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## Sessions 9 and 10: Aspirin and NSAID's in cancer prevention: Attempts for an international consensus

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### S35. Introduction into the consensus topic

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Aspirin & non-steroidal anti-inflammatory drugs (NSAIDs) have been investigated for their cancer preventive properties for more than four decades. During that time, reports from experimental & clinical research have provided strong evidence of Aspirin's benefits in reducing the risk of colorectal cancer; suggestive evidence indicates it may be beneficial for cancers of the esophagus, prostate, breast, & pancreas in women. Aspirin & NSAIDs may prevent cancer through anti-inflammatory or anti-angiogenic actions, or through some as yet unknown mechanism-of-action. For example, Aspirin acts as an anti-inflammatory agent by inhibiting prostaglandin synthesis by cyclo-oxygenase enzymes, which are produced by the body during inflammation. In addition, NSAIDs such as cyclo-oxygenase-2 (cox-2) inhibitors specifically inhibit cox-2 which is overexpressed in some polyps & colorectal cancers & stimulates pathways that promote cell proliferation & inhibit cell death. Because Aspirin & NSAIDs appear to have favorable safety profiles for many people, there has been interest in using these drugs for cancer prevention, although the balance of benefits & risks for the person as a whole needs to be taken into account.

Results from a number of clinical trials of Aspirin & cancer have been mixed. For example, the Cancer Prevention Study II Nutrition Cohort found a 15 percent reduction in overall cancer incidence for men & women who took an adult strength (360mg) dose of Aspirin daily for at least 5 years compared to

those who did not. Long term daily Aspirin use also resulted in an approximately 30 percent decrease in colorectal cancer incidence. Prostate cancer incidence was reduced by 20 percent & female breast cancer by 15 percent, although the reduction in breast cancer was not statistically significant. The Nurses' Health Study found that taking more than two 325 mg tablets per week reduced colorectal cancer incidence (RR=0.77) but significant reduction was observed only after more than 10 years of use. A systematic review of the evidence for colon cancer prevention by Aspirin prepared for the United States Preventive Services Task Force found an RR of 0.82 for randomized controlled trials & 0.87 for case-control studies; a 22 percent reduction in adenoma occurrence was observed for cohort studies. The Prevention of Colorectal Sporadic Adenomatous Polyps Trial & the Adenoma Prevention with Celecoxib Trial tested daily doses of cox-2 inhibitors & found that although occurrence of adenomas was decreased, a troubling increase in cardiovascular events were observed in participants using these drugs.

The use of Aspirin & NSAIDs, which are widely used in most societies, could benefit many individuals, particularly those at high colo-rectal cancer risk, particularly as we learn better how to avoid their use for groups with an increased susceptibility to adverse effects. Although the evidence for colo-rectal cancer is strong, it is important to consider the impact on overall quality of life & longevity.