

# 肥胖治疗与菌群移植

张发明

南京医科大学第二附属医院

**74.29% 的经过第1次FMT治疗的IBD患者愿意接受第2次FMT**

张发明团队数据

**74%的德国肥胖患者没听说过FMT**

德国待发表数据

**中国不足1%的人知晓FMT**

**中国不足10%的医生真正理解FMT**

Filters

Apply Clear

Status

Recruitment ⓘ :

- Not yet recruiting
- Recruiting
- Enrolling by invitation
- Active, not recruiting
- Suspended
- Terminated
- Completed
- Withdrawn
- Unknown status†

Expanded Access ⓘ : +

Eligibility Criteria

Age ⓘ :

years OR

Age Group ⓘ :

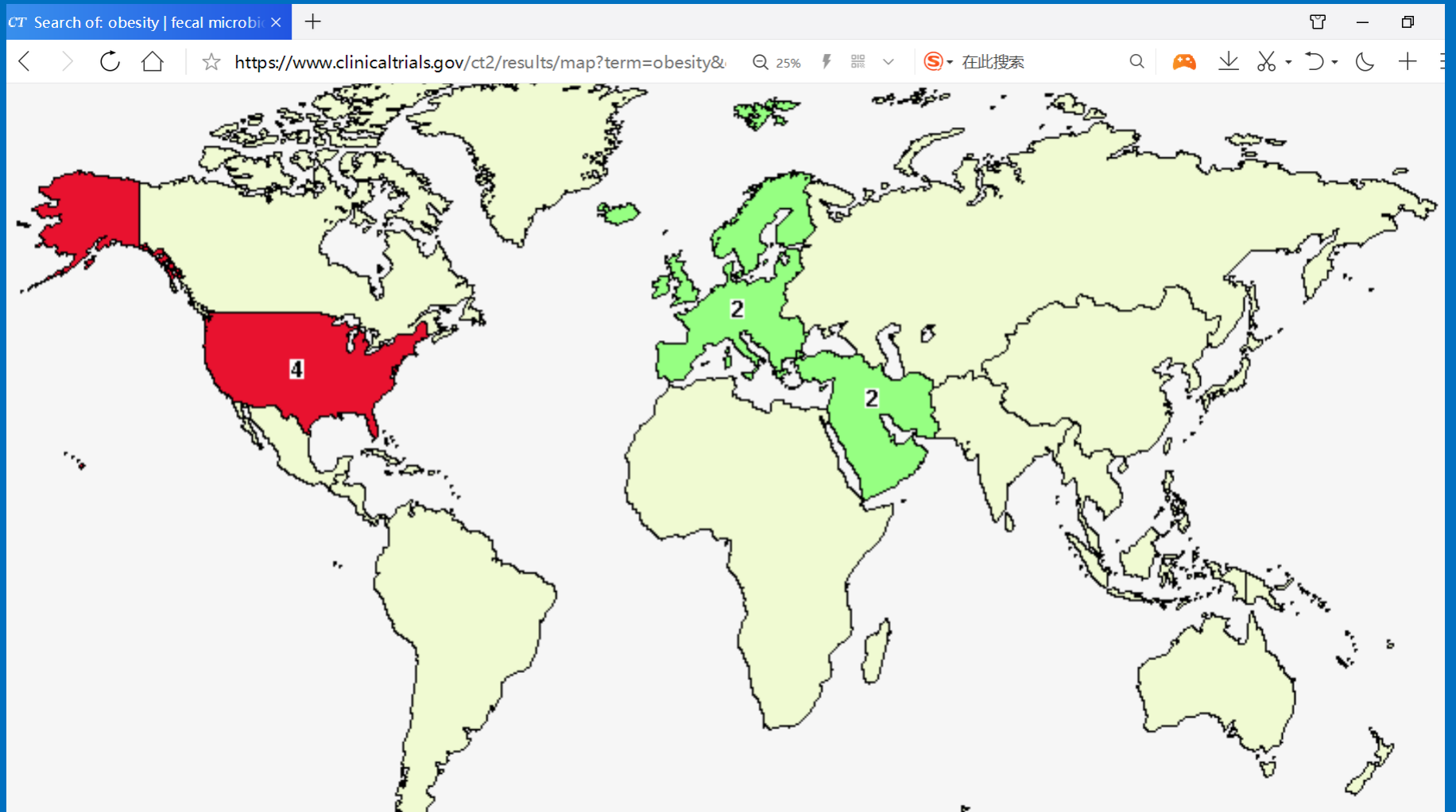
- Child (birth–17)
- Adult (18–64)
- Older Adult (65+)

Sex ⓘ :

- All
- Female

Showing: 1-10 of 11 studies 10 studies per page Show/Hide Columns

Row	Saved	Status	Study Title	Conditions	Interventions	Locations
1	<input type="checkbox"/>	Active, not recruiting	<a href="#">Fecal Microbiota Transplantation for the Treatment of Obesity</a>	• Obesity	<ul style="list-style-type: none"> <li>• Biological: Fecal Microbiota Transplantation</li> <li>• Other: Placebo</li> </ul>	<ul style="list-style-type: none"> <li>• Brigham and Women's Hospital Boston, Massachusetts, United States</li> </ul>
2	<input type="checkbox"/>	Not yet recruiting	<a href="#">Randomized Controlled Trial of Fecal Microbiota Transplantation in Severe Obesity</a>	• Obesity, Morbid	<ul style="list-style-type: none"> <li>• Other: Fecal microbiota transplantation</li> <li>• Other: Placebo: fecal microbiota transplantation</li> </ul>	
3	<input type="checkbox"/>	Unknown †	<a href="#">Fecal Microbiota Transplantation for Diabetes Mellitus Type II in Obese Patients</a>	<ul style="list-style-type: none"> <li>• Diabetes Mellitus, Type 2</li> <li>• Obesity</li> </ul>	<ul style="list-style-type: none"> <li>• Procedure: gastroscopy</li> <li>• Drug: Fecal Microbiota Transplantation</li> <li>• Other: high fat low fiber diet</li> <li>• (and 2 more...)</li> </ul>	<ul style="list-style-type: none"> <li>• Department of Gastroenterology Tel Aviv, Israel</li> </ul>
4	<input type="checkbox"/>	Recruiting	<a href="#">FAECAL MICROBIOTA TRANSPLANTATION IN OBESITY</a>	• Obesity, Morbid	<ul style="list-style-type: none"> <li>• Other: Fecal microbiota transplantation</li> </ul>	<ul style="list-style-type: none"> <li>• Helsinki University Hospital Helsinki, Finland</li> <li>• Päijät-Häme Central Hospital Lahti, Finland</li> </ul>
5	<input type="checkbox"/>	Unknown †	<a href="#">Proposal to Examine the Effect of Fecal Transplantation on Obesity</a>	• Disorientation as to People, Time and Place	<ul style="list-style-type: none"> <li>• Other: fecal material</li> <li>• Other: normal saline</li> </ul>	<ul style="list-style-type: none"> <li>• Kaplan Medical Center Rehovot, Israel</li> </ul>
6	<input type="checkbox"/>	Unknown †	<a href="#">Fecal Microbiota Transplantation to Treat Recurrent C. Difficile Associated Diarrhea Via Retention Enema or Oral Route</a>	• C. Difficile	<ul style="list-style-type: none"> <li>• Biological: Frozen Microbiota</li> <li>• Biological: Lyophilized Microbiota</li> </ul>	<ul style="list-style-type: none"> <li>• University of Texas Health Science Center at Houston Houston, Texas, United States</li> </ul>
7	<input type="checkbox"/>	Unknown †	<a href="#">Fecal Microbiota Transplantation for the Treatment of Metabolic Syndrome</a>	• Metabolic Syndrome	<ul style="list-style-type: none"> <li>• Other: fecal microbiota transplantation from healthy lean donors</li> </ul>	<ul style="list-style-type: none"> <li>• Catholic University of Sacred Heart - "A. Gemelli" University Hospital Rome, Italy</li> </ul>
8	<input type="checkbox"/>	Recruiting	<a href="#">Fecal Microbiota Transplantation (FMT) in Nonalcoholic</a>	• Nonalcoholic Fatty	<ul style="list-style-type: none"> <li>• Drug: Fecal Microbiota</li> </ul>	<ul style="list-style-type: none"> <li>• Rhode Island Hospital</li> </ul>

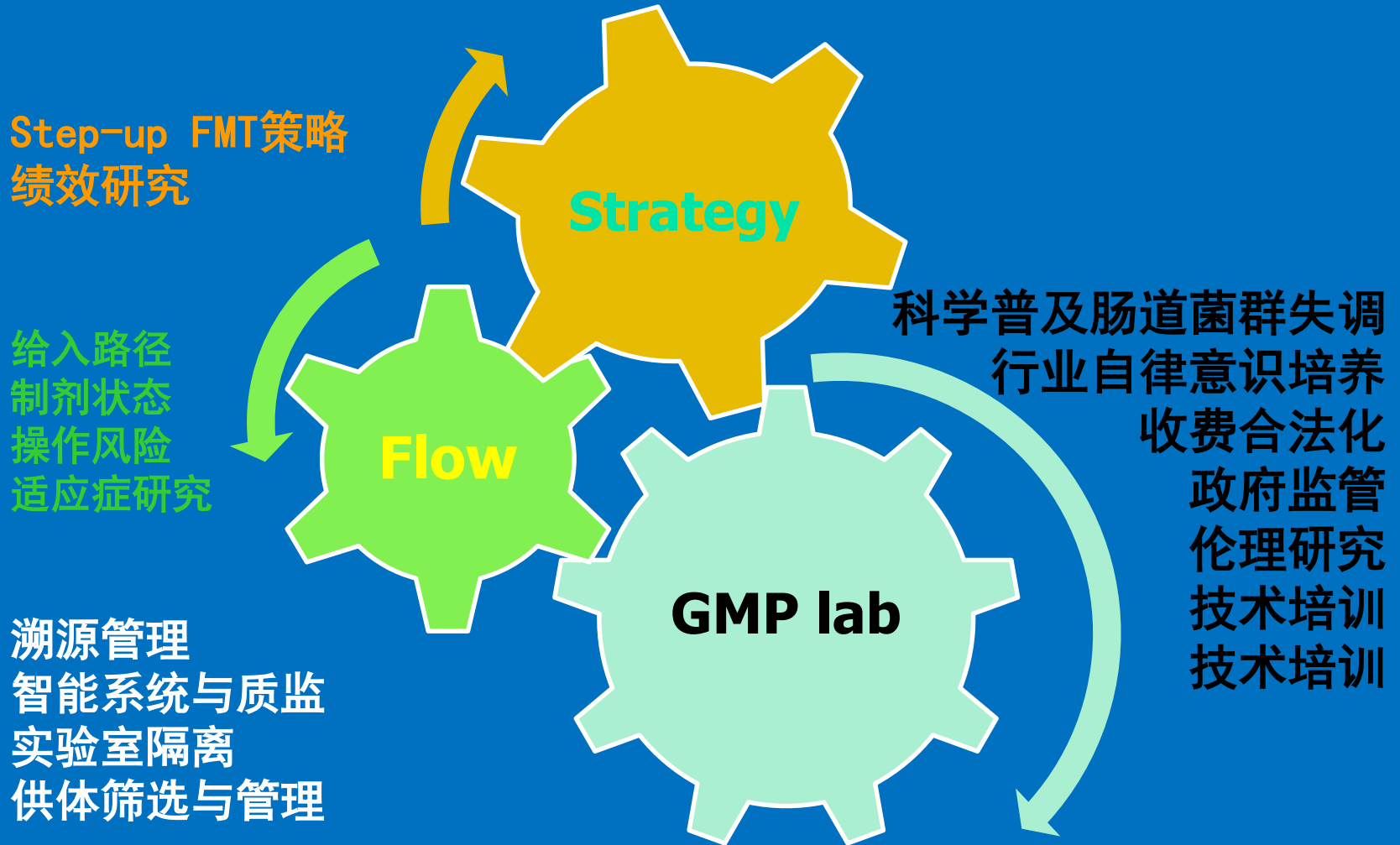


注册FMT治疗肥胖的临床试验：北美5，欧洲2，中东2

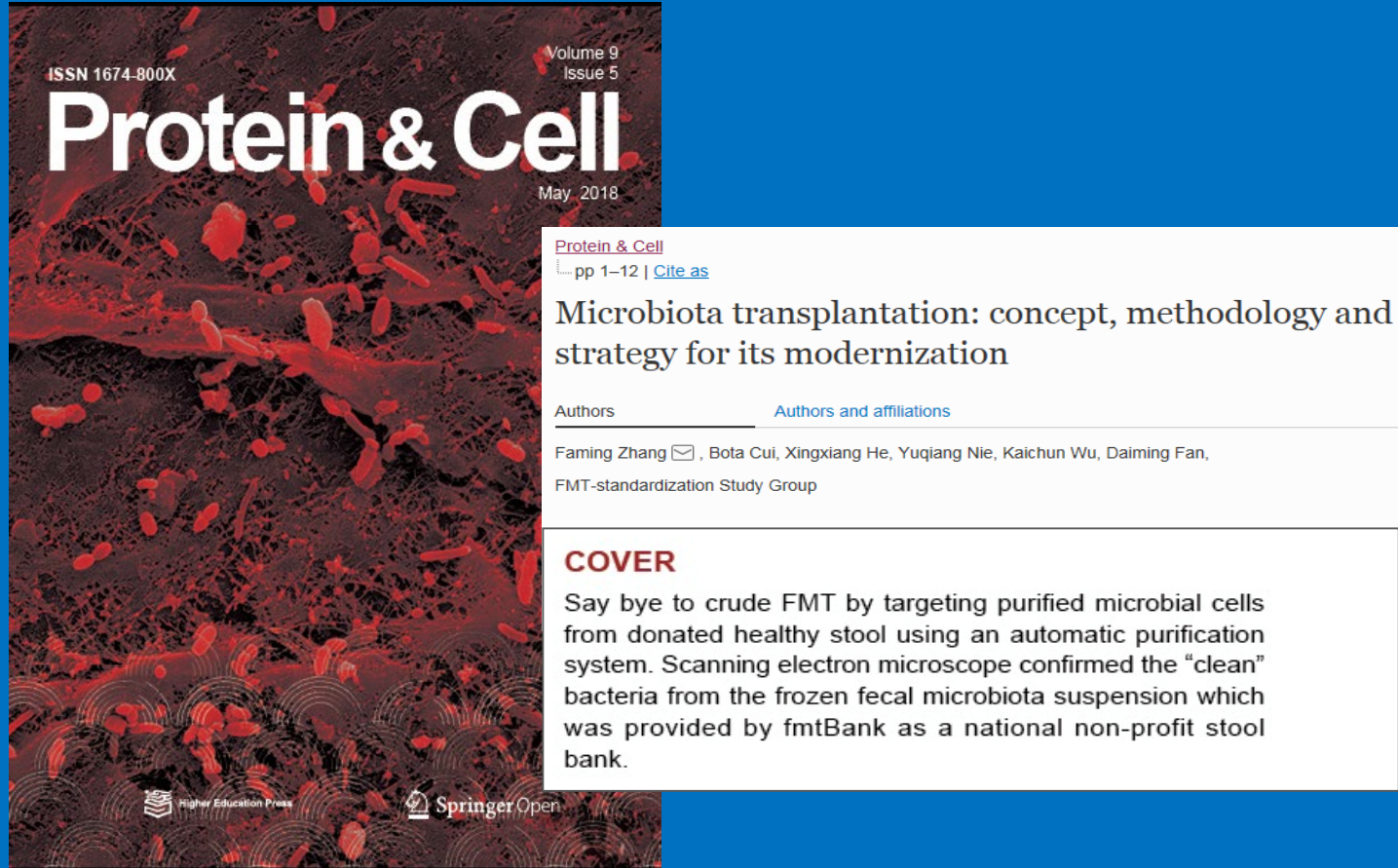
新抓手：**FMT** | **TET**

菌群移植体系  
**Microbiota Transplantation System**

# Microbiota Transplantation System



# 菌群移植体系研究与应用：长期的历程



Zhang Faming et al. FMT-standardization Study group. Protein Cell. 2018

# Safety and quality control of FMT

## 1. Total AEs at low level----**safety data level**

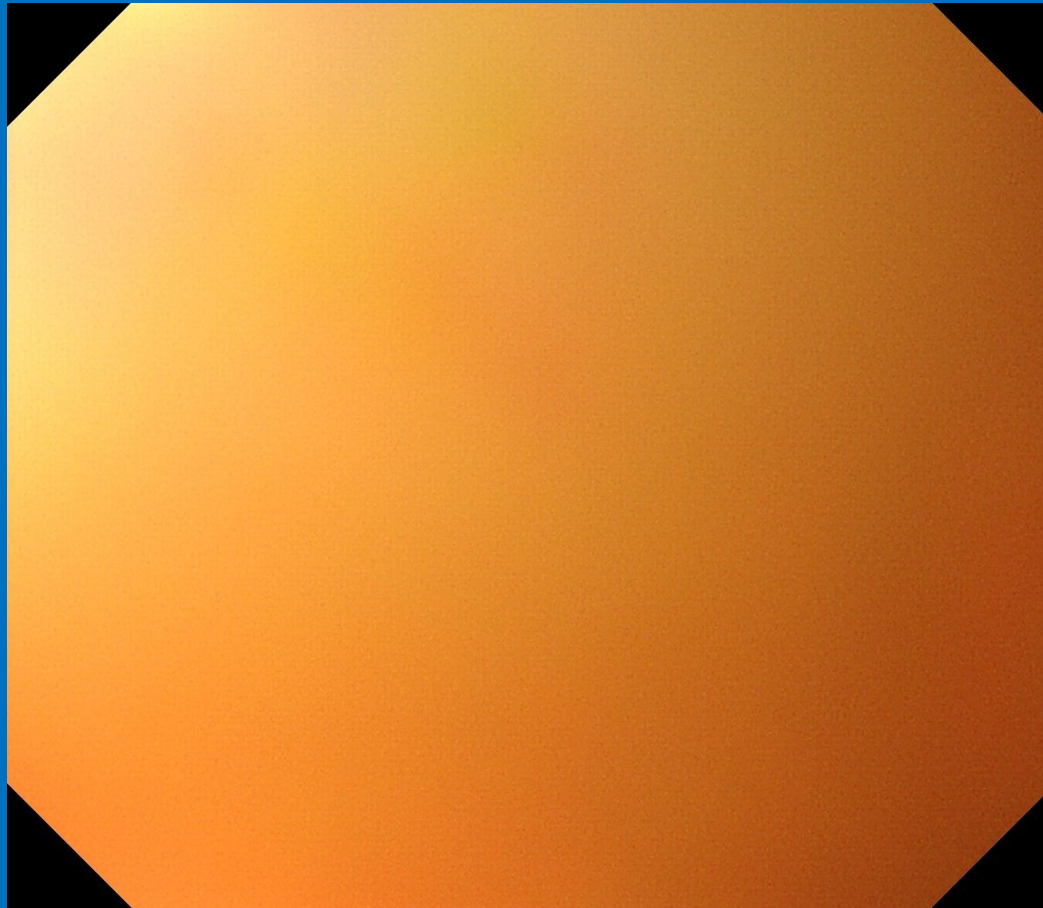
Exclusive lab room for preparation is required, but GMP-lab is the future

## 2. Maintaining functional microbiota in short process time----**efficacy data level**

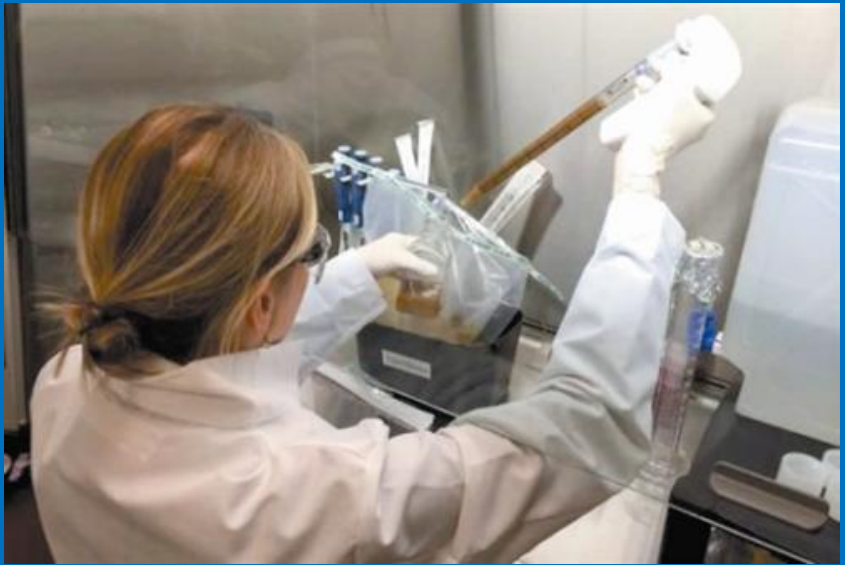
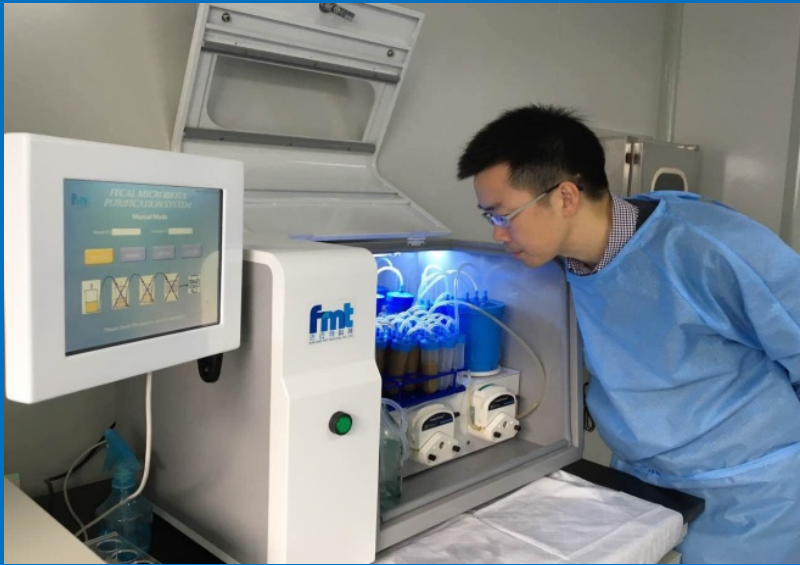
## 3. Sources traceability: donors' fecal samples stored for > two years---**Law level**



菌群分离纯化系统GenFMTer处理后菌液  
内镜放大条件下无颗粒物质



# 全球最大的两大非营利性粪菌库 fmtBank | openBiome



Nanjing, China | Boston, USA

# 全球仅有的两个粪菌库GMP实验室 Nanjing | Nanjing



**Clean FMT: 解放医患双方依靠GMP**



图 1 临床实践中诊疗伪膜性肠炎的简易流程. 灌肠后直乙结肠内镜检查(a)及发现典型团簇状渗出物及其底部溃疡(b), 可依此快速诊断伪膜性肠炎, 并直接在内镜下植入TET管建立FMT结肠给药途径并满足便捷的重复治疗(c).

张发明. 科学通报. 2018, 63:1-6

**FMT procedure related AEs: could be prevented**

**Mid-gut FMT: inappropriate techniques and procedures**

**two reported deaths could be avoided?**

**aspiration is the direct reason of death**

Gweon et al. Gastroenterol Res Pract. 2016

Furuya-Kanamori et al. J Clin Gastroenterol. 2017

FMT-standardization Study Group. Protein Cell. 2018

# Long term monitoring providing safety data

<http://cmts.ydata.org>

## 中国菌群移植平台

CHINA MICROBIOTA TRANSPLANTATION SYSTEM

旨在建立一个为中国菌群移植（含FMT和mini-FMT）提供  
**决策判别、治疗记录、疗效评估、风险监管**  
的集临床服务、数据管理和新技术研究为一体的公共服务平台

卡医学、赢在整合！  
——张发明

学术支持：  
南京医科大学第二附属医院  
第四军医大学西京医院 • 国家消化系统疾病临床医学研究中心

技术支持：  
慧方科技 医数据



张发明

NIH U.S. National Library of Medicine

# ClinicalTrials.gov

NCT03325855

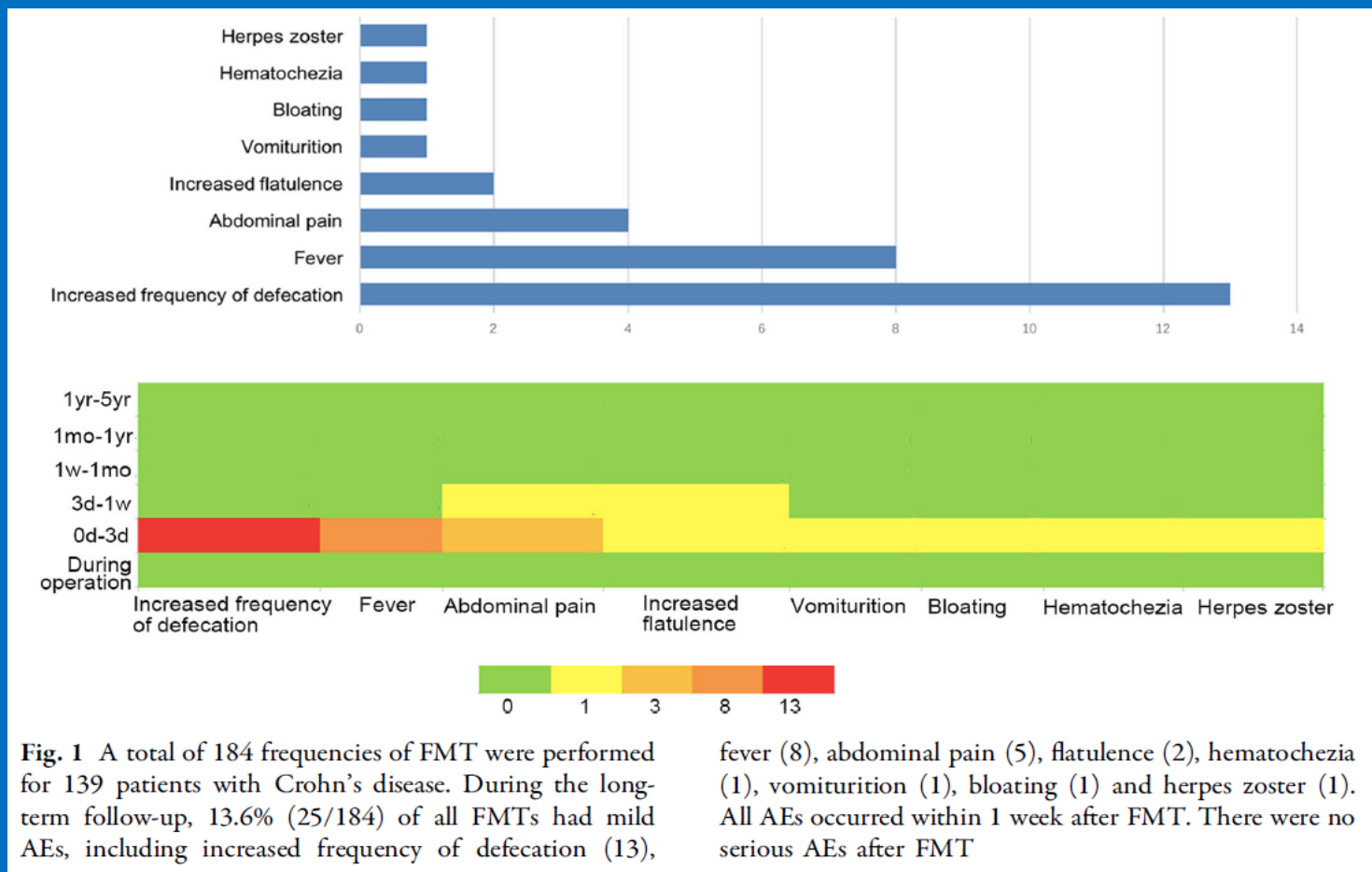
Study Type ⓘ: Observational [Patient Registry]  
Estimated Enrollment ⓘ: 4000 participants  
Observational Model: Other  
Time Perspective: Prospective  
Target Follow-Up Duration: 10 Years  
Official Title: Fecal Microbiota Transplant National **Registry**  
Actual Study Start Date ⓘ: September 20, 2017  
Estimated Primary Completion Date ⓘ: August 2021  
Estimated Study Completion Date ⓘ: August 2026

10-year follow-up for donors and patients

AGA's FMT national registry

Kelly et al. Gastroenterology. 2017  
FMT-standardization Study Group. Protein Cell. 2018

# 来自中国菌群移植平台的发表数据



Wang Honggang, et al. Zhang Faming. Adv Ther. 2018  
FMT短期与长期不良事件的分界线：1个月

# 来自中国菌群移植平台的发表数据

## The safety of fecal microbiota transplantation for Crohn's disease: Findings from long-term study (n=139)

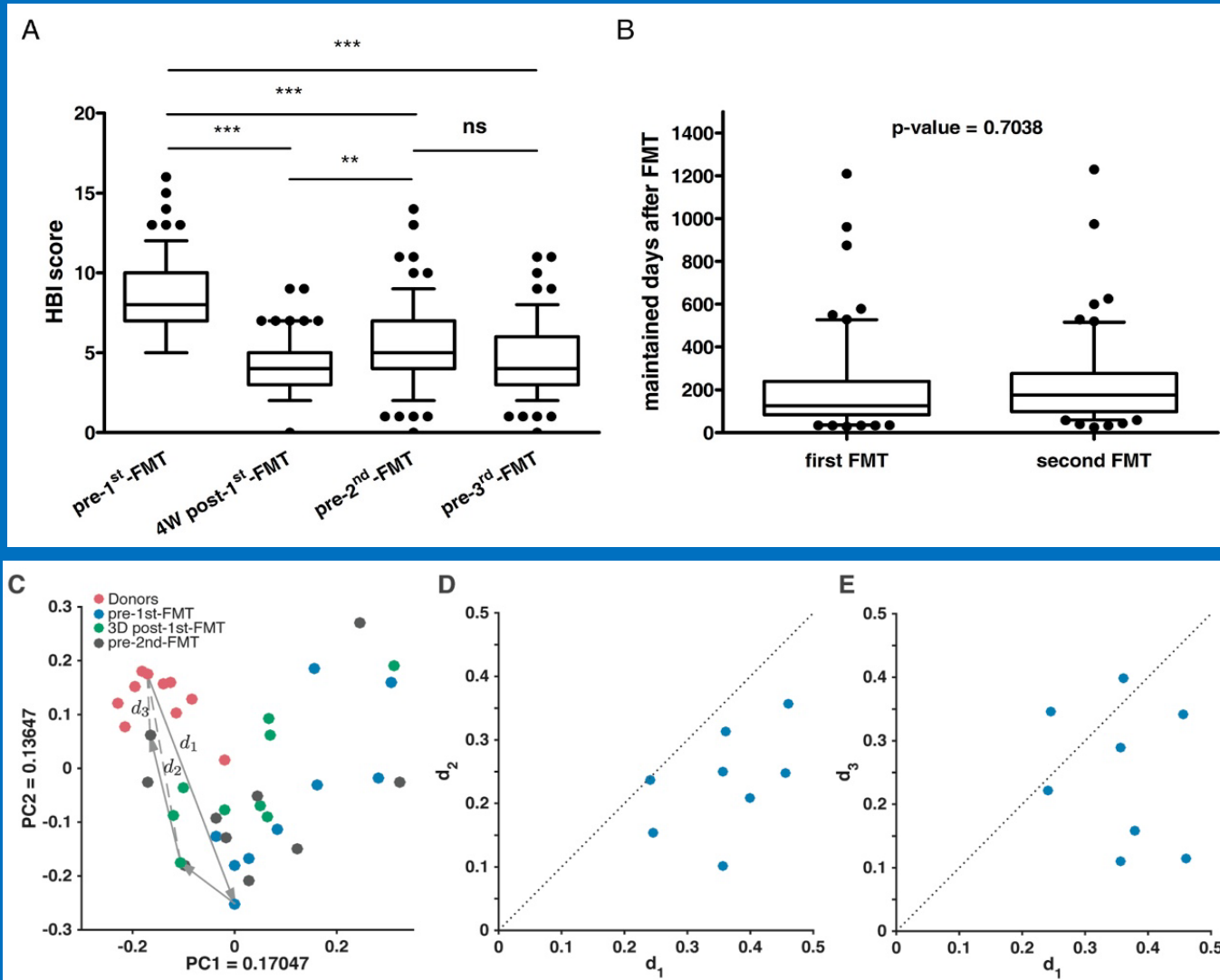
Purification for fecal microbiota reduced the rate of AEs without affecting efficacy (total 184 FMTs in 139 CD pts)

疗效和不良事件与供体无关，结论是有前提条件的！！

Methods	% of adverse events	p	% of improvement	p
Manual (before April 2014)	21.7% (15/69)	0.005	77.6% (52/67)	0.108
Automation (after April 2014)	8.7% (10/115)		65.3% (47/72)	

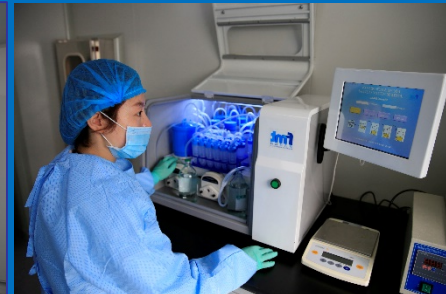
Wang Honggang et al. Zhang Faming. Adv Ther. 2018

# Timing of FMT for Crohn's disease: 3 months



## *fmtBank* providing national non-profit service

- Safety and quality management
- Government and hospital supports
- Social challenge
- Financial difficulty
- Team building



# From FMT to selective microbiota transplantation (SMT)

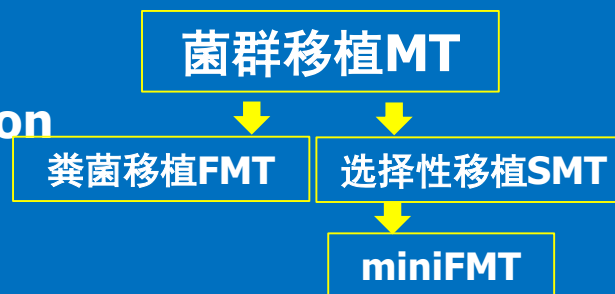
Table 2. Possible usage of microbiota transplantation in human diseases

Types	Sites	Microbiota profile	Suitable dosage forms	Possible management in policy
FMT	Microbiota to gut	Whole	Pill, suspension	Medical technology or drug
SMT/mini-FMT	Microbiota to gut	Selected	Pill, powder, suspension	Medical technology or drug
SMT	Microbiota to sinus	Selected	Powder, spray, suspension	Medical technology, drug or health products
SMT	Microbiota to vagina	Selected	Pill, powder, suspension	Medical technology or drug
SMT	Vaginal microbiota to skin	Selected/whole	Powder, spray, suspension	Medical technology, drug or health products

**FMT** = fecal microbiota transplantation

**SMT** = Selective microbiota transplantation

**mini-FMT** = 旨在模拟FMT的SMT，用于肠道



新抓手：**FMT** | **TET**

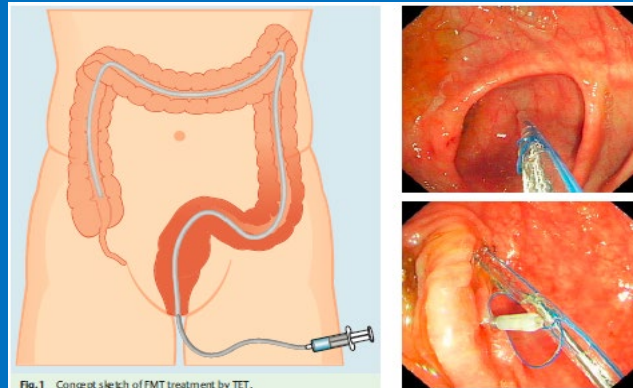
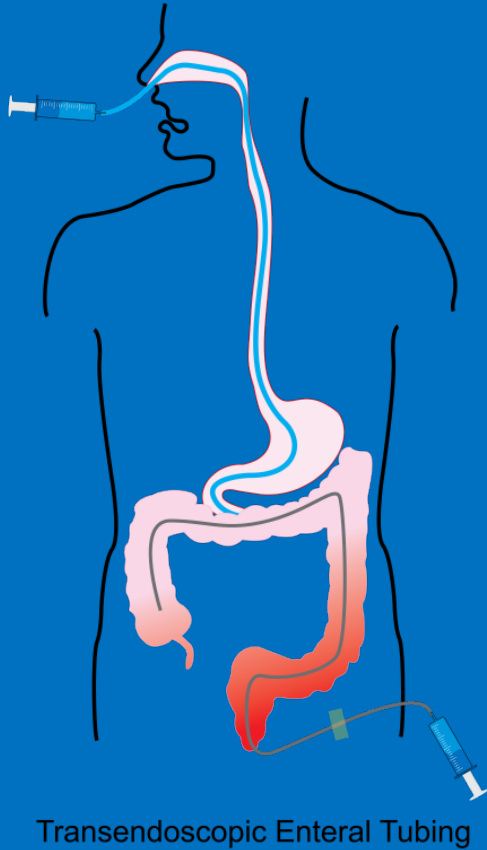
# 全结肠给药：结肠TET

## Transendoscopic Enteral Tubing | TET

# TET：从中国走向全球



# 结肠TET：1-4周全结肠灌肠+多次FMT



www.thieme.com

Colonic transendoscopic enteral tubing: A novel way of transplanting fecal microbiota

10.1055/s-0042-105205  
Endosc Int Open 2016; 4: E610-E613

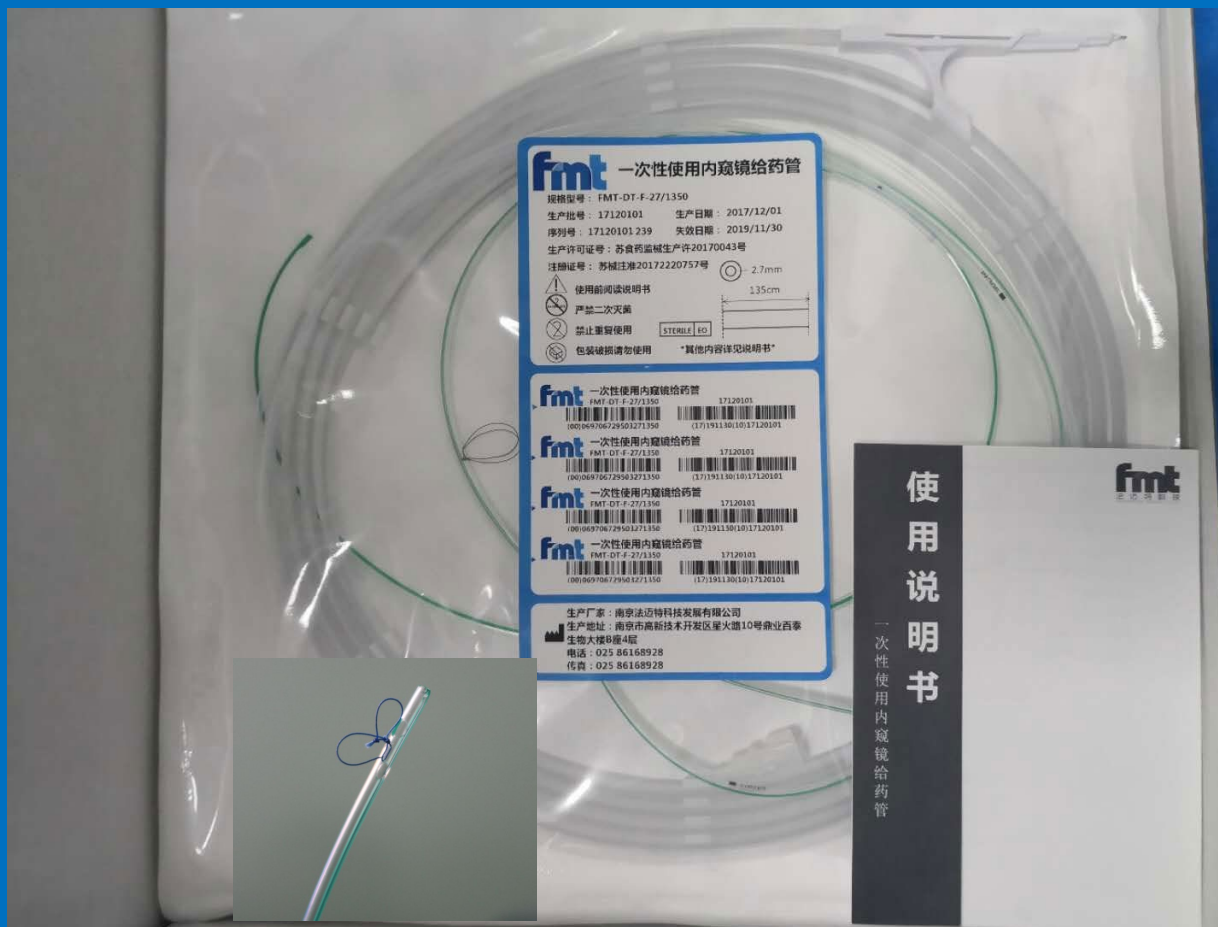
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Georg Thieme Verlag KG  
Rüdigerstraße 14  
70469 Stuttgart  
ISSN 2364-3722

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 Thieme

张发明团队. 结肠途径TET. Endosc Int Open. 2016



内窥镜给药管，南京法迈特科技，中国**2017**批准进入临床  
 全世界第一个用于全结肠重复给药的植入器械，即将进入欧洲

# 结肠TET效果：前瞻性评估

**Table 1** Characteristics of patients undergoing FMT through colonic TET.

Characteristics	N (%)
Total number	54 (100)
Age, mean $\pm$ SD, years	34.5 $\pm$ 10.4
Male	32 (59)
Disease category	
Ulcerative colitis	23 (42.5)
Crohn's disease	16 (29.6)
Unexplained chronic diarrhea	5 (9.3)
Constipation	5 (9.3)
Small intestinal bacterial overgrowth	3 (5.6)
Irritable bowel syndrome	2 (3.7)
TET success rate, n (%)	54 (100)
Tubing time, mean $\pm$ SD, min	14.8 $\pm$ 5.8
Retention time of tube, mean $\pm$ SD, days	12.4 $\pm$ 2.3
Removal of tube	
Tube falling out	35 (64.8)
Tube extraction	19 (35.2)
Satisfaction survey for FMT via TET	53 (98.1)

满意度 **98%**! Peng. et al. Endosc Int Open. 2016

## 结肠TET：适应证

溃疡性结肠炎广泛结肠型,需要广泛给药  
结肠弥漫性渗血需要广泛给药  
为择期FMT准备给入通路  
为重复FMT保留给入通路

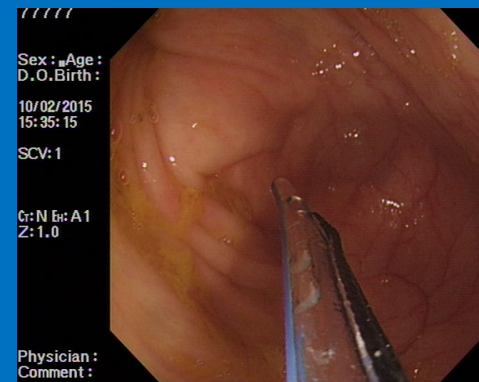
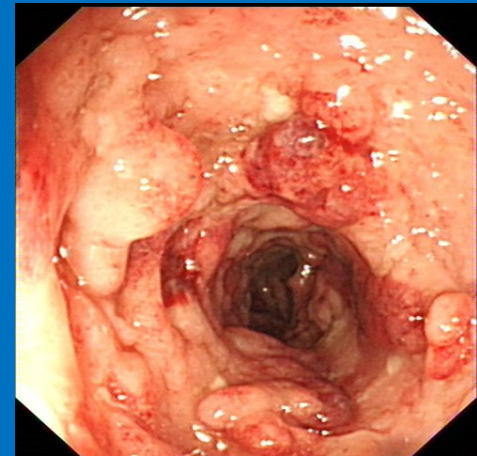
## 结肠TET：适应年龄

目前结肠TET植入最小年龄3岁

儿童也可在家人配合时清醒条件下植管  
推荐儿童在非麻醉时选择左半结肠植管

## 结肠TET：禁忌(相对)禁忌证

不能接受内镜检查  
腔道狭窄影响内镜操作  
溃疡很深  
钛夹固定固定区严重溃疡  
肛周复杂瘘



提醒：不要插入阑尾孔，回盲部直视下回旋

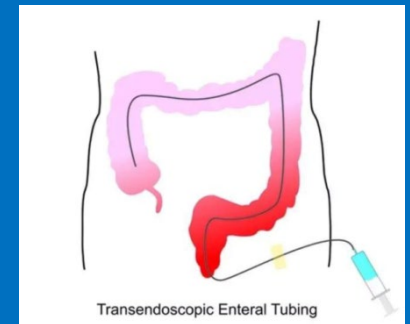
# 目前结肠TET植入最小年龄3岁 儿童要考虑植入后配合度



## TET适应证及优势

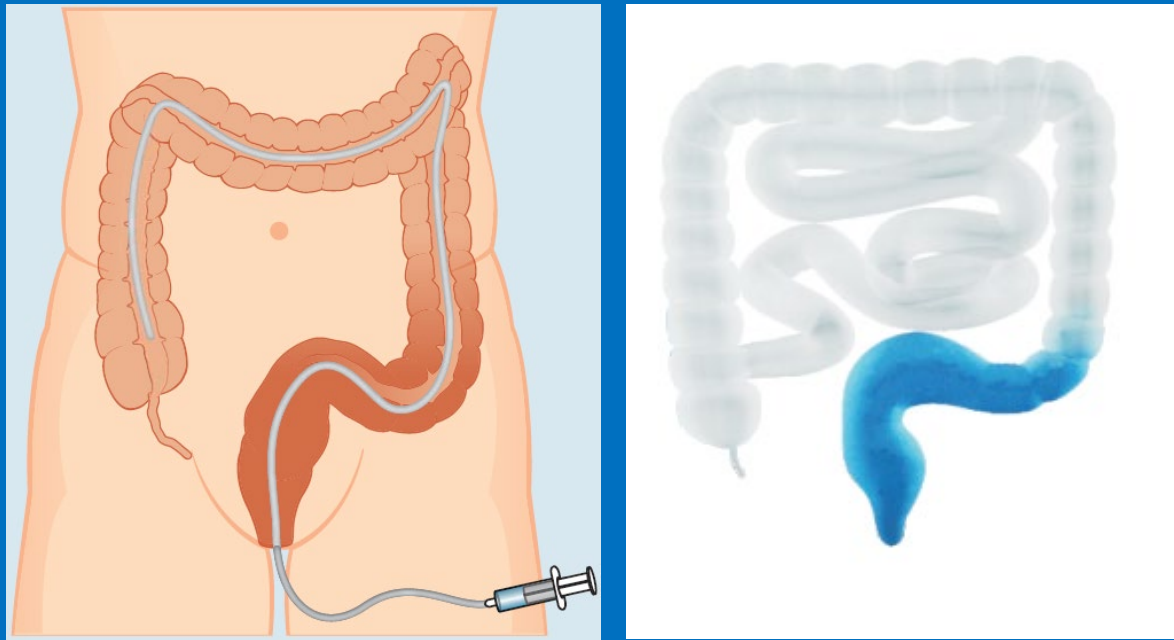
结肠TET是一种全新的简单快捷的内镜技术

1. 结肠任何部位可固定
2. 操作简单
3. 全结肠给药：FMT、美沙拉嗪、止血药
4. 受众面很广的全新技术



张发明. 从粪菌移植到菌群移植. 科学通报. 2018  
Zhang F, et al. FMT-standardization study group. Proten Cell. 2018

# 结肠TET作为**介入IBD新技术**改变IBD进程



掌握介入IBD技术不与时代说再见

## 结肠TET | 常见问题

1. 病人痛苦吗？ ---满意度98%，洗澡爬山都行
2. 医生自己加工？ ---No. 这是CFDA批准器械
3. 多少钛夹？ ---依据保留时间，2-4个居多
4. 怎么拔出来？ ---手动拔很简单
5. 能自行脱落？ ---当然能自然脱落
6. 会堵管吗？ ---液体或混选就不会堵
7. 温度有要求吗？ ---要求38-40度，避免低温
8. 一定要到回盲部？ ---横结肠和降结肠也可
9. 还有哪些？ ---中药及创新药物给药途径研究

# 结肠TET | 介入IBD新技术

给药部位深远  
留置管道持久  
医护方便操作  
体现医技价值

# 快速中消化道植管：**mid-gut TET**


**Transendoscopic Enteral Tubing | TET**

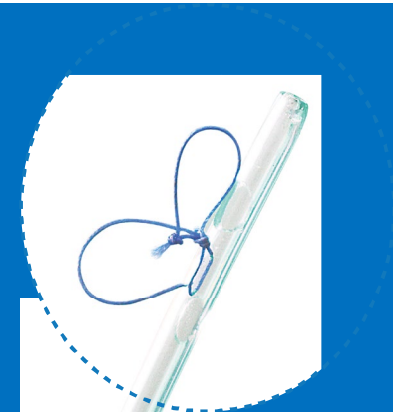
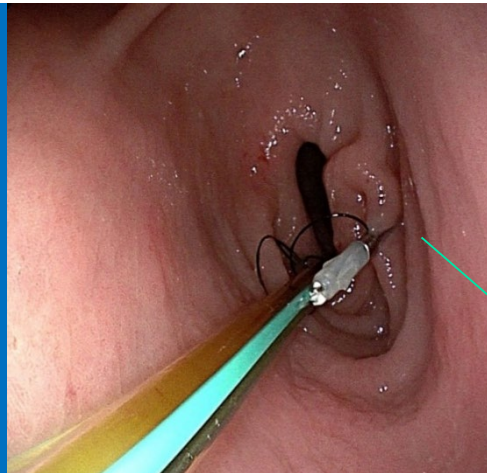
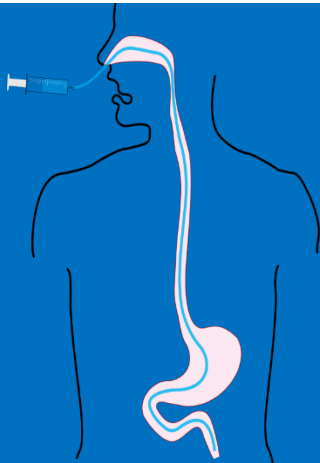
TECHNICAL ADVANCE

Open Access

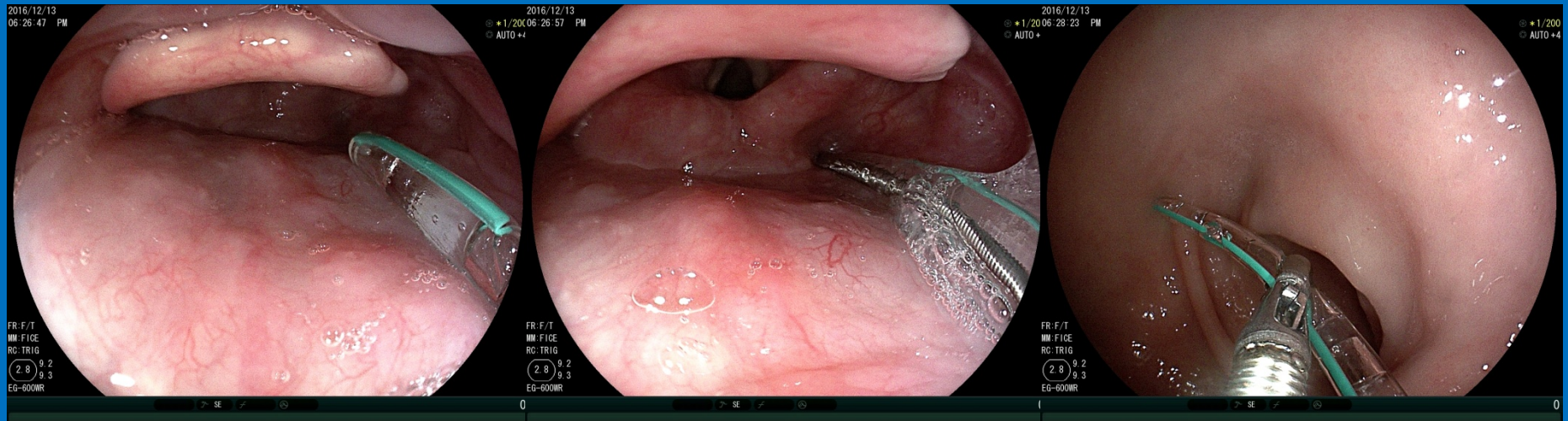


# A novel quick transendoscopic enteral tubing in mid-gut: technique and training with video

Chuyan Long<sup>1,2</sup>, Yan Yu<sup>1,3</sup>, Bota Cui<sup>1,2</sup>, Sabreen Abdul Rahman Jagessar<sup>1,2</sup>, Jie Zhang<sup>1</sup>, Guozhong Ji<sup>1,2</sup>, Guangming Huang<sup>1,2</sup> and Faming Zhang<sup>1,2,4\*</sup> 

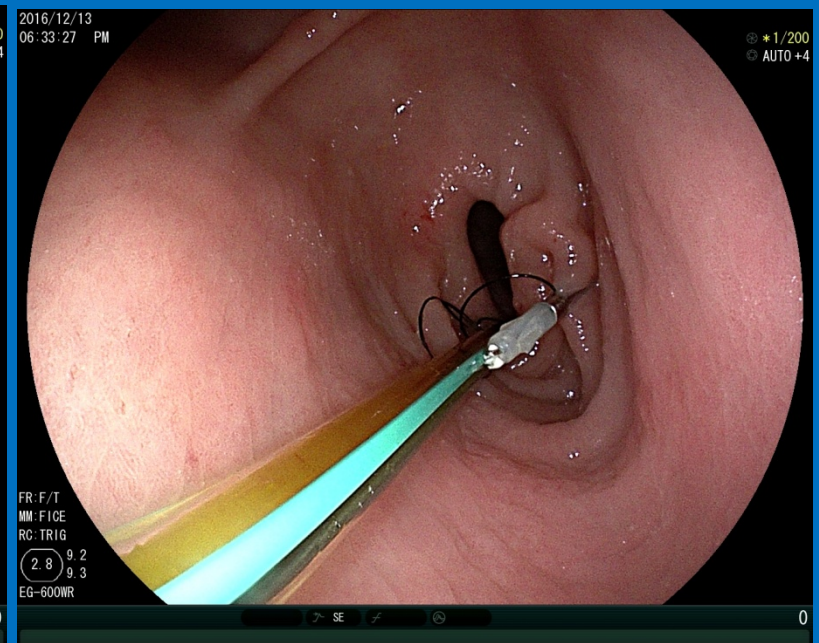
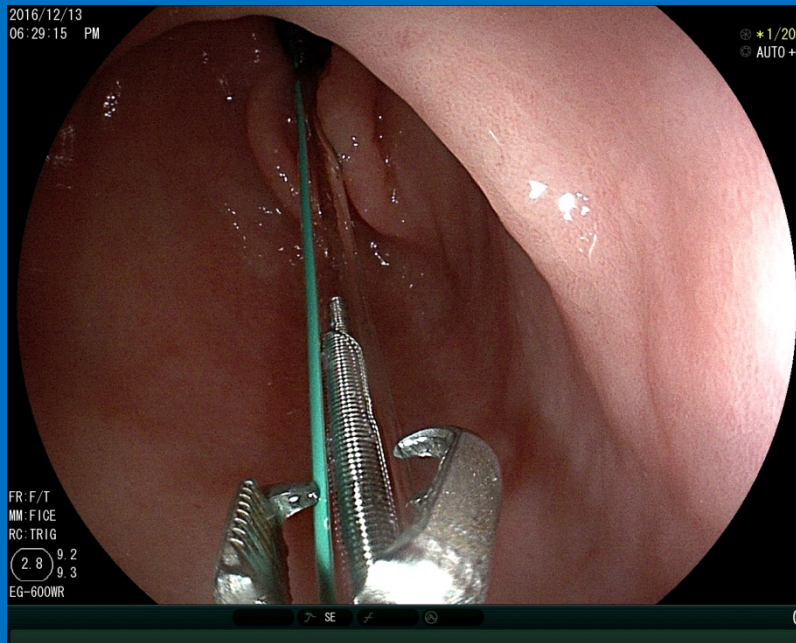


# 经鼻空肠TET



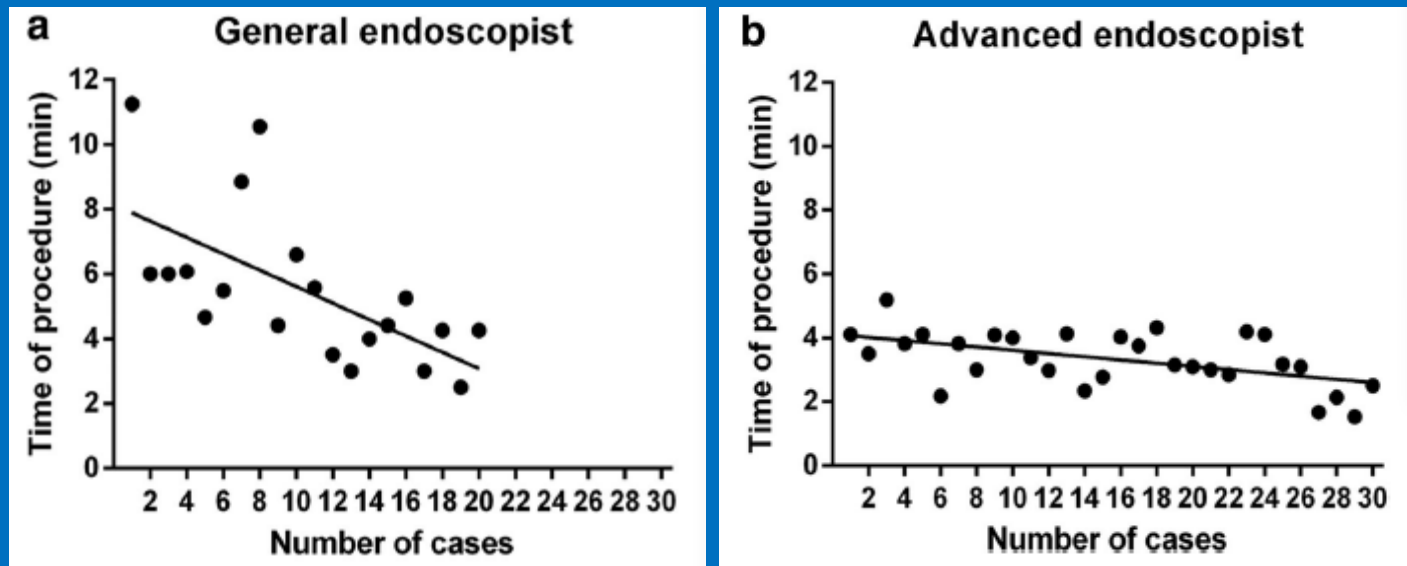
Long et al. BMC Gastroenterol. 2018  
TET器械（南京法迈特）

# TET的方法：经鼻空肠TET



Long et al. BMC Gastroenterol. 2018  
TET器械（南京法迈特）

# 中消化道TET应用解析



Long Chuyan, et al, Zhang. BMC Gastroenterol. 2018

# 中消化道TET应用解析

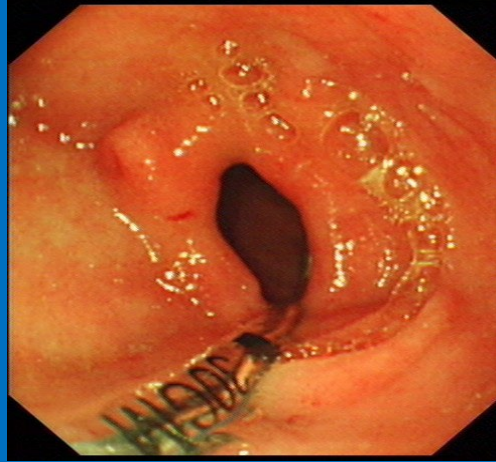
**Table 2** Comparison of different nasojejunal tube insertion methods

	Success rate (%)	Tubing time(min)	Advantages	Disadvantages
TET	98.8	4.2	Endoscopic view, time saving, no need of switch tube from mouth to nasal orifice, no need of confirmation by X-ray	Interventional endoscopy
Blind insertion [24, 25]	17–68	–	Safe and less cost	Time-consuming, low success rate, need confirmation of the location
DSA [10, 26, 27]	84–96	14.9–17.0	Safe and less cost	Time-consuming, X-ray exposure
EM-guided [10, 28, 29]	43–98	6.2–20.0	Operation by trained nurses bedside, no need of fasting	Time consuming, the evidence for altered upper GI anatomy after surgery is scarce
Traditional endoscopic [10, 13, 15, 16, 30]	36–100	6.6–28.0	Under endoscopic view	Interventional endoscopy, time consuming, tube location changing, switching tube from mouth to nasal orifice

TET, transendoscopic enteral tubing; DSA, digital subtraction angiography; EM, electromagnetic

Long Chuyan, et al, Zhang. BMC Gastroenterol. 2018

# 鼻-空肠TET：一次成功+肠内营养+多次FMT



新技术：一次定点放置成功，不需X线确认  
只要有腔，经鼻十二指肠TET一定成功

## 经鼻空肠TET：提醒麻烦事的处理

禁忌/相对禁忌  
不能接受内镜检查  
腔道狭窄影响内镜操作  
咽部病变

如果拔不出来  
直接在外接口注射医用石蜡油



# FMT | TET | CAES | 全国科技名词委审定



全国科学技术名词审定委员会  
China National Committee for Terms in Sciences and Technologies

## 粪菌移植 编辑

“粪菌移植”（Fecal microbiota transplantation, FMT），其定义是，将健康人粪便中的功能菌群，移植到患者胃肠道并重建新的肠道菌群，实现肠道及肠道外疾病的治疗。也被少数人称为Fecal transplantation、Fecal bacteriotherapy和Intestine microbiota transplantation，可分别译为“粪便移植”、“粪菌治疗”和“肠菌移植”或“肠微生态移植”。迄今，全世界已有约3万患者接受粪菌移植治疗<sup>[1]</sup>。

中文名	粪菌移植	外文名	Fecal microbiota transplantation
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## 经内镜肠道植管术 锁定

经内镜肠道植管术（transendoscopic enteral tubing, TET），指经内镜辅助植入定管并固定于肠道深部外界相通。通常包括结肠途径TET和鼻空肠途径TET，均可用于肠道内长时间保留<sup>[1]</sup>。

中文名	经内镜肠道植管术	英文缩写	TET
外文名	Transendoscopic Enteral Tubing	技术起源	中国


## 透明帽辅助内镜下硬化术 收藏 锁定

透明帽辅助内镜下硬化术（Cap-assisted endoscopic sclerotherapy, CAES）是一种利用透明帽辅助内镜治疗内痔、肛膜脱垂等病变的新型内镜下微创治疗手段<sup>[1-2]</sup>。其特点是：内镜手术视野非常清楚，使用专用长针，硬化剂可以精准注射，安全。

中文名	透明帽辅助内镜下硬化术	英文缩写	CAES
外文名	Cap-assisted endoscopic sclerotherapy	技术起源	中国, 2015

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## 经内镜肠道植管术 锁定

经内镜肠道植管术（transendoscopic enteral tubing, TET），指经内镜辅助植入定管并固定于肠道深部外界相通。通常包括结肠途径TET和鼻空肠途径TET，均可用于肠道内长时间保留<sup>[1]</sup>。

中文名	经内镜肠道植管术	英文缩写	TET
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## Disclosure statement

The inventor of GenFMter (FMT medical. Nanjing)

The inventor of TET devices (FMT medical. Nanjing)

The sponsor of non-profit national microbiota bank fmtBank



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# Disclosure statement

The inventor of GenFMTer (FMT medical. Nanjing)

The inventor of TET devices (FMT medical. Nanjing)

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**Thanks to  
the FMT-standardization Study Group members as follows:**

Baisui Feng, The Second Affiliated Hospital of Zhengzhou University

Dongfeng Chen, Daping Hospital of The Third Military Medical University

Jianlin Ren, Zhongshan Hospital of Xiamen University

Mingming Deng, The Affiliated Hospital of Southwest Medical University

Ning Li, The Tenth People's Hospital of Tongji University

Pengyuan Zheng, The Fifth Affiliated Hospital of Zhengzhou University

Qing Cao, Shanghai Children's Medical Center

Shaoqi Yang, General Hospital of Ningxia Medical University

Xingxiang He, The First Affiliated Hospital of Guangdong Pharmaceutical University

Yu Liu, Sir Run Run Hospital of Nanjing Medical University

Yuqiang Nie and Yongjian Zhou, Guangzhou First People's Hospital of Guangzhou MU

Daiming Fan, Kaichun Wu and Yongzhan Nie, Xijing Hospital of Digestive Diseases

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