

PERFECT SOLUTION FOR GESTATIONAL DIABETES

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Start and end time: 2019-09-01 to 2020-06-30

I、 Research tasks and objectives

People's pursuit of healthy living has increased the demand for nutrition and health. Healthy life depends on three major support: reasonable nutrition intake, proper regular exercise, and healthy psychological status. Nutritional health management is influenced by many factors such as individual, age, gender, physical condition, medical history, living habits and environmental conditions. Different people need different nutritional diet management programs to deal with the same health problem, personalized needs are fundamentally more in line with the concept of nutrition theory, while products of prevention and treatment with specific diseases as the core are becoming new intervention model to be promoted in society .

Pregnant women, newborns and children are a social health symbol and an important part of social productivity and overall national strength. Paying attention to nutrition and health in the early stages of life is a major livelihood issue and an important socio-economic issue. Although there are a series of effective maternal and child nutrition improvement interventions in China, the actual nutrition management support in providing health services is often insufficient, and there are also lack of corresponding evaluation indicators, technical service standards, norms and professional and technical personnel.

In October 2018, the first phase of the “Perfect Pregnant Mother Training Camp” exploration project provided a practical basis for this study. In this study, we will undertake a centralized, group-based health management model combine with nutrition, exercise, psychology, and on-line health management, in which the core value lies in providing more professional and personalized nutrition intervention programs and products through exploration of health management models and the interpretation of multidimensional data , and exploring the importance of incorporating adult chronic disease prevention and control into the early life health management system.

II、 Research methods and technical routes to be adopted

1. The study subjects will be from Peking Union Medical College Hospital. It is planned to include 60 subjects with good compliance for centralized health management projects, which was divided into three groups: 20 in the healthy group, 20 in the high-risk group (no intervention), 20 in the high-risk group (intervention) (not less than 20 in each group). Subjects need to sign informed consent forms, fill in questionnaires according to the test requirements, and wear mobile blood glucose meters and help to offer Samples of saliva, blood, feces, urine etc. the intervention to GDM high-risk groups to explore effective interventions are mainly from the diet, combined with curriculum guidance.

2. Subject enrollment and exclusion criteria, the study subjects are pregnant women

(1) Entry criteria

- a) Age: 20-45 years old;
- b) Natural pregnancy
- c) pregnant with a single child
- d) Pregnancy 8 ~ 13⁺⁶ weeks;
- e) Overweight, obesity, family history of diabetes, PCOS, GDM history, arbitrarily satisfy one;
- f) Cooperate with health management content requirements and sample retention;

(2) Exclusion criteria

- a) Have smoking or drinking habits;
- b) Use antibiotics 1 month before enrollment;
- c) Pregnancy with hypertension, diabetes ,chronic hepatitis, nephritis, chronic gastritis, gastric ulcer, chronic colorectal inflammation, hyperthyroidism, hypothyroidism and blood diseases etc.;
- d) Have a long history of medication
- e) Subjects refused to sign informed consent.

3. Research process

(1) screening subjects

According to the medical records, pregnant women who met the enrollment conditions in the 8~13⁺⁶ weeks of pregnancy were screened and signed the informed consent form, and could Check in after 12 weeks of pregnancy.

(2) Questionnaire survey

All subjects completed the questionnaire:

- a) Record the basic condition (age, sex), prenatal weight, current weight, premature birth or not, production mode (caesarean section or delivery), pregnancy with hypertension or not, use of antibiotics, diabetes, eating habits, medication history, etc.
- b) Dietary survey: The 24-hour dietary record method was used to record the type and intake of food ingested daily during the intervention period;
- c) Frequency of questionnaires:

Different questionnaires were recorded at enrollment, after One month intensive intervention, 24 to 28 weeks of pregnancy, 42 days after delivery.

(3) Check-in arrangement

Check-in time: expected to star at 10.26

- **the first week** from 25th night to 28th morning (check-in at 5 pm, 20th October, leave at 8:00am 28th October), three night & two day;
- **the second week** at home ,remote health management;
- **the third week** from 5th night to 8th morning, November (check-in at 5 pm, 5th november, leave at 8:00am 8th november), three night & two dayxx
- **the fourth week** at home ,remote health management;

4. sample collection point: 4 times

Enrollment, after One month intensive intervention, 24 to 28 weeks of pregnancy, 42 days after delivery.

5. sample:

No.	Sample Type	Test
1	Feces	16s rDNA + metagenome
2	Saliva	Metabonome/proteome
3	Blood	Metabolome: short-chain fatty acids, bile acids, choline, phenols, indoles, polyamines, lipids, vitamins, hormones, etc.
4		Immunomics: lipopolysaccharide, polysaccharide A, interleukin 1, 2, 6, 8, 10, 22; biochip detection of about 100 biomarkers such as tumor necrosis factor and nuclear transcription factor KB. Currently customizing a chip includes 60 factors: 10-15 lipid metabolism related factors, such as Adiponectin/FGF-19/FGF-21 Inflammatory immune related factors 30-40 such as MCP-1/CD23/ICAM-3/IL-10/TNF Alpha Insulin-related factors 5-10, such as IGF-1/IGF-2 5-10 angiogenesis related factors, VEGF-A/VEGF-C
5		Blood routine
6		Liver function (ALT, Cr, Alb)
7		Kidney function
8		blood lipids (FFA\LDC, TG, TC)
9		Fasting blood glucose (FBG)
10		HsCRP (supersensitive C-reactive protein)
11		Glycated hemoglobin(HbA1c)
12		Glycated albumin
13		Fasting Insulin
14		Fasting C-peptide
15		Proinsulin
17		urine
18	RT (urine routine)	
19	ISO-PGE2 (urinary prostaglandin)	

5. CGM monitor: The enrollment pregnant women were given continuous blood glucose monitoring and monitored by Abbott FreeStyle Libre equipment:

Enrollment (for 4 weeks), after 1 month intensive intervention (for 2 weeks), 24 to 28 weeks of pregnancy (for 2 weeks), 42 days after delivery (for 2 weeks)

6. Course schedule during the check-in:

First week / third week

date	First week			
	Friday	Saturday	Sunday	Monday
7:30-8:00		Collecting samples		
		Sampling room		
8:00-8:50		breakfast	breakfast	breakfast/leave
		1st floor restaurant	1st floor restaurant	
9:00-10:00		Opening Salon (Ma)	Oral health during pregnancy	
		17st floor event room	17st floor event room	
10:00-10:30		Rest / meal / outdoor activities	Rest / meal / outdoor activities	
10:30-12:00		Recognize ingredients 1	Recognize ingredients 2	
12:00-1:00		lunch	lunch	
		1st floor restaurant	1st floor restaurant	
1:00-2:00		break	break	
		Room	Room	
2:00-4:00		Pregnancy exercise (six-step method)	Pregnancy exercise (six-step method)	
		17st floor event room	17st floor event room	
4:00-4:30		Rest / meal	Rest / meal	
		How to cook healthy food 1	How to cook healthy food 1	
4:30-6:00	Check-in at 17:00 pm	17st floor event room	17st floor event room	
		dinner	dinner	
6:00-7:00	Familiar with living and surrounding environment	1st floor restaurant	1st floor restaurant	
		Mental health during pregnancy	ending Salon (Ma)	
7:00-8:00	Introduce health management requirements and precautions	17st floor spa room	17st floor event room	
8:00-8:30		Meal	Meal	
8:30-9:30		Rest/finish	Rest/finish	
9:30		go to bed	go to bed	

date	The thrid week			
	Friday	Saturday	Sunday	Monday
7:30-8:00				Collecting samples
				Sampling room
8:00-8:50		breakfast	breakfast	breakfast/leave

9:00-10:00		1st floor restaurant	1st floor restaurant
		Opening Salon (Ma)	Oral health during pregnancy
10:00-10:30		17st floor event room	17st floor event room
		Rest / meal / outdoor activities	Rest / meal / outdoor activities
10:30-12:00		Recognize ingredients 1	Recognize ingredients 2
		17st floor event room	17st floor event room
12:00-1:00		lunch	lunch
		1st floor restaurant	1st floor restaurant
1:00-2:00		break	break
		Room	Room
2:00-4:00		Pregnancy exercise (six-step method)	Pregnancy exercise (six-step method)
		17st floor event room	17st floor event room
4:00-4:30		Rest / meal	Rest / meal
		How to cook healthy food 1	How to cook healthy food 1
4:30-6:00	Check-in at 17:00 pm	17st floor event room	17st floor event room
		dinner	dinner
6:00-7:00		1st floor restaurant	1st floor restaurant
		Mental health during pregnancy	ending Salon (Ma)
7:00-8:00	Familiar with living and surrounding environment ;Introduce health management requirements and precautions	17st floor spa room	17st floor event room
8:00-8:30		Meal	Meal
8:30-9:30		Rest/finish	Rest/finish
9:30		go to bed	go to bed

7. Course introduction (check-in)

(1) Nutritional intervention techniques.

Nutritional intervention techniques based on susceptibility genes、 gut microbiota and physical identification have formed individualized nutritional intervention guidelines and nutritional intervention programs , fianlly achieve balanced nutrition, quantification, facilitation and operability of dietary interventions.

(2) Exercise intervention techniques.

By the multi-source information-based motion target technology, a sports risk assessment model was established, and a personalized exercise guidance program was constructed through key technologies such as structured expression of exercise prescription, precise exercise intensity control, and online monitoring of sports energy consumption.

(3) Psychological intervention techniques.

Integrating TCM theory and Western art psychology, through art、psychology、Chinese medicine、brain science、multimedia and other technical means, developed an emotional conditioning system and psychological adjustment program based on art therapy to achieve the purpose of treating diseases and improving health.

(4) Oral intervention technique 。

8. Health manager management content

Please add BY the health manager

9. Take an intensive intervention for 1 month, distribute the main meal (lunch/dinner), and record the diet diary (dietary diary standard)

III、 Research plan	
time	work content
2019.9-2019.11	Health Management Project Design Launch
2019.11-2019.12	Project development, data summary
2019.12-2020.06	Detection, analysis, summary

IV、 List of project team members and labor division					
all of them are coming from Beijing Union Medical College Hospital					
N0.	Name	Title /position	Department	Actual input /month	Duties
1	Ma Liangkun	Attending physician	gynaecology and obstetrics	10	Team leader
2	Yu Miao	Associate chief physician	Endocrinology department	10	member
3	He Shuli	Attending physician	Nutrition department	3	
4	Zhang Xin	Attending physician	stomatology department	3	
5	Zhang Suhan	Scientific research management	gynaecology and obstetrics	10	

6	Tian Ying	current master student	gynaecology and obstetrics	6
7	Liu Jieying	researcher	Central laboratory	10
8	Sun Wei	researcher	Basic research department	3
9	Li Honglei	detector	Test department	3
10	Lin Hang	research assistant	gynaecology and obstetrics	6
11	Huang Feilin	research assistant	gynaecology and obstetrics	6

V、staff budget

完美妊糖解决方案

PERFECT SOLUTION FOR GESTATIONAL DIABETES

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起止时间: 2019-09-01 至 2020-06-30

(一)研究任务及目标

人们对健康生活的追求的同时也增加了对营养健康的需求,健康的生活依赖于三大支持:合理营养摄入、适当规律运动、健康心理状况。而营养健康管理受个体、年龄、性别、身体状况、病史、生活习惯、环境情况等多因素的影响。同一种健康问题,不同的人群需要不同的营养饮食管理方案,个性化的需求从根本上更符合营养学的理念,同时以针对特定疾病为核心的预防、治疗的产品正在成为新的干预模式在社会推广。

孕妇、新生儿和儿童是一个社会的健康标志,同时也是社会生产力和综合国力的重要组成部分。关注生命早期的营养与健康是重大的民生问题,也是重要的社会经济问题。虽然我国也有一系列有效的母婴营养改善干预措施,但在提供卫生服务中实际的营养管理支持常常是不足的,同时也缺乏相应的评估指标,技术服务标准、规范和专业技术人员。

2018年10月第一阶段“完美孕妈训练营”探索项目为本次研究提供了实操基础,本次研究我们将结合营养、运动、心理、线上健康管理的集中群体式模式,研究的核心价值在于通过对健康管理模式的探索以及多维度数据的解读来提供更专业地、个性化地营养预防方案和产品,探索将成人期慢性病防控纳入生命早期健康管理具有重要的意义。

(二)拟采取的研究方法、技术路线

1. 研究对象来自北京协和医院,拟纳入60位依从性好的受试者进行集中健康管理项目,分为三组,分别是:健康组20例、高危组(不干预)20例、高危组(干预)20例(每组不少于20例),受试者均签署知情同意书,按照试验要求填写调查问卷,并连续佩戴移动血糖仪,留取唾液、血液、粪便、尿液等样本,通过对GDM高危人群的干预,本次主要从饮食方面为主,结合课程指导,探索有效的干预手段。

2. 受试者入组及排除标准,研究对象为孕妇

(1) 入组标准

- a) 年龄：20-45 岁；
- b) 自然妊娠；
- c) 单胎；
- d) 孕 8~13⁶周；
- e) 超重、肥胖、糖尿病家族史、PCOS、GDM 史，任意满足一项；
- f) 配合健康管理内容要求和留样；

(2) 排除标准

- a) 有吸烟或饮酒习惯；
- b) 入组前 1 个月使用抗生素；
- c) 孕前合并高血压、糖尿病、慢性肝炎、肾炎、慢性胃炎、胃溃疡、慢性结直肠炎、甲亢、甲减及血液病等；
- d) 有长期用药史；
- e) 受试者拒绝签署知情同意。

3. 研究流程

(1) 筛选受试者入组

根据医疗记录筛选孕 8~13⁶周符合入组条件的孕妇，签署知情同意书，满 12 周后开始入住。

(2) 问卷调查

所有受试者均填写调查问卷：

- a) 记录孕妇基本状况（年龄，性别）、产前体重、当前体重、是否早产、生产方式（剖腹产或顺产）、是否妊娠高血压、是否使用抗生素、糖尿病、饮食习惯、用药历史等。
- b) 膳食调查：干预期间每日采用 24h 膳食记录法详细记录摄入食物的种类和摄入量；
- c) 问卷频次：

入组、强化干预后 1 个月、24~28 周、分娩后 42 天，分别进行不同的问卷记录。

(3) 入住安排

a) 入住时间：

预计开展时间 10.26

第一周 入住时间 10.25 晚-10.28 早(具体入住时间 10.25 下午 5 点以后,离开时间 10.28 早 8 点)，三晚两天；

第二周 住家，远程健康管理；

第三周入住时间 11.15 晚-11.8 早（具体入住时间 11.5 下午 5 点以后，离开时间 11.8 早 8 点），三晚两天

第四周 住家，远程健康管理；

4. 采样时间点：4次

入组、强化干预后1个月、24~28周、分娩后42天

5. 样本：

样本类型	项目
唾液	代谢组学/蛋白组学

血液	血常规
	肝功 (ALT、Cr、Alb)
	肾功
	血脂三项 (FFA/LDC、TG、TC)
	空腹血糖
	超敏 C 反应蛋白
	糖化血红蛋白
	糖化白蛋白
	空腹胰岛素
	空腹 C 肽
	胰岛素原
	代谢组: 短链脂肪酸、胆汁酸、胆碱、酚类、吡啶类、多胺类、脂类、维生素、激素等。
	免疫组: 脂多糖、多糖 A、白介素 1、2、6、8、10、22; 肿瘤坏死因子、核转录因子 KB 等约 100 个生物标记物的生物芯片检测。 目前定制一款芯片包括 60 个因子: 脂代谢相关因子 10-15 个如, Adiponectin/FGF-19/FGF-21 炎症免疫相关因子 30-40 个如, MCP-1/CD23/ICAM-3/IL-10/TNF alpha 胰岛素相关因子 5-10 个如, IGF-1/IGF-2 血管生成相关因子 5-10 个如, VEGF-A/VEGF-C
	RT(尿常规)
PCR+ACR (尿蛋白肌酐比+尿蛋白肌酐比)	
ISO-PGE2 (尿前列腺素)	
大便	16s rDNA+宏基因组

5. 动态血糖监测: 入组孕妇进行连续的血糖监测, 采用雅培顺感设备做监测; 入组 (4周)、强化干预1个月后 (2周)、24~28周 (2周)、分娩后42天 (2周)

6. 入住期间课程安排:

第一周/第三周

日期	第一周			
星期	星期五	星期六	星期日	星期一
7:30-8:00		搜集样本		
		采样间		

8:00-8:50		早餐	早餐	早餐 / 离开
		1 层餐厅	1 层餐厅	1 层餐厅
9:00-10:00		开题沙龙（马大夫）	孕期口腔健康	
		17 层活动室	17 层活动室	
10:00-10:30		休息/加餐/户外活动	休息/加餐/户外活动	
10:30-12:00		认识食材 1	认识食材 2	
		17 层活动室	17 层活动室	
12:00-1:00		午餐	午餐	
		1 层餐厅	1 层餐厅	
1:00-2:00		午休	午休	
		房间	房间	
2:00-4:00		孕期运动（六步法）	孕期运动（六步法）	
		17 层活动室	17 层活动室	
4:00-4:30		休息/加餐	休息/加餐	
4:30-6:00		如何烹饪健康食物 1	如何烹饪健康食物 1	
	17:00 后开始入住	17 层活动室	17 层活动室	
6:00-7:00	熟悉居住和周边环境	晚餐	晚餐	
	介绍健康管理要求和注意事项	1 层餐厅	1 层餐厅	
7:00-8:00		孕期心理健康	结题沙龙（马大夫）	
		17 层 spa 间	17 层活动室	
8:00-8:30		加餐	加餐	
8:30-9:30		休息/整理	休息/整理	
9:30		睡觉	睡觉	
日期	第三周			
星期	星期五	星期六	星期日	星期一
7:30-8:00				搜集样本
				采样间

8:00-8:50		早餐	早餐	早餐 / 离开
		1层餐厅	1层餐厅	1层餐厅
9:00-10:00		开题沙龙（马大夫）	孕期口腔健康	
		17层活动室	17层活动室	
10:00-10:30		休息/加餐/户外活动	休息/加餐/户外活动	
10:30-12:00		认识食材 1	认识食材 2	
		17层活动室	17层活动室	
12:00-1:00		午餐	午餐	
		1层餐厅	1层餐厅	
1:00-2:00		午休	午休	
		房间	房间	
2:00-4:00		孕期运动（六步法）	孕期运动（六步法）	
		17层活动室	17层活动室	
4:00-4:30		休息/加餐	休息/加餐	
4:30-6:00		如何烹饪健康食物 1	如何烹饪健康食物 1	
	17:00 后入住	17层活动室	17层活动室	
6:00-7:00		晚餐	晚餐	
	熟悉居住 和周边环 境，介绍 健康管理 要求和注 意事项	1层餐厅	1层餐厅	
孕期心理健康		结题沙龙（马大夫）		
17层 spa 间		17层活动室		
加餐		加餐		
8:00-8:30		休息/整理	休息/整理	
8:30-9:30		睡觉	睡觉	

7. 入住课程介绍

(1) 营养干预技术。

基于易感基因、肠道菌群和体质辨识的营养干预技术，形成了个体化的营养干预指导原则及与其匹配的营养干预方案，实现了饮食干预营养均衡、定量化、便利化和可操作性。

(2) 运动干预技术。

基于多源信息的运动目标推理技术，建立了运动风险评估模型，并通过运动处方结构化表达、精准运动强度控制、运动能耗在线监测等关键技术构建了个性化运动指导方案，实现了运动处方可实施性。

(3) 心理干预技术。

融合中医理论和西方艺术心理学，通过艺术、心理学、中医、脑科学、多媒体等技

术手段，研发了基于艺术治疗的情志调理系统和心理状况调节方案，达到治疗疾病、增进健康的目的。

(4) 口腔干预技术。

8. 健康管理师管理内容

请健康管理师补充

9. 采取强化干预1个月，配送主餐（午餐/晚餐），同时记录饮食日记（饮食日记标准）

(三)时间计划

时间	工作内容
2019. 9-2019. 11	健康管理项目设计启动
2019. 11-2019. 12	项目开展、数据汇总
2019. 12-2020. 06	检测、分析、总结

(四)项目组成员名单及分工

序号	姓名	技术职称/职务	工作单位/科室	实际投入/人月	职责
1	马良坤	主任医师	北京协和医院/妇产科	10	组长
2	于淼	副主任医生	北京协和医院/内分泌科	10	成员
3	何书励	主治医师	北京协和医院/营养科	3	成员
4	张欣	主治医师	北京协和医院/口腔科	3	成员
5	张素菡	科研管理	北京协和医院/妇产科	10	成员
6	田莹	研究生在读	北京协和医院/妇产科	6	成员

7	刘洁颖	研究员	北京协和医院/中心实验室	10	成员
8	孙伟	研究员	北京协和医学院/基础所	3	成员
9	李洪雷	检验师	北京协和医院/检验科	3	成员
10	林航	科研助理	北京协和医院/妇产科	6	成员
11	黄菲玲	科研助理	北京协和医院/妇产科	6	成员

(五) 人员经费预算