Deutsche Krebshilfe
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DEUTSCHES
KREBSFORSCHUNGSZENTRUM
IN DER HELMHOLTZ-GEMEINSCHAFT

Memorandum on cancer prevention research in Germany

With support from

NATIONALES
KREBSPRÄVENTIONSZENTRUM

dkfz. DEUTSCHES
KREBSFORSCHUNGSZENTRUM
IN DER HELMHOLTZ-GEMEINSCHAFT

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German Cancer Aid (Deutsche Krebshilfe) was founded on September 25, 1974 by Dr Mildred Scheel. The aim of the nonprofit organization is to fight cancer in all its forms. Following the motto "Helping. Researching. Informing," German Cancer Aid supports projects to improve prevention, early detection, diagnosis, treatment, medical follow-up care, and psychosocial care, including cancer self-care. Its mandate also covers research and health policy activities. It is one of the initiators of Germany's National Cancer Plan and a partner of the National Decade Against Cancer. German Cancer Aid is the largest source of private funding for efforts to fight cancer, including cancer research, in Germany. It finances its entire activities solely from donations and voluntary financial contributions from the population.

With more than 3,000 employees, the **German Cancer Research Center** (DKFZ) is Germany's largest biomedical research institute. Researchers at DKFZ study how cancer develops, identify cancer risk factors, and search for new strategies to prevent people from developing cancer. They are also devising new methods to diagnose tumors more precisely and treat cancer patients more successfully. DKFZ's Cancer Information Service (KID) provides patients and their families, interested members of the general public, and healthcare professionals with individual answers to all their cancer-related questions.

To transfer promising approaches from cancer research to clinical practice and thus improve the prognosis of cancer patients, DKFZ runs translational centers in collaboration with excellent university hospitals and research institutions throughout Germany:

- National Center for Tumor Diseases (NCT, six sites)
- German Cancer Consortium (DKTK, eight sites)
- Hopp Children's Cancer Center (KiTZ) Heidelberg
- Helmholtz Institute for Translational Oncology (HI-TRON) Mainz – a DKFZ Helmholtz Institute
- DKFZ-Hector Cancer Institute at the University Medical Center Mannheim
- National Cancer Prevention Center (jointly with German Cancer Aid)

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IN OUR SOCIETY**
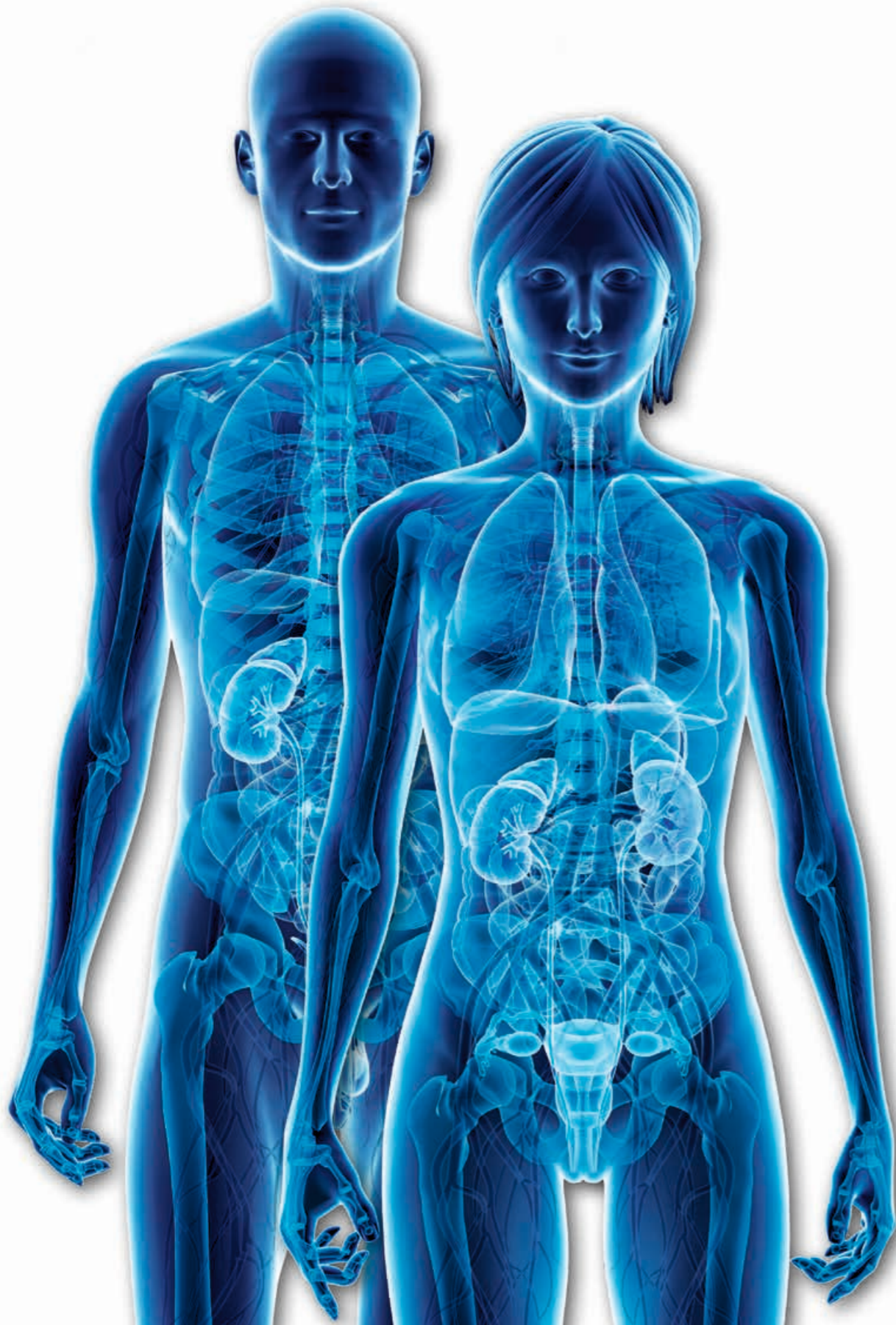
MEMORANDUM BY GERMAN CANCER AID AND THE GERMAN CANCER RESEARCH CENTER ON CANCER PREVENTION RESEARCH IN GERMANY

1. PREAMBLE

Experts anticipate around **523,000** new cases of cancer a year in **2025,** with figures set to rise further.

Experts forecast that the current incidence of cancer will rise from an estimated 510,000 to around 523,000 in 2025, due partly to demographic developments and the associated considerable increase in the proportion of older people in the population.

Yet around half of the current new cases of cancer could be avoided by changes in behavior. Better early detection could improve the cancer-specific ten-year survival rate from the current figure of approximately 53% to 75% by 2030.

To realize these opportunities, changes need to be made relating to research and structures. Primary and secondary prevention must take a translational and multidisciplinary approach, one that is not well developed in Germany.

The present memorandum by German Cancer Aid and the German Cancer Research Center (DKFZ) addresses these requirements and proposes options to implement them.

A healthy lifestyle is the best way to proactively prevent cancer.

510,000 NEW CASES OF CANCER A YEAR IN GERMANY

There are currently more than 4 million people living in Germany who have or have had cancer.

Estimated number of new cases per year*	Men	Women	Total
Prostate	70,100	–	70,100
Breast	770	66,800	67,570
Lung	34,700	25,000	59,700
Bowel	33,100	25,000	58,100
Malignant melanoma**	20,600	19,600	40,200
Non-Hodgkin lymphoma	11,800	9,300	21,100
Pancreas	10,700	10,300	21,100
Bladder	14,600	5,200	19,800
Mouth and throat	9,700	4,900	14,600
Kidney	9,300	5,200	14,500
Stomach	8,800	5,300	14,100
Leukemia	6,200	5,600	11,800
Womb	–	10,600	10,600
Liver	7,400	3,100	10,500
Esophagus	6,300	2,000	8,300
Central nervous system	4,300	3,500	7,800
Thyroid	2,200	5,000	7,200
Ovaries	–	6,800	6,800
Multiple myeloma	3,100	3,400	6,500
Gall bladder and gall ducts	2,600	2,500	5,100
Soft tissue without mesothelioma	2,500	2,400	4,900
Cervix	–	4,100	4,100
Testicles	4,100	–	4,100
Vulva	–	3,700	3,700
Larynx	2,600	640	3,240
Hodgkin lymphoma	1,600	1,200	2,800
Mesothelioma	1,400	340	1,740

* Source: Robert Koch Institute, new cases of cancer in Germany (selected types of cancer), prognosis for 2022
** Source: Association of Population Based Cancer Registries in Germany (GEKID), 2022

2. INTRODUCTION

2.1 Prevention and the population

Alongside medical care, prevention can be seen as the second pillar of healthcare for the population. It is the overarching term for measures designed to reduce the occurrence and spread of diseases by minimizing or eliminating causes of disease, identifying and treating risks of disease at an early stage, and avoiding the progression of an existing disease. Prevention can actively influence both mortality and morbidity and their negative impacts on quality of life and participation and on the direct and indirect costs of disease for society. This can only be achieved if preventive measures actually reach the population or rather the relevant sections of the population. Starting points for preventive measures thus include lifestyle, maintaining health, the stage of disease, and the extent of the risk of disease in the target population along with the level of intervention and the degree of influence on existing general conditions for cancer-relevant behaviors.

Designing effective prevention measures requires a knowledge of cancer risk behaviors, development stages, and stages and rate of disease progression, the degree to which the population can be reached, research on impact to design effective prevention measures, and research on their implementation and long-term sustainability.

2.2 Historical reasons for prevention research in Germany

Germany has a very particular deficit in the field of prevention research and practice. This becomes very obvious if we take the need for prevention services as a benchmark or compare them with the situation in other countries. There are a wide variety of reasons for this deficit. One of the reasons suggested is that Germany already has a highly effective healthcare system. From a historical point of view, particularly after the inhumane abuse of public health and prevention in the past under the National Socialist regime, promoting prevention research was avoided for decades. Initial support initiatives in the 1980s were marked by failure. There was a lack of research infrastructure consisting of sufficient researchers able to work in the field of prevention research. Despite favorable developments in public health research in the past ten years, this is still having an impact today and means that Germany is lagging behind other countries in prevention research and practice too.

2.3 Potential of prevention to reduce the incidence of cancer

Potential for reducing the incidence of cancer could be harnessed in particular by avoiding behavior that increases the risk of cancer (primary prevention) and by promoting protective lifestyle factors such as physical activity and appropriate diet. Structural prevention also plays a key role here in creating framework conditions that promote preventive behavior or reduce exposure to cancer risks. In addition, screening programs to detect and remove not only early-stage cancer but also precursors (e.g., cervical carcinoma, bowel cancer) can also make a considerable contribution to reducing incidence.

2.4 Conclusions from international assessments: potential of prevention to reduce disease and optimize medical care

For 2030, a full care continuum that includes translational research on personalized and precision medicine and on prevention aims to achieve a cancer-specific survival rate of 75% of patients diagnosed in an EU member state with a well-developed healthcare system. Programs have been initiated by the International Agency for Research on Cancer (IARC) (e.g., the European Code Against Cancer) and the European Commission (e.g., Europe's Beating Cancer Plan and Horizon 2020) to harness this potential in European countries. According to the World Health Organization (WHO), 30% of all cancer cases throughout the world could be prevented through primary prevention measures, while the figure given for Europe is 40–60%.

These primary prevention measures include eating a healthy diet and maintaining an active lifestyle, reducing the consumption of tobacco, alcohol, and other noxious substances demonstrated to be carcinogenic (e.g., UV and radon exposure), and avoiding specific pathogens that cause infections. Moreover, for the first time, WHO has included air quality as a key risk factor to prevent noncommunicable diseases, including cancer.

Further studies are required that cover the entire range of prevention research – from mechanistic basic research to studies on the effectiveness and implementation of cancer prevention strategies at individual and population level. Epidemiologic data suggests that the incidence and prognosis of many types of cancer can be attributed to similar lifestyle-related risk factors, such as smoking, excess weight, UV exposure, and insufficient physical activity (see above). Primary and tertiary prevention programs to reduce these risk factors therefore have the potential to have a positive impact on a wide variety of types of cancer. The reduction of cancer risk factors may also have a positive effect on the development, course, and medical care of other major chronic diseases, such as coronary heart disease and stroke, because smoking, diet, and exercise have a crucial influence on the development and severity of their biological precursor diseases, type 2 diabetes and hypertension.
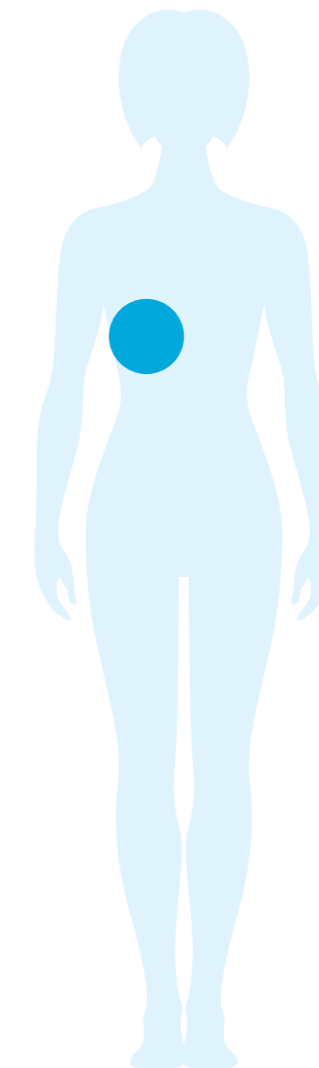
40–60 %
of cancer cases could be prevented by primary prevention measures.

THE MOST COMMON TYPES OF NEW CASES OF CANCER IN MEN AND WOMEN*

70,100
new cases of prostate cancer
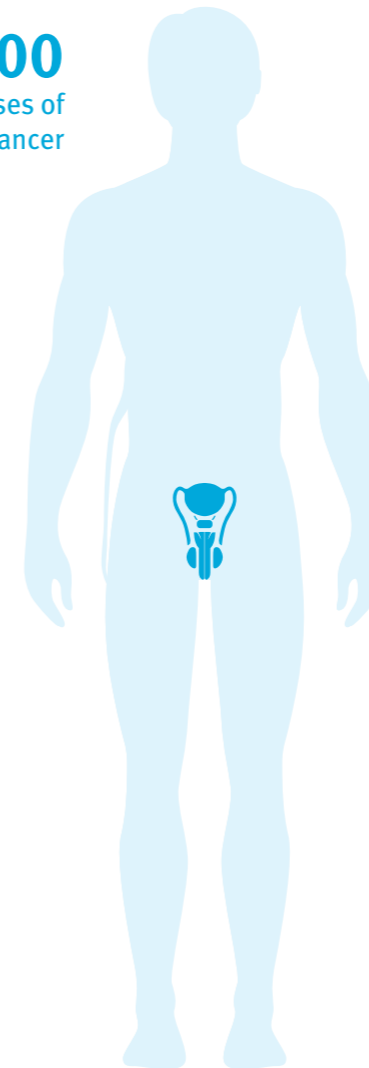
66,800
new cases of breast cancer

* Source: Robert Koch Institute, new cases of cancer, prognosis for 2022

Preventing cancer
before it develops –
by adopting a healthy
lifestyle.

Ways to reduce cancer risk

DO NOT
SMOKE

DRINK ALCOHOL IN
MODERATION

HAVE
VACCINATIONS

MAINTAIN
A HEALTHY
WEIGHT

EAT A
HEALTHY DIET

GET PLENTY
OF EXERCISE

AVOID EXCESSIVE
UV EXPOSURE

AVOID CANCER-
CAUSING
SUBSTANCES

3. CURRENT SITUATION IN GERMANY

3.1 Primary prevention

3.1.1 Lack of focus of individual and broad-based activities (e.g., campaigns) on topics of the European Code Against Cancer

Based on the relevant evidence, the European Code Against Cancer identifies 12 specific ways of reducing the risk of cancer in three areas:

- avoiding health risk behaviors (not smoking, avoiding second-hand smoke, maintaining a healthy weight, being physically active, eating a healthy diet, limiting alcohol intake, breastfeeding, and limiting the use of hormonal therapy (women)),

- avoiding exposure to pollutants (too much sun, cancer-causing substances in the workplace, high radon levels),

- taking part in vaccination programs (hepatitis B and human papillomavirus (HPV)) and screening (using cancer screening programs).

In Germany, not enough research focuses on these 12 target behaviors. There is a lack of basic strategies for research and of approaches addressing one or several of the 12 ways of reducing cancer. There is also a lack of research to identify the most efficient "intervention packages" to achieve all 12 target behaviors (implementation research). In order to be able to use the available high-level research results from epidemiology and intervention research on individual behaviors for relevant research programs, longer-term support is needed for suitable research projects and programs.

In addition, research results that address specific population groups in a targeted way are not sufficiently translated into prevention practice at present. For primary prevention, findings from basic research are not adequately integrated to develop behavioral and structural prevention measures, particularly where this calls for an interdisciplinary approach. In particular, biomedical methods in the omics field offer new starting points for personalized prevention and new options for stratification. The programs and campaigns carried out in practice often lack evaluations. Furthermore, the findings obtained from epidemiologic surveys need to be fed back into research and care in a structured way across the board.

It would appear necessary to integrate existing structures (clinical centers such as the Comprehensive Cancer Centers), large-scale infrastructure and population-based cohorts (National Cohort), and other institutions (research, information, communication, and education institutions, secondary and tertiary health sector, medical insurers, and policymakers) into prevention planning through comprehensive initiatives that reach the various population groups.

3.2 Secondary prevention

3.2.1 Lack of focus on target groups in campaigns

One of the major problems in secondary prevention in Germany is the fact that campaigns are not sufficiently geared toward the target groups. For example, there is insufficient uptake of existing screening programs and they are not adapted to specific population groups in line with the relevant risk profiles. Screening programs for specific tumor entities that only cover smaller population groups but that would nevertheless be relevant to prevention goals are only hesitantly implemented, if at all. For example, although legal provisions are certainly communicated successfully, there is a lack of further-reaching coordinated campaigns by state-run bodies on integrated prevention measures.

Coordinated measures need appropriately clear goals:

1. addressing sections of society that conventional campaigns do not reach, such as less well educated groups and individuals with a migration background and language or religious/ethnic barriers that make it more difficult for them to take part in particular preventive measures,

2. making the topic of secondary prevention easier to understand, e.g., by having content and communication instruments reviewed by focus groups from the population in a structured and systematic way to check that they are easy to understand and have the intended effect.

By doing so, campaigns can be geared more effectively toward the experience and knowledge of members of the target group, enabling them to take informed decisions.

3.2.2 Lack of specificity to target groups of screening programs on different entities (bowel, breast, cervical, prostate, skin cancer) in a heterogeneous field

There are established screening programs in Germany for some common types of cancer (bowel, breast, cervix). Apart from defining the target groups by age and sex, however, there is largely no further differentiation of the target groups. For cervical cancer screening, initial steps have been taken toward risk stratification as a result of the introduction of HPV testing (since January 2020). Skin cancer screening is not carried out by invitation, and low-dose computed tomography (CT) screening for the early detection of lung cancer and the prostate-specific antigen (PSA) test for the early detection of prostate cancer are not yet part of the statutory cancer early detection program.

Yet epidemiologic studies have long since identified risk factors and preventive factors associated with a higher or lower risk of these types of cancer. Based on the results of genome-wide association studies, a large number of genetic variants have also been identified that enable the genetic risk to be increasingly clearly differentiated using polygenic risk scores. Moreover, large cohort studies have identified an increasing number of non-genetic biomarkers that can also play a major role in risk stratification. A new generation of biomarkers that can be determined using digital methods also promises earlier and more individualized

Detecting cancer
at an early stage
so that it is easier
to treat.

diagnoses within the different screening programs. Defining target groups more effectively using meaningful risk stratification is hugely important for screening programs, as the cost-benefit and harm-benefit ratios are usually very much better in high-risk population groups than in ones with a low risk.

3.3 Overarching deficits and challenges

3.3.1 Lack of research on public health impact

Public health impact is considered to be a success criterion in prevention research. Determining the public health impact of an intervention requires evidence relating to the share of the population that took part in the intervention, the share of the population in which the intervention was successful, the extent to which the participating institutions actually carried out the intervention, the extent to which the intervention was realized in line with the idea behind it, and the extent to which the intervention was upheld in the long term. Further important factors include the social impact, i.e., the impact in populations of different socio-economic status, and issues concerning the cost and benefit of the interventions. These criteria and features have not been sufficiently reflected in studies conducted in Germany to date. Systematic prevention research is required, however, including the provision of long-term funding and human resources and the inclusion of patient-reported outcomes (PROs), to enable the public health impact of interventions to be assessed.

Prevention research on **public health impact** is essential for planning and evaluating interventions.

3.3.2 Lack of research on the success of integrated prevention involving targeted initiatives, projects, and communication campaigns

Integrated prevention involves prevention initiatives designed to implement overall strategies drawn from different areas of action. The focus here is on creating integrated support over people's lifetimes (prevention chains) that goes beyond individual entities. Prevention research plays a very important role in these discussions, because it provides evidence on the public health impact of prevention services and can hence demonstrate the effectiveness of strategies and interventions. Public health impact is a crucial criterion for the usefulness of interventions.

There is a considerable need for targeted initiatives, projects, and communication campaigns. Such measures have great potential to impact on cancer throughout the entire care continuum (prevention, diagnosis, treatment, follow-up care, palliative care) and hence to make a key contribution to improving cancer-related medical care for the population.

3.3.3 Lack of health literacy

In Germany, two representative surveys on health literacy in the population in all the federal states showed that more than half (59%) of the individuals surveyed found it difficult to use health information appropriately. This means that around one in two people in Germany have problems finding, understanding, and assessing health-related information and applying it to their own situation (health literacy). Health literacy has decreased over the past six years in all age

groups and in all dimensions. Digital health literacy and people's ability to find their way around the healthcare system are particularly limited. Tasks connected with promoting health are felt to be particularly difficult. These difficulties are especially pronounced in people with a low social status, those with a migration background, older people, and people with chronic illnesses. Individual factors and to a great extent factors relating to society, personal experience, and social conditions all affect health literacy. Promoting health literacy must therefore be seen as a challenge for society as a whole.

3.3.4 Untapped digital potential

Digital behavioral interventions, for example using smartphone apps, may potentially be effective prevention measures that have a broad impact and can be tailored to individuals; flanked by scientific studies, interventions of this kind should become increasingly important in the years to come. Existing preventive medical examinations that reach and affect several millions of people in Germany every year could be improved on a broad scale using digital assistance systems taken from the field of machine learning.

3.3.5 Lack of strategic focus and funding for primary and secondary cancer prevention research

Considerable funding from the public sector and industry is being devoted to research on developing new approaches to diagnose and treat oncology patients. In contrast, relatively few resources are invested in prevention research. Health policymakers, the public sector, and self-administered bodies still do not see prevention research as the basis for developing a healthy population. The same applies to the private sector. Here, too, prevention has so far not been seen as a market worth investing in, possibly because there is little scope for large profit margins.

Overall, funding for primary, secondary, and tertiary cancer prevention services is extremely limited, particularly if compared with funding for diagnostic and therapeutic measures, despite the fact that there are already well-documented examples of cost-effective measures at both intervention and program level. Cost-benefit analyses show that primary and secondary prevention not only provide health benefits for the population, but can also be associated with reduced costs in the health sector and with lower economic losses.

On the basis of this, the urgently needed budgets should be allocated to basic research and implementation research in the field of cancer prevention so that new cancer prevention approaches can be identified and then implemented using translational concepts; moreover, measures shown to be successful can thus be made strategically available to the population and can be used by all.

59 %
of the population finds it difficult to use health information appropriately.

Cost-benefit analyses show that prevention measures reduce costs in the health sector.

3.3.6 Lack of focus of healthcare structures on cancer prevention (outpatient, inpatient, public health services), lack of specialists

The German healthcare system is primarily geared toward treating illnesses. Medical services – mainly secondary cancer prevention – are usually provided in physicians' offices in Germany. Social security providers, company-based physicians, and the public healthcare system have a broad range of duties and do not specifically focus on cancer prevention. Conversely, there are well-qualified professional groups in this context, such as academically trained sport scientists/ sport therapists and nutritionists, whose potential is not yet being harnessed.

Against this backdrop, numerous citizen-centered actors outside the healthcare system have become active in the primary prevention of cancer: Childcare facilities and schools, providers of health information and health education, commercial providers, for example in the field of exercise and diet, and the media are all addressing prevention-related topics. Products are also being developed for this sector by (digital) businesses. Many services are not evidence based – there is a lack of evidence on effectiveness and safety. This carries the risk not only of undersupply but also oversupply and inappropriate supply of prevention services for the population. Cancer prevention has not been systematically included in biomedical research and in medical training and continuing education up to now. This means that there are not enough specialists (Bachelor of Science (BSc), Master of Science (MSc), physicians) with sound scientific training and practical experience in the field of cancer prevention.

The Cancer Early Detection and Register Act *(Krebsfrüherkennungs- und -register-gesetz, KFRG)* of 2013 and the Act on Strengthening Health Promotion and Prevention *(Gesetz zur Stärkung der Gesundheitsförderung und der Prävention, PrävG)* of 2015 partly created the basis for implementing and evaluating primary and secondary cancer prevention interventions, campaigns, and programs. These alone are not sufficient, however.

By setting up the National Cancer Prevention Center, German Cancer Aid and the German Cancer Research Center (DKFZ) have reached an important milestone in establishing an institution for comprehensive, multi-professional, and translational prevention, which was previously missing in Germany.

3.3.7 Lack of political will, untapped (health) policy and regulatory scope for action (primordial, primary, secondary)

Effective, sustainable cancer prevention requires the will of health policymakers to use structural measures to shape living conditions and healthcare in such a way that people find it easy to adopt a healthy lifestyle and take advantage of statutory cancer early detection examinations. In Germany, section 20 (primary prevention and health promotion) and section 25 (medical examinations) of the Fifth Book of the Social Code (*Sozialgesetzbuch, SGB*) create joint scope for action and targets for prevention efforts at statutory level. In the field of primary prevention in particular, measures of this kind are implemented on the basis of initiatives launched by individuals in a relatively uncoordinated way, however. As a result, these political formulations alone are not strategically suitable for integrating prevention structurally/sustainably into people's lives in line with the "health in all policies" approach adopted by WHO and for reducing the rising numbers of cancer

cases. Although some institutions have become established in the field of scientific policy advice, they are not yet strong enough overall to influence political decision-making accordingly. Political regulatory scope for action to mainstream cancer prevention at a structural level in Germany is therefore not yet being sufficiently harnessed. Targeted and effective regulatory measures to reduce risk factors such as smoking, alcohol intake, excess weight, a lack of physical activity, and artificial UV radiation, measures to increase vaccination rates (HPV vaccination), and measures to promote healthy lifestyles are lacking or are not being implemented fully or resolutely enough. Moreover, there is a lack of long-term strategic focus. Regulatory, organizational scope for action in health policy that would facilitate access to statutory cancer early detection services and hence increase the uptake of these services is also not being sufficiently harnessed.

Preventing cancer
before it develops –
by adopting a healthy
lifestyle.

4. NEED FOR ACTION TO DEVELOP CANCER PREVENTION RESEARCH

4.1 Primary prevention

4.1.1 Mechanisms of pathogenesis (genomics, microbiome, inflammation)

Singular genetic factors, such as inherited mutations in DNA repair or metabolism genes, are responsible for only about 5% of all cancer cases. In contrast, 90–95% of the genetic changes needed for cancer to develop are acquired during the course of a person's lifetime.

In addition to chemical carcinogens, the role of microbial pathogens (viruses, bacteria) in cancer pathogenesis has already been well established. Comprehensive availability of a vaccine that protects against cervical carcinoma can be seen as a particular achievement of primary cancer prevention in this context. In addition to lifestyle factors such as poor diet, excess weight, and a lack of activity, prevention research is increasingly also focusing on factors such as the microbiome. One key feature that these risk factors have in common is chronic inflammation, which increases the risk of DNA damage and also prevents the immune system from fighting the tumor effectively. The individual cancer risk is determined to a large part by the highly complex interaction between a person's genetic predisposition, acquired mutations, and lifestyle factors. One of the major tasks of prevention research is therefore to identify the molecular mechanisms of cancer pathogenesis under the influence of multifactorial risk factors.

90–95 %

of the genetic mutations that lead to cancer are acquired during a person's lifetime.

A further aspect is the identification of hitherto unknown risk factors, e.g., as a result of the occurrence of new pathogens. This is the only way to develop reliable indicators for a personalized risk assessment, which would enable people to be given effective individual advice and would allow informed health policy measures to be implemented.

4.1.2 Infections as a trigger of oncologic diseases

Around 15–20% of all cancer cases throughout the world are associated with infections (e.g., hepatitis B/C; human papillomavirus, HPV; Helicobacter pylori; Epstein-Barr virus, EBV; human herpesvirus 8, HHV-8), which are therefore the third most common cause of cancer worldwide after smoking and excess weight. This highlights the need for strategic and targeted programmatic prevention measures. Cancer linked to infections can be prevented comparatively easily by primary and secondary prevention measures. This makes it all the more important to implement effective testing and vaccination programs.

In addition, researchers have presumably not yet identified all of the pathogens that are relevant to oncogenesis. Modern sequencing and analytic methods enable researchers to look for possible associations between these viruses and selected tumor entities. A knowledge of such associations forms the basis for new basic research and the development of diagnostic and therapeutic agents and vaccines that can prevent infection-related carcinomas too.

4.1.3 Identification of intervention options at the premorbid stage (e.g., vaccinations)

The search for intervention options should be led by target behaviors, as evidenced in the European Code Against Cancer, and by the public health impact. Based on these two factors, the degree to which populations can be reached and motivated (motivational phase) to take part in interventions and/or adopt healthy behaviors on a long-term basis (volitional phase) is important. More prevention research should therefore be directed at the extent to which people can be reached and motivated. In addition to the behavioral level, the structural level is also highly relevant to prevention, and it is important to identify and modify structures and contexts that influence health and disease.

A prevention measure particularly suitable for infection-related tumors that should therefore be integrated into research questions involves identifying pathogen-specific biomarkers, which enable a prediction to be made about the risk of particular types of tumors. Identifying viral or bacterial biomarkers either directly (by detecting the genome or antigen of the pathogen) or indirectly (in this context particularly pathogen-specific antibodies) provides an efficient way of detecting small, fairly easily treatable tumors or their precursors at an early stage (e.g., screening for virus-associated nasopharyngeal carcinomas using antibodies against EBV and HPV, or screening for bowel cancer using histologic antibody staining in bowel tissue). Vaccination plays a particular role in infection-associated tumors. Vaccination rates thus need to be improved by means of systematic education programs or – if a vaccine does not yet exist – by developing effective vaccines against tumor-relevant pathogens (e.g., hepatitis C virus, EBV). Ethical questions arising in this context should be addressed at an early stage.

Another opportunity to implement interventions arises on the basis of new findings on tumors triggered by chronic inflammatory processes. One important aspect concerns cancer that develops as a result of a high-calorie diet or alcohol abuse and a lack of exercise. Liver cancer induced by fatty liver disease is an example in this context. Here, suppression of inflammation and reduction of fatty liver (through therapeutic and/or lifestyle interventions) can greatly reduce the risk of developing liver cancer.

These examples highlight the fact that basic research is important in order to understand the molecular and cellular effects of a healthy lifestyle and to harness these mechanisms for preventive treatments.

4.1.4 Individualized prevention research

Individualized prevention research in the field of primary prevention offers new opportunities. Population groups can be reached while nevertheless taking account of the particular circumstances of each individual. This includes identifying further factors and their combinations, whereby cancer risk profiles can be created. Examples include genetic and lifestyle factors. By identifying high-risk groups, cancer prevention measures can be made more effective. Moreover, personalized prevention research is thought to be a particularly promising way to support the desired changes in behavior. Taking account of individual factors when translating programs into practice – such as motivation to change behaviors, health litera-

Prevention research provides necessary insights into how **people can be reached** and **motivated to change their behavior.**

cy, social aspects, and subjective perceptions and needs – can help enhance acceptance among those affected and can improve the success of the programs.

4.2 Secondary prevention

4.2.1 Biomarkers and imaging methods for early diagnosis and diagnosis of recurrence

Many of the particularly serious types of tumors (e.g., pancreatic cancer, lung cancer) are associated with an unfavorable prognosis because they cause few symptoms in the early stages and are therefore detected too late. Yet in many cases an earlier diagnosis could enable patients to be cured by surgery. One example here is bowel cancer, which can be detected at an early stage using simple tests. There are a large number of biomarkers for the early detection of tumors: Imaging methods (e.g., magnetic resonance imaging (MRI), multiparametric MRI, computed tomography (CT), positron emission tomography (PET-CT), sonography, X-ray) can be used to detect tissue areas that look abnormal. Endoscopic methods, e.g., for the lung or the gastro-intestinal tract, provide a direct image of tissue damage that might be a precursor of cancer. Techniques of this kind can also be used to take samples to look for molecular changes. Molecular biomarkers are also used to diagnose virus-associated tumors (cervical cancer, head and neck tumors) or genetic and epigenetic mutations in precision oncology. Methods of this kind use not only tissue samples but also secretion, blood, urine, and stool samples. In the past, however, individual biomarkers were mainly used for the early detection of tumors. The next major step will involve achieving a better understanding of the interaction between the various factors and biomarkers. To do so, interdisciplinary efforts will be required to develop multimarker combinations to predict a person's individual cancer risk. For example, it is certainly conceivable that imaging methods combined with molecular biomarkers from blood and urine will offer considerably better options for detecting a tumor at an early stage or predicting tumor progression in future.

To achieve this goal, the population needs to be stratified into risk groups defined not only by the cancer risk but also by diet and inflammatory factors; app-based participation by individuals could also play a key role here. The potential of various German Health Research Centers could be harnessed to network their interactions and develop common definitions of risk factors. New biomarkers identified from these risk groups for early detection could also be validated in the medium term using the resources of the National Cohort.

4.2.2 Identification of intervention options in early stages of disease

The key goal of secondary prevention is to identify clinically manifest early stages or precursors of cancer before symptoms of the disease occur. This gives rise to considerable potential for intervention in early stages. This is already being done for colorectal carcinomas, skin and breast tumors, HPV-associated anogenital carcinomas, and in particular cervical carcinoma. Here, removal of precancerous polyps or intraepithelial neoplasms can help not only detect cancer at an early stage but also actually prevent cancer from developing. In other tumor entities, there are no ways of diagnosing tumors at an early stage to enable early intervention.

The need for research includes developing and refining methods for early diagnosis and the diagnosis of recurrence with a high level of specificity and sensitivity along with predictive methods for a more precise assessment of the risk of malignant transformation and of risk factors. The aim must be to detect early stages in a more targeted way and use nuanced treatment approaches to avoid overtreatment. Research approaches that need to be explored in greater depth address innovative predictive and diagnostic biomarkers and combinations of biomarkers and their interpretation with a view to using them initially in risk populations but subsequently in the general population too. Another area of research in this context involves new functional imaging methods such as PET-MRI with innovative tracers and the use of deep learning algorithms to assess conventional images, as in the field of endoscopy and skin cancer screening.

From a systematic perspective, research must focus on evaluating, designing, and refining early detection programs, particularly against the backdrop of the aforementioned new developments. This also includes patient-centered and holistic intervention advice with joint decision-making. Care must be taken right from the start to translate the interpretation and implications of modern early detection methods into a language that laypeople can understand and to consider patients' individual preferences and values, which requires the relevant communication skills on the part of healthcare professionals. Patient representatives should be included in research as a valuable component here.

4.2.3 Research on risk-adapted early detection (personalized and integrated prevention)

Risk-adapted early detection plays a key role in secondary prevention: Innovative approaches need to be used to avoid overdiagnosis and overtreatment in normal-risk groups while identifying high-risk groups to make prevention efforts considerably more effective, e.g., in terms of the frequency and extent of early detection measures. To do so, groups with differing risk profiles need to be clearly differentiated beyond existing profile characteristics, e.g., using molecular markers still to be established. Risk-adapted early detection also involves adapting the invasiveness of screening measures to the risk. In other words, the lower the risk, the less invasive and easier to carry out the early detection measure should ideally be. In this context, particularly tests that use samples that are easy to obtain, such as breath, urine, stool, or blood, are highly suitable. If these strategies can be established across the board for all tumor entities, it can be assumed that this kind of risk-adapted "personalized" early detection will become considerably more efficient and at the same time will help significantly increase the acceptance of these measures among the relevant target population.

In the field of risk-adapted early detection, there are essentially two different but combinable approaches at genetic level. First, using a genetic profile, a higher familial risk, e.g., due to germline mutations, can be identified. Second, tumors have genetic features (known as somatic mutations) that may be able to be found at an early stage (e.g., through circulating DNA). In some tumor entities (breast and ovarian cancer, bowel cancer), the genetic predisposition has already been well studied, while in others (prostate, lung) useful studies still

Detecting cancer early so that it is easier to treat.

Cancer early detection programs and methods must be continually **evaluated,** designed anew, and **refined.**

need to be conducted. In particular, longitudinal studies of clinically normal to clinically abnormal results are lacking in which genetic developments can be identified sufficiently early to ensure that early interventions would be feasible if necessary. By understanding the exact molecular mechanisms that lead to the development of cancer, targeted pharmacologic and immunologic prevention strategies can be developed.

Several factors (e.g., age, family history, particular lifestyle factors such as smoking) are usually combined in clinical risk prediction. In addition to germline and tumor genetics, considerable progress has been made in recent years in imaging in particular (e.g., multiparametric MRI). This means that high-risk individuals can be identified even more precisely using modern imaging methods before invasive diagnostic procedures are performed. Here, too, there is a considerable need for research, because the subjectiveness of assessment – and hence quality assurance – in imaging methods currently prevents them from being used across the board. Imaging methods are a key part of the secondary prevention of many types of tumors (e.g., breast, prostate, lung cancer). The need for research includes developing better noninvasive, low-radiation and radiation-free imaging methods and increasing the precision of these met-hods by including comprehensive anamnestic, clinical, and molecular biology information. Artificial intelligence methods will help researchers use the complex and extensive datasets from cohorts. The aim must be to develop individual early detection measures involving the targeted, risk-adapted use of imaging methods. Examinations for prostate carcinoma and for mammary carcinoma point to assessments that are more readily standardized.

A further relevant goal in prevention research is the early identification of combinations of risks in lifestyle factors such as physical activity and diet. Data obtained to date suggests that poor diet and a lack of exercise may be a prognostic factor in certain tumor entities. There is a lack of validated screening programs to identify risks in this area, but also a lack of strategies for effective and sustainable implementation of exercise and diet programs.

The aim of the areas mentioned above is to create an individual risk profile as a combination of genetic and clinical information and then to determine precisely justifiable additional examinations. For almost all types of tumors, more precise early detection can thus be established, thereby reducing overdiagnosis and overtreatment rates.

4.3 Need for research on overarching prevention topics

4.3.1 Research on public health impact (implementation, barriers)

The relevance of public health impact in reducing cancer rates and the fact that in-cidence is nevertheless still increasing show that, in addition to the other measu-res described, research should also be conducted on the way in which prevention measures are implemented in real-life healthcare settings.

The transfer of prevention measures that prove effective, for example in a randomized control group study, depends in practice on factors such as the level of funding and on the interests and other conditions that prevail in the institutions involved. As a result, the measures are altered in some cases and are no longer exactly the same as the interventions that have been shown to be effective in the studies. The impact of these changes needs to be studied. This also applies to potential barriers that affect implementation and uptake of the measures. In practice, the target population might differ from the participants in the studies previously conducted.

4.3.2 Research on outcomes

The success of most primary and secondary prevention measures is not reflected in epidemiologic figures until much later, particularly due to the fact that latency periods are very long in some cases. It is therefore only possible and useful to a limited extent to evaluate effectiveness in cancer prevention using conventional study designs such as randomized intervention studies. Large study populations and very long follow-up times mean that in many cases the interventions are often already deemed to be outdated and no longer appropriate by the time they are evaluated. Research is therefore particularly needed to identify sensitive intermediary endpoints to be measured much earlier, e.g., specific biomarker signatures, and to develop modeling studies that can reliably predict the anticipated effectiveness and cost-effectiveness of specific prevention measures in long-term follow-up.

4.3.3 Epidemiologic research

Epidemiologic research is the core discipline for identifying and quantifying the role of risk factors and preventive factors in the individual cancer risk and the incidence and consequences of cancer at population level. By including the latest technologies (e.g., omics technologies, digital media, imaging), an increasingly nuanced quantification of cancer risks and the chances of prevention should be able to be achieved. There is also considerable need for research in clinical epidemiology to develop and evaluate innovative tests and strategies for more effective and, where appropriate, risk-adapted early detection of cancer involving the use of modern biomarkers, imaging methods, and analytic methods for highly dimensional data.

4.3.4 Research on health literacy

The limited extent of health literacy among the German population has now been well researched and is regularly reviewed using surveys. Research therefore mainly needs to be carried out in the field of evidence-based strategies and interven-tions to promote health literacy at an individual and systems level, particularly with a view to the associated promotion of healthy behaviors and the reduction of lifestyle-related cancer risk. It is important to promote health literacy in all areas of everyday life (cf. National Action Plan on Health Literacy) and to enhance it using approaches that address society as a whole (such as a patient-centric approach in the healthcare system) while identifying effective strategies.

Prevention measures must be able to be **applied in a targeted way** in practice.

4.3.5 Research on the opportunities provided by digitalization

Increasing digitalization in the health sector offers considerable opportunities and possibilities for new approaches and far-reaching prevention. This potential can only be leveraged through broad methodological and interdisciplinary research, ranging from engineering, data science, and medicine through to the social sciences. Crucial factors include data blending (e.g., from citizens, healthcare facilities, registers, medical insurers), integration of data classes (e.g., genetics, environment, lifestyle/medical history), and data collection over as long a period as possible and from large cross-sections of the population. If this integration is successful, use of the data thus obtained will lead to a better understanding of risk factors and their influences, the quantitative assessment of personalized risk profiles, and the definition of tailored recommendations on action to be taken to minimize risk.

The possibilities described above are predicated on successful technical development and research, for example effective, efficient use of wearables compliant with regulations (e.g., smartwatches, fitness trackers, medical sensors) in order to allow digital measurement of lifestyle factors and provide new ways of carrying out targeted personalized behavior prevention measures. Furthermore, the establishment of new participation models and structures ranging from data donation to elaborate citizen science approaches would be welcomed.

5. SUMMARY, REQUIREMENTS AND DEMANDS MADE OF POLICYMAKERS

Continually rising cancer incidence rates are a clear indication that the possibilities of cancer prevention and cancer prevention research have not been sufficiently harnessed in the past. Consistently implemented prevention measures in the field of primary prevention have the potential to reduce the rate of new cancer cases in Germany by 40%. In the long run, additional measures in the field of early detection (secondary prevention) could increase the survival rate of cancer patients to up to 75%.

This will require basic research to achieve a better understanding of cellular functional mechanisms and of cancer development processes along with research and measures on translational implementation, early detection, and implementation of programs geared toward population groups. This can only be done if targeted measures are implemented in a concerted and strategically coordinated way within Germany and with European partners. Interinstitutional partnerships must be supported in this context to ensure the necessary interdisciplinarity.

German Cancer Aid and DKFZ call on health and research policymakers to draw on all the options and requirements set out in this position paper in the context of the National Cancer Plan and the National Decade Against Cancer and to initiate concerted, targeted action. This is the only way to reduce rising incidence rates and to continue to improve cancer treatment.

This includes:

- adequate financing of cancer prevention research (basic research, implementation research, epidemiologic research),

- development and financing of structures for the use of cancer prevention,

- support for cancer prevention through political initiatives,

- implementation of targeted, population-related cancer prevention initiatives,

- implementation of risk-adapted, target group-specific cancer screening programs,

- improvement/strengthening of health literacy in the population,

- support in developing and using digital options.

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SUSTAINBLE PROMOTION OF CANCER PREVENTION

National Cancer Prevention Center

The German Cancer Research Center (DKFZ) and German Cancer Aid have agreed to establish the National Cancer Prevention Center with a new building in Heidelberg as part of a long-term partnership. The aim is to combine high-level prevention research, training and continuing education, public relations work, and policy consulting under one roof and to implement them nationwide using outreach programs and networking. Researchers from various disciplines will team up to conduct research on cancer prevention here – from basic research to implementation in practice. In addition, a prevention outpatient clinic and an information center for the population will be established. The aim is to develop prevention programs geared toward the target groups with a view to ideally benefiting everyone in Germany. More information is available here › www.dkfz.de/ncpc

National Cancer Prevention Week

German Cancer Aid and DKFZ announced the first National Cancer Prevention Week in September 2019 to mark the start of their partnership. The German Cancer Society (DKG) became a partner of the campaign in 2021. The three organizations use the week to draw attention to the great potential of prevention. Every year, the campaign focuses on a different lifestyle factor that affects cancer risk. More information is available here › www.krebshilfe.de/krebspraeventionswoche

FORMS OF PREVENTION

Primary prevention

Preventing cancer before it develops – by adopting a healthy lifestyle.

Secondary prevention

Detecting cancer at an early stage so that it is easier to treat.

Tertiary prevention

Preventing recurrence of cancer after patients have recovered.