**Can Cost-effectiveness Analysis Inform Genotype-Guided Aspirin Use for Primary Colorectal Cancer Prevention?**

**Biltaji et al. | Page 1106**

Emerging data indicates genetic polymorphisms may affect the efficacy of aspirin for chemoprevention of colorectal cancer and may be used as a tool to improve risk assessment and identify individuals that are likely to benefit. Biltaji and colleagues created a decision analytical model to assess the potential benefit of a genotype-guided aspirin strategy for colorectal cancer chemoprevention in an average risk population. The authors concluded the approach was cost-effective and improved clinical outcomes. This model establishes a framework and the potential clinical utility for a precision medicine approach to targeted chemoprevention of colorectal cancer.

---

**Long-term Patterns of Excess Mortality among Endometrial Cancer Survivors**

**Anderson et al. | Page 1079**

Examining excess mortality among cancer survivors relative to the general population can inform planning for surveillance and follow-up after cancer treatment. Anderson and colleagues examined patterns of excess mortality among women with endometrial cancer identified in the Surveillance, Epidemiology and End Results (SEER) database. Overall, endometrial cancer survivors had little excess mortality compared to the general population beyond 4 years post-diagnosis. However, excess mortality was greater for Black survivors and those with more advanced stage or higher-grade disease. Strategies to mitigate long-term mortality disparities among endometrial cancer survivors are needed.

---

**Type 2 Diabetes and Cancer**

**Pearson-Stuttard et al. | Page 1218**

Type 2 diabetes (T2DM) has been associated with an increased risk of developing several common cancers, but it is unclear whether this association is causal. Pearson-Stuttard and colleagues aimed to summarize the evidence on T2DM and cancer and evaluate the validity of associations from both observational and Mendelian randomization (MR) studies. This study provides a comprehensive update of the observational evidence linking type 2 diabetes and cancer risk across 21 different sites and is substantially enhanced by the inclusion of MR studies which address potential causation and mechanisms. The most robust observational evidence was detected for T2DM and increased risk of colorectal, breast, endometrial, gallbladder, hepatocellular and pancreatic cancer, while MR studies supported a causal association between genetically predicted T2DM and/or fasting insulin concentrations and risk of endometrial, breast and pancreatic cancer, as well as with lung, kidney and cervical cancer.

---

**The Effects of Lifetime Estrogen Exposure on Breast Epigenetic Age**

**Sehl et al. | Page 1241**

Accelerated breast tissue aging is thought to contribute to an elevated incidence of breast cancer in younger women. Estrogen stimulation and cell cycling are thought to underlie this accelerated aging process. Sehl and colleagues investigated methylation-based estimates of epigenetic aging in normal breast tissue of healthy women donors, focusing analysis on Grim age, an epigenetic age measure whose acceleration in peripheral blood is associated with time to cancer. The study found that earlier age at menarche and higher body mass index are associated with acceleration in Grim age in breast tissue, supporting the hypothesis that lifetime estrogen exposure drives epigenetic aging in healthy female breast tissue.