

# Cancer Association of South Africa (CANSA)

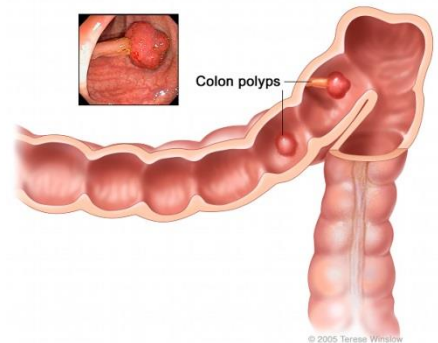


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## Fact Sheet on Familial Adenomatous Polyposis

### Introduction

A polyp is an abnormal growth of tissue projecting from a mucous membrane. If it is attached to the surface by a narrow elongated stalk, it is said to be pedunculated. If no stalk is present, it is said to be sessile. Polyps are commonly found in the colon, stomach, nose, sinus(es), urinary bladder and uterus. They may also occur elsewhere in the body where mucous membranes exist like the cervix, vocal folds, and small intestine. (Wikipedia).



[Picture Credit: Polyp]

### Familial Adenomatous Polyposis (FAP)

Familial adenomatous polyposis (FAP) is a rare, inherited condition that causes extra tissue (polyps) to form in one's large intestine and in the upper part of the small intestine (duodenum). If FAP is untreated, these polyps in the large intestine almost always become cancerous by age 40.

Most people with familial adenomatous polyposis eventually need surgery to remove the upper part of the large intestine (colon) to prevent cancer. The polyps in the duodenum (first part of the small intestine) can also develop cancer, but it can usually be managed by removing the polyps regularly. (Mayo Clinic).

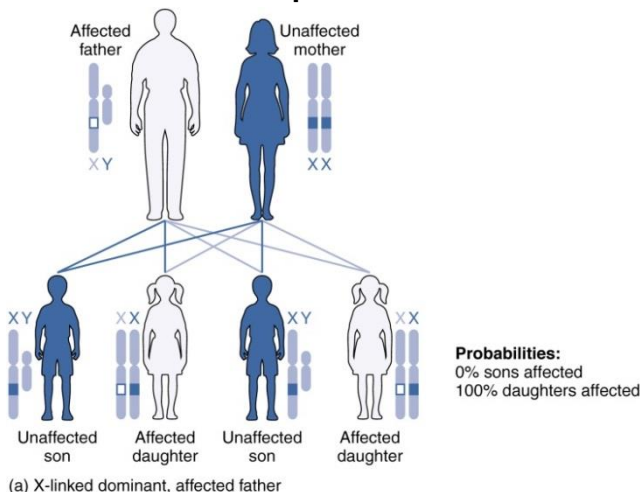
Familial adenomatous polyposis (FAP) is characterised by cancer of the large intestine (colon) and rectum. People with the classic type of familial adenomatous polyposis may begin to develop multiple non-cancerous (benign) growths (polyps) in the colon as early as their teenage years – and sometimes even earlier. Unless the colon is removed, these polyps will become malignant (cancerous). The average age at which an individual develops colon cancer in classic familial adenomatous polyposis is 39 years. Some people have a variant of the disorder, called attenuated familial adenomatous polyposis, in which polyp growth is delayed. The average age of colorectal cancer onset for attenuated familial adenomatous polyposis is 55 years.

In people with classic familial adenomatous polyposis, the number of polyps increases with age, and hundreds to thousands of polyps can develop in the colon. Also of particular significance are non-cancerous growths called desmoid tumours. These fibrous tumours usually occur in the tissue covering the intestines and may be provoked by surgery to remove the colon.

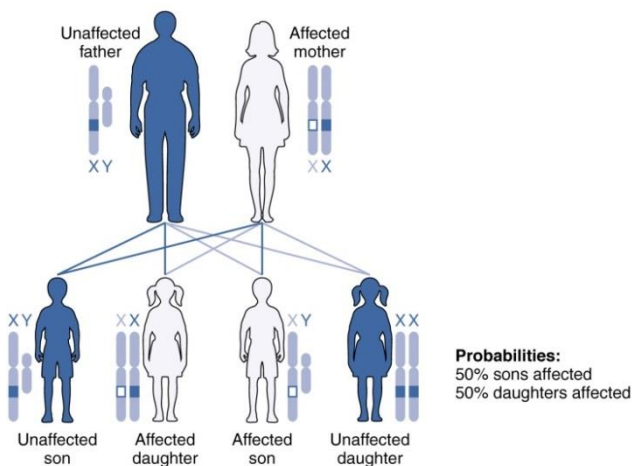
Desmoid tumours tend to recur after they are surgically removed. In both classic familial adenomatous polyposis and its attenuated variant, benign and malignant tumours are sometimes found in other places in the body, including the duodenum (a section of the small intestine), stomach, bones, skin, and other tissues. People who have colon polyps as well as growths outside the colon are sometimes described as having Gardner syndrome.

A milder type of familial adenomatous polyposis, called autosomal recessive familial adenomatous polyposis, has also been identified. People with the autosomal recessive type of this disorder have fewer polyps than those with the classic type. Fewer than 100 polyps typically develop, rather than hundreds or thousands. The autosomal recessive type of this disorder is caused by mutations in a different gene than the classic and attenuated types of familial adenomatous polyposis. (Genetics Home Reference).

### Gene Mutations Responsible for Familial Adenomatous Polyposis



(a) X-linked dominant, affected father



(b) X-linked dominant, affected mother

Mutations in the *APC* gene cause both classic and attenuated familial adenomatous polyposis. These mutations affect the ability of the cell to maintain normal growth and function. Cell overgrowth resulting from mutations in the *APC* gene leads to the colon polyps seen in familial adenomatous polyposis. Although most people with mutations in the *APC* gene will develop colorectal cancer, the number of polyps and the time frame in which they become malignant depend on the location of the mutation in the gene.

[Picture Credit: Autosomal Dominant Inheritance]

Normally, every cell has two copies of each gene: one inherited from one's mother and one inherited from one's father. FAP follows an autosomal dominant inheritance pattern. In autosomal dominant inheritance, a mutation happens in only one copy of the gene. This means that a parent with a gene mutation may pass along a copy of their normal gene or a copy of the gene with the mutation. Therefore, a child who has a parent with a mutation has a 50% chance of inheriting that mutation. A

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December 2015

brother, sister, or parent of a person who has a mutation also has a 50% chance of having the same mutation.

(Genetics Home Reference).

Mutations in the *MUTYH* gene cause autosomal recessive familial adenomatous polyposis (also called MYH-associated polyposis). Mutations in this gene prevent cells from correcting mistakes that are made when DNA is copied (DNA replication) in preparation for cell division. As these mistakes build up in a person's DNA, the likelihood of cell overgrowth increases, leading to colon polyps and the possibility of colon cancer.

(Genetics Home Reference).

[Picture Credit: Autosomal Recessive Inheritance]

The root cause of familial adenomatous polyposis is, therefore, understood to be a genetic mutation – a flaw in the body's tumour suppressor genes that prevent development of tumours. The flaw allows numerous cells of the intestinal wall to develop into potentially cancerous polyps when they would usually reach the end of their life – inevitably one or more will eventually progress and give rise to cancer. The risk for this to happen is:

- 7% risk by age 21
- 87% risk by age 45
- 93% risk by age 50

The flawed genes do not trigger cancer, but rather, they reduce the body's ability to protect against the risk of aged cells becoming cancerous. Even with the flawed gene, it may still take time before a cell actually does develop that is cancerous as a result, and the gene may in some cases still partially operate to control tumours. It is because of this that cancer from familial adenomatous polyposis takes many years to develop and is almost always an adult-onset disease.

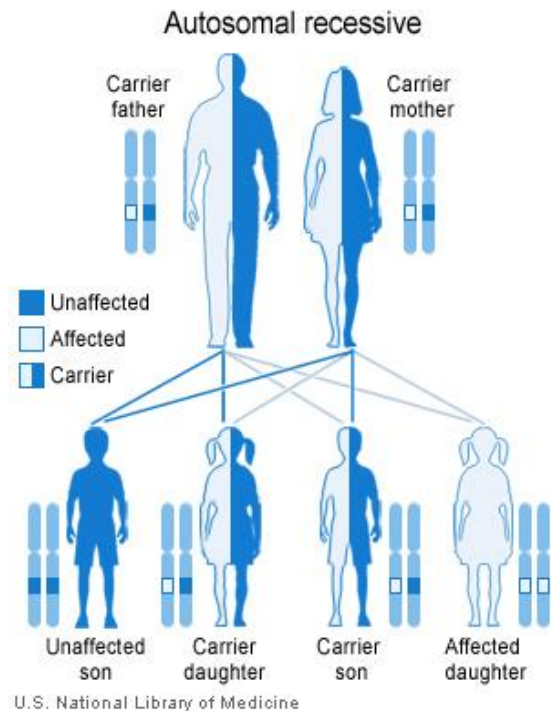
There are three subtypes of classic FAP:

- Attenuated FAP (AFAP)
- Gardner syndrome
- Turcot syndrome

(Mayo Clinic; eMedicine).

### **Incidence of Familial Adenomatous Polyposis (FAP) in South Africa**

The National Cancer Registry (2010) does not provide information regarding the different types of cancers of the colon.



According to the National Cancer Registry, the following cases of colorectal cancer were histologically diagnosed during 2010 (the most recent formal statistics available for South Africa):

Group - Males 2010	No of Cases	Lifetime Risk	Percentage of All Cancers
All males	1 295	1:114	4,77%
Asian males	100	1:51	13,62%
Black males	407	1:264	3,84%
Coloured males	180	1:79	5,64%
White males	608	1:50	4,83%

Group - Females 2010	No of Cases	Lifetime Risk	Percentage of All Cancers
All females	1 132	1:182	3,80%
Asian females	71	1:97	7,39%
Black females	397	1:389	2,54%
Coloured females	144	1:103	4,66%
White females	520	1:71	5,17%

The frequency of histologically diagnosed cases of colorectal cancer in South Africa for 2010 was as follows (National Cancer Registry, 2010):

Group - Males 2010	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All males	6	32	74	151	302	332	278	98
Asian males	0	0	6	4	26	29	24	2
Black males	5	20	42	65	101	78	49	15
Coloured males	0	4	11	29	33	49	33	11
White males	0	7	13	47	130	161	159	61

Group - Females 2010	0 – 19 Years	20 – 29 Years	30 – 39 Years	40 – 49 Years	50 – 59 Years	60 – 69 Years	70 – 79 Years	80+ Years
All females	3	26	65	172	228	288	228	111
Asian females	0	1	4	12	15	19	14	3
Black females	2	15	37	82	87	69	60	24
Coloured females	0	2	4	20	27	47	30	8
White females	1	6	17	55	91	139	115	74

N.B. In the event that the totals in any of the above tables do not tally, this may be the result of uncertainties as to the age, race or sex of the individual. The totals for 'all males' and 'all females', however, always reflect the correct totals.

### Diagnosis of Familial Adenomatous Polyposis (FAP)

Diagnosis is based primarily on clinical findings and family history. Molecular genetic testing may be used to clarify diagnosis in individuals with ambiguous findings, or for early identification of at-risk family members.

#### Diagnostic criteria

Familial Adenomatous Polyposis (FAP) is diagnosed in an individual with one of the following:

- One hundred or more colorectal adenomatous polyps
- Fewer than 100 adenomatous polyps and a relative with FAP 10 -100 adenomatous polyps and a first degree relative with FAP
- Detection of a deleterious germline mutation in the *APC* gene.

### First Diagnostic Steps

- Document patient and family polyp and cancer history
- When possible, confirm diagnoses through record review, paying particular attention to quantity and histology of polyps.
- Consider genetic testing to confirm diagnosis, clarify diagnosis in ambiguous cases, and provide information for at-risk family members. Results could alter decisions about screening, surgical prophylaxis, and life/reproductive planning.

### Testing Strategy

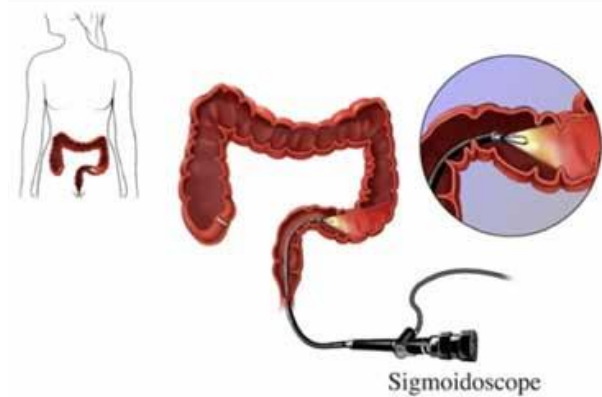
Testing is indicated for the following patients:

- hepatoblastoma <age 7
- when the above clinical diagnostic criteria are met
- Perform targeted genetic testing for the single specific *APC* gene mutation identified in a relative.
- First-tier: sequencing and deletion/duplication analysis of the *APC* gene. (Detects a mutation in ~90% of individuals with classic FAP, while detection rate is lower in those with an attenuated presentation.)
- Second-tier: testing of other genes associated with polyposis (see Differential Diagnosis)
- When no disease-causing mutation is identified in an affected individual, but a familial cancer syndrome is still suspected, genetics consultation is appropriate.

(GeneFacts).

Although familial adenomatous polyposis (FAP) is a serious condition that may become life-threatening, it can be detected early and treated successfully. With prompt treatment, FAP patients lead normal, healthy lives. Untreated FAP will, however, lead to colon cancer.

Because this condition is always hereditary, family members of those with the condition also are at risk of developing it. FAP can be diagnosed by a blood test to detect a genetic mutation in the *APC* gene, which causes FAP, or by flexible sigmoidoscopy, a simple, painless examination of the lower colon that is performed at a doctor's office. Those at risk are strongly advised to consider genetic testing or flexible sigmoidoscopy done either by a family physician or by a specialist.



[Picture Credit: Sigmoidoscopy]

In its early stages, FAP has no symptoms. That is why genetic testing or endoscopic screening starting at puberty when polyps first appear is so important. The diagnosis can, and should, be made before symptoms and colorectal cancer occur.

If untreated, polyps will increase in number and size. Patients may have hundreds of polyps in their colon without symptoms. As the condition progresses, patients may experience blood in the stool, diarrhoea, mucous discharge, crampy abdominal pain, anaemia, weight loss and intestinal obstruction. However, these symptoms may not occur until the condition has become cancerous.

(Cleveland Clinic).

## **Surgical Treatment of Familial Adenomatous Polyposis (FAP)**

Prophylactic colectomy in classic FAP is usually performed shortly after polyps are discovered on surveillance colonoscopy. When polyps are diagnosed in the early teenage years, surgery can be deferred until the patient reaches maturity in their late teens or early twenties. Four options exist:

- total abdominal colectomy with ileorectal anastomosis (TAC+IRA)
- total proctocolectomy with ileal pouch anal anastomosis (TPC+IPAA)
- total proctocolectomy with end ileostomy (EI)
- total proctocolectomy with continent ileostomy (TPC+CI) .

The choice of operation depends on many factors and should be individualised. The most important determinants are rectal polyp burden, presence of cancer or severe dysplasia, age, symptoms, continence, genotype, and patient compliance. Dysplasia (from Ancient Greek *δυσ-* *dys-*, "bad" or "difficult" and *πλάσις* *plasis*, 'formation') is an ambiguous term used in pathology to refer to an abnormality of development or an epithelial anomaly of growth and differentiation (epithelial dysplasia).

Patients and their surgeon will typically be faced with the choice between TAC+IRA and TPC+IPAA. While both operations preserve continence, the resultant bowel function is inferior to what the patient had experienced prior to surgery. The advantage of TAC+IRA is that this change in function is less severe than that resulting from TPC+IPAA. The advantage of the latter is that removal of the rectum virtually eliminates the risk of rectal cancer, although several cases following IPAA have been reported worldwide.

**TAC+IRA** can be performed safely, and should, therefore, be favoured, in the following situations:

- In patients with mild to moderate colonic polyposis and <20 polyps in the rectum.
- In genotyped patients with mutations in exons 3, 4, or the 3'end of exon 15. These mutations are associated with the 'attenuated' form of FAP, where the development of severe rectal polyps or rectal cancer is extremely rare.
- In teenaged patients where the relatively poor function of an IPAA may have severe social ramifications and where the pelvic dissection associated with proctectomy may alter both male and female sexual function and fertility. In these cases, the patient can be followed closely with annual or bi-annual proctoscopy with proctectomy deferred until rectal polyposis can no longer be controlled with the combination of endoscopic polypectomy and NSAIDs.

In addition, all patients being offered TAC+IRA must have adequate sphincter function and should be willing to enter a surveillance proctoscopy program. Studies in patients with FAP have shown perioperative morbidity rates to be lower following TAC+IRA compared to TPC+IPAA. In addition, patients undergoing TAC+IRA have fewer stools (both daily and night time), less incontinence, and wear pads less often than those treated with TPC+IPAA. Rates of rectal cancer following TAC+IRA in FAP have varied widely (5% to 37%) and are clearly related to patient selection and the availability of surgical options. This is best illustrated by a study from the Cleveland Clinic which looked at outcomes in patients having TAC+IRA in the era before the availability of IPAA and compared it to those having surgery after IPAA became available at that institution. Thirteen percent of patients having TAC+IRA in the pre-IPAA era developed rectal cancer versus none in the post-IPAA era. Likewise, the

proctectomy rate following TAC+IRA was much higher in the pre-IPAA era patients (32%) compared to those in the post-IPAA era (2%).

**TPC+IPAA** is required in the following situations:

- Patients with severe polyposis
- Patients with >20 polyps in the rectum
- Patients with cancer or severe dysplasia
- Patients with the exon 15G mutation (predicts severe disease)

An area of controversy in the management of FAP patients is whether or not to perform a mucosectomy and handsewn IPAA. Data from patients with ulcerative colitis has shown that functional outcomes are worse in patients undergoing mucosectomy (M) compared to those having preservation of the anal transitional zone by the more common double-stapled IPAA (DS). In FAP, the benefit of improved function must be balanced against the risk of developing adenomas (25-30%) or rectal cancer in the retained anal transitional zone/low rectal mucosa. Surgeons tend to perform M in most patients with FAP, reserving DS for women who have had previous vaginal deliveries or patients where body habitus (tall/obese/long, narrow anal canal) may make the extra several centimetres of pouch reach needed after M difficult to obtain.

Another area of controversy is the patient with FAP who presents with rectal cancer. The decision to offer the patient IPAA versus permanent end ileostomy (EI) should be made following sound oncologic principles. If a clear distal and radial margin can be obtained and sphincter function is adequate, then IPAA can be pursued. In these cases, radiation therapy should always be given pre-operatively as radiating an existing pelvic pouch will lead to poor pouch function and eventual pouch excision in most cases. It is for this reason that practitioners tend to treat *all* rectal cancers in FAP patients with neoadjuvant therapy, regardless of stage, in order to avoid the dilemma of post-operative radiation in a patient whose tumour was understaged by endorectal ultrasound.

**TPC+EI** is reserved for patients with poor sphincter function, those not willing to undergo yearly adenoma surveillance following IPAA, or those favouring the convenience and low morbidity of an ileostomy over a restorative procedure. It is also the procedure of choice when an intra-abdominal desmoid tumour precludes IPAA or IRA.  
(NYU Langone Medical Center; American Society of Colon and Rectal Surgeons).

### **Medical Treatment of Familial Adenomatous Polyposis (FAP)**

Sulindac, a non-steroidal anti-inflammatory drug, and celecoxib, a COX-2 antagonist, have both been shown to cause regression of colorectal adenomas in FAP. Unfortunately, the response is rarely complete and in most cases all that is seen is a modest reduction in the number and size of polyps. No protective effect against the development of cancer has yet been definitively demonstrated and these drugs cannot replace the role of prophylactic colectomy in FAP. Their best use is in controlling pouch or ATZ polyposis after prophylactic surgery. Several small studies have shown a reduction in polyp load ranging from 12% to 44%.

(American Society of Colon and Rectal Surgeons).

## **About Clinical Trials**

Clinical trials are research studies that involve people. These studies test new ways to prevent, detect, diagnose, or treat diseases. People who take part in cancer clinical trials have an opportunity to contribute to scientists' knowledge about cancer and to help in the development of improved cancer treatments. They also receive state-of-the-art care from cancer experts.

### Types of Clinical Trials

Cancer clinical trials differ according to their primary purpose. They include the following types:

**Treatment** - these trials test the effectiveness of new treatments or new ways of using current treatments in people who have cancer. The treatments tested may include new drugs or new combinations of currently used drugs, new surgery or radiation therapy techniques, and vaccines or other treatments that stimulate a person's immune system to fight cancer. Combinations of different treatment types may also be tested in these trials.

**Prevention** - these trials test new interventions that may lower the risk of developing certain types of cancer. Most cancer prevention trials involve healthy people who have not had cancer; however, they often only include people who have a higher than average risk of developing a specific type of cancer. Some cancer prevention trials involve people who have had cancer in the past; these trials test interventions that may help prevent the return (recurrence) of the original cancer or reduce the chance of developing a new type of cancer.

**Screening** - these trials test new ways of finding cancer early. When cancer is found early, it may be easier to treat and there may be a better chance of long-term survival. Cancer screening trials usually involve people who do not have any signs or symptoms of cancer. However, participation in these trials is often limited to people who have a higher than average risk of developing a certain type of cancer because they have a family history of that type of cancer or they have a history of exposure to cancer-causing substances (e.g., cigarette smoke).

**Diagnostic** - these trials study new tests or procedures that may help identify, or diagnose, cancer more accurately. Diagnostic trials usually involve people who have some signs or symptoms of cancer.

**Quality of life or supportive care** - these trials focus on the comfort and quality of life of cancer patients and cancer survivors. New ways to decrease the number or severity of side effects of cancer or its treatment are often studied in these trials. How a specific type of cancer or its treatment affects a person's everyday life may also be studied.

### Where Clinical Trials are Conducted

Cancer clinical trials take place in cities and towns in doctors' offices, cancer centres and other medical centres, community hospitals and clinics. A single trial may take place at one or two specialised medical centres only or at hundreds of offices, hospitals, and centres.

Each clinical trial is managed by a research team that can include doctors, nurses, research assistants, data analysts, and other specialists. The research team works closely with other health professionals, including other doctors and nurses, laboratory technicians, pharmacists, dieticians, and social workers, to provide medical and supportive care to people who take part in a clinical trial.



### Research Team

The research team closely monitors the health of people taking part in the clinical trial and gives them specific instructions when necessary. To ensure the reliability of the trial's results, it is important for the participants to follow the research team's instructions. The instructions may include keeping logs or answering questionnaires. The research team may also seek to contact the participants regularly after the trial ends to get updates on their health.

### Clinical Trial Protocol

Every clinical trial has a protocol, or action plan, that describes what will be done in the trial, how the trial will be conducted, and why each part of the trial is necessary. The protocol also includes guidelines for who can and cannot participate in the trial. These guidelines, called eligibility criteria, describe the characteristics that all interested people must have before they can take part in the trial. Eligibility criteria can include age, sex, medical history, and current health status. Eligibility criteria for cancer treatment trials often include the type and stage of cancer, as well as the type(s) of cancer treatment already received.

Enrolling people who have similar characteristics helps ensure that the outcome of a trial is due to the intervention being tested and not to other factors. In this way, eligibility criteria help researchers obtain the most accurate and meaningful results possible.

### National and International Regulations

National and international regulations and policies have been developed to help ensure that research involving people is conducted according to strict scientific and ethical principles. In these regulations and policies, people who participate in research are usually referred to as "human subjects."

### Informed Consent

Informed consent is a process through which people learn the important facts about a clinical trial to help them decide whether or not to take part in it, and continue to learn new information about the trial that helps them decide whether or not to continue participating in it.

During the first part of the informed consent process, people are given detailed information about a trial, including information about the purpose of the trial, the tests and other procedures that will be required, and the possible benefits and harms of taking part in the trial. Besides talking with a doctor or nurse, potential trial participants are given a form, called an informed consent form, that provides information about the trial in writing. People who agree to take part in the trial are asked to sign the form. However, signing this form does not mean that a person must remain in the trial. Anyone can choose to leave a trial at any time—either before it starts or at any time during the trial or during the follow-up period. It is important for people who decide to leave a trial to get information from the research team about how to leave the trial safely.

The informed consent process continues throughout a trial. If new benefits, risks, or side effects are discovered during the course of a trial, the researchers must inform the participants so they can decide whether or not they want to continue to take part in the trial. In some cases, participants who want to continue to take part in a trial may be asked to sign a new informed consent form.

New interventions are often studied in a stepwise fashion, with each step representing a different “phase” in the clinical research process. The following phases are used for cancer treatment trials:

### Phases of a Clinical Trial

Phase 0. These trials represent the earliest step in testing new treatments in humans. In a phase 0 trial, a very small dose of a chemical or biologic agent is given to a small number of people (approximately 10-15) to gather preliminary information about how the agent is processed by the body (pharmacokinetics) and how the agent affects the body (pharmacodynamics). Because the agents are given in such small amounts, no information is obtained about their safety or effectiveness in treating cancer. Phase 0 trials are also called micro-dosing studies, exploratory Investigational New Drug (IND) trials, or early phase I trials. The people who take part in these trials usually have advanced disease, and no known, effective treatment options are available to them.

Phase I (also called phase 1). These trials are conducted mainly to evaluate the safety of chemical or biologic agents or other types of interventions (e.g., a new radiation therapy technique). They help determine the maximum dose that can be given safely (also known as the maximum tolerated dose) and whether an intervention causes harmful side effects. Phase I trials enrol small numbers of people (20 or more) who have advanced cancer that cannot be treated effectively with standard (usual) treatments or for which no standard treatment exists. Although evaluating the effectiveness of interventions is not a primary goal of these trials, doctors do look for evidence that the interventions might be useful as treatments.

Phase II (also called phase 2). These trials test the effectiveness of interventions in people who have a specific type of cancer or related cancers. They also continue to look at the safety of interventions. Phase II trials usually enrol fewer than 100 people but may include as many as 300. The people who participate in phase II trials may or may not have been treated previously with standard therapy for their type of cancer. If a person has been treated previously, their eligibility to participate in a specific trial may depend on the type and amount of prior treatment they received. Although phase II trials can give some indication of whether or not an intervention works, they are almost never designed to show whether an intervention is better than standard therapy.

Phase III (also called phase 3). These trials compare the effectiveness of a new intervention, or new use of an existing intervention, with the current standard of care (usual treatment) for a particular type of cancer. Phase III trials also examine how the side effects of the new intervention compare with those of the usual treatment. If the new intervention is more effective than the usual treatment and/or is easier to tolerate, it may become the new standard of care.

Phase III trials usually involve large groups of people (100 to several thousand), who are randomly assigned to one of two treatment groups, or “trial arms”: (1) a control group, in which everyone in the group receives usual treatment for their type of cancer, or 2) an investigational or experimental group, in which everyone in the group receives the new intervention or new use of an existing intervention. The trial participants are assigned to their individual groups by random assignment, or randomisation. Randomisation helps ensure that the groups have similar characteristics. This balance is necessary so the researchers

can have confidence that any differences they observe in how the two groups respond to the treatments they receive are due to the treatments and not to other differences between the groups.

Randomisation is usually done by a computer program to ensure that human choices do not influence the assignment to groups. The trial participants cannot request to be in a particular group, and the researchers cannot influence how people are assigned to the groups. Usually, neither the participants nor their doctors know what treatment the participants are receiving.

People who participate in phase III trials may or may not have been treated previously. If they have been treated previously, their eligibility to participate in a specific trial may depend on the type and the amount of prior treatment they received.

In most cases, an intervention will move into phase III testing only after it has shown promise in phase I and phase II trials.

Phase IV (also called phase 4). These trials further evaluate the effectiveness and long-term safety of drugs or other interventions. They usually take place after a drug or intervention has been approved by the medicine regulatory office for standard use. Several hundred to several thousand people may take part in a phase IV trial. These trials are also known as post-marketing surveillance trials. They are generally sponsored by drug companies.

Sometimes clinical trial phases may be combined (e.g., phase I/II or phase II/III trials) to minimize the risks to participants and/or to allow faster development of a new intervention.

Although treatment trials are always assigned a phase, other clinical trials (e.g., screening, prevention, diagnostic, and quality-of-life trials) may not be labelled this way.

### Use of Placebos

The use of placebos as comparison or “control” interventions in cancer treatment trials is rare. If a placebo is used by itself, it is because no standard treatment exists. In this case, a trial would compare the effects of a new treatment with the effects of a placebo. More often, however, placebos are given along with a standard treatment. For example, a trial might compare the effects of a standard treatment plus a new treatment with the effects of the same standard treatment plus a placebo.

### Possible benefits of taking part in a clinical trial

The benefits of participating in a clinical trial include the following:

- Trial participants have access to promising new interventions that are generally not available outside of a clinical trial.
- The intervention being studied may be more effective than standard therapy. If it is more effective, trial participants may be the first to benefit from it.
- Trial participants receive regular and careful medical attention from a research team that includes doctors, nurses, and other health professionals.
- The results of the trial may help other people who need cancer treatment in the future.
- Trial participants are helping scientists learn more about cancer (e.g., how it grows, how it acts, and what influences its growth and spread).

### Potential harms associated with taking part in a clinical trial

The potential harms of participating in a clinical trial include the following:

- The new intervention being studied may not be better than standard therapy, or it may have harmful side effects that doctors do not expect or that are worse than those associated with standard therapy.
- Trial participants may be required to make more visits to the doctor than they would if they were not in a clinical trial and/or may need to travel farther for those visits.

### Correlative research studies, and how they are related to clinical trials

In addition to answering questions about the effectiveness of new interventions, clinical trials provide the opportunity for additional research. These additional research studies, called correlative or ancillary studies, may use blood, tumour, or other tissue specimens (also known as 'biospecimens') obtained from trial participants before, during, or after treatment. For example, the molecular characteristics of tumour specimens collected during a trial might be analysed to see if there is a relationship between the presence of a certain gene mutation or the amount of a specific protein and how trial participants responded to the treatment they received. Information obtained from these types of studies could lead to more accurate predictions about how individual patients will respond to certain cancer treatments, improved ways of finding cancer earlier, new methods of identifying people who have an increased risk of cancer, and new approaches to try to prevent cancer.

Clinical trial participants must give their permission before biospecimens obtained from them can be used for research purposes.

### When a clinical trial is over

After a clinical trial is completed, the researchers look carefully at the data collected during the trial to understand the meaning of the findings and to plan further research. After a phase I or phase II trial, the researchers decide whether or not to move on to the next phase or stop testing the intervention because it was not safe or effective. When a phase III trial is completed, the researchers analyse the data to determine whether the results have medical importance and, if so, whether the tested intervention could become the new standard of care.

The results of clinical trials are often published in peer-reviewed scientific journals. Peer review is a process by which cancer research experts not associated with a trial review the study report before it is published to make sure that the data are sound, the data analysis was performed correctly, and the conclusions are appropriate. If the results are particularly important, they may be reported by the media and discussed at a scientific meeting and by patient advocacy groups before they are published in a journal. Once a new intervention has proven safe and effective in a clinical trial, it may become a new standard of care. (National Cancer Institute).

### **Medical Disclaimer**

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## Sources and References

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