

Summaries of PredictAYA Work Packages (WPs)

WP 1 - Project Management and Coordination, Data Management, IPR and Ethics

WP1 ensures that the PredictAYA project runs smoothly, stays on track, and meets all its goals. It sets up the structure for managing the project, including clear rules, responsibilities, and communication channels between all partners.

This work package handles day-to-day coordination, monitors progress, manages risks, and ensures that all legal, financial, and ethical requirements are met. It also oversees reporting to the European Commission and organizes regular meetings to keep everyone informed and aligned with the project goals and timelines.

WP1 includes the creation of a project handbook, ethics and gender equality plans, and a data management strategy to protect personal information and support responsible data sharing. It also manages the Scientific and Ethical Advisory Board, which includes patient representatives, clinicians, and industry experts who provide valuable guidance throughout the project.

Overall, WP1 provides the foundation for successful collaboration and high-quality research across the PredictAYA consortium.

WP 2 - Understanding Long-Term Health Effects in Young Cancer Survivors

WP2 focuses on understanding how cancer and its treatment affect the long-term health of adolescents and young adults (AYAs) across Europe. Using large population-based registries, this work package studies how common and how severe reproductive organ damage is after cancer treatment, and what factors (such as age, type of cancer, treatment or social background) might increase the risk.

WP2 also studies how reproductive problems may be linked to other health issues like hormonal, heart, or brain-related conditions. WP2 aims to find out when it's best to start screening for these late effects and who is most at risk.

Another key goal is to evaluate how safe and effective fertility preservation methods are for AYAs with cancer, and to understand their chances of natural conception later in life. To achieve these goals WP2 also studies pregnancy outcomes, IVF use and the health of children born to cancer survivors.

Patient and relative representatives can provide valuable insights into lived experiences, helping to shape research questions, interpret findings, and ensure that the outcomes are meaningful and relevant to those affected.



The data collected will help generate new research questions and support the development of better follow-up care and guidelines for young cancer survivors.

WP 3 - Pharmacogenetic modelling - Understanding How Cancer Treatments Affect Fertility and Long-Term Health

Many young people who survive cancer face long-term side effects from their treatment. One of the most serious is damage to reproductive organs, which can lead to infertility or early menopause. WP3 aims to understand why some people experience these problems while others do not, and to find ways to predict and prevent them in the future.

Our researchers will study how common cancer drugs affect reproductive cells and tissues in the laboratory, and how genetic differences between people might explain their sensitivity to these treatments. We will use data from large European biobanks and patient groups to identify genetic markers linked to fertility problems or other long-term toxicities. We will also establish a **European database of whole-genome sequences** from young cancer survivors, focusing on those who have experienced reproductive side effects. This will help us explore the complete genetic landscape of treatment-related toxicity. Using artificial intelligence and machine learning, we will develop **prediction models** that can estimate an individual's risk of reproductive or other organ damage after cancer treatment. The long-term goal is to make it possible to personalise treatment and follow-up care—so that therapy remains effective while protecting patients' future health and fertility.

This work will help us develop **prediction models** that could one day allow doctors to personalize cancer treatment—reducing the risk of infertility and other toxicities while keeping therapy effective.

We would like the members of the **Patient and Relatives Advisory Board (PRAB)** to play a role in guiding how genetic information is used in an ethical and respectful way, especially given the sensitivity of fertility and reproductive health information. Their perspectives will help ensure that we communicate clearly about what genetic findings mean (and what they do not mean) for patients and families. The PRAB can also provide valuable advice on their thoughts of using machine learning and AI and how to present the results in understandable terms.

WP 4 - Clinical research on ovarian toxicity from large cohorts across Europe

This part of the project focuses on understanding how cancer and its treatments affect fertility in young women and how fertility preservation can help. A **new European study group (cohort)** of female cancer patients will be created. These patients received counselling about the risk of infertility and fertility preservation options before cancer treatment and are followed-up after cancer therapy.

At the same time, we will look into **existing European studies** from different centres that already follow women treated for cancer. Data will be **merged** to form a large dataset, allowing powerful analysis. This will make it possible to compare short-, medium-, and long-term fertility outcomes across different cancer types, treatments, and age groups.

The data collected will help us understand how different cancer therapies influence ovarian function and fertility, and how effective different fertility preservation measures, such as freezing eggs, are, how often women conceive naturally or with assisted methods after cancer treatment, and how satisfied women are with the counselling they received.

WP 5 - Late effect of cancer therapies on fertility and reproduction in males

Cancer treatments such as chemotherapy can affect fertility and testosterone production in young men. However, the long-term effects on the function of the testicles are still not well understood. The *PREDICT-AYA-TEST* study aims to fill this important knowledge gap by developing methods to predict testicular damage in adolescent and young adult (AYA) cancer survivors. The study will follow about 1,000 male cancer survivors aged 15–39 years who have been treated for testicular cancer or lymphomas at several hospitals across Europe.

Researchers will collect detailed information before and after treatment, including hormone levels, semen quality, lifestyle factors, and sexual health. This information will help identify which patients are most likely to experience infertility or low testosterone after chemotherapy. In selected participants, tests on DNA collected from blood and sperm will also be performed to understand why some individuals are more vulnerable to long-term side effects. The study will further explore whether cancer treatments can cause “accelerated aging” and how this may relate to reproductive health.

By bringing together data from many European centres, this study will develop reliable tools to predict fertility risks and guide personalized follow-up and counselling for young male cancer survivors. The findings will help doctors provide better advice on fertility preservation, safe timing for conception, and long-term hormone health—ultimately improving quality of life and reproductive options for young men after cancer.

WP 6 - Postcancer reproductive health, sexuality and quality of life

WP 6 studies **how cancer and its treatments affect the ability to have children** safely, and **how cancer treatments can influence sexual health and quality of life** in adolescent and young adult (AYA) cancer survivors. PredictAYA will first examine how safe it is to become pregnant after cancer, both for the health of the mother and the health of the child. The study will compare natural pregnancies, assisted reproduction, and pregnancies following fertility preservation, as well as how



the timing of pregnancy after cancer treatment affects outcomes. PredictAYA will use large European datasets, to assess risks such as premature birth, pregnancy complications, and the impact of different cancer types and treatments on health outcomes.

We will also look at **pregnancies that occur during cancer treatment** and the potential impact of this on the risk of cancer coming back. Another aspect of the project is to look into **unintended pregnancies** in cancer survivors and the possible reasons for this. This will help to understand how to improve contraception counselling and access for AYA cancer patients and survivors.

Finally, researchers will study how cancer might influence the **sexual health and quality of life** of male and female AYA cancer survivors. The aim is to investigate problems in sexual function and challenges such as loss of desire, pain, or hormone-related issues, and guide better support during follow-up care.

WP 7 - Communications, dissemination, stakeholder engagement, policy, and European initiative clustering

In W7, **PredictAYA connects and engages with key interest groups** (called stakeholders) in the adolescent and young adult (AYA) cancer field, including AYA cancer patients and survivors, healthcare professionals, researchers, and policymakers. With this, we want to ensure that our results are relevant and useful for these groups, also after the project end. Through PredictAYA's own social media accounts, website, events, or project partners' networks, we will share our goals, activities, progress and results. We will also use our platforms to **raise public awareness** about late effects in AYA cancer survivors and aspects such as fertility preservation.

PredictAYA will collaborate with other EU-funded projects in the AYA cancer field to address critical research topics, and ensure that AYA cancer is an important policy issue for decision-makers in Europe. For this, PredictAYA is part of a group of projects brought together by the European Commission under the theme "**Quality of life (AYA)**". Together, this so-called "Cluster" contributes to the objectives of the **EU Cancer Mission**, a key initiative combining research, innovation and public health policies to address the burden of cancer in Europe.

In this WP, PredictAYA will also study **how young cancer survivors experience fertility preservation care and counselling**. Based on the results, we will develop **new guidelines** on reproductive health and fertility after cancer for healthcare professionals to improve current practices.

We will organise online meetings and physical events to which interested stakeholders will be invited. This also includes the **Patient and Relatives Advisory Board (PRAB)**, which will involve AYA cancer patients, survivors and relatives from different European countries to share their lived experiences, ensuring PredictAYA remains meaningful and relevant to AYAs. PRAB members can contribute, for instance, through supporting advocacy efforts and providing feedback on our new guidelines.

WP 8 - Data Management and Clinical Study Support

WP8 focuses on organizing and harmonizing clinical and population-based data collected across Europe for the PredictAYA project. It helps ensure that all research teams collect and manage data in a consistent way, making it easier to compare results and draw reliable conclusions.

This work package supports the planning and approval of clinical studies, coordinates a steering committee to oversee them, and manages the collection of data and biological samples. It also helps identify missing data and ensures that all study sites are aligned in their methods.

WP8 plays a key role in combining data from different sources, such as hospitals, registries, and patient surveys, into a shared database. This harmonized data will be used to better understand the long-term effects of cancer treatment on fertility and other health outcomes. Finally, WP8 provides expert statistical support to help design the studies, calculate sample sizes, and analyze the results accurately.

Patient representatives can contribute by, for example, helping to shape the design of surveys and questionnaires, by identifying how best to reach out and by ensuring that the data collected reflects the priorities of cancer survivors.

WP 9 – Ethics

WP9 ensures that all research in the PredictAYA project is carried out ethically and in full respect of human rights. It focuses on protecting participants, and most especially children and vulnerable individuals, when their personal or health data is used. Before starting any research activities, the project must show how informed consent is obtained from all study participants, how national laws are followed, and how sensitive data is protected.

Because the project uses artificial intelligence (AI) to study long-term health effects after cancer treatment, WP9 also includes a detailed review of how AI is developed and used responsibly. This includes checking for risks like bias or discrimination, making sure people understand how the AI works, and ensuring that humans stay in control of important decisions.

Patient representatives can provide valuable input by helping to ensure that the research respects participants' rights and communicates study information clearly, both at inclusion of study participants and in sharing results from the project.

An independent Ethics Advisory Board with expertise in data protection, AI, and vulnerable populations will review the project regularly and report to the funding authority. This helps ensure that ethical standards are met throughout the project.