



Does daily intake of resistant starch reduce the acute bowel symptoms in pelvic radiotherapy? RCT



PV-0124

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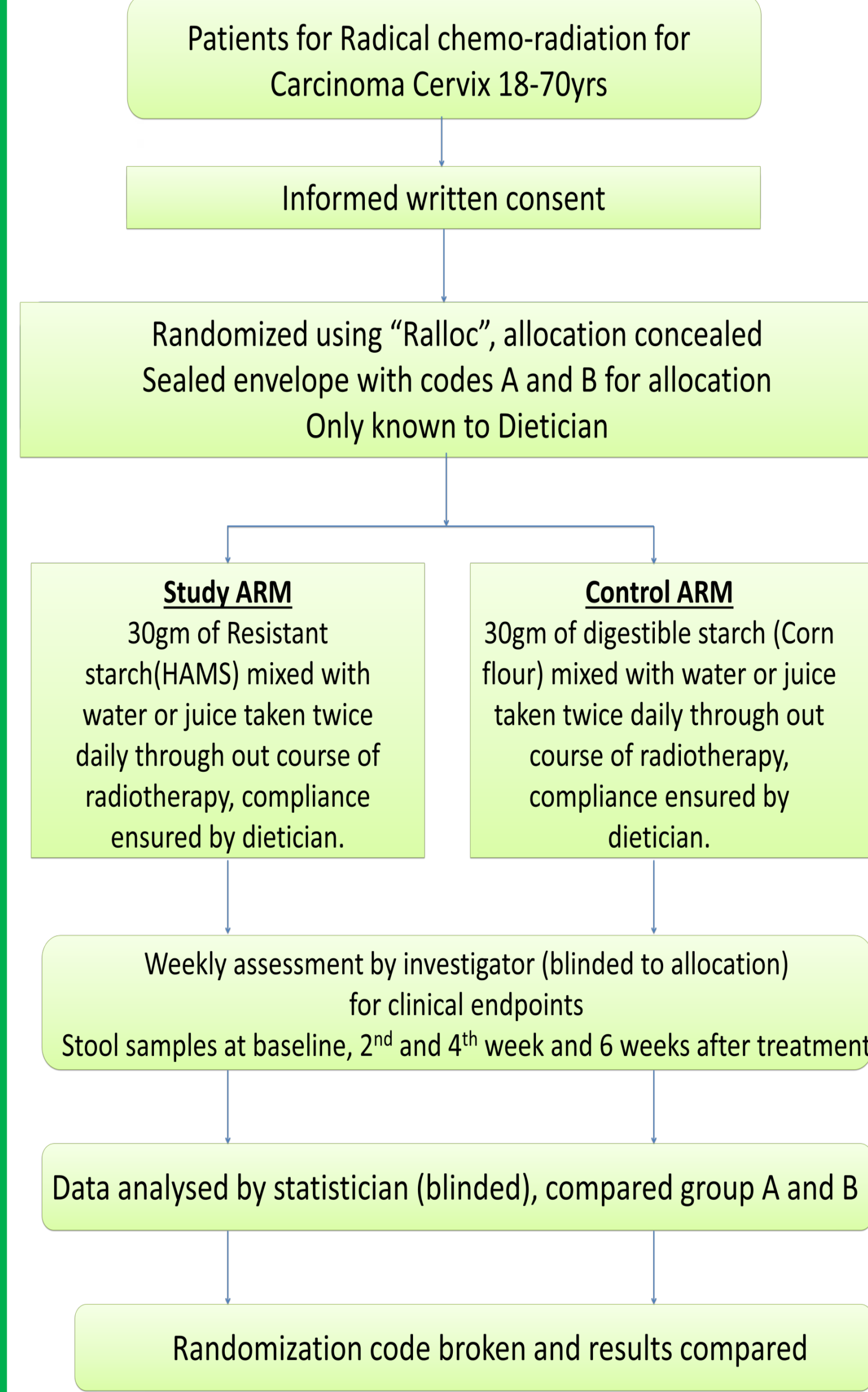
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BACKGROUND

- Acute Radiation proctitis is a distressing symptom of pelvic radiotherapy¹
- 8-20% incidence, causes diarrhoea and rectal pain.
- Butyrate (Short chain fatty acid) a natural anti-inflammatory product of fermentation of non-digested carbohydrate by probiotics in the intestine, was proven to be beneficial when used as enema in radiation proctitis².
- Orally fed resistant starch (High amylose Maize Starch – HAMS) can lead to increased butyrate levels in colon and has proven beneficial in IBD^{3,4,5}.
- This study postulates that orally fed HAMS may alleviate and reduce incidence of radiation proctitis and enteritis.
- This was tested in a phase II double blinded randomized control trial.

METHODS



Exclusion : Crohn's disease, ulcerative colitis, IBS, Rectal extension of carcinoma, diversion surgeries of the colon, patients with intestinal obstruction, previous pelvic irradiation.

Standard of care: Standard radiotherapy protocol 50Gy in 25 fractions prescribed to 95% isodose delivered over 5 weeks, fourfield box technique with shaped beams and weekly concurrent chemotherapy with 40mg/m² Cisplatin(3-4cycles) followed by LDR or HDR brachytherapy boost.

Primary outcome/s: Incidence of Grade 2, 3 and 4 functional and clinical proctitis and diarrhoea graded in CTC V 3.0 and RTOG toxicity criteria.

Secondary Outcome/s:

•Estimate the short chain fatty acid concentration of stool samples in both groups of patients.

•Pattern of stool microflora changes during the course of radiotherapy both arms.

Sample size : Assumed baseline incidence of 35% (from in-house trials), $\delta= 25$, $\alpha=0.05$, $\beta=20\%$ (80% power), calculated sample was 43 in each arm.

Analyses

•The outcomes (Proctitis and diarrhoea) were categorized into two groups (below grade 2, grade 2 and above). The change of grade over the time between the two groups was compared. Generalized estimated equations (GEE) analysis was used to find the change over the time between the two types of STARCH.

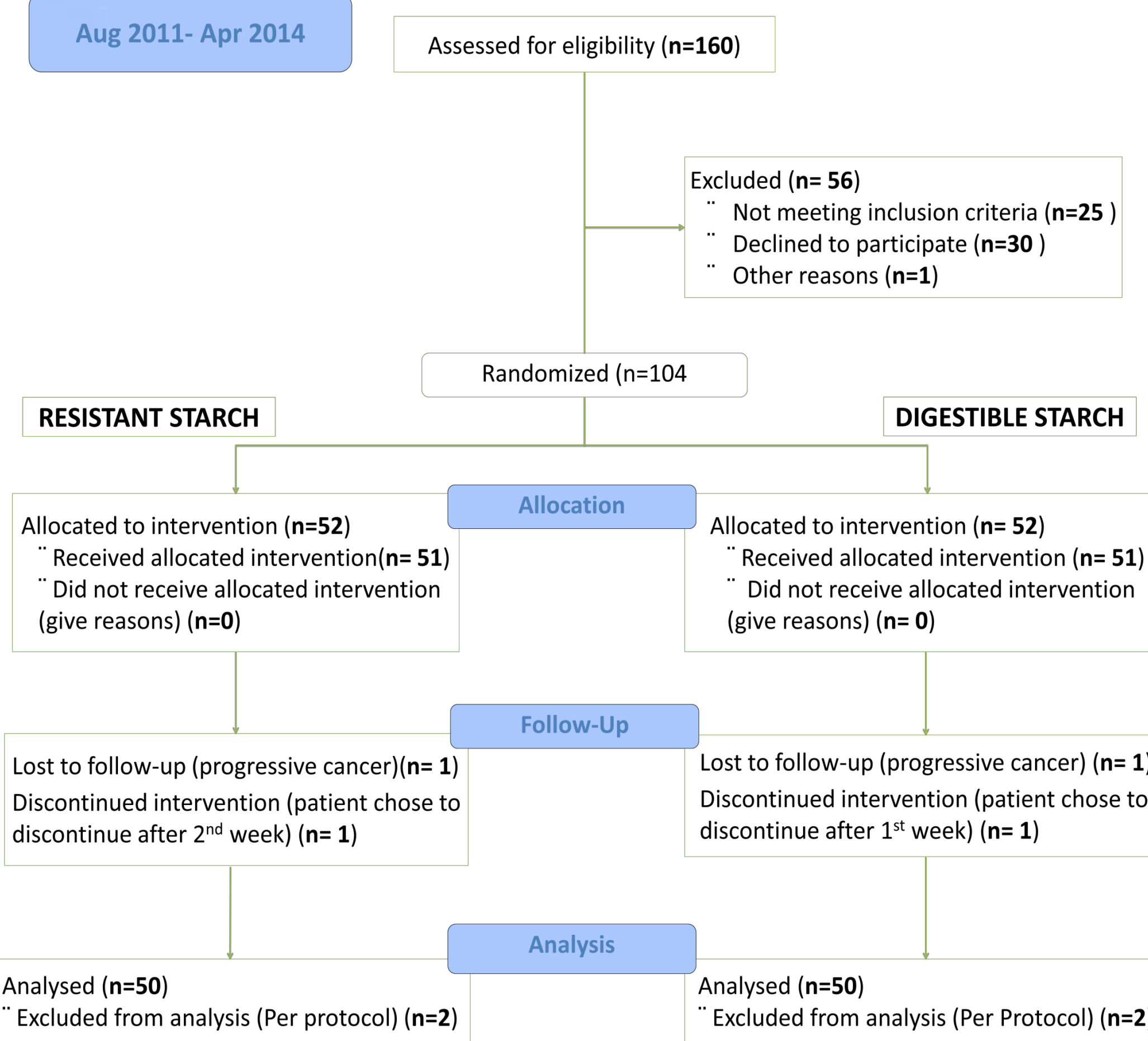
•The proportion of stool fatty acid estimates (gas chromatography) collected at baseline week 2,4 and first follow up(6weeks post treatment) were compared between 2 groups.

•Quantitative PCR for predominant bacterial groups and Sci Genome sequencing for qualitative data on microflora was used.

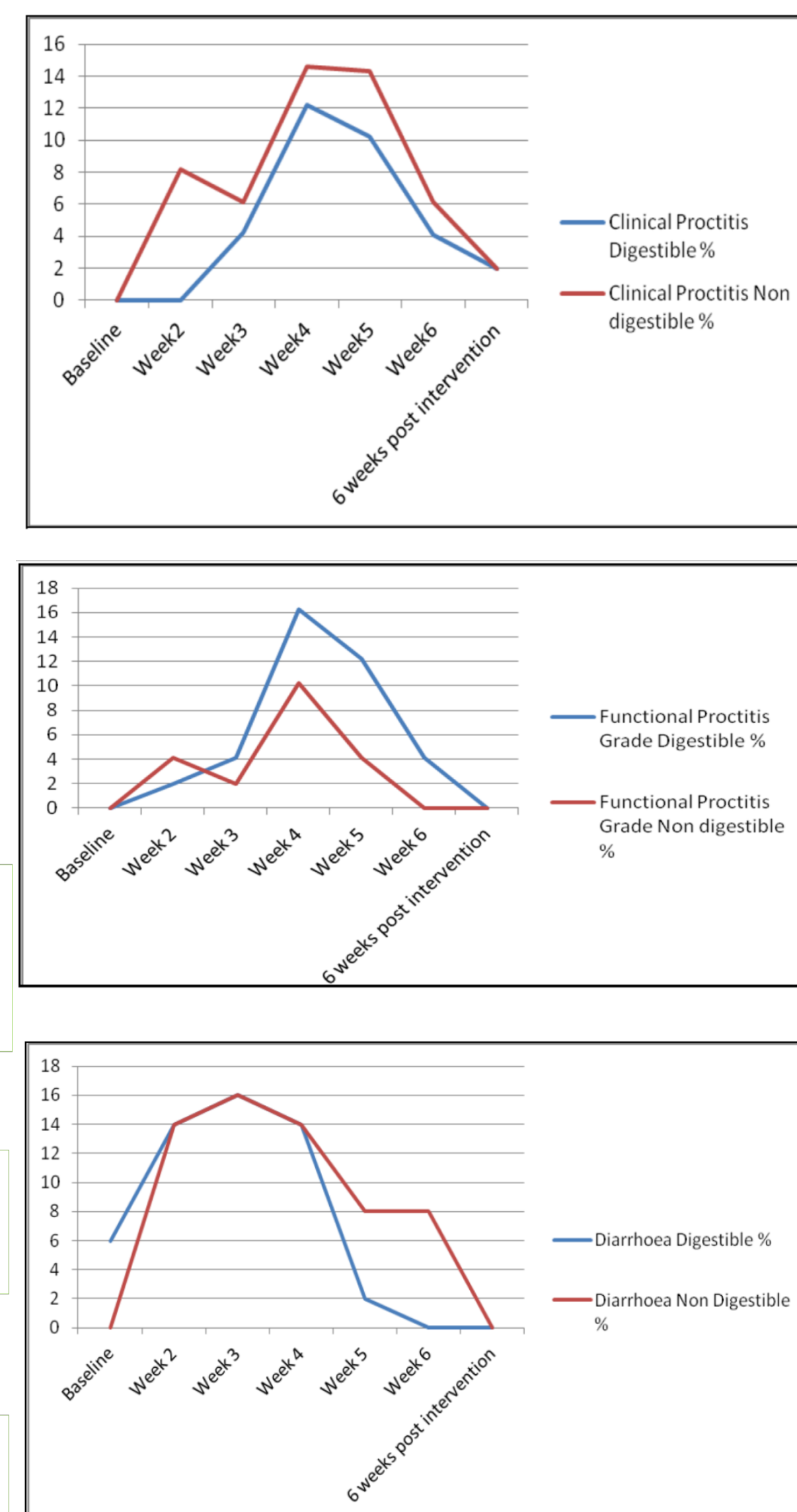
RESULTS



CONSORT Flow Diagram: Starch Trial

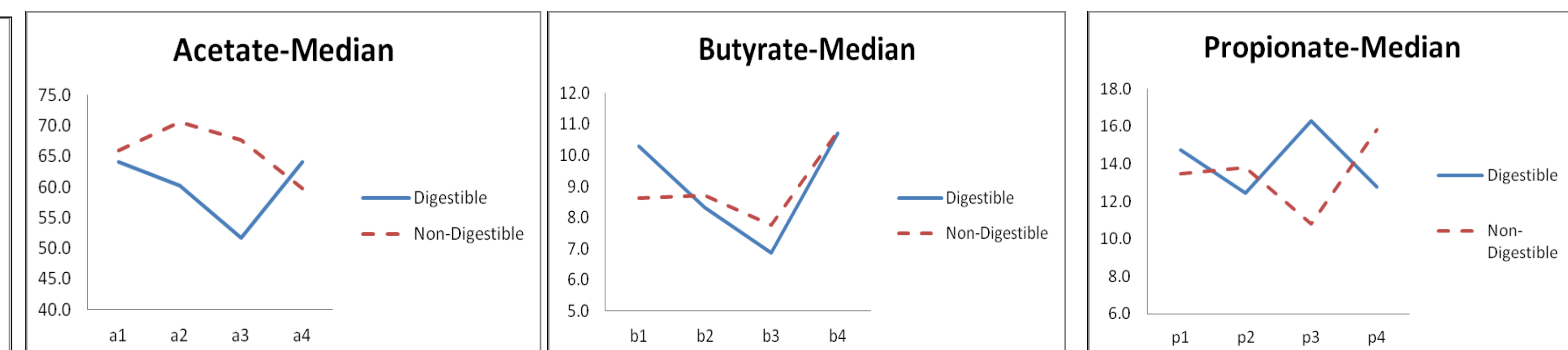


Incidence of toxicity / grade 2 or more



Stool fatty acid concentration for study and control groups

Variables (µmoles/g wet weight of the fecal sample)	Digestible			Non-Digestible			
	n	Mean(SD)	Median(min,max)	n	Mean(SD)	Median(min,max)	
Acetate	Time a1	49	66.41(19.2)	64.07(22.4,120.3)	49	69.74(27.9)	65.99(17.2,141.6)
	Time a2	48	66.7(33.9)	60.26(23.4,181.1)	44	71.82(30.8)	70.57(23.9,158.1)
	Time a3	46	62.41(27.78)	51.68(24.3,134.3)	43	73.02(36.4)	67.72(18.2,151.7)
	Time a4	39	69.49(25.6)	64.04(25.9,129.7)	36	69.74(33.8)	59.68(17.1,169.3)
Propionate	Time b1	48	10.9(5.9)	10.29(1.5,24.2)	48	10.64(6.3)	8.64(2.4,30.5)
	Time b2	45	11.09(8.5)	8.34(0,35.9)	43	9.91(7.6)	8.73(1.2,37.2)
	Time b3	42	9.48(6.9)	6.88(0.03,28.8)	42	9.38(8.0)	7.76(0.1,40.8)
	Time b4	39	12.76(7.7)	10.72(2.3,34.3)	35	11.81(7.2)	10.76(1.5,30.1)
Butyrate	Time p1	48	19.48(13.8)	14.73(1.3,60.23)	49	16.85(11.9)	13.48(0.8,60.23)
	Time p2	47	14.99(10.6)	12.45(0,56.4)	44	14.31(7.3)	13.82(2.6,30.9)
	Time p3	45	15.79(11.2)	16.3(0.3,48.1)	43	16.5(15.5)	10.82(0.5,82.9)
	Time p4	39	18.51(13.6)	12.76(1.3,56.3)	36	19.61(15.1)	15.82(2.3,85.0)



CONCLUSIONS

- Daily intake of resistant starch during pelvic radiotherapy did not reduce the incidence of acute bowel symptoms
- The study was designed to find a 25% reduction in incidence of toxicity in the intervention arm assuming baseline incidence of 35%. In retrospect, this could be considered as an overestimate or the incidence of toxicity could have been lower in both arms due to a daily intake of starch. A third arm without any dietary intervention may have answered this.
- The estimates of stool short chain fatty acid concentration did not reveal any significant difference in both the arms. A comparison with known estimates in other patients could be undertaken as these patients in the trial were most often having diarrhoea and hence there will be dilution of the estimates.
- The third objective of the trial to establish the profile of bacterial flora in the intestine pre and post radiotherapy is the first such initiative and it has not been completed yet. *The knowledge of the pattern of change in quality and quantity of microbia in the bowel during radiation may help us introduce better prebiotic/probiotic supplements in future.*

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