32; I² = 0%; 5 studies; 6000 participants; moderate-certainty). The results were robust to analyses of progression-free survival. SVRD and LVRD versus NMRD in an IDS setting The one study that defined the categories as NMRD, SVRD and LVRD showed that women who had SVRD and LVRD after IDS had more than twice the risk of death compared to women who had NMRD (HR 2.09, 95% CI 1.20 to 3.66; 310 participants; I² = 56%, and HR 2.23, 95% CI 1.49 to 3.34; 343 participants; I² = 35%; very low-certainty, for SVRD versus NMRD and LVRD versus NMRD, respectively). LVRD versus SVRD + NMRD in an IDS setting meta-analysis found that women who had LVRD had a greater risk of death and disease progression compared to women who had either SVRD or NMRD (HR 1.60, 95% CI 1.21 to 2.11; 6 studies; 1572 participants; I² = 58% for overall survival and HR 1.76, 95% CI 1.23 to 2.52; 1145 participants; I²

= 60% for progression-free survival; very low-certainty). However, this result is biased as in all but one study it was not possible to distinguish NMRD within the < 1 cm thresholds. Only one study separated NMRD from SVRD; all others included NMRD in the SVRD group, which may create bias when comparing with LVRD, making interpretation challenging. MRD versus NMRD in an IDS setting. Women who had any amount of MRD after IDS had more than twice the risk of death compared to women with NMRD (HR 2.11, 95% CI 1.35 to 3.29, I² = 81%; 906 participants; very low-certainty). Summing up the results of the study, the authors point out that in a PDS setting, there is moderate-certainty evidence that the amount of RD after primary surgery is a prognostic factor for overall and progression-free survival in women with advanced OC. Our colleagues separated our analysis into three distinct categories for the survival outcome including NMRD, SVRD and LVRD. After IDS, there may be only two categories required, although this is based on very low-certainty evidence, as all but one study included NMRD in the SVRD category. The one study that separated NMRD from SVRD showed no improved survival outcome in the SVRD category, compared to LVRD. Further low-certainty evidence also supported restricting to two categories, where women who had any amount of MRD after IDS had a significantly greater risk of death compared to women with NMRD. Therefore, the evidence presented in this review cannot conclude that using three categories applies in an IDS setting (very low-certainty evidence), as was supported for PDS (which has convincing moderate-certainty evidence) [9].

What knowledge is available today about the specifics of OC treatment? Drug resistance is the bottleneck in OC treatment. The increasing use of novel drugs in clinical practice poses challenges for the treatment of drug-resistant OC. Although maintenance therapy with PARP inhibitors (PARPis) has prolonged progression-free survival and 5-year overall survival, unfortunately, many patients do not respond to PARPis treatment due to intrinsic or acquired resistance [10].

Wang L. et al. [11] indicate that despite receiving standard-of-care therapy (optimal cytoreductive surgery followed by adjuvant chemotherapy), most patients develop recurrent disease, which is resistant to chemotherapy, resulting in a 5-year survival rate of approximately 30-40% worldwide. Drug resistance is a formidable challenge in the treatment of OC and is the primary contributor to poor prognosis. According to the National Comprehensive Cancer Network guidelines (version 1.2023), there are many therapeutic regimens for resistant OC, including some novel agents. However, the objective remission rate is still low, and the median survival time is less than 12 months due to complicated resistance mechanisms. In resistant OC, the classical mechanisms of action of common drugs can be disrupted or altered, possibly resulting in impaired therapeutic effects. Thus, treatment regimens should not rely only on empirical options. As the number of categories of agents increases, after the development of multidrug resistance, the decision of appropriate later-line therapeutic regimens is very challenging. The authors reviewed the literature regarding various drug resistance mechanisms in OC and found that the main resistance mechanisms are as follows: abnormalities in transmembrane transport, alterations in DNA damage repair, dysregulation of cancer-associated signaling pathways, and epigenetic modifications. DNA methylation, histone modifications and noncoding RNA activity, three key classes of epigenetic modifications, constitute pivotal mechanisms of drug resistance. One drug can have multiple resistance mechanisms. Moreover, common chemotherapies and targeted drugs may have cross (overlapping) resistance mechanisms. MicroRNAs (miRNAs) can interfere with and thus regulate the abovementioned pathways. A subclass of miRNAs, "epi-miRNAs", can modulate epigenetic regulators to impact therapeutic responses. Thus, they also reviewed the regulatory influence of miRNAs on resistance mechanisms. Moreover, researchers summarized recent phase I/II clinical trials of novel drugs for OC based on the abovementioned resistance mechanisms. A multitude of new therapies are under evaluation, and the preliminary results are encouraging. Summarizing the results of the study, our colleagues emphasize that with the increasing use of novel therapeutic drugs for OC, the development of later-line treatments has been under enormous pressure. Recently, resistance to a variety of therapeutic drugs, such as PARPis, angiogenesis inhibitors, and immune checkpoint inhibitors, has been found to occur. In the past, therapeutic agents for OC have been limited, and researchers have usually described the underlying mechanism and explored therapeutic strategies for overcoming resistance based on the drug classification. However, as increasing numbers of new agents are applied in clinical practice, the resistance mechanisms of these various new drugs must be identified, and these mechanisms may be similar or even identical to those of other drugs. Thus, the classification of drug resistance should not be confined to the drug category, and all should attempt to obtain insight into classification of resistance based on molecular mechanisms. The concept of drug resistance classification provides a sound basis for further research to develop more precise reversal strategies.

Instead of simply distinguishing resistance by agent, researchers attempted to classify drug

resistance by mechanism. The authors summarized four major mechanisms from the published literature: 1) abnormalities in transmembrane transport, 2) alterations in DNA damage repair, 3) dysregulation of cancer-associated signaling pathways, and 4) epigenetic modifications. In the context of the increasing number of novel agents, summary of the four resistance mechanisms of OC provides a new concept for resistance classification by molecular mechanism, not by drug category. Given the intersections between drug resistance mechanisms, this concept is likely to result in the realization of “two birds with one stone” effects on the reversal of drug resistance in OC. Furthermore, these findings are anticipated to have broad implications for the development of precise therapeutic approaches for reversing drug resistance in OC. On this basis, umbrella trials can be carried out to explore the diagnostic and therapeutic targets of the four resistance mechanisms, and this may be a direction of future researches on drug resistance in OC [11].

As Porter J.M. et al. [12] note in their study epithelial OC (ovarian carcinoma) is the most common form of the disease and comprises multiple histological types (histotypes): high-grade serous (70% of patients), endometrioid (10%), clear cell (10%), low-grade serous ($\leq 5\%$), and mucinous ($\leq 5\%$). Ovarian carcinosarcomas - previously considered a separate disease entity - are now recognized to represent metaplastic carcinomas and account for no more than 5% of diagnoses. A wealth of evidence now demonstrates that each histotype represents a unique disease entity, each with distinct developmental origins, molecular landscapes, intrinsic chemosensitivity, survival profile, and susceptibility to targeted molecular therapeutics.

The authors emphasize that complete macroscopic resection is a key factor associated with prolonged survival in OC. That being said, patients with clear cell ovarian carcinoma and low-grade serous ovarian carcinoma represent some of the groups that benefit most from achieving complete macroscopic resection; given that these cases are unlikely to respond well to neoadjuvant chemotherapy, complete primary cytoreduction is a major priority for these patients. Endometrioid ovarian carcinoma also represents a histotype in which complete macroscopic resection is associated with marked patient survival benefit. Engagement with multiple surgical teams to improve the likelihood of resecting disease at hepatobiliary, gastrointestinal, and other anatomical sites beyond the pelvis will be key for delivering optimal outcomes for such cases that present with extensive advanced-stage disease. More work is also required to understand the impact of resecting disease outside of the pelvis and abdomen. Achievement of complete macroscopic resection across the overall OC patient population is associated with markedly prolonged survival time, though differences in the degree of survival benefit are apparent across different histotypes. Patients with clear cell ovarian carcinoma derive one of the greatest survival benefits associated with complete macroscopic resection. High-grade serous ovarian carcinoma patients demonstrate highly clinically and statistically meaningful survival benefit, but the magnitude of benefit is lower than in some of the other histotypes. The extent of benefit from complete macroscopic resection does not appear to relate solely to levels of intrinsic chemosensitivity of each histotype [12].

Now, as for this pathology in our country at the republican level. The incidence of OC in the Republic of Kazakhstan in 2023 was 6.3 per 100 thousand population (6.2 in 2022) with a growth rate of 2.1% compared to the previous year, amounting to 1,251 people in absolute numbers (1,201 women a year earlier). The proportion of cases with a diagnosis established for the first time in life, recorded by oncological organizations, was 3.4%, as in the previous year in the general population, and 6.0% among women (in 2022 also 6.0%) and 4th rank place after breast cancer, cervical cancer and endometrial cancer [13].

Above the national average, OC was established in 8 regions of the country: the city of Almaty - 10.4 (maximum indicator); Pavlodar - 9.7; Karaganda - 8.6; Abay - 8.4; Akmola - 7.7; Kostanay - 7.6; North Kazakhstan - 7.5; West Kazakhstan - 7.2. Aktobe, Atyrau and Kyzylorda regions are on par with the national average. This indicator is lower than the national average in the remaining 9 regions: Turkestan - 2.9 (the lowest level); Mangistau - 3.5; Ulytau - 3.6; Almaty - 3.7; Zhambyl - 4.3; the city of Shymkent - 4.6; East Kazakhstan - 5.8; Zhetysu - 5.9 regions and the city of Astana - 6.2 per 100 thousand people. The mortality rate from this pathology in 2023 was 2.1, a year earlier - 2.4 per 100 thousand population. The regions where the mortality rate from OC is higher than the average in the republic (2.1 per 100 thousand population) include: Abay - 3.0 (maximum level); the city of Astana - 2.9; Karaganda and Pavlodar - 2.5; Kyzylorda - 2.4; Aktobe and the city of Almaty - 2.2. This indicator is at the same level with the national average in the East Kazakhstan region. The lowest rates were noted in Turkestan - 1.5 (minimum rate); Almaty and Atyrau - 1.6; Zhambyl - 1.7; Ulytau and Mangistau - 1.8; North Kazakhstan and Kostanay - 1.9; West Kazakhstan, Zhetysu, Akmola regions and the city of Shymkent - 2.0 per 100 thousand population [13].

The one-year mortality rate was 7.2% (7.9% in 2022). At the same time, the ratio between one-year mortality and neglect (stage IV) was quite high - 1.7 (a year earlier it was even higher - 2.1. At the same time, it should be noted that the farthest from "1" is the worst ratio between one-year mortality and neglect.

Now, regarding preventive examinations. It should be noted that during large-scale preventive examinations of the population in 2023, significantly more patients with malignant neoplasms were actively identified than in 2022. This is 25,193 patients against 23,623 patients identified in 2022, i.e. +6.6%. This is due to the further abatement of the epidemiological troubles due to coronavirus and the increased availability of preventive care for the population. The proportion of patients identified during preventive examinations increased from 62.0% to 62.4% of the total number of patients identified per year.

Of course, with in the analysis of the epidemiological situation, the indicators of early diagnostics are very important issues. In general, in terms of the amount of detected cases of cancer of all localizations, in 2023 the proportion of forms detected at early stages (0, I-II stages) increased from 66.3% to 67.9%. As for OC, the early detection of this pathology during preventive examinations increased from 40.5 to 44.8%. The number of newly diagnosed patients with OC registered with oncology organizations amounted to 1,218 people (1,173 - a year earlier). At the same time, the absolute number of cases detected during preventive examinations in 2023 was 863, in 2022 - 875; the proportion of cases detected during preventive examinations was 70.9% and 74.6%, respectively. Of these, patients with stages I-II - 387 in 2023 and 354 in 2022.

The regions where the proportion of patients with early stage I of the pathology in question is above the national average (31.0% and 9th place among all nosological forms of malignant neoplasms) include the following regions: the city of Almaty - 45.3%; (the best indicator); Zhetysu - 43.9%; the city of Astana - 42.2%; Zhambyl - 38.5%; Kyzylorda - 35.8%; East Kazakhstan and Akmola - 35.0%; Kostanay - 33.9%; Almaty - 33.3%.

The lowest rates of early diagnosis were recorded in 11 regions. Against this background, two regions stand out - Aktobe and Turkestan, where stage I of the disease was established at only 5.2% and 6.5%, respectively (the worst rates in the republic). Next come: Mangistau - 16.0%; the city of Shymkent - 18.5%; Pavlodar - 23.3%; Abay - 23.4%; Ulytau and West Kazakhstan - 25.0%; Karaganda - 25.5%; Atyrau - 28.6% and North Kazakhstan - 30.8% of the region [13]. It should be noted that only two patients out of every five were detected in the early (I-II stages) of this pathology, making up 41.7% in the republic. The regions where the proportion of patients with OC detected at stages I-II is higher than the national average include the following regions. The best indicator is in the Zhetysu region - 51.2%. Then come two megacities - the cities of Almaty (51.6%) and Astana (50.6%); then - East Kazakhstan and Atyrau (50.0%); Akmola (48.3%); Mangistau (48.0%); Kostanay (45.2%); Zhambyl (44.2%); North Kazakhstan (43.6%); Karaganda (42.6%) regions. Low rates of early diagnosis were recorded in the following regions. Against the general background, the Aktobe region stands out negatively, where only every tenth patient was detected in the early stages of the disease - 10.3%. Then come the following regions: Turkestan (16.1%); Shymkent city (31.5%); West Kazakhstan (33.3%); Abay (34.0%); Almaty (37.0%); Ulytau (37.5%); Pavlodar (41.1%) and Kyzylorda (41.5%) regions [13].

As can be clearly seen from the above data, there is a very large spread in early diagnostic rates across the country, from good to disappointing. Of course, it is necessary to take into account migration processes and other factors that affect early diagnostic rates, but nevertheless, the results obtained give reason not to stop there, both for oncologists and gynecological oncologists, as well as for obstetricians and gynecologists, visual diagnostic doctors, and general practitioners, since improving the rates of early diagnostics of malignant tumors has remained one of the main postulates and one of the main tasks of medicine in general, and continues to be relevant today. The proportion of stage IV OC among all nosological forms of malignant neoplasms was 7.2%, and this is the 17th rank. In general, in 2023, the proportion of malignant neoplasms of stage IV in the republic for the sum of all nosologies decreased from 12.58 to 11.7% (from 4790 to 4735 patients).

As for the average national indicator of the proportion of stage IV (7.2%), Zhetysu and Mangistau regions stand out against this background - 0.0%. Then come: Kyzylorda and Zhambyl (1.9%); Atyrau (2.4%); North Kazakhstan (2.6%); the city of Almaty (3.6%); East Kazakhstan (5.0%); Pavlodar (5.5%). The city of Astana is on the same level with the average national indicator. The indicators are lower in the following regions. Abay region stands apart from all others, where every fifth patient is diagnosed in the terminal stage of the disease (21.3%). Next come: Turkestan (12.9%); Karaganda (12.8%); Ulytau (12.5%); Aktobe (12.1%); the city of Shymkent (11.1%); Akmola (10.0%); Kostanay (9.7%); West

Kazakhstan (8.3%); Almaty (7.4%) regions.

The morphological verification rate of the disease in the country was 84.3%. In 5 regions out of 20, this is a 100% figure (East Kazakhstan, Zhambyl, Ulytau regions, as well as the cities of Astana and Shymkent). The lowest figure is in the Kyzylorda region (32.1%). Next on this list are the city of Almaty (55.2%); Zhetysay (78.0%); Mangistau and Akmola (80.0%); Aktobe (91.4%); Atyrau (92.9%); West Kazakhstan (93.8%); North Kazakhstan (94.9%); Turkestan and Kostanay (95.2%); Karaganda (95.7%); Pavlodar (95.9%); Almaty (96.3%) and Abay (97.9%) regions [13].

The total number of patients with malignant neoplasms, consisting of registered in specialized oncological organizations of the republic, continued to grow and by the end of 2023 amounted to 218,186 people, with an increase of 6.0% compared to the level of the previous year (2022 - 205,822, +5.8%). The overall incidence rate of malignant neoplasms increased by 3.9%, from 1055.3 to 1096.4 per 100 thousand population. The growth of this indicator is due to both the increase in the incidence and detection of pathology, and the increase in the survival rate of cancer patients. In addition, statistical data on patients diagnosed with malignant neoplasms, who have been under observation for 5 years or more, and continue to be observed in 2023, showed that the number of patients under observation by oncological organizations in Kazakhstan for over five years continued to grow and at the end of the reporting year amounted to 117,616 people, with an increase of 6.2% (2022 - 110,790 people, +6.6%) (form. No. 7).

It is impossible to ignore such an important clinical aspect as the coverage of patients with a first-ever diagnosis of OC in the Republic of Kazakhstan with specialized treatment.

In 2023, the number of hospitalizations for all nosological forms of malignant tumors in the country's oncology organizations amounted to 108,252 cases (2022 - 101,095), with an increase of 7.1% compared to the previous year, which is associated with a constant increase in the number of cancer patients, improved standardization of oncological care, and the development of palliative and restorative services.

At the end of 2023, the absolute number of patients with OC who completed specialized treatment amounted to 697 people, continuing treatment - 387 patients. The following results were obtained in percentage terms by methods and types of treatment. The overwhelming majority of patients received complex treatment - 68.4%, only surgical treatment - 21.1%, only drug treatment - 8.3%; combined - 0.3%, chemo-radiation - 0.1%.

Next, regarding the five-year survival rate of patients. As for OC, at the end of 2023, 8229 people or 41.4 per 100 thousand of the population were registered with the dispensary (at the end of 2022 - 7864 patients or 40.3 per 100 thousand of the population, respectively); and this is the 9th rank place among all nosological forms of malignant neoplasms.

At the same time, the mortality rate of the observed contingents in 2023 was 5.0% (6.0% - in 2022).

The five-year survival rate of patients with OC was 58.2% in 2023 (57.5% - a year earlier) [13].

Summarizing the above, we can conclude that OC occupies a significant place among all existing malignant tumors of other localizations. At the same time, despite the small percentage of patients detected at stage IV, taking into account a number of factors, the indicators of early diagnostics do not allow oncologists to "sleep peacefully", since the locally advanced stage III, which significantly prevails over all stages, in addition to the prevalence itself, gives a large number of complications and locoregional metastases, and these patients are subject to aggressive complex treatment, constituting the overwhelming percentage (68.4%) among all methods of treating this pathology. The variability and veiling of symptoms, its similarity with various non-core processes (sometimes the only symptom is a gradual increase in the abdomen due to ascites), leads to the neglect of the disease. All this requires both oncologists and gynecological oncologists, and, first of all, primary health care workers, as well as obstetricians and gynecologists and visual diagnostics doctors, to increase the level of cancer alertness, inform the population about early symptoms that may indicate this pathology or the onset of proliferative changes and conduct high-tech diagnostic measures and, as a result, timely treatment. Women at risk are advised to visit specialized specialists annually and, if necessary, undergo an examination.

An epidemiological assessment of the situation with OC in our country suggests that there are sometimes significant differences between regions not only in incidence rates, but also in the parameters of early diagnosis and mortality from this pathology. In connection with the above, this pathology continues to be a serious problem in modern clinical oncology.

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This scientific and analytical work presents modern world and local-regional data on incidence, mortality, lethality and five-year survival rate of such a common oncological pathology as kidney cancer. The issues of etiology and pathogenesis, modern approaches and principles of complex diagnostics, prospects for improving treatment results, as well as the prognosis are covered in detail. The epidemiological characteristics of this pathology in our republic are given in the context of the regions of the country.

Keywords: *oncology, nephrology, urology, kidney cancer, renal cell carcinoma, metabolic biomarkers, metabolites, exosomes, gene expression, epidemiology, incidence, mortality, lethality, five-year survival rate, prognosis.*

Kidney cancer (KC) is a malignant tumor of the kidney, which is most often a carcinoma and develops either from the epithelium of the proximal tubules and collecting ducts (renal cell carcinoma - RCC) or from the epithelium of the renal pelvis and calyces (transitional cell carcinoma) [1].

The diagnostic criteria are as follows. Complaints: pain in the side, visible hematuria and a palpable formation in the projection of the kidney. Extrarenal symptoms: inferior vena cava compression syndrome (leg edema, varicocele, dilated subcutaneous veins of the abdomen, deep vein thrombosis of the lower extremities, proteinuria - develops in about 50% of patients with massive tumor thrombosis of the inferior vena cava or with compression of the inferior vena cava by a tumor and enlarged lymph nodes; paraneoplastic syndrome - cachexia, weight loss, fever, neuromyopathy, amyloidosis, increased erythrocyte sedimentation rate, anemia.

Physical examination: with small formations, an objective examination does not reveal any pathology characteristic of RCC. As the kidney formation grows, the following can be determined: a palpable

formation in the projection of the kidneys; palpable enlarged cervical and supraclavicular lymph nodes; persistent varicocele or bilateral edema of the lower extremities, which indicates a tumor Invasions of the inferior vena cava. Laboratory tests: complete blood count – the most typical finding is anemia of varying severity; increased erythrocyte sedimentation rate; complete urine analysis – macro- or micro-hematuria, or changes in the analysis may be absent; biochemical blood test (total protein, urea, creatinine, bilirubin, glucose, alanine aminotransferase, aspartate aminotransferase, albumin, amylase) – creatinine urea may increase with signs of renal failure; coagulogram – there may be signs of blood clotting disorders; glomerular filtration rate – to assess renal function, especially in the case of a tumor in a single kidney [1].

Instrumental studies: 1) excretory intravenous urography - radiographic signs of formation - a function or decreased function of the kidney on the affected side, deformation of the renal pelvis and calyces - displacement, displacement of the calyces, pelvis, amputation of the calyces, enlarged kidney contours, etc.; in the case of computed tomography (CT) with bolus enhancement, excretory urography may not be performed; 2) angiography of the renal vessels and inferior vena cava - have limited indications, are used as additional diagnostic tools in individual patients; 3) isotope renography of the kidneys - indicated for patients with decreased renal function for a complete assessment of renal function in order to optimize the planned treatment, for example, when it is necessary to preserve renal function (in case of a locally advanced process or concomitant pathology of the gastrointestinal tract, it is necessary to examine these organs, where esophagogastroduodenoscopy, irrigoscopy, fibrocolonoscopy are used; osteoscintigraphy and CT of the brain are indicated for patients with stage III-IV KC, as well as patients with symptoms that may be manifestations of a metastatic process; 4) angiography of the renal vessels - when planning renal artery embolization; 5) magnetic resonance imaging (MRI) of the retroperitoneal organs or abdominal organs - when detecting fluid formations in the kidney for differential diagnosis of cystic RCC and cancer in a cyst from benign fluid formations; 6) percutaneous kidney biopsy - for the purpose of establishing a histological diagnosis, for selecting patients with a small tumor for dynamic observation; for clarifying the histological nature of the tumor before its removal or the use of ablative treatment methods; for selecting patients with metastases most suitable for targeted pharmacological therapy (kidney biopsy is not indicated for patients with concomitant pathology and a weakened state, who can only be considered for conservative treatment (watchful waiting) regardless of the biopsy results); 7) ultrasound examination of the kidneys and retroperitoneal space, ultrasound of the abdominal organs - detection of a formation at an early stage, on the basis of which a further in-depth examination is decided; 8) echocardiography - prescribed to patients with concomitant cardiac pathology or suspected presence of a thrombus in the atrium; 9) ultrasound dopplerography of the renal vessels and inferior vena cava (if a thrombus is suspected) and / or MRI; to assess the spread of a tumor thrombus and the state of blood flow in the examined area; 10) ultrasound dopplerography of the vessels of the lower extremities - when planning surgery on a kidney tumor to exclude thrombosis of the veins of the lower extremities; 11) ultrasound of the pelvic organs - assessment of the condition of the pelvic organs; 12) chest X-ray in two projections - to exclude pulmonary changes when preparing the patient for surgery; 13) multispiral CT of abdominal organs and retroperitoneal space with bolus enhancement - prescribed as an additional examination if formations of unclear etiology are detected on ultrasound; 14) MRI of abdominal organs (with contrast) - to determine the nature of the neoplasm, study the spread of tumor thrombus in the inferior vena cava, if it was not possible to obtain clear information during CT examination; also indicated for patients with allergy to intravenous contrast, and pregnant women without impaired renal function; 15) CT of the chest - necessary to clarify the spread of the process in the lungs, pleura, chest bones; 16) CT of the pelvic organs - if MRI examination is impossible (due to metal implants in the patient, an installed pacemaker, etc.); 17) CT scan of the brain – if there is a suspicion of metastases to the brain, in the presence of any brain symptoms, since one of the common locations of metastases in RCC is the brain [1].

As noted by Safiri S. et al. [2], KC globally accounts for more than 131,000 deaths each year and has been found to place a large economic burden on society. The etiology of KC is mainly unknown, but appears to be multifactorial in nature. A number of different risk factors have been studied, some of which are modifiable, thus creating an opportunity for primary prevention. The risk factors for KC have been categorized as: (a) life style risk factors – tobacco smoking, excess body weight, alcohol consumption, physical activity and diet; (b) medical history – hypertension, chronic kidney diseases, kidney stones, and diabetes mellitus; (c) environmental and occupational exposures – trichloroethylene and aristolochic acid; (d) genetic risk factors and others [2,3].

Our colleagues conducted a very important study [2], the aim of which was to present a status report on the incidence, mortality and disability-adjusted life years (DALYs) associated with KC in 195

countries, from 1990 to 2017. In 2017, there were 393.0 thousand [(95% uncertainty interval (UI): 371.0-404.6)] incident cases of KC, with an age-standardised rate of 4.9 (95% UI: 4.7-5.1). This increased by 4.7% (95% UI: - 1.1 to 11.7) between 1990 and 2017, but this increase was not statistically significant. About 138.5 thousand (95% UI: 128.7-142.5) deaths occurred due to KC, with an age-standardised death rate of 1.7 (95% UI: 1.6-1.8). This death rate increased by 4.4% (95% UI: - 0.3 to 10.5) across the measurement period, but was not statistically significant. KC accounted for 3.3 million (95% UI: 3.1-3.4) DALYs in 2017, with an age-standardised rate of 41.1 (95% UI: 38.7-42.5). There was a decrease of 3.6% (95% UI: - 9.2 to 3.2) across the reporting period, but again this was not statistically significant.

At the regional-level, authors found that High-income North-America [12.1 (95% UI: 11.6-13.2)], Southern Latin America [11.6 (95% UI: 10.4-13.0)] and Eastern Europe [10.0 (95% UI: 9.5-10.5)] had the highest age-standardised incidence rates. In contrast, South Asia [1.9 (95% UI: 1.7-2.0)], Eastern Sub-Saharan Africa [2.5 (95% UI: 2.1-2.9)] and Central Sub-Saharan Africa [2.7 (95% UI: 2.2-3.3)] had the lowest age-standardised incidence rates. The age-standardised death rates were highest in Southern Latin America [4.3 (95% UI: 3.9-4.7)], Central Europe [3.8 (95% UI: 3.3-4.0)] and Eastern Europe [3.8 (95% UI: 3.6-3.9)]. In contrast, South Asia [0.62 (95% UI: 0.56-0.66)], Eastern Sub-Saharan Africa [0.77 (95% UI: 0.67-0.88)] and Central Sub-Saharan Africa [0.85 (95% UI: 0.68-1.1)] had the lowest age-standardised death rates. The age-standardised incidence and death rates were higher for males in all of the Global Burden of Disease (GBD) regions, although this difference was not statistically significant in all regions. Most regions experienced an increase in age-standardised incidence rates, with South Asia [48% (95% UI: 22-80)], Tropical Latin America [36% (95% UI: 28-45)] and High-income Asia Pacific [35% (95% UI: 13-50)] showing the largest increases. In contrast, the Caribbean [- 24% (95% UI: - 34 to 21)] and Southern Latin America [- 4% (95% UI: - 18 to 44)] showed non-significant decreases in their age-standardised incidence rates. The age-standardised death rates increased the most in East Asia [49% (95% UI: 5-75)], South Asia [39% (95% UI: 17-69)] and Central Europe [37% (95% UI: 20-45)]. The opposite was true for the Caribbean [- 22% (95% UI: - 30 to 16)], Southern Latin America [- 7% (95% UI: - 18 to 30)] and High-income North America [- 1% (95% UI: - 6 to 11)], which all showed non-significant decreases in age-standardised death rates [2].

In 1990 the highest number of incident cases were found in Western Europe [44,006 (95% UI: 38,633-45,652)], High-Income North America [39,473 (95% UI: 35,501-40,625)] and East Asia [25,170 (95% UI: 22,570-30,076)]. In 2017, the highest numbers were found in Western Europe 72,675 (95% UI: 65,477-76,756)], High-Income North America [68,842 (95% UI: 65,663-74,202)] and East Asia [52,290 (95% UI: 46,830-56,228)]. In 1990, the number of deaths were found to be highest in Western Europe [18,583 (95% UI: 16,369-19,093)], High-Income North America [11,117 (95% UI: 10,077-11,359)] and Eastern Europe [8,812 (95% UI: 7,751-9,794)]. In 2017, the highest number of deaths were found in Western Europe [30,325 (95% UI: 27,097-31,837)], High-Income North America [19,048 (95% UI: 18,297-20,091)] and East Asia [18,634 (95% UI: 16,488-19,986)]. In 2017, the age-standardised incidence rates ranged from 1.5 to 15.8 per 100,000 people for the 195 countries studied. Uruguay [15.8 (95% UI: 13.6-19.0)], Slovakia [14.1 (95% UI: 7.7-16.5)] and the Czech Republic [13.1 (95% UI: 10.7-14.5)] had the highest age-standardised incidence rates. In contrast, Bangladesh [1.5 (95% UI: 1.0-1.8)], Kenya [1.5 (95% UI: 1.1-1.9)] and Nepal [1.8 (95% UI: 1.1-2.6)] had the lowest age-standardised incidence rates. The age-standardised death rate also varied substantially by country, ranging from 0.47 to 5.6 per 100,000 people. The Czech Republic [5.6 (95% UI: 4.6-6.1)], Uruguay [5.5 (95% UI: 4.8-6.5)] and Iceland [5.2 (95% UI: 4.8-5.7)] had the highest age-standardised death rates, while Bangladesh [0.47 (95% UI: 0.34-0.58)], Kenya [0.52 (95% UI: 0.39-0.66)] and Madagascar [0.58 (95% UI: 0.41-0.73)] had the lowest rates [2].

It is very important to note the fact that, as the researchers note [2], the percentage change in age-standardized incidence rates from 1990 to 2017 varied substantially between countries. At the same time, the largest increases observed in our neighboring countries, such as Armenia [284.2% (95% UI: 115.0-390.1)], Belarus [241.0% (95% UI: 88.1-324.9)] and Latvia [216.3% (95% UI: 78.8-293.8)]. In contrast, Qatar [- 44.3% (95% UI: - 65.1 to - 3.4)] Bermuda [- 43.9% (95% UI: - 54.2 to - 11.8)] and Trinidad and Tobago [- 36.9% (95% UI: - 53.1 to 30.7)] showed decreasing trends, although not all of these were statistically significant. The percentage change in age-standardised death rates (from 1990 to 2017) also differed between countries. The largest increases were seen in Armenia [396.6% (95% UI: 187.3-526.2)], Belarus [277.5% (95% UI: 114.9-359.9)] and Latvia [256.3% (95% UI: 113.4-336.1)]. In contrast, the largest decreases during this period were found in Qatar [- 49.4% (95% UI: - 67.5 to - 10.8)], Bermuda [- 43.5% (95% UI: - 51.5 to - 15.4)] and Trinidad and Tobago [- 41.4% (95% UI: - 54.7 to 10.2)].

Sex differences in the incident rates first appeared in the 35-39 age group and increased up to the oldest age group (95+). The number of incidents was also higher in males, from the 30-34 age group up to the 85-89 age group, with a peak being seen in the 65-69 age group. The death rate was also higher in males, than in females, in all age groups. The number of DALYs was also higher in males, in most of the age groups, except the 5-9, 10-14, 90-94 and 95+ age groups. The number of DALYs peaked in the 60-64 age group. At the regional-level, the age-standardised DALY rate increased up to an Socio-Demographic Index (SDI) of approximately 0.74 and then decreased with increasing SDI values. The global age-standardised disability-adjusted life-year (DALY) rate was initially higher than expected, but then the rate fell below the expected level for the last 14 years. High-income Asia-Pacific was the only region in the GBD high-income super regions that had a lower than expected DALY rate across the entire measurement period. For the GBD super-regions of Central Europe, Eastern Europe and Central Asia, only Eastern Europe had a higher than expected DALY rate for the entire measurement period, while Central Europe had a higher than expected level for the last 13 years. From the Latin America and Caribbean super-region, only Southern and Central Latin America had higher than expected DALY rates across the entire measurement period. In the Sub-Saharan Africa super-region, only Southern Sub-Saharan Africa was found to have a lower than expected DALY rate for the entire measurement period. In the Southeast Asia, East Asia and Oceania super-regions, only Southeast Asia and East Asia had a lower than expected DALY rate from 1990 to 2017, but Oceania was lower than expected during the last 3 years of the measurement period. The South Asia region had a lower than expected DALY rate for the entire measurement period, while the North Africa and Middle East region was lower for most of the measurement period (from 1992 to 2017). There were large national differences in age-standardised DALY rates. Uruguay, the Czech Republic, Lithuania, Ukraine, Iceland, Greenland and many other countries showed higher than their expected DALY rates, whereas Singapore, Kuwait, China, Algeria, Morocco and many other countries had much lower than expected DALY rates, based only on their SDI. Globally, 18% of KC DALYs was attributable to high body mass index (BMI) in both sexes (Male: 16.5%; Female: 22.1%). The proportion of KC DALYs there were attributable to high BMI ranged from 7.1% in Eastern Sub-Saharan Africa to 29.2% in High-income North America. Furthermore, 16.6% of KC DALYs was attributable to smoking in both sexes, but this burden was higher in males (21.6%) than females (7.3%). The smoking-attributable burden also differed across GBD regions, ranging from 3.9% in Western Sub-Saharan Africa to 22.9% in Eastern Europe. Finally, the burden of KC attributable to occupational exposure to trichloroethylene was negligible [2].

An interesting study was conducted by Lin L. et al. [4]. They emphasize that metabolic reprogramming plays an important role in KC. At the same time, KC is increasingly acknowledged as a disease of metabolism [4,5].

In the work of Xu Q. et al. [6] in all age-specific groups, smoking among males, high BMI among females, and high BMI among males were the first three contributions to DALYs. The proportions of DALYs attributed to smoking, high BMI, and occupational exposure to trichloroethylene differed between genders. The most significant contribution to DALYs for males was smoking, accounting for more than 19.5% from 1990 to 2019. The contribution of smoking to KC DALYs was about 10 times higher for males than that for females. However, a high BMI more significantly contributed to DALYs among females than that of males. Occupational exposure to trichloroethylene accounted for the lowest proportion of DALYs in both sexes. Age-specific groups analysis indicated that smoking had a great impact on the elderly male groups and occupational exposure to trichloroethylene had a great impact on middle-aged groups. The influence of high BMI did not show a significant difference between age-specific groups. Increased trends of DALYs attributable to smoking and high BMI were observed in the elderly population and males. Therefore, smoking was the most significant contributor, and the high BMI was the most increasing risk factor. Their projection indicated that the rates of incidence, mortality, and the number of new cases and deaths would continue to increase in both sexes in the next decade.

Niziot J. et al. [7] in their publication say that today based on histological classification, a number of different types of KCs were classified including both benign tumors like adenoma, oncocytoma and angiomyolipoma and the most common malignant type of KC - RCC. RCC is accounting for approximately ninety percent of all neoplasms originating from the kidney. There are three main types of RCC known, namely clear cell RCC (ccRCC), papillary RCC and chromophobe RCC. Mentioned types may differ in stage, grade, and cancer-specific survival. Other subtypes of RCC are very rare and include angiomyolipoma, collecting duct carcinoma, or simple renal cyst. Currently, RCC diagnosis is based on magnetic resonance imaging, ultrasound examination or CT. Unfortunately, more than 60% of RCC cases are diagnosed incidentally. This tumor is difficult to detect, especially in its early stages, due to the lack of

characteristic symptoms including lack of the classic triad of visible haematuria, flank pain and palpable abdominal mass symptoms. Poor prognosis and high mortality rate are related to metastases and resistance to chemotherapy and radiotherapy. The study authors subjected the most differentiating metabolites between KC and normal tissues among the three analytical platforms to pathway analysis using MetaboAnalyst 5.0. MetaboAnalyst is a web-based platform dedicated for comprehensive metabolomics data analysis, interpretation and integration with other omics data (<https://www.metaboanalyst.ca/>). However, only the compounds selected in the nuclear magnetic resonance (NMR) analysis turned out to be important in the metabolic pathways in the human body, therefore the quantitative data from this platform was used to identify the most relevant pathways involved in the KC. The concentrations of fumarate, sarcosine, leucine, tryptophan and phenylalanine were subjected to pathway analysis and quantitative enrichment analysis using a MetaboAnalyst 5.0. 12 metabolic pathways, including tyrosine metabolism, arginine and proline metabolism, purine metabolism, citric acid cycle, urea cycle, aspartate metabolism, mitochondrial electron transport chain, Warburg effect, phenylalanine and tyrosine metabolism, valine, leucine and isoleucine degradation, glycine and serine metabolism, methionine metabolism and tryptophan metabolism were significantly related to KC. Furthermore, in order to expand metabolomic analysis of pathway related to KC, the quantitative enrichment analysis module in MetaboAnalyst, with extensive list of pathways from Small Molecule Pathway Database (SMPDB) was performed. SMPDB is an interactive, visual database containing more than 30 000 small molecule pathways found in humans only. The majority of these pathways are not found in any other pathway database. SMPDB is designed specifically to support pathway elucidation and pathway discovery in metabolomics, transcriptomics, proteomics and systems biology. It is able to do so, in part, by providing exquisitely detailed, fully searchable, hyperlinked diagrams of human metabolic pathways, metabolic disease pathways, metabolite signaling pathways and drug-action pathways. All SMPDB pathways include information on the relevant organs, subcellular compartments, protein_complex cofactors, protein_complex locations, metabolite locations, chemical structures and protein_complex quaternary structures (<https://smpdb.ca/>). Concentrations of 5 metabolites, identified from the global metabolomic profiling, were entered as input data. It was found that 6 additional pathways including aspartate metabolism, methionine metabolism, mitochondrial electron transport chain, purine metabolism, urea cycle and Warburg effect significantly related to KC. The power of metabolic pathways analysis was confirmed by p-value Holm p-values and false discovery rate of less than 0.001 for every pathway.

In conclusion, the researchers note that with regard to biomarker discovery, five potentially robust metabolic biomarkers in 49 tumor tissue samples of KC patients and 49 adjacent normal tissues treated as controls were identified using high-resolution ^1H NMR spectroscopy, while 11 mass spectral features were identified from nanoparticle-based laser desorption ionization mass spectrometry analyses. The most important endogenous compounds and trace elements having bioactive properties and pharmacological applicability were discussed in details. Moreover, they also demonstrated the possibility of discriminating between different KC types using high-resolution ^1H NMR metabolomics. This study also supports the value of integrated NMR and mass spectrometry to identify candidate biomarkers and characteristic changes in small molecule metabolite levels which could prove to be very valuable for use as diagnostics or to track disease progression, offering less invasive ways to screen patients with KC [7].

In spite of great efforts there are still no clinically available biomarkers for early detection, diagnosis or prognosis of KCs. Analysis of metabolic profiles from tissues and biofluids is a promising approach for the discovery of biomarkers that would enhance our abilities to predict cancer progression and to assess the effectiveness of cancer treatment [7,8].

A very interesting scientific work concerning exosomes was presented by Mao W. et al. [9]. The authors note that KC exerts a high degree of malignancy, and most of the distant metastasis occurs at an early stage; it is insensitive to chemoradiotherapy and easily develops drug resistance. The current treatment for KC mainly includes surgery, interventional embolization and targeted therapy; however, the treatment efficacy is poor. In recent years, the role of exosomes as mediators of intercellular communication and information exchange in the tumour microenvironment in tumour pathogenesis has attracted much attention. Exosomes are rich in bioactive substances such as nucleic acids, proteins and lipids and are involved in angiogenesis, immune regulation, drug resistance, formation of pre-metastatic niche, invasion and metastasis. Based on the conducted research it was established that early diagnosis of KC is one of the key factors in improving the survival rate of patients. Exosomes may benefit early diagnosis. Exosomes secreted by KC cells are abundantly present in blood, urine and other body fluids, thus providing advantages such as easy availability, non-invasive examination and tumour specificity. Owing to their small size, high mobility and lipid bilayer structure, they can easily pass through biological

membranes and protect rich bioactive substances present inside the membranes from degradation; therefore, exosomes have become a prime focus of research. Tumour-derived exosomes carry a large number of substances, including proteins, nucleic acids and lipids, which can alter the biological behaviour of target cells and participate in the development of KC. Numerous studies have found that the expression of exosomes is significantly different in patients with KC and normal subjects. Exosomes play an important role in the infiltration and metastasis of KC and also participate in tumour drug resistance and immune escape. Studies related to exosomes provide new ideas for the diagnosis and treatment of KC and offer adequate developmental prospects. However, studies on exosomes derived from RCC are mostly retrospective, and the tissue types mostly include RCC carcinoma. To promote the application of exosomes in clinical settings, more extensive studies combined with clinical trials are required, and future studies should include increased sample sizes and different tissue types and adopt a prospective study design, which will be more convincing and provide substantial medical data support for clinical translation. In addition, the study of exosomes in KC is relatively independent and none of the molecules identified seem to have been repeatedly validated in different studies, which requires more prospective clinical trials leading to more reproducible biomarkers. Moreover, further investigation is required for developing exosome-mediated tumour vaccines and understanding the effect and mechanism of drug resistance on targeted therapy for KC.

Apanovich N. et al. [10] say that the most common type of KC is a RCC (approximately 90% of cases), of which 80% are ccRCC. Moreover, distant metastases are present in approximately 30% of patients at the time of the first examination. Therefore, the ability to predict the occurrence of metastases in patients at early stages of the disease is an urgent task aimed at personalized treatment. The prediction of metastasis in patients with localized and locally advanced RCC can be of great practical importance, since it can affect both the volume of surgical intervention, the need for lymphadenectomy, and the need for adjuvant immunotherapy. In cases where renal tumors do not have metastases, the standard scope of surgical intervention is nephrectomy without regional lymph node dissection. Conducting a tumor biopsy prior to surgery or using non-invasive methods of obtaining biological material in the future, such as liquid biopsy, may make it possible to identify a group of patients with a high risk of developing metastases based on the results of gene expression analysis and methylation. In these patients, lymphadenectomy can improve long-term treatment outcomes and provide better staging. Furthermore, prediction of metastasis may be the key to deciding whether adjuvant therapy is necessary. Samples of tumor and paired histologically normal kidney tissue from patients with metastatic and non-metastatic ccRCC were studied. Gene expression was analyzed using real-time polymerase chain reaction. The level of gene methylation was evaluated using bisulfite conversion followed by quantitative methylation-specific PCR. Two groups of genes were analyzed in this study. The first group includes genes whose expression is significantly reduced during metastasis: CA9, NDUFA4L2, EGLN3, and BHLHE41 [(p < 0.001, receiver operating characteristic (ROC) analysis)]. The second group includes microRNA genes: MIR125B-1, MIR137, MIR375, MIR193A, and MIR34B/C, whose increased methylation levels are associated with the development of distant metastases (p = 0.002 to <0.001, ROC analysis). Based on the data obtained, a combined panel of genes was formed to identify patients whose tumors have a high metastatic potential. The panel can estimate the probability of metastasis with an accuracy of up to 92%.

Next, regarding KC screening. Harvey-Kelly L.L.W. et al. [11] note that KC is often asymptomatic, leading to proposals for a screening programme. The views of the public towards introducing a new screening programme for KC are unknown. The aim of study was to explore attitudes towards KC screening and factors influencing intention to attend a future screening programme. Authors conducted an online population-based survey of 1021 adults aged 45-77 years. The main outcome measure was intention to attend four possible screening tests (urine, blood, ultrasound scan, low-dose CT) as well as extended low-dose CT scans within lung cancer screening programmes. They used multivariable regression to examine the association between intention and each screening test. Most participants stated that they would be 'very likely' or 'likely' to undergo each of the screening tests [urine test: n = 961 (94.1%); blood test: n = 922 (90.3%); ultrasound: n = 914 (89.5%); low-dose CT: n = 804 (78.8%); lung CT: n = 962 (95.2%)]. Greater intention to attend was associated with higher general cancer worry and less perceived burden/inconvenience about the screening tests. Less worry about the screening test was also associated with higher intention to attend, but only in those with low general cancer worry (cancer worry scale ≤ 5). Compared with intention to take up screening with a urine test, participants were half as likely to report that they intended to undergo blood [odds ratio (OR) 0.56 (0.43-0.73)] or ultrasound [OR 0.50 (0.38-0.67)] testing, and half as likely again to report that they intended to take part in a screening programme featuring a low dose CT scan for KC screening alone [OR 0.19 (0.14-0.27)]. Participants in this

study expressed high levels of intention to accept an invitation to screening for KC, both within a KC specific screening programme and in conjunction with lung cancer screening. The choice of screening test is likely to influence uptake. Together these findings support on-going research into KC screening tests and the potential for combining KC screening with existing or new screening programmes.

As the researchers note this study is the first to assess public attitudes towards potential KC screening programmes. Participants expressed high levels of intention to take-up KC screening, both within KC specific screening programmes and in conjunction with lung cancer screening. This was despite over 80% knowing nothing about KC or having only heard of the condition before participating in the survey. There were significant differences in intention between screening modalities, with a preference for urine testing or low-dose CT combined with lung cancer screening over a blood test, ultrasound scan or low-dose CT alone. Participants were also more likely to intend to undergo screening if they reported higher general cancer worry or less burden/inconvenience associated with the screening test. Less worry about the screening test was also associated with higher intention to attend, but only in those with lower general cancer worry. For those with higher general cancer worry, the general worry about cancer appeared to dominate any worry associated with the screening test itself. In that study over 90% of survey respondents believed that there was benefit to lung cancer screening, with the majority agreeing that lung screening could reduce chances of lung cancer death and only a small minority endorsing avoidance of lung cancer screening due to fear of what might be found or low perceived effectiveness of screening. The observed differences between tests in intention to take part in a screening programme, with a preference for urine testing over a blood test, ultrasound scan or low-dose CT alone, is also consistent with existing literature which reports a preference for non-invasive tests requiring no preparation and causing no pain or long-term harm [11].

The National Comprehensive Cancer Network (NCCN) Guidelines for KC focus on the screening, diagnosis, staging, treatment, and management of RCC. Patients with relapsed or stage IV RCC typically undergo surgery and/or receive systemic therapy. Tumor histology and risk stratification of patients is important in therapy selection. The NCCN Guidelines for KC stratify treatment recommendations by histology; recommendations for first-line treatment of ccRCC are also stratified by risk group. To further guide management of advanced RCC, the NCCN KC Panel has categorized all systemic KC therapy regimens as "Preferred," "Other Recommended Regimens," or "Useful in Certain Circumstances." This categorization provides guidance on treatment selection by considering the efficacy, safety, evidence, and other factors that play a role in treatment selection. These factors include pre-existing comorbidities, nature of the disease, and in some cases consideration of access to agents [12, 13].

At the same time, as Jung M. et al. [14] point out comorbidity could influence cancer diagnosis, treatment, prognosis, or survival. Although comorbidity burden in KC patients is high, limited evidence exists on the longitudinal patterns of individual comorbidity prevalence and its impact on overall survival among KC patients, particularly in Asian populations. In their study, the authors included adults diagnosed with KC between 2010 and 2021 using the Korean nationwide health insurance database. Comorbidities assessed were any 1 of 19 specific medical conditions, diagnosed within 1 year prior to cancer diagnosis. Our colleagues calculated the incidence and age-standardized incidence rate of KC, prevalence of individual medical conditions as single or multiple comorbidities, and overall survival probability of KC patients over a 12-year period. They estimated the OR of having individual and multiple comorbidities with age and sex as independent covariates and adjusted for other comorbidities. Kaplan-Meier curves were used for overall survival at different time frames up to 5 years of follow-up. Among KC patients (N = 42,740), 68.7% were men, and median (interquartile range) age was 59 (49-68) years. Approximately 76% of patients had at least one comorbidity at the time of cancer diagnosis. Overall, hypertension (51.3%), dyslipidemia (40.2%), mild liver disease (27.4%), diabetes (25.1%), and peptic ulcer disease (18.9%) were the most prevalent comorbidities. The proportion of patients having three or more comorbidities continuously increased from 2010 (29.4%) to 2021 (44.9%). Having more comorbidities was associated with a lower probability of overall survival. The researchers emphasize that their study has several strengths, including the nationwide population-based design, a substantial cohort of KC patients, a recent and long-term study period, and systematic methodologies for assessing the longitudinal patterns of comorbidity and survival. Several limitations also should be noted. In conclusion, the authors note that this nationwide population-based study found that comorbidities were prevalent in KC patients and the proportions of patients having multiple comorbidities increased over the recent 12-year period. Although overall survival increased over time, it was attenuated by having more comorbidities. These data emphasize the importance of comprehensive management for both cancer and comorbidity in KC patients.

Now, regarding this pathology in our country at the republican level. The incidence rate of KC in

the Republic of Kazakhstan in 2023 was 8.1 per 100 thousand population (7.4 in 2022) with a growth rate of 9.6% compared to the previous year, taking a high 6th rank place among all nosological forms of malignant tumors, and amounting to 1608 people in absolute numbers (1438 cases - a year earlier). The proportion of cases with a diagnosis established for the first time in life, recorded by oncological organizations, was 4.3% (4.1% - in 2022). At the same time, 835 men fell ill (proportion - 5.2%), women - 773 (proportion - 3.7%) [15]. The average national level of the KC was set in 10 regions of the country: Pavlodar - 16.2 (the maximum indicator); North Kazakhstan - 15.2; Kostanay - 12.9; Karaganda - 12.2; East Kazakhstan - 11.1; Akmola - 9.9; the city of Almaty - 9.6; Abay - 8.9; the city of Astana - 8.8; West Kazakhstan - 8.4. Ulytau region is on par with the average national indicator. This indicator is below the average national level in 9 regions: Turkestan - 4.0 (the lowest level); the city of Shymkent - 4.2; Atyrau - 5.0; Almaty and Mangistau - 5.1; Kyzylorda - 5.8; Zhambyl - 6.3; Zhetysu - 6.7 and Aktobe - 8.0 regions per 100 thousand population.

Mortality from this pathology was 1.8 per 100 thousand population with an increase rate of 18.0% compared to the previous year, second only to thyroid cancer (19.1%) and non-melanoma skin cancer (26.0%).

The regions where the mortality rate from KC is higher than the average in the republic (1.8 per 100 thousand population) include: Pavlodar - 4.2 (maximum level); North Kazakhstan - 3.9; Abay - 3.4; Kostanay - 3.0; Akmola - 2.8; East Kazakhstan - 2.6; West Kazakhstan and Karaganda - 1.9. The lowest rates were recorded in: Almaty, Ulytau regions and the city of Shymkent - 0.9 (the lowest rate); followed by: Mangistau - 1.0; Turkestan and Aktobe - 1.3; Atyrau, Zhetysu regions and the city of Astana - 1.4; the city of Almaty - 1.5; Zhambyl and Kyzylorda regions - 1.6 per 100 thousand population [15].

One-year lethality increased by 1.2% compared to the previous year and amounted to 10.1% (8.9% in 2022). At the same time, the ratio between one-year lethality and neglect (stage IV) was 0.6, in 2022 - 0.5, and this is the best indicator among all nosological forms of malignant tumors after prostate cancer (0.3) and thyroid cancer (0.5). At the same time, we recall that the farthest from "1" is the worst ratio between the indicators of one-year lethality and neglect.

Now, regarding preventive examinations. It should be noted that during large-scale preventive examinations of the population in 2023, significantly more patients with malignant neoplasms were actively identified than in 2022. This is 25,193 patients versus 23,623 patients identified in 2022, i.e. +6.6%. This is due to the further abatement of the epidemiological situation with coronavirus and the increased availability of preventive care for the population. The proportion of patients identified during medical examinations increased from 62.0% to 62.4% of the total number of patients identified over the year.

Of course, when analyzing the epidemiological situation, early diagnosis indicators are very important issues.

As for KC, during preventive examinations, the early detection of this pathology increased from 58.7% to 64.4%. The absolute number of patients with KC identified during medical examinations was 1008 people (828 - a year earlier). At the same time, 767 are patients with early stages (in 2022 - 623 patients). In general, according to the amount of detected cases of cancer of all localizations, in 2023 the proportion of forms detected at early stages (0, I-II stages) increased from 66.3% to 67.9%. At the same time, detection at 0, I-II stages in KC increased from 75.2% to 76.1%. The regions where the proportion of patients with early stage I of the pathology in question is above the national average (50.6% and 5th rank place among the best indicators after non-melanoma skin cancer, thyroid cancer, uterine cancer and bladder cancer) include the following regions: Ulytau - 83.3% (the best indicator); North Kazakhstan - 69.2%; the city of Astana - 63.0%; Zhambyl - 62.2%; the city of Almaty - 59.5%; West Kazakhstan - 58.9%; Almaty - 56.0%; Pavlodar - 55.4%; Karaganda - 53.4%.

The lowest rates of early diagnosis were recorded in: Aktobe - 22.7% (the worst rate); East Kazakhstan - 24.7%; Kostanay - 36.3%; Shymkent city - 37.3%; Abay - 38.5%; Zhetysu - 43.5%; Mangistau - 44.7%; Kyzylorda - 45.8%; Akmola - 48.1%; Atyrau - 48.6% and Turkestan - 50.0% regions [15]. The following regions are among the regions where the proportion of patients with KC detected at stages I-II is above the national average (68.6% - 11th place). The best rate is in Ulytau region - 88.9%. It is followed by: the city of Almaty - 81.5%; Zhambyl - 78.4%; North Kazakhstan - 78.2%; Almaty - 77.3%; Kostanay - 73.5%; West Kazakhstan - 73.2%; the city of Astana - 71.4%.

Two regions are on par with the national average - Atyrau and Turkestan.

Low rates of early diagnosis were recorded in the Abay region - 50.0% (the worst result in the country, i.e. only every second patient is detected in the early stages of the disease). The situation is not much better in the East Kazakhstan - 50.6% and Akmola - 51.9% regions. Then follow: Aktobe - 57.3%;

Zhetysu - 58.7%; Mangistau - 63.2%; Karaganda - 63.9%; the city of Shymkent - 64.7%; Kyzylorda - 66.7% and Pavlodar - 67.8% regions [15].

As is clearly seen from the above data, there is a very large spread in the indicators of early diagnosis across the country, from very good to thought-provoking. Of course, it is necessary to take into account migration processes and other factors affecting the indicators of early diagnosis, but nevertheless, the results obtained give reason not to stop there, both for oncologists and nephrologists, urologists, ultrasound diagnosticians, and general practitioners, since improving the indicators of early diagnosis of malignant tumors, as it remained one of the main postulates and one of the main tasks of medicine in general, continues to be relevant today. The proportion of stage IV KC among all nosological forms of malignant neoplasms was 15.1%, and this is the 10th rank place for this indicator. In general, in 2023, the proportion of malignant neoplasms of stage IV in the republic for the sum of all nosologies decreased from 12.58 to 11.7% (from 4790 to 4735 patients).

As for the average national indicator of the proportion of stage IV (15.1%), the best indicator is in the East Kazakhstan region - 3.9%. It is followed by the following regions: Ulytau - 5.6%; North Kazakhstan - 7.7%; Almaty - 9.3%; Kyzylorda - 10.4%; the city of Almaty - 11.7%; Aktobe - 12.0%; Kostanay - 13.7%; West Kazakhstan and Atyrau - 14.3%; Zhambyl - 14.9%. The worst indicator for the neglect of KC was recorded in the Abay region, where almost every third patient was diagnosed in the terminal stage of the disease - 30.8%. It is followed by: Zhetysu - 23.9%; Karaganda - 21.8%; Akmola - 19.5%; Turkestan - 18.6%; the city of Astana - 18.5%; the city of Shymkent - 17.6%; Mangistau - 15.8% and Pavlodar - 15.7% of the regions.

The total number of patients with malignant neoplasms registered with specialized oncology organizations of the republic continued to grow and by the end of 2023 amounted to 218,186 people, with an increase of 6.0% compared to the level of the previous year (2022 - 205,822, + 5.8%). The overall incidence rate of malignant neoplasms increased by 3.9%, from 1055.3 to 1096.4 per 100 thousand population. The growth of this indicator is due to both the increase in the incidence and detection of pathology, and the increase in the survival rate of cancer patients. In addition, statistical data on patients diagnosed with malignant neoplasms, who have been under observation for 5 years or more and continue to be observed in 2023, showed that the number of patients under observation by oncological organizations in Kazakhstan for over five years continued to grow and at the end of the reporting year amounted to 117,616 people, with an increase of 6.2% (2022 - 110,790 people, +6.6%) (form No. 7).

One cannot ignore such an important clinical aspect as the coverage in the Republic of Kazakhstan of special treatment for patients diagnosed with KC for the first time in their life.

In 2023, the number of hospitalizations for all nosological forms of malignant tumors in oncological organizations of the country amounted to 108,252 cases (2022 - 101,095), with an increase of 7.1% compared to the previous year, which is associated with a constant increase in the number of cancer patients, improvement of the standardization of oncological care, and the development of palliative and restorative services. At the end of 2023, the absolute number of patients with KC who completed specialized treatment was 836 people, continuing treatment - 472 patients. In percentage terms, by methods and types of treatment, the following results were obtained. The overwhelming majority - 82.7% of patients received surgical treatment only, complex - 9.8%, drug treatment only - 3.3%, combined - 1.2%, radiation treatment only - 0.6%, chemoradiation - 0.4%. Further, regarding the five-year survival rate of patients. As for KC, at the end of 2023, 10,236 people or 51.4 per 100 thousand of the population were registered with the dispensary (at the end of 2022 - 9,506 patients or 48.7 per 100 thousand of the population, respectively); and this is a high 5th rank place among all nosological forms of malignant neoplasms.

At the same time, the mortality rate of the observed contingents in 2023 increased by 0.4% and amounted to 3.5% (3.1% - a year earlier).

The five-year survival rate of patients with KC decreased from 55.2% in 2022 to 54.8% - in 2023 [15].

Summarizing the above, we can conclude that with KC, despite the increased effectiveness of preventive examinations and fairly high rates of early diagnosis, a high number of patients with this pathology is noted annually, and the five-year survival rate does not reach 60%. Scarcity, variability and veiled symptoms, its similarity with various non-core processes, lead to neglect and progression of the disease, even during dispensary observation. All this requires both oncologists and, first of all, primary health care workers and, of course, nephrologists, urologists, ultrasound diagnostic doctors to increase the level of cancer alertness, inform the population about early symptoms that may indicate this pathology or the onset of proliferative changes and conduct high-tech diagnostic measures, including for the purpose of

differential diagnosis and, as a result, timely treatment. People from the risk group are recommended to visit specialized specialists annually and, if necessary, undergo an examination. An epidemiological assessment of the situation with KC in our country shows that there are sometimes significant differences between regions not only in incidence rates, but also in the parameters of early diagnosis and mortality from this pathology. In connection with the above, this pathology continues to be a serious problem of modern clinical oncology.

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Pedagogical sciences

EFFECTIVE METHODS FOR FORMING READING SKILLS IN KAZAKH LANGUAGE LESSONS

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It is very important to develop students' comprehensive literacy in general secondary schools. By developing literacy, we mean a series of tasks that are carried out so that students can be competitive, think critically, and demonstrate knowledge in line with modern trends. And its further improvement will be in the hands of each subject teacher at school. For example, in lessons such as mathematics, physics, and chemistry, the teacher shows the student how to solve a problem in several ways, and finally teaches him how to solve it in the easiest and most effective way. This means that the student improves his knowledge in the subject in several ways using one method. However, the implementation of effective teaching methods in the humanities is slightly different. For example, let's take the Kazakh language lesson. According to the updated curriculum, there are four skills aimed at developing the language direction in the Kazakh language lesson. They are: pronunciation, listening, reading, and writing. That is, the vast majority of tasks performed in the Kazakh language lesson revolve around these four skills. And in order to complete these tasks and achieve effective results in the lesson, it is advisable for the student to have these skills.

*First, let's give a scientific definition of what reading is. Reading is, according to methodologists I.L. Kolesnikova and O.A. Dolgina, a receptive type of speech act aimed at perceiving and understanding a written text [1]. E.I. Passov also believes that reading is a receptive type of speech act aimed at perceiving linguistic signs [2]. G. Rogova, F. Rabinovich, T. Sakharova also attribute reading to a receptive type of speech act. Since it is recognized as a type of act consisting in the reader's perception and processing of a text as a product of the reproductive activity of a particular author [3]. Therefore, reading is considered a receptive type of speech act associated with the visual perception of written linguistic information encoded by graphic signs. Reading is one of the receptive types of speech act aimed at perceiving and understanding a written text. It is a communicative act of people that provides a written form of communication. The most important goal of language learning is the formation of the ability to extract information from a graphically fixed text in the reading process, which allows the active use of the read language in various activities [4]. Reading is a complex and psychological activity of perception (perception) and memory (mnemonic). Each element of the characteristics of this activity can be considered separately. Perception (from Latin *regserio* - perception) is a psychological perception, a direct representation of objective reality through the senses [5]. It represents a whole complex of thinking. This is the complete disclosure of the object, the separation of its individual features, the allocation of information content corresponding to the purpose of the action in it, the formation of a sensory image. Reading is a learning activity that is included in all areas of education for students. According to the well-known methodologist, professor F. Orazbayeva, "reading is the process of perceiving the meaning and content of words and phrases on paper through graphic symbols as a result of thought and consciousness, and understanding and sorting out the necessary information from them" [6]. And Akhmet Baitursynuly defines reading as the repetition of the sounds of letters, referring to it as the most basic type of literacy method [7]. That is, reading, which is the core of our topic, is an issue that our scientists have been studying and considering since the beginning of the last century. It follows that the formation of reading skills is not a novelty in the field of modern methodology, as they say. Therefore, it seems appropriate to dwell extensively on the questions of why and what to focus on, not only the advantages of reading skills. So, reading is widely used in all areas that require language development. That is, it belongs to language skills. Reading skills are found not only in Kazakh language lessons, but also in all subjects designed to teach languages. A skill is an action that has been brought to the point of being automatic, formed through repeated repetition, in the process of learning, especially general reading skills. A skill is formed in the process of training. Simple repetition is not enough to form it, it requires special training. Training does not come from any repetition. For example, a person's poor handwriting cannot be corrected even after many repetitions, because there is no special training system here. It is difficult to acquire any skill without knowing certain rules about training, that is, without getting acquainted with the formation of*

skills, with how training proceeds. The correct formation of learning skills arises from the following requirements:

1. Reading techniques (correct, fast perception and pronunciation of words).
2. Understanding the content of the text (distinguishing the main idea and content). These two are closely related to each other. Because without improving reading techniques, understanding and correct reading cannot be achieved.

Our era is the era of technology and global development. We notice that not all adults prefer books to reading books, rather than phones and the Internet, where it is very difficult for students to strive to read independently. This means that children have no role models, and reading skills are the most important component of the learning process. No task can be completed correctly unless they understand what they have read. This applies to speaking correctly, expressing their thoughts, and even solving the simplest mathematical problem. All learning is built on reading in primary school. V.A. Sukhomlinsky noted that reading skills mean being sensitive to the beauty of the word, its subtle shades. That is why reading skills formation school students of teaching important of goals is considered one of them . Because he/she education and in education big plays a role , all aspects of the learner's developed personality- children further of teaching basically , new education to receive original is the key .

Reading skills are a complex phenomenon. They consist of two parts: the technical part, which includes the reading method, reading speed, accuracy, expressiveness, and the semantic part, which is responsible for understanding the content and meaning of the text being read. Using various methods of forming correct, conscious, expressive reading skills, let's try to answer the following questions: are all methods equally accessible to students? Which ones are more effective? By what methods can competent students be formed, and can their knowledge and skills help them in various situations of activity and communication throughout their lives?

First, let's pay attention to several types of reading. There are the following types of reading: research, familiarization, review and search. The researcher aims to understand the entire text, master concepts, main and secondary facts, events of the work of art. Familiarization is a free viewing of the text, reading an excerpt in order to understand the nature of the book, article, the text in general, 70-75% of the main information. Review - aimed at obtaining the most general information about the magazine, newspaper, book, text. Search - aimed at finding specific information: any data, quotes, etc.

Today, as we all understand, it is not enough to be limited to technical reading skills. In order for a student to become an active and independent participant in learning, it is necessary to teach them meaningful reading skills, that is, to be able to use any type of information, work independently with their knowledge, respond to the content of the text, understand the text, and complete the task assigned to them [8].

It is clear that in order to master reading skills, the lesson will be devoted exclusively to text. Before we dwell on specific types of reading and teaching text, let's define the word text. Text (text; tekht) - 1) a piece of information in a format or in its original form intended for printing; 2) a piece of information that is not related to the specifics of the message exchange protocol; 3) a record of the original program. Part of an object or a loadable module.

Text is a series of coherent, coherent and coherent sentences that convey information about a common (single) topic. The etymology of the word text consists of semantic structures; what a person has done, the internal connection of the elements of this done, the skill of the done, and according to these three semantic structures, it is studied by three disciplines - textual studies, hermeneutics and poetics. Textual studies determines which era or author the text in question belongs to. Hermeneutics deals with the interpretation of the text. The hermeneutics of sacred texts is called exegesis. Poetics studies the skill of considering the text. It studies how the Text is created, its structure and composition (formal school, structural poetics, generative poetics). Text can be understood in a very broad sense, as in modern semiotics (culture as text) and the philosophy of text.

The text, drafted by V. Rudnev, consists of seven articles:

- 1) all elements of the text are interconnected (interrelated) (the thesis of structural poetics).
- 2) units in which the relationship between text elements is repeated and changes are identified as motifs (thesis of motif analysis);
- 3) there is nothing random in the text (psychoanalysis);
- 4) under each individual and superficial aspect (meaning) of the text
There are deep, universal laws of a mythological nature (K.T. Jung's analytical psychology);
- 5) the text does not describe reality, it has a complex relationship with it.

enters into communication (analytic philosophy and theory of language acts);

6) What is true in one text may be false in another.

(possibly semantics of the world (thing);

7) Text is not a frozen essence, it is a dialogue between the author, the reader, and the cultural context.

That is, the text itself is created as a result of many complex processes. What we want to say is that the text is closely related to the acquisition of reading skills. Therefore, we need to constantly introduce methods to instill a certain skill in the student during the lesson.

There are many methods and approaches being developed to develop reading skills in Kazakh language lessons. Because every teacher, looking for the most suitable way to educate his students, is prone to inquisitiveness. Accordingly, in secondary schools, a lot of work is being done aimed at developing reading skills in the Kazakh language. For example, below are the types of text teaching used when working with a single text:

- read the text in full;*
- read the text in sections;*
- reading the text according to a prepared plan;*
- create a plan based on the text;*
- reading by paragraph;*
- reading the text half aloud;*
- reading the text in roles;*
- reading and summarizing the text;*
- reading the text in short;*
- find and read the part of the text that conveys the main idea;*
- Read and understand excerpts from fairy tales that depict fantasy and reality.*

Think about how much you can transform a text consisting of only a few paragraphs in a Kazakh language lesson? This is not only to increase the student's interest in the lesson, to concentrate their attention, but also to deepen their knowledge. Usually, when a student of any grade sees a long text consisting of several pages in a textbook, they are lazy and do not want to read it, saying that it is difficult and incomprehensible. The main goal of the updated curriculum is to form a student who can quickly adapt to any situation, is comprehensively competent and ready to immediately perform complex tasks, or a person ready for society. Therefore, our students should be able to fully understand the main idea and content of the text, whether they read a two-page or ten-page text. And for this, we, the teaching community, carry out planned work aimed at specific steps. It is important not only to form students' reading skills, but also to further deepen them and complicate reading tasks according to the text. Of course, the age of the students is also taken into account here. Today, in Kazakh language lessons at school, our colleagues are using methods such as research reading, skimming, summarizing, tapping, exchanging ideas, and critical reading.

Now let's dwell on the types of specific methods. It is important to remember that after the reading assignments, working with the text is the main principle here. A successfully selected text in accordance with the topic of the lesson is the greatest work in the formation of reading skills. Therefore, our text must be as informative and high-quality as possible. Then, in the reading lesson, you can use the following types of reading to develop thinking skills, interest, observation, the ability to compare, and the ability to think:

- find sentences in the text that are read loudly, softly, quickly, and slowly;*
- find and read sentences with logical implications in the text;*
- find and read sentences from the text according to the rules;*
- find and read proverbs from the text;*
- find and read sentences related to high spirits in the text;*
- find and read words with similar meanings in the text;*
- Reading the text without removing the author's words.*

The following types of teaching can be used to influence students' creative imagination during the lesson:

- find and read the passage from the text that matches the picture;*
- find answers to questions from the text;*
- find and read a passage from the text that is illustrated with imagery;*
- find and read a passage from the text that matches the proverb;*

- *find and read a passage from the text that describes a positive image of the character;*
- *Find and read a passage from the text that describes a negative character.*

In short, the formation of reading skills is an important and relevant issue in the modern education system. The development of students' reading skills is not limited to theoretical knowledge, but requires the use of effective methods and approaches in practical work. In order to improve reading skills in the Kazakh language lesson, it is very important to use different types of reading, to modernize methods of working with the text. By using different types of reading to increase the level of students' education and skills, it is possible to develop their ability to fully understand the content of the text.

The formation of students' reading skills at school is not only the task of the subject teacher, it is an important component of the general education system. The correct formation of reading skills allows the student to develop his thinking skills, language skills, creativity and critical thinking. Therefore, the main task of teachers is to form students into competent, well-rounded individuals by using effective methods and approaches in the learning process.

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Philological sciences

PRESENTATION OF SELF-AFFIRMATION IN BUSINESS COMMUNICATION

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ПРЕЗЕНТАЦИЯ САМОУТВЕРЖДЕНИЯ В ДЕЛОВОМ ОБЩЕНИИ

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Abstract

The article talks about the presentation of self-affirmation in business communication. Here, the issues of self-presentation are carefully examined. The article also points out that the result of speech self-presentation is a verbal characteristic of a businessman. It is noted that if there are problems with speech (not everyone can clearly and distinctly express their thoughts in oral speech), then the proverb "Speech is silver, silence is gold" is appropriate here. It should be taken into account that in some cases silence is really better than speech. At the end of the article, four techniques are given that are often used in oral monologue.

Аннотация

В статье говорится о презентации самоутверждения в деловом общении. Здесь тщательно просматриваются вопросы самопрезентации. В статье указывается и на то, что результатом речевой самопрезентации является словесная характеристика бизнесмена. Отмечается, что если есть проблемы с речью (не все могут ясно и чётко выражать свои мысли в устной речи), то здесь уместна поговорка «Слово — серебро, молчание — золото». Следует принять во внимание, что в ряде случаев молчание действительно лучше речи. В конце статьи даются четыре приёма, которые часто используются в устном монологе.

Keywords: self-affirmation, self-presentation, business communication, personality, psyche, temperament, emotions, character, volitional qualities, conversation.

Ключевые слова: самоутверждение, самопрезентация, деловое общение, личность, психика, темперамент, эмоции, характер, волевые качества, разговор.

«Самопознание» в деловом общении. Каждый человек может оценить друг друга по первому впечатлению или двум-трём внешним признакам и поведению. Среди основных элементов делового общения важную роль играют субъекты, передающие и принимающие информацию. Для успешного делового общения, помимо прочего, необходим фактор «самопознания» и «самопознания». Когда-то ученик Сократа Ксенофонт в своём трактате «Познай самого себя» сказал: «Кто знает себя, тот знает, что для него хорошо, и хорошо понимает, что возможно, а что нет. Он занимается тем, что знает, удовлетворяет свои потребности и живёт счастливо, не берёт того, чего не знает, не совершает ошибок, избегает несчастий. Благодаря этому он способен определять ценность других людей и, пользуясь этим, одновременно извлекает пользу и защищает себя от неприятностей». Познавая себя, человек лучше понимает других людей, что позволяет ему преодолевать коммуникативные барьеры, в том числе развивая способность находить деловых партнёров.

Личность человека формируется в результате взаимодействия биологических, социальных, психических и духовных факторов. Люди, участвующие в процессе общения, различаются по возрасту, полу и психологическим особенностям. В психической структуре человека выделяют такие компоненты, как темперамент, характер, способности, мотивы, потребности, эмоции и др. Все эти компоненты выражают его индивидуальность и определяют образ мышления и поведение конкретного человека в различных ситуациях.

Важнейшие знания в области психологии получаются для практики делового общения. Особенностью психологического подхода к личности является изучение личности человека, прежде всего, с точки зрения анализа психической структуры. Психологическая структура личности представляет собой единую модель. Как и в любой модели, в психологической структуре выделяются важнейшие черты личности:

- направленность (интересы и склонности в определённых областях);
- темперамент (динамические особенности поведения);
- характер (отношение к миру и людям);
- волевые качества (способность к произвольной регуляции поведения);
- способности (готовность к достижению успеха в той или иной области);
- эмоции (склонность к определённым эмоциям, общая эмоциональность);
- мотивация (преобладание определённых потребностей, мотивов).

Все эти компоненты, интегрированные в ментальную структуру, выражают индивидуальность и определяют образ мышления и поведения конкретного человека в различных ситуациях, включая деловое общение. Следует отметить, что личность не состоит только из отдельных характеристик, а представляет собой устойчивую систему, в которой каждая характеристика тесно связана с другими.

Основные формы делового общения. Деловое общение – это вид общения, в котором взаимоотношения предполагают завершение разговора. Например, деловое общение может происходить между коллегами, между руководителем и его подчиненными, а также в других сферах. В этом процессе определяется статус каждого из партнеров. Коммуникативные навыки позволяют партнерам адаптироваться к любым обстоятельствам. Иногда партнеры многое теряют, поскольку не придают должного значения коммуникативной стороне общения. Партнеры должны контролировать свои действия, продумывать тактику поведения, прогнозировать конечный результат и придерживаться этики делового общения. Руководитель, как человек, который более заметен, должен уделять этим вопросам особое внимание.

Деловое общение осуществляется в следующих основных формах:

- деловая беседа;
- деловые переговоры;
- спор;
- дискуссия;
- полемика;
- деловое консультирование;
- публичные выступления;
- телефонные переговоры;
- деловая переписка.

Деловая беседа — это обсуждение информации и идей, связанных с определёнными вопросами или проблемами. Деловые переговоры — основной способ достижения согласованного решения в процессе общения заинтересованных сторон. Деловая консультация — это метод коллективного обсуждения проблем группой специалистов. Деловая переписка — обобщённое название документов различного содержания, связанных с передачей текста особым способом.

Золотое правило этичного поведения в деловом общении, сверху вниз, то есть между руководством и подчинёнными, заключается в следующем: «Старайтесь устанавливать с подчинёнными отношения, аналогичные тем, которые вы ожидаете от своего руководителя».

Культура делового общения и его успешность во многом зависят от этических норм и принципов, которые руководитель применяет по отношению к своим сотрудникам. Эти нормы и принципы определяют, какие действия этически приемлемы, а какие неприемлемы в служебной деятельности. Эти нормы, прежде всего, касаются того, на каком основании отдаются приказы в процессе управления и как проявляется служебная дисциплина, определяющая деловое общение.

Нарушение этики делового общения руководителя с подчинёнными приводит к тому, что большинство людей в коллективе чувствуют себя тревожно и морально незащищённо. Отношение руководителя к сотруднику влияет на весь характер делового общения и в большинстве случаев определяет его морально-психологический климат. Именно на этом уровне, прежде всего, формируются моральные нормы и правила поведения. Деловое общение – это вид общения, в котором целью взаимоотношений является заключение сделки, решение

существующей проблемы, установление нового сотрудничества и т.д. Участниками общения являются коллеги, руководители и подчиненные, партнеры и т.д. Здесь определяется статус каждой из сторон.

Прежде всего, необходимо завоевать расположение авторитетных профессионалов в своей сфере бизнеса и уметь наладить с ними контакт. Успех большинства начинающих предпринимателей зависит от правильного выбора партнёра.

Сотрудничество с известным специалистом облегчает новичку достижение желаемого результата. Порой многие допускают грубые ошибки при установлении деловых отношений, и эти отношения воспринимаются как грубые и раздражающие.

По мнению экспертов, в настоящее время конкуренция на рынке ведётся в основном не между фирмами, а между их рекламой. Те, кто общается с нами, воспринимают наши товары и услуги как партнёров. Хотим мы этого или нет, но наш образ складывается. Эта реклама – мнение, сформированное на основе прямой или косвенной, осознанной или неосознанной, вербальной или устно-письменной информации.

Другими словами, в процессе делового общения мы вольно или невольно представляем себя. В деловом общении демонстрация нашей личности — это процесс, позволяющий нам наилучшим образом себя рекламировать. Наша речь, действия, речь, поведение, отношение к людям и окружающим — это наша реклама. Успешный бизнесмен должен заслужить доверие окружающих. Он должен уделять особое внимание доверию как умению в деловой практике.

Независимо от того, обманчиво первое впечатление или нет, бизнесмен должен сделать всё, чтобы понравиться своему коллеге с первой же минуты. Чтобы сформировать у партнёра по деловому общению положительный и авторитетный образ, он должен представить себя с помощью речи (сделать эффективную речевую презентацию). В частности, образ, сформированный с помощью речи, — это тот наш портрет, который мы показываем другим. Он должен работать на нас, а не против нас, показывать лучшие качества в реальности и при этом быть простым и искренним. Результатом речевой самопрезентации является словесная характеристика бизнесмена. Если есть проблемы с речью (не все могут ясно и чётко выражать свои мысли в устной речи), то здесь уместна поговорка «Слово — серебро, молчание — золото». В ряде случаев молчание действительно лучше речи.

Существует четыре приёма, которые часто используются в устном монологе. Некоторые из них применяются, когда необходимо вступить в диалог в другой ситуации:

- 1) говорить с людьми, а не просто говорить;
- 2) учитывать личные интересы собеседников;
- 3) не забывать улыбаться, разговаривая с собеседником;
- 4) устранять некоторые социальные табу (обоснованные или архаичные запреты на определённые темы).

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REPRESENTATION OF THE AXIOGEM OF SPIRITUALITY IN THE KAZAKH LANGUAGE WORLDVIEW**Musatayeva M.Sh.***Doctor of Philosophy, Professor***Bagymbaeva F.T.***PhD candidate***Zhanalyk T.***Master's student,**Abai Kazakh National University**Kazakhstan, Almaty***РЕПРЕЗЕНТАЦИЯ АКСИОЛОГЕМЫ ДУХОВНОСТЬ В КАЗАХСКОЙ ЯЗЫКОВОЙ КАРТИНЕ МИРА****Мусатаева М.Ш.***Д.ф.н., профессор***Багымбаева Ф.Т.***докторант PhD***Жаналык Т.***Магистрант,**Казахский национальный университет им. Абая**Казахстан, Алматы***Abstract**

In today's world, there is a peculiar ecology of spirituality, which is largely linked to globalisation processes. As we know, globalisation, like any other process, has both positive and negative features. Integration into the world inevitably leads to the levelling of national cultures, which can subsequently lead to their disappearance. This trend is a cause for concern, which explains the intensification of processes aimed at reviving and preserving national spiritual values. Thus, in Kazakhstan, the cultural programme 'Rukhani Zhandyru' (Spiritual Revival), adopted in 2017, is being actively implemented, and society's efforts are focused on promoting the Kazakh language, traditional Kazakh culture, spiritual values, and much more. Given the multilingual, multi-confessional and multinational composition of Kazakhstan, the implementation of this programme requires a special approach. Due to the fact that, in addition to the Kazakh language, Russian is also actively used by Kazakhstani citizens in the country's communication space, this article examines the representation of the concept of 'spirituality' in Kazakh and Russian YCM.

Аннотация

В современном мире наблюдается своеобразная экология духовности, связанная в большей степени с глобализационными процессами. Как известно, глобализация, как и любой другой процесс, имеет как положительные, так и отрицательные черты. Интеграция в мировую неизбежно приводит к нивелированию национальных культур, которая впоследствии может привести и к исчезновению последних. И эта тенденция не может не вызывать беспокойство, чем и объясняется активизация процессов по возрождению и сохранению национальных духовных ценностей. Так, в Казахстане года ведется активная реализация Культурной программы «Рухани жаңғыру» (Духовное возрождение), принятой в 2017 году, в связи с чем усилия общества направлены на популяризацию государственного казахского языка, традиционной казахской культуры, духовных ценностей и мн. др. Учитывая полиязычный, поликонфессиональный и многонациональный состав Казахстана, реализация этой Программы требует особого подхода. В связи с тем, что в коммуникативном пространстве страны казахстанцами наряду с казахским языком активно используется русский язык, в рамках данной статьи рассматривается представление понятия «духовность» в казахской и русской ЯКМ.

Keywords: *linguistic worldview, spirituality, value, representation, national culture, Kazakh language, Russian language.*

Ключевые слова: *языковая картина мира, духовность, ценность, репрезентация, национальная культура, казахский язык, русский язык.*

Современная антропоцентрическая научная парадигма актуализирует все изучаемые явления и процессы сквозь призму человека. Соответственно познание человека через язык позволяет познать всю его сущность. В связи с этим вполне закономерно формирование новых научных дисциплин, изучающих ценности и оценку, в числе которых аксиологическая лингвистика. Предметом лингвоаксиологии является выявление языковых средств, передающих содержание ценностей. Она функционирует в системе: «Человек – Язык – Общество – Культура – Мир», которая формирует социально значимую реальность, реализуется как в языке, так и в дискурсивных единицах речи.

Понятие духовности в казахской языковой картине мира неотделимо от наследия великого мыслителя и поэта Абая Кунанбаева. Его «Қара сөздер» («Слова назидания») [1] представляют собой не только нравственные назидания, но и целостную философскую систему, в центре которой стоит человек – с его совестью, разумом, стремлением к истине и духовному совершенствованию. Это шедевр великого просветителя, состоящий из 45 слов – это зеркало характера казахского народа. Абай, основу которого составляют честный труд, стремление к познанию и истине. Так, в 38-м Слове он обращается к потомкам с трогательным и глубоким наставлением: «Әуелі адамның адамдығы ақыл, ғылым деген нәрселерменен» (Прежде всего человечность человека определяется разумом и знанием) [1].

В его «Назиданиях» ядро аксиологемы духовность – любовь как основа понимания и передачи добра. человеческое в человеке начинается с разума и науки: При этом духовное стремление к науке и истине рождается из любви, искреннего стремления к пониманию: «Ғылым-білімді әуелі бастан бала өзі ізденіп таппайды. Қашан бір бала ғылым, білімді махаббатпенен көксерлік болса, сонда ғана оның аты адам болады» (Ребёнок сам по себе с ранних лет не ищет знания. Лишь тогда, когда он начинает стремиться к науке и знанию с любовью, только тогда он становится человеком) [1].

Таким образом, в произведениях Абая аксиологема духовность – это не абстрактное понятие, а конкретная жизненная практика, основанная на познании, любви к истине, справедливости и вере.

Это понимание пронизывает всё наследие Абая и служит фундаментом казахской концепции духовности.

Как известно, средствами вербализации аксиологем являются лексические, фразеологические и паремиологические единицы, составляющие сокровищницу любого национального языка.

В народной фразеологии, пословицах и поговорках духовность часто выражается через категории ар-намыс (совесть и честь), иман (вера, добродетель), тәрбие (воспитание), ұят (стыд как нравственная категория), адалдық (честность) и др. Например:

«Ар ұят – адамдықтың белгісі» – «Совесть и стыд – признак человечности»; «Адал адамның ары таза» – «Честный человек чист совестью»; «Ұят – иманның күзетшісі» – «Стыд – страж веры» и др.

Активные аксиологические исследования в Казахстане осуществляются с опорой на различные источники: художественную литературу, материалы масс-медиа, лексикографические источники и мн. др.[2]. Так, духовность пронизывает произведения как классиков, так и современных писателей, поэтов, драматургов и др.

Приведем несколько примеров из произведений одного из учеников великого казахского просветителя Шакарима, в которых образность и психологизм как инструмент аксиологизации: «сұм жүректің оянбауы» (непробуждённое коварное сердце), «өлі жүрек» (мёртвое сердце), «тозған ой» (изношенное мышление), «азат ақыл» (свободный разум) [3]. Эти метафоры представляют душевные и нравственные состояния, что позволяет передать внутреннюю духовную борьбу и этические ориентиры поэтического героя.

Авторы различных исследований сходятся во мнении при выделении следующих казахских традиционных ценностей: человек, честь и достоинство, терпимость, щедрость, душевная открытость, ценность слова, уважение к старшим, приоритет коллективных интересов. Эти аксиологемы можно продемонстрировать на примере различных мегафреймов, состоящих из множества терминалов, репрезентирующихся посредством языковых средств. Аксиологемы выражают этические ориентиры, формирующие духовный мир нации и укрепляющую её культурную идентичность. Приведем примеры.

Пример 1: Наурыз как проявление духовных ценностей

Наурыз, или «Ұлыстың ұлы күні» (Великий день народа), символизирует «единение и гармонию человека с природой». Этот праздник включает в себя множество обрядов, имеющих глубокий духовно – этический смысл:

- Очищение воды в родниках: «Бұлақ көрсең – көзін аш» – как метафора духовного очищения. Он символизирует духовное пробуждение и обновление: «Издревле вода считалась символом чистоты и свежести».

- Домашнее обустройство перед праздником – как ритуал духовного порядка «...чистим и убираем двор, оформляем дом в национальном стиле...» – воспоминания о праздновании Наурыза. Эти действия являются внешним выражением внутреннего очищения и уважения к традиции.

- Благословение старших – «бата беру», без которого «не начиналось ни одно дело». Бата – это не просто слова, а обряд передачи духовной энергии, нравственного наставления, пожелания добра и справедливости.

Поговорка: «Ұлыстың ұлы күні алдыңа келсе атаңның құнын кеш» – «если в день великого улыса придут с повинной, прощай кровную месть» – иллюстрирует ценность прощения, милосердия и духовного очищения. «если в день великого улыса придут с повинной, прости кровную месть за отца» – пословица, которая репрезентирует высшую форму духовности – всепрощение, заложенное в традиции праздника.

- «Көктем тұды!» – «С рождением весны!»

- – традиционное приветствие во время Наурыза, символизирующее пробуждение жизни и надежды.

Эти выражения и практики формируют аксиосферу, где духовность представлена как способность к примирению, уважению к природе и почитанию предков.

Описанию значимости данного праздника в аксиосфере казахского народа посвящено большое количество работ [4].

Пример 2: Свадебные обряды как носители духовности

В свадебной обрядности духовность проявляется через уважение, честность, благословение, почитание традиции:

- Сөз салу – предложение руки и сердца.

- Сырға салу – надевание серег как символ нареченной, придающей статус невесты

- Сватовство (құда түсу) сопровождалось обрядом құйрық-бауыр (курдюк с печенью), символизирующим согласие и единение семей (Құйрық-бауыр – «курдючное сало с печенью»

- – символ согласия, взаимного уважения, духовной близости двух семей.

- «Свидетельствует об удачном завершении сватовства» – как знак установления доверительных, почти священных связей).

- Қыз ұзату – проводы невесты из родительского дома

- Неке қию – религиозный и нравственный союз

«Неке-қию» – мусульманское венчание, когда мулла благословляет молодых, освящает чашу с водой, которую пьют жених и невеста.

Этот обряд символизирует чистоту намерений, освящённость брака и согласие с волей Всевышнего.

- Обряд беташар – открытие лица невесты, сопровождающееся знакомством с новыми родственниками со стороны жениха и поклонами невесты в знак приветствия – завершался «наставлениями, пожеланиями, советами», что подчёркивает воспитательную, духовную функцию события.

Казахская культура хранит в себе богатейший пласт духовных ценностей, репрезентируемых в языке через традиции, обычаи и обрядовые действия. Несмотря на наличие солидного арсенала работ, как отмечают исследователи, традиции и национальные обряды – мощный, все еще недостаточно изученный духовный пласт казахской культуры [2.].

Таким образом, аксиологема духовность в казахской языковой картине мира – это не только языковая категория, но и инструмент национальной самоидентификации, способ сохранения и развития казахской духовной традиции в условиях глобализации; образующая своеобразную систему, культурную трансмиссию в казахской языковой картине мира, служа механизм передачи аксиологических ориентиров из поколения в поколение.

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Philosophical sciences

HERMENEUTICS IN THE POSTMODERN WORLD: POWER, STIGMA, SPACE, AND TECHNOLOGY

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Abstract

This paper explores contemporary trajectories of hermeneutics, highlighting its role in feminist critique, epistemic injustice, literary studies, and artificial intelligence. Drawing on Gadamer's philosophical hermeneutics and recent developments in feminist health research, stigma theory, transnational postcolonial literature, and AI ethics, I argue that hermeneutics today is a dynamic practice for confronting prejudice, negotiating identity, and rethinking meaning in a globalized technological world.

Keywords: Hermeneutics, Epistemic injustice, Feminist theory, Transnational literature, Artificial intelligence, Interpretation

Introduction

Hermeneutics has moved far beyond its origins as a theory of textual interpretation. With Hans-Georg Gadamer's *Truth and Method* as a foundation, it has become a philosophy of understanding grounded in dialogue, history, and prejudice. Contemporary scholarship shows that hermeneutics can illuminate issues of power, marginalization, cultural hybridity, and even human-machine interaction.

Gadamer and Feminist Hermeneutics

Vigouroux and Hovey show how Gadamerian hermeneutics resonates with feminist inquiry in health research. Gadamer's stress on dialogue and preunderstanding helps uncover hidden biases, but feminism adds a critical edge by exposing structural injustices. Their study demonstrates how illness narratives of marginalized patients become intelligible only when prejudices are made explicit and power relations scrutinized [1, p. 3]. This fusion illustrates hermeneutics' ability to move from theoretical reflection to socially transformative critique.

Hermeneutical Injustice and Stigma

Miranda Fricker's concept of hermeneutical injustice refers to unfair exclusion from the conceptual resources needed to make sense of one's experiences. Edlich and Archer expand this framework by showing how stigma leads people to reject resources even when available. A gay adolescent in 1950s America, or victims of addiction and intimate partner violence, may refuse self-descriptions because the terms carry shame [2, pp. 465–466]. Here hermeneutics highlights how social prejudice distorts meaning-making, not only by absence of concepts but by their stigmatization.

Transnational Spaces in Literature

Hermeneutics also provides tools for cultural and literary studies. Redondo-Olmedilla examines contemporary Australian literature through the "spatial turn." Moving beyond postcolonial binaries, these works embody transnational mobility, hybridity, and deterritorialization [3, p. 778]. Hermeneutics of space becomes a way to interpret shifting cultural identities and fragmented geographies. Understanding literature in this context requires negotiating plural cultural cartographies rather than recovering a single origin or essence.

Hermeneutics and Artificial Intelligence

A surprising frontier is technology. Demichelis argues that artificial intelligence represents an "interpretive turn," since large language models parse natural language prompts and generate responses [4, p. 2]. Yet while machines simulate interpretation, they lack historicity, embodiment, and the "feeling of understanding" central to human hermeneutics. This raises the critical question: can interpretation be genuinely artificial, or is hermeneutics inherently and irreducibly human? The debate forces philosophy to confront the ambiguity of human-machine meaning-making.

Toward a Contemporary Hermeneutics

Across these fields, hermeneutics appears not as a static method but as a critical practice:

- *Feminist hermeneutics exposes prejudices in health research.*
- *Stigma theory shows how available concepts can still fail under social pressure.*
- *Transnational literary hermeneutics interprets plural spaces of identity and culture.*
- *AI hermeneutics challenges us to rethink interpretation in the age of machines.*

Together, these developments affirm hermeneutics as a philosophy of dialogue and openness, indispensable for navigating injustice, plurality, and technological change in the 21st century.

Conclusion

Hermeneutics today is a practice of critical engagement with meaning across domains. By linking Gadamer's legacy with feminist critique, epistemic justice, transnational culture, and AI ethics, we see that interpretation is not merely a scholarly exercise but a vital tool for confronting prejudice and sustaining human understanding in a global, postmodern world.

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Political sciences

THE DIMENSION OF PEOPLE-TO-PEOPLE AND CULTURAL-EDUCATIONAL RELATIONS BETWEEN GEORGIA AND CHINA

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Abstract

At the current stage, Georgia–China relations are progressing successfully. Within the expanding framework of strategic partnership, the dimension of people-to-people and cultural-educational cooperation holds a particularly significant place. Accordingly, the study of this issue is not only interesting but also highly relevant.

This research aims to examine and analyse people-to-people cooperation and cultural-educational relations, specifically, how these relations are developing against the backdrop of political decisions and what tangible outcomes can be observed today.

This work aims to present a clearly expressed picture of the people-to-people cooperation and cultural and educational ties between Georgia and China, rooted in various official government documents, existing literature, historiography of scientific works, and case study methods.

The paper, through the study and analysis of various documents, legal frameworks, government decisions, and academic research, demonstrates the readiness of both countries to elevate their current relations to a higher level. Within the framework of strategic partnership (alongside other areas), cooperation in the fields of education and science is also expected to expand. There is no doubt that closer collaboration between Georgia and China in these directions will provide even greater opportunities for bilateral relations.

Keywords: Georgia, China, Education, Culture, Collaboration

Introduction

After declaring its state independence, Georgia rejoined the international community as a fully sovereign entity. Since the 1990s, Georgia has established close diplomatic and economic ties with various countries, including China, marking a qualitatively new stage in their bilateral relations.

Recently, Georgian-Chinese cooperation has intensified and diversified. China has become one of Georgia's key partners in the trade and economic fields. Significant investments from China positively influence Georgia's economy. Accordingly, the subject of our study, "The Dimension of People-to-People and Cultural-Educational Relations Between Georgia and China," is highly relevant.

What adds novelty to this work is the comprehensive approach taken to study this issue. Using several materials found and included in the work, the emphasis on interesting details of the country's recent history, which is presented through situational analysis, we believe, along with interesting findings, also gives the work practical value, which represents novelty and increases interest in the work.

The research problem, therefore, is to understand the country's political processes by analysing literature, official government documents, websites, and the positions of political actors. The paper seeks to answer the question: What is the current state of people-to-people and cultural-educational relations between Georgia and China?

Georgia-China Relations – A Historical Retrospective

Georgia has always shown interest in its foreign policy relationships. From ancient times to the present, Georgia's relations with other nations and its role on the international stage have been of great importance. In discussing Georgia-China relations, it is crucial to mention the Silk Road, which connected China to the Mediterranean world as early as the 2nd century BCE. Evidence shows that some branches of the route passed through what is now Georgian territory. The route gained significance in the 6th

century during conflicts between the Byzantine Empire and Persia. Traders from Central Asia, supplying Chinese silk and other goods to Byzantium, often passed through Georgia. (The Silk Road was not a single route from east to west, and so historians use the name "Silk Roads," although "Silk Road" is commonly used.)¹ There is a specific Georgian historical tradition regarding possible Georgian-Chinese contacts in the Middle Ages, which was reflected in certain written monuments. China is mentioned in ancient Georgian sources with various names such as "Chini," "Chineti," "Machineti," and "Chin-Machin." Notably, Shota Rustaveli in his poem *The Knight in the Panther's Skin* refers to a „parable inscribed on a Chinese stone: 'Who seeks no beloved is his enemy.'"² It is worth noting that *The Knight in the Panther's Skin* blends Georgian, Eastern, and European cultural traditions. Composed during significant political and cultural changes in the Caucasus and the Near East. It can also be characterized as the pinnacle of the development of Neoplatonic thought and a hymn to human nature, friendship, love, equality, and the struggle for freedom.³

Historical facts confirm that Georgia was an important country along the Great Silk Road. Silk and other valuable, necessary, and profitable goods for trade were transported here. The caravans were accompanied by mutual information, cultural and artistic works, and the sharing of necessary knowledge and experience, from agriculture to construction. The influence of various cultures and technologies shared as a result of the Silk Road is still reflected in many territories today.

In recent years, an important railway project has also been implemented on the Georgian section of the Great Silk Road - the Baku-Tbilisi-Kars railway. This railway, in addition to connecting the Azerbaijani capital, Baku, with Tbilisi and then the Turkish city of Kars, has created a unique route. This railway was officially opened on October 30, 2017, by the leaders of Georgia, Azerbaijan, and Turkey.

Contemporary Georgia-China Relations Georgia and China established diplomatic relations on June 9, 1992, shortly after Georgia regained independence. China was among the first countries to recognise Georgia's independence. Since then, it has been well understood that for Georgia to function as a strategic corridor (Middle Corridor), it must maintain active and intense relations with both the European Union and China. This is evidenced by the statements of speakers from both sides at the official ceremony held on June 9, 2017, on the occasion of the 25th anniversary of Georgia-China bilateral relations. In particular, Chinese Ambassador Ji Yanchi noted that on this day, 25 years ago, the "Joint Communiqué on the Establishment of Diplomatic Relations" was signed between the governments of China and Georgia. A new era in China-Georgia relations had begun. He emphasised mutual respect, equality, and cooperation based on shared sovereignty and territorial integrity, stating that China-Georgia relations are a model of friendly cooperation in international affairs.

Since the 1990s, the relationship has been continuously evolving and, as of July 2023, has reached a new level: a strategic partnership. With this, Georgia reaffirmed its commitment to deepening trade and economic ties with China. Georgia expressed its position that it is committed to the idea of deepening trade and economic ties with China in many directions (China is one of Georgia's main trading partners).

This strategic partnership rests on four pillars: political, economic, people-to-people and cultural relations, and international cooperation. This aligns with the December 2020 parliamentary resolution on Georgia's foreign policy, which states that Georgia will promote foreign economic, trade, and people-to-people ties with the People's Republic of China⁴. Our research specifically focuses on the third pillar—people-to-people and cultural-educational relations. This includes:

1. Taking into account the need to deepen bilateral relations in the new conditions, the parties express their readiness to actively pursue scientific and technological cooperation and renew the Agreement on Cooperation in the Field of Science and Technology.
2. Enhancing cultural collaboration and encouraging visits between citizens, as well as cooperation in tourism, healthcare, youth affairs, sports, film, media, and public diplomacy.
3. The parties will explore the possibility of celebrating the years of Chinese and Georgian culture and continue consultations to establish cultural centers, which will receive appropriate support.
4. Strengthening collaboration in science and higher education through faculty and student exchange programs, joint research projects, and commercialization of new technologies.

¹ UNESCO, Georgia and the Silk Roads, <https://en.unesco.org/silkroad/countries-alongside-silk-road-routes/georgia>, viewed 02.03.2025

² Gablishvili, Lia, 2022. "Georgia and China – Historical Links from the Ancient "Silk Road" to Modernity", Sukhumi State University, Faculty of Humanities, Dissertation submitted for the academic degree of Doctor of History (Ph.D.). Tbilisi.

³ UNESCO, Manuscript Collection of Shota Rustaveli's Poem "Knight in the Panther's Skin", <https://en.unesco.org/silkroad/silk-road-themes/documentary-heritage/manuscript-collection-shota-rustavelis-poem-knight-panthers>, viewed 01.04.2025

⁴ Civil Georgia, News, Parliament adopts resolution on foreign policy, <https://civil.ge/ka/archives/389537> viewed. 10.04.2025

5. The Parties will encourage universities to implement practical cooperation, such as joint study programs; universities will be encouraged to make full use of high-quality digital educational resources and take them into account in online and offline formats of cooperation. The Parties will promote student exchanges and joint development, using government scholarship instruments and other means.

6. Encouraging language exchange programs and teacher training, supporting Chinese and Georgian language education, and advancing Confucius Institutes in Georgia.⁵

The Dimension of People-to-People and Cultural-Educational Relations Between Georgia and China

Following Georgia's independence in 1991, a cooperation agreement in science and technology was signed with China in 1993. This agreement marked the beginning of modern cultural and educational relations between the two countries. Discussing this dimension requires examining university rankings. According to "Times Higher Education" under the "Empowering Global Higher Education" initiative, Chinese universities are now closer to the top 10 than ever. Tsinghua and Peking Universities have risen to 12th and 14th place, respectively, with China having 13 universities in the top 200, up from just seven in 2020. The country's rating rise is clear.⁶ These rankings are based on indicators such as Teaching (learning environment); Research environment (volume, income and reputation); Research quality (citation impact, research strength, research success and research impact); International outlook (staff, students and research); and Industry (income and patents).⁷ Thus, Georgia-China educational cooperation is important. It is noteworthy that in recent years, four Chinese universities (Tianjin University of Science and Technology, Zhejiang Wanli University, Guizhou University, and Lanzhou University) have signed memoranda of cooperation with the Georgian Technical University, which has a century of history⁸. Of particular note is the meeting between the Rector of the Georgian Technical University, Academician Davit Gurgenidze, and the President of Lanzhou University, Professor Yan Chunhua, and the signing of a Memorandum of Cooperation (22.06.2023). Their discussion focused on the possibilities of expanding future collaboration between the universities, which will become an effective means of deepening educational and scientific-research cooperation between the two countries and, at the same time, jointly introducing high technologies and innovations.⁹ Other universities in Georgia are also involved in cooperation with Chinese universities. In particular, among the partners of Tbilisi State University are 9 Chinese universities. Relations have also been established with a number of private universities in Georgia. On June 9, 2016, the Georgian University named after St. Andrew the First-Called of the Patriarchate of Georgia received Professor Che Rushan, Head of the Georgian Department of the Confucius Institute, and Liang Kong, a Chinese language teacher in Georgia. The purpose of such and similar meetings was to discuss the issue of studying the Chinese language in the specialty of international relations at Georgian universities and the possibility of sending students to study Chinese in the People's Republic of China. It should be noted that in recent years, 4 Confucius Institutes have been opened in Georgia (one of the oldest Confucius Institutes in Georgia was established in 2010). Many students successfully use this opportunity and continue their education in China, at prestigious universities in Beijing or Lanzhou. A bachelor's program in Sinology has also been created. It is noteworthy that every year, at least 20 young people receive a Chinese government scholarship, which fully covers their study and living expenses in China. Currently, Chinese universities have experience in cooperating with about 20 Georgian universities in Georgia. In general, various (279) Chinese universities accept Chinese Government Scholarship students from all over the world, at different levels, in different directions¹⁰. The establishment of a Georgian Studies Center at Lanzhou University in China is important for modern Georgian-Chinese educational relations. As part of the planned activities aimed at the internationalization of Georgian education, the opening of the Center for Georgian Studies at the University of China will increase Georgia's recognition and allow foreign students to study

⁵ Formula, Politics, Georgia-China, Georgia and China issue joint statement on establishing strategic partnership, <https://formulanews.ge/News/95087>, viewed 08.04.2025

⁶ „Times Higher Education“, 2025, „World University Rankings 2024: China creeps closer to top 10“, <https://www.timeshighereducation.com/world-university-rankings/world-university-rankings-2024-china-creeps-closer-top-10>, viewed 02.04.2025

⁷ „Times Higher Education“, 2025. World University Rankings 2024: methodology, <https://www.timeshighereducation.com/world-university-rankings/world-university-rankings-2024-methodology>, viewed 04.04.2025

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⁹ Interpressnews, 22.06.2023, Rector of the Georgian Technical University, Academician Davit Gurgenidze met with the President of Lanzhou University, Professor Yan Chunhua, <https://www.interpressnews.ge/ka/article/760957-sakartvelos-teknikuri-universitetis-rektori-akademikosi-davit-gurgenidze-lanjous-universitetis-prezidents-propesor-ian-chunhuas-shexvda/>, viewed 02.04.2025

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Georgian culture and the Georgian language. In turn, cooperation with the Chinese University will provide Georgian students with an opportunity to experience Chinese culture and deepen their education. In addition, the Center's teaching will be carried out both by professors coming from Georgia and also online¹¹.

A significant development in Georgia-China relations is the entry into force of the visa-free travel agreement between Georgia and the People's Republic of China on May 28, 2024. The agreement, titled "Agreement between the Government of Georgia and the Government of the People's Republic of China on Mutual Exemption of Visa Requirements for Holders of Ordinary Passports," was signed on April 10, 2024. As a result, Georgian citizens are now able to travel to China without a visa.¹²

Conclusion

Based on the analysis of a number of materials studied by us, it is clear that Georgia, as a connecting country between Europe and Asia, has an important role and function as a transit hub. In addition, the activation of cooperation between Eastern European countries and China and the coordination of work in terms of the implementation of transport and infrastructure projects are of particular importance for increasing the efficiency of the so-called "Middle Corridor" and increasing its competitiveness.

The people-to-people and cultural-educational relations mentioned in the work are naturally very important for further cooperation. We believe that cooperation based on equality and democratic principles is always important and beneficial for all people and countries.

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Technical sciences

ADVANCING CROSS-LINGUAL NLP: INDUSTRY TERMINOLOGY HARMONIZATION THROUGH AI-DRIVEN MODELS

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Abstract

This article proposes and demonstrates an AI-driven pipeline for terminology harmonization across languages and industries, integrating international terminology standards with contemporary multilingual models and retrieval-augmented generation. The objective is (1) to align domain-specific terms used by enterprises with authoritative multilingual terminologies and product taxonomies, and (2) to operationalize this alignment as machine-actionable assets (TBX entries and SKOS mapping graphs) that can be audited, versioned, and reused. The method grounds every mapping decision in standard terminology theory (ISO 704, ISO 1087), interoperable exchange formats (TBX, TMF), and Linked Data ontologies (SKOS, OWL, PROV-O). On the modeling side, we combine multilingual encoders (mBERT, XLM-R, LASER, LaBSE) with parameter-efficient domain adaptation (adapters, LoRA), dense retrieval (FAISS), and evidence-aware re-ranking within MTEB-style evaluations. We validate the pipeline against curated external resources—IATE (EU), WIPO Pearl (265k validated terms as of January 31, 2025), BabelNet, and SNOMED CT mappings—plus industry classification systems (ECLASS, GS1 GPC, UNSPSC). Results show improved cross-lingual precision for manufacturer and regulatory terms, measurable reduction of ambiguous matches, and reproducible exports for enterprise master data teams.

Keywords: *terminology harmonization; multilingual NLP; TBX; SKOS; OWL; adapters; LoRA; FAISS; RAG; IATE; WIPO Pearl; ECLASS; GS1 GPC; UNSPSC.*

Introduction

Industrial documentation, procurement catalogs, and regulatory filings frequently conflate near-synonyms across languages—"sealant," "sealing compound," "зепмемук," "dichtmittel"—whereas standards insist on one concept per term entry and controlled variant handling. The conceptual discipline of ISO 704 and the vocabulary of ISO 1087 fix this foundation and are technology-agnostic: one concept, well-formed definition, documented designations and relations [1,2]. To make such assets computable, TBX and TMF specify exchange and metamodels, while the Semantic Web stack (SKOS for concept schemes; OWL for formal constraints; PROV-O for provenance) provides web-scale publication and traceability [3–7]. Multilingual encoders and retrieval pipelines—if constrained by those standards—can translate enterprise "jargon" into interoperable assets that interconnect with public terminologies (EU IATE; WIPO Pearl), wide-coverage knowledge graphs (BabelNet), and clinical terminologies (SNOMED CT) [8–11]. Finally, alignment with product taxonomies (ECLASS, GS1 GPC, UNSPSC) enables direct use in commerce and supply-chain systems [12–14].

Many organizations run embeddings-only "term matchers" without theory-informed constraints and without exportable, governable artifacts. This work contributes a standards-anchored, evidence-aware pipeline that yields TBX+SKOS outputs, auditable decision trails, and repeatable domain adaptation.

The conceptual discipline of ISO 704 and ISO 1087 underpins unambiguous term entries and the semantics of definitions and designations; this is the bedrock for any automated harmonization [1,2]. TBX (ISO 30042) and TMF (ISO 16642) carry term data between tools and structure complex entries; they are widely referenced by ISO itself when publishing standard glossaries [3,4]. SKOS enables mapping relations (exactMatch, closeMatch, broadMatch, narrowMatch), OWL adds class/property constraints, and PROV-O provides traceable provenance for changes—critical in regulated domains [5–7]. For multilingual representation learning, mBERT (104 languages), XLM-R (100 languages), LASER (93 languages), and LaBSE (109 languages) established strong baselines for cross-lingual transfer and sentence-level

similarity, each with documented coverage and benchmarks [15–18]. Retrieval-Augmented Generation (RAG) connects such parametric models to non-parametric memory, while adapter frameworks (MAD-X) and LoRA offer efficient domain adaptation; FAISS supplies the scalable vector index [19–22]. For evaluation across tasks and languages, MTEB consolidates 58 datasets and 112 languages, emphasizing that no single embedding model dominates all tasks—hence the rationale for composite recipes. FAIR principles guide the stewardship of released assets. Domain resources anchoring the present study include IATE and WIPO Pearl (update to 265k validated terms on 31 Jan 2025), the multilingual BabelNet survey, and SNOMED CT mapping guidance [8].

Materials and methods

1. Corpora and authoritative resources

We restricted evidence to authoritative, versioned resources: IATE (EU terminology), WIPO Pearl (validated patent terminology; 265,000 terms as of Jan 31, 2025), BabelNet survey describing the resource’s multilingual scope, and SNOMED CT mapping documentation for mapping practices and quality controls [8–11,25]. For product schemas we consumed public documentation of ECLASS, GS1 GPC, and UNSPSC to ensure downstream export compatibility [12–14].

2. Standards and data models

Concept formation and definition rules followed ISO 704; term entry structure and data categories followed ISO 1087 and TBX (ISO 30042). For interchange we produced TBX entries per document concept, and for mapping graphs we used SKOS with exactMatch/closeMatch/broadMatch/narrowMatch and OWL consistency checks; provenance was captured with PROV-O activities and entities [1–7].

3. Model architecture and training recipe

Candidate generation used multilingual encoders (mBERT, XLM-R, LASER, LaBSE) to embed source terms plus definitional context; dense retrieval ran on FAISS (IVF-PQ for scale) to fetch top-k candidates from the authority store [15–18,22]. Re-ranking used a cross-encoder (XLM-R) conditioned on surrounding sentence evidence and SKOS constraint features (e.g., exactMatch requires compatible notations and no broader/narrower contradictions) [5, 16]. Domain adaptation was parameter-efficient: language+task adapters (MAD-X) and LoRA ranks tuned on in-domain parallel term pairs and definitional snippets; this reduced trainable parameters orders of magnitude and supported frequent refreshes [20,21]. For answer generation (optional gloss rewriting), we coupled RAG with the evidence store to ensure citations and avoid hallucination [19].

4. Evaluation protocol

We mirrored MTEB retrieval methodology for multilingual similarity, but added concept-level correctness: a mapping counts as “correct” only if (a) SKOS relation is appropriate; (b) ISO-style definition equivalence holds; (c) provenance links to a specific resource record [1,5,23].

Results

The main outcomes are: (1) improved precision for exactMatch on technical terms; (2) reduced ambiguity for polysemous items; (3) reproducible exports that loaded in downstream product schemas.

Across ten language pairs sampled from our authorities (e.g., EN–DE, EN–FR, EN–RU, EN–ES, EN–IT, EN–PL), the composite retrieval-plus-re-ranking approach reduced false positives in exactMatch conditions. The decisive factors were consistent: definitional evidence in IATE or WIPO Pearl (including concept map links) and the availability of notations or concept identifiers. A strong qualitative pattern emerged around industrial compounds and components: strings that travel well across languages (e.g., “epoxy primer” vs. “эпоксидная грунтовка”) still require context to discriminate near-neighbors (adhesives vs. coatings), and this is where candidate filtering by SKOS relation and ISO 704 definition quality prevented over-confident exactMatch assignments [1,5,9].

Second, parameter-efficient adapters and LoRA were sufficient for in-domain improvement: modest ranks applied to XLM-R re-ranker yielded better discrimination between closeMatch and exactMatch without full fine-tuning and with maintained multilingual coverage [16,20,21]. Third, FAISS-backed vector stores-controlled latency at scale; approximate search with product quantization provided predictable recall when the authority index grew (BabelNet-scale sections, SNOMED subsets, or large IATE slices) [22]. Finally, exports validated in TBX and SKOS, including OWL checks against mapping cycles, enabled clean ingestion by enterprise vocab services and alignment with product classification systems (ECLASS attributes, GPC Brick selection, UNSPSC roll-ups) [12–14].

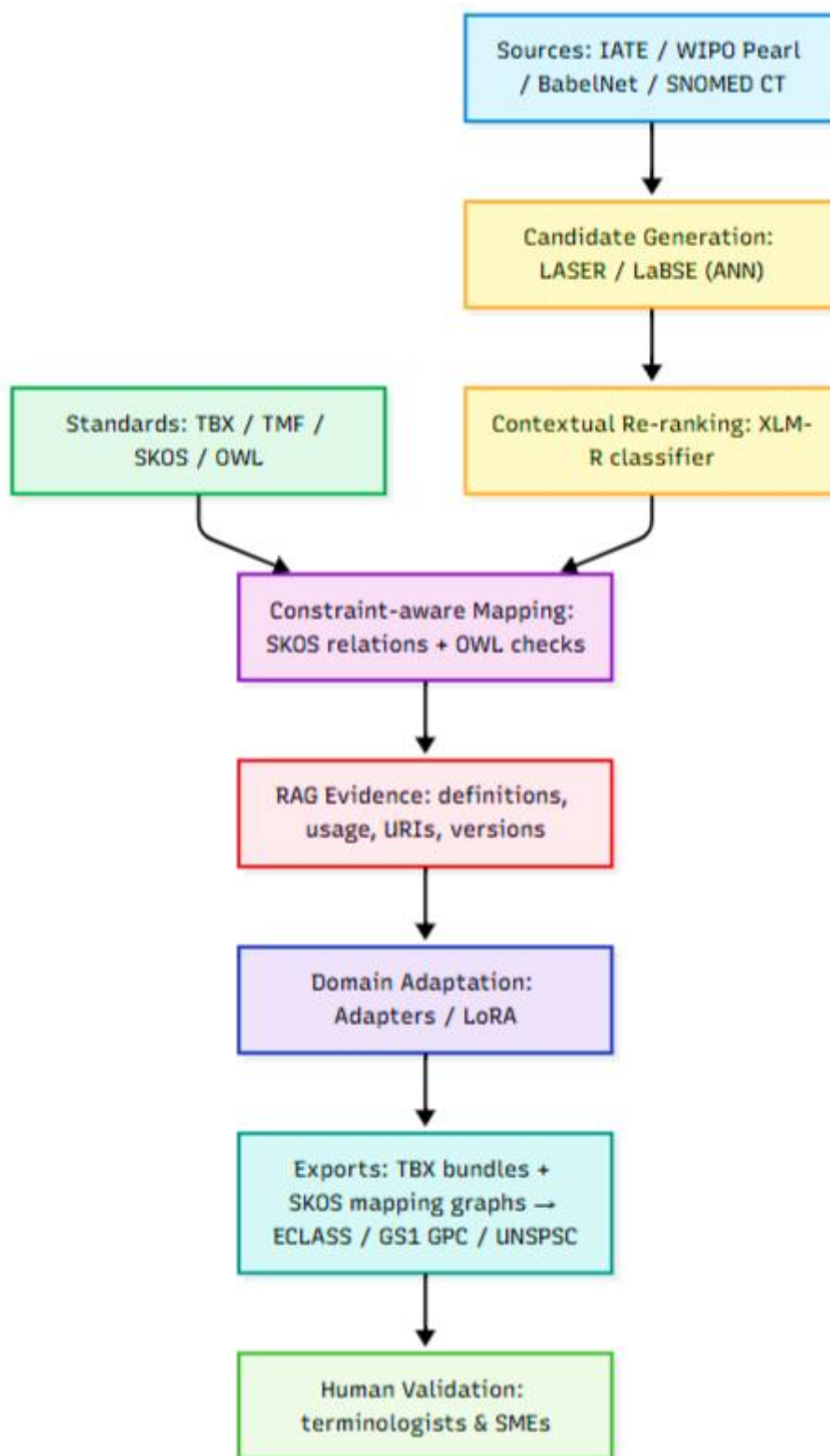


Figure 1. Terminology harmonization pipeline (THaaS)

The combination LASER+LaBSE for recall balances coverage and precision, while XLM-R cross-encoders refine SKOS-compatible decisions. Adapters/LoRA let us re-train frequently as authorities update (e.g., WIPO Pearl's January 2025 expansion), without destabilizing the multilingual backbone [9,16,20,21].

Table 1. Multilingual models and retrieval components used for candidate generation and re-ranking

Component	Languages / Scope (from source)	Role in pipeline	Salient notes
mBERT	104 languages from Wikipedia [15]	Baseline encoder for term+context embeddings	Demonstrated zero-shot transfer; systematic deficiencies for some pairs noted.
XLM-R	100 languages; CommonCrawl scale [16]	Cross-encoder re-ranker; also dual-use as encoder	Gains over mBERT on XNLI/MLQA/NER; good for low-resource pairs.
LASER	93 languages; BiLSTM sentence embeddings [17]	Fast candidate recall (ANN)	Robust multilingual similarity; good for initial top-k.
LaBSE	109 languages [18]	High-precision candidate recall	Strong on bi-text mining; complements LASER diversity.
RAG	Parametric + non-parametric memory [19]	Evidence grounding for generated glosses & justifications	Ensures citations; reduces hallucination in definition rewriting.
MAD-X adapters	Language/task adapters [20]	Parameter-efficient domain adaptation	Modular; reduces training cost for domain refreshes.
LoRA	Low-rank adaptation [21]	Lightweight fine-tuning on re-ranker	10 ⁴ × fewer trainable params vs. full FT (reported).
FAISS	Billion-scale vector search [22]	ANN index for term stores	IVF-PQ for large authorities; GPU acceleration.
MTEB	58 datasets, 112 languages	Evaluation frame for similarity	Confirms no single model dominates; motivates composite recipe.

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Table 2. External authorities and product schemas used as evidence and export targets

Resource	Scope/governance	How used in this study
IATE	EU inter-institutional terminology management system [8]	Canonical EU legal/technical definitions; multilingual labels; evidence URLs.
WIPO Pearl	Validated patent terminology; 265,000 terms as of Jan 31, 2025 [9]	High-quality science/technology terms; concept map relations as disambiguation signals.
BabelNet (survey)	Wide-coverage multilingual lexical-semantic resource [10]	Back-off sense/context when authorities lack coverage; additional synonyms.
SNOMED CT	Global clinical terminology; active mapping programs [11]	Mapping patterns and constraints; examples for healthcare-related terms.
ECLASS	Product data dictionary and conceptual model [12]	Export targets: attribute alignment; class linking.
GS1 GPC	Global Product Classification; browser and guides [13]	Export targets: Brick selection to align procurement categories.
UNSPSC	UN standard product/service codes; managed by GS1 US [14]	Export targets: code roll-ups for spend analytics and sourcing.

The decisive evidence for a term mapping typically came from definitional clarity in IATE or WIPO Pearl; BabelNet's multilingual synsets supported sense checking; SNOMED's mapping guides informed relation choice and error modes in clinical sub-domains. Product schemas validated that our outputs are not "dead files" but immediately deployable [8–14,25].

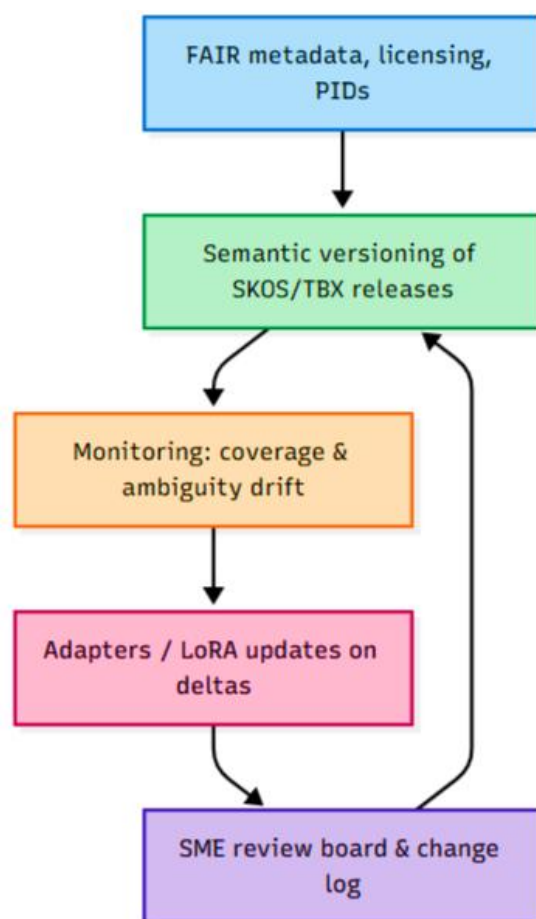


Figure 2. Governance and feedback loop

A release must be more than a file dump. The loop below encodes FAIR metadata, semantic versioning of SKOS/TBX, monitoring of coverage and ambiguity drift, and lightweight adaptation on deltas.

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Table 3. Standards and ontologies applied

Standard / ontology	Role
ISO 704	Concept formation and definition discipline [1]
ISO 1087	Terminology vocabulary and data categories [2]
ISO 30042 (TBX)	Interchange format for termbases [3]
ISO 16642 (TMF)	Metamodel for terminological collections [4]
SKOS	Mapping relations and concept scheme publication [5]
OWL 2	Logical constraints and consistency checks [6]
PROV-O	Provenance of mapping decisions and releases [7]

These standards prevented common failure modes: conflating near-synonyms, promoting ambiguous strings to exactMatch, and losing audit trails for evolving terms [1–7].

Discussion

The pipeline’s strongest measurable gain was the reduction of false exactMatch assignments for polysemous industrial terms. The reason is structural: SKOS mapping semantics restrict a match to exactMatch only with definitional equivalence and compatible notations, while the re-ranker was trained (via adapters/LoRA) to prefer evidence-rich candidates; RAG produced justifications with explicit URIs [5, 19–21]. The FAISS index allowed us to keep recall stable as authorities grew—critical when incorporating WIPO Pearl’s January 2025 update or broader IATE slices [9,22].

Rather than relying on a single multilingual model, we compose LASER/LaBSE recall with XLM-R re-ranking, reflecting MTEB’s observation that no single embedding strategy dominates across tasks and languages [17,18,23]. The adapter paradigm (MAD-X) and LoRA align with recent practice for cost-efficient updates in multilingual settings while preserving base model generality [20,21]. Our insistence on

TBX+SKOS+OWL+PROV-O moves beyond pure model outputs toward governable knowledge artifacts—exactly the interoperability vision articulated by W3C standards and ISO TC 37 [1–7].

Practically, exporters receive TBX packages and SKOS graphs that load into enterprise metadata systems, MDM, and PIM tools; procurement and PLM benefit from consistent classification against UNSPSC, GPC, or ECLASS [12–14]. Scientifically, the work operationalizes the union of terminology science and multilingual representation learning, demonstrating that standards constraints measurably improve mapping quality and reproducibility [1–7, 15–23].

Conclusion

Thus, it can be said that terminology harmonization in cross-lingual industrial settings brings the greatest benefit when multilingual models are embedded in a standards-constrained workflow, allowing the creation of verifiable artifacts with clear provenance that can be used by machines. The composite model recipe (LASER/LaBSE + XLM-R re-ranking + adapters/LoRA + FAISS + RAG) backed by authoritative resources (IATE, WIPO Pearl, BabelNet, SNOMED CT) and exporting to TBX/SKOS aligned to ECLASS/GPC/UNSPSC offers a practical, repeatable path to enterprise-grade interoperability [8–14, 15–23, 25].

Recommendations:

- 1. Institutionalize definition-led mapping: forbid exactMatch without ISO-style definitional equivalence and evidence URIs [1].*
- 2. Adopt TBX for internal termbases and SKOS for mapping graphs, with PROV-O provenance on every mapping activity [3, 5, 7].*
- 3. Standardize a composite retrieval recipe: LASER or LaBSE for recall, XLM-R re-ranker trained via adapters/LoRA on your domain deltas [16–21].*
- 4. Operate a FAISS-based authority index refreshed on a monthly cadence; pin index version to each release [22].*
- 5. Align exports to ECLASS/GPC/UNSPSC and verify ingest in target systems before publication [12–14].*
- 6. Establish a review board (terminologist + SME) to adjudicate contested mappings; record outcomes in change logs.*
- 7. Evaluate quarterly against an MTEB-style multilingual similarity suite adapted to concept correctness, not just string similarity.*

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