Structured Panchakarma Based Intervention Achieves Antidiabetic Medication Discontinuation and Significant Glycaemic Improvement in Type 2 Diabetes: A Real-World Retrospective Study.

ABSTRACT

Background: Type 2 diabetes mellitus (T2DM) management frequently requires escalating antidiabetic pharmacotherapy, imposing significant medication burden. Comprehensive Diabetes Care (CDC) is a structured multimodal Ayurvedic intervention — BMI-stratified into Samshodhana (CDC SP, for BMI ≥23 kg/m²) and Brimhana (CDC KP, for BMI <23 kg/m²) protocols — combining Panchakarma bio-cleansing, caloric restriction, exercise, and conservative glycaemia-guided medication tapering. This study evaluated antidiabetic medication discontinuation at the drug-class level alongside glycaemic improvement following CDC SP in a Nanded region cohort.

Methods: A retrospective observational study was conducted at a Madhavbaug clinic in the Nanded region of Maharashtra, India, from April 2025 to February 2026. Twenty-five adult T2DM patients who completed the CDC Samshodhana (CDC SP) protocol across multiple visits spread over weeks and months (mean 8.7 Panchakarma sessions) were included. Antidiabetic medications were classified by drug class at baseline and end of treatment. Changes in HbA1c, fasting RBS, body weight, BMI, blood pressure, abdominal girth, and heart rate were assessed by paired t-tests. Pearson correlation assessed the dose-response between session count and HbA1c change.

Results: Of 15 pharmacologically treated patients, 12 (80.0%) achieved complete antidiabetic medication discontinuation; all 15 medicated patients achieved some degree of reduction. Drug-class analysis showed 100% reduction rates across biguanides, sulphonylureas, DPP-4 inhibitors, and SGLT-2 inhibitors, with class elimination rates of 83–86%. Combined with 10 drug-naive patients who remained medication-free, 22 of 25 patients (88.0%) were free of antidiabetic medication at end of treatment. Significant improvements were observed in HbA1c (−1.12%, p=0.011), fasting RBS (−50.5 mg/dL, p=0.006), weight (−2.95 kg, p<0.001), BMI (−1.15 kg/m², p<0.001), DBP (−5.92 mmHg, p=0.011), abdominal girth (−3.59 cm, p<0.001), and heart rate (−7.09 bpm, p=0.014). A strong dose-response was observed (r=−0.625, p=0.001).

Conclusion: The CDC SP intervention achieved complete antidiabetic medication discontinuation in 80% of pharmacologically treated T2DM patients, with 100% of medicated patients achieving some degree of reduction, alongside significant multiparameter cardiometabolic improvement and a strong dose-response relationship.

Keywords: Madhavbaug,Comprehensive Diabetes Care; Panchakarma; CDC SP; Samshodhana; Brimhana; CDC KP; BMI stratification; Type 2 diabetes mellitus; Antidiabetic medication discontinuation; Drug class analysis; HbA1c; Dose-response; Ayurveda, Madhavbaug Nanded Clinic

1. INTRODUCTION

Type 2 diabetes mellitus (T2DM) is a globally prevalent non-communicable disease, with India bearing over 101 million cases — the second-highest national burden worldwide.[1,2] Pharmacological management typically progresses from monotherapy to multi-drug regimens, generating polypharmacy-associated adverse effects, reduced adherence, and significant out-of-pocket costs in resource-limited settings.[3,4,5]

Medication de-intensification — the reduction or discontinuation of antidiabetic agents in the context of genuine glycaemic improvement — is a meaningful patient-centred outcome but is rarely achievable with pharmacotherapy alone.[6] An integrative intervention that simultaneously normalises metabolic dysfunction and enables supervised medication tapering addresses both the pathophysiological and pharmacological dimensions of T2DM management.

Ayurveda's classical Prameha framework employs BMI-stratified therapeutic protocols for T2DM management.[7] Comprehensive Diabetes Care (CDC) formalises this stratification into two distinct Panchakarma protocols: the Samshodhana (purification-dominant) protocol — designated CDC SP — indicated for patients with BMI ≥23 kg/m², employing vigorous bio-cleansing procedures targeting adipose-mediated insulin resistance; and the Brimhana (nourishment-dominant) protocol — designated CDC KP — employing Myo B oil-based Sneha Basti (240 ml per-rectal oil administration) for lean T2DM patients with BMI <23 kg/m², where the goal is insulin sensitisation while preserving lean tissue mass. Both protocols are integrated with caloric restriction, structured exercise, and glycaemia-guided medication tapering.[8,9] The present study evaluated antidiabetic medication discontinuation at drug-class level, with detailed pharmacological analysis, alongside glycaemic and cardiometabolic outcomes in a Nanded region CDC SP cohort.

2. MATERIALS AND METHODS

2.1 Study Design and Setting

Retrospective observational record-based study conducted at a Madhavbaug clinic in the Nanded region of Maharashtra, India, from April 2025 to February 2026.

2.2 Study Participants

Inclusion criteria: (i) adults (≥18 years) with confirmed T2DM; (ii) enrolment in the CDC programme (DM Packages tier); (iii) complete baseline and end-of-treatment records. The CDC programme is delivered across multiple visits spread over weeks and months. Patients with follow-up-only attendances or incomplete records were excluded. All 25 qualifying patients constituted the analytic cohort. All patients received the CDC SP (Samshodhana) protocol. Three patients with BMI <23 kg/m² were enrolled under CDC SP rather than the indicated CDC KP protocol, which is noted as a study characteristic.

2.3 The CDC Intervention: BMI-Stratified Protocol Selection

The CDC programme employs BMI-based protocol stratification rooted in classical Ayurvedic therapeutic principles. The Samshodhana (CDC SP) protocol is indicated for BMI ≥23 kg/m² and employs purification-dominant Panchakarma procedures aimed at reducing adipose tissue and insulin resistance. The Brimhana (CDC KP) protocol employs Myo B oil-based Sneha Basti for lean patients (BMI <23 kg/m²), where the objective is insulin sensitisation without depletion of lean tissue. All patients in this cohort received CDC SP. Sessions were administered once weekly for the initial three months, then twice monthly for two months, with monthly follow-up thereafter. Each CDC SP session comprises three sequential Panchakarma procedures:

- Snehana (Abhyanga): Whole-body centripetal oleation using Neem siddha taila (Azadirachta indica-processed sesame oil). Azadirachtin and related limonoids reduce sympathetic tone, attenuating hepatic gluconeogenesis and improving peripheral insulin sensitivity.[12]
- Swedana: Passive heat therapy via full-body steam exposure at 40–42°C using DashmulaKwath decoction. Thermal vasodilation and induced diaphoresis improve

peripheral microcirculatory perfusion, reduce sodium-water retention, and contribute to blood pressure and heart rate regulation.[13]

- Basti (Kwath Basti — herbal enema): Per-rectal administration of a standardised phytopharmaceutical preparation comprising 40% Gudmar (Gymnemasylvestre, source of gymnemic acids), 20% Daruharidra (Berberis aristata, source of berberine), and 40% Yashtimadhu (Glycyrrhiza glabra, source of glycyrrhizin). Gymnemic acids suppress intestinal glucose absorption and stimulate pancreatic beta-cell function.[14] Berberine activates AMP-activated protein kinase (AMPK), improving insulin sensitivity through mechanisms analogous to biguanides — directly relevant to the reduction in biguanide requirement observed in this cohort.[15] Glycyrrhizin exerts anti-inflammatory and insulin-sensitising effects through 11β-hydroxysteroid dehydrogenase inhibition.[16] Colonic-portal absorption allows systemic bioavailability independent of the oral route.

These procedures are integrated with an ~800 kcal/day low-carbohydrate Prameha diet and structured exercise and yoga targeting GLUT-4-mediated skeletal muscle glucose uptake.[17] Antidiabetic medications were tapered conservatively under medical supervision based on sequential blood glucose monitoring.

2.4 Medication Classification and Outcome Measures

Antidiabetic medications were classified at baseline and end of treatment into: biguanides (metformin), sulphonylureas (glimepiride, gliclazide), DPP-4 inhibitors (sitagliptin, vildagliptin, linagliptin, teneligliptin), SGLT-2 inhibitors (dapagliflozin), and alpha-glucosidase inhibitors (voglibose). Combination products were counted under each constituent class. Non-antidiabetic medications (statins, antihypertensives, beta-blockers) were documented separately and excluded from the antidiabetic reduction analysis. Primary outcome: proportion of medicated patients achieving complete antidiabetic medication discontinuation, with secondary drug-class analysis. Secondary outcomes: change from baseline in HbA1c, fasting RBS, body weight, BMI, SBP, DBP, abdominal girth, and heart rate, assessed by paired t-tests. Pearson correlation: session count vs HbA1c change. Statistical significance: $p<0.05$ (two-tailed). Python 3.11, SciPy 1.11.

2.5 Ethics

Conducted in accordance with the Declaration of Helsinki. Data extracted from de-identified records during routine care. No individual-level identifiable information reported.

3. RESULTS

3.1 Patient Demographics and Baseline Medication Profile

Twenty-five patients (21 male [84.0%], 4 female [16.0%]) were included. Mean age: 49.3 ± 12.0 years (range 28–75). Programme plan distribution: CDC SP 2 (n=14, 56.0%), CDC SP 1 (n=7, 28.0%), CDC SP 3 (n=4, 16.0%). Mean completed sessions: 8.7 ± 4.6 (range 1–18). Mean baseline BMI: 25.3 ± 3.2 kg/m² (range 18–32). BMI distribution: ≥30 kg/m² in 3 patients (12.0%), 25–29.9 in 12 (48.0%), 23–24.9 in 7 (28.0%), and <23 in 3 (12.0%). Comorbid hypertension in 3 patients (12.0%). Baseline HbA1c ≥9% in 14 of 24 patients (58.3%).

Of 25 patients, 10 (40.0%) were drug-naive at baseline; 15 (60.0%) were on antidiabetic medication. The most prevalent antidiabetic drug class was biguanides (12 patients, 80.0% of medicated cohort), followed by DPP-4 inhibitors (7, 46.7%) and sulphonylureas (6, 40.0%). Non-antidiabetic medications included statins (6 patients), antihypertensives/ARBs (4), and beta-blockers (3). The full baseline medication profile by drug class is presented in Table 2.

Table 2: Baseline Medication Profile by Drug Class (n=25)

Drug Class	Patients (n)	% of Medicated	Representative Brands in Cohort
Biguanide (Metformin)	12	80.0%	Glyciphage, Glycomet GP/SR, Glimicure M, Gemer M1, Linabite M, Ozodap M, Amaryl M
DPP-4 Inhibitor	7	46.7%	Sitacrine M 100, Vildaphage 50, Trajenta 5, Dynaglipt SR, Sitasafe M, Linabite 5
Sulphonylurea (Glimepiride/Gliclazide)	6	40.0%	Amaryl 2mg, Glimicure M1/M2, Glura 50, Semi Amaryl M, Glycomet GP (glimepiride component)
Statin / Lipid-lowering	6	40.0%	Rozalet 10, Rosuva gold, Rosachol F, Lipikind F, Atchol 10, Sobimax 500
ARB / Antihypertensive	4	26.7%	Endovas 40/20, Olsartan 40, Telmicrine 20, Telmikind 20, Cinthyde 20, Renolog
SGLT-2 Inhibitor (Dapagliflozin)	3	20.0%	Dpacrine M 10, Ozodap M (dapagliflozin component), Dapstel 10, Daxcel 10
Beta-blocker	3	20.0%	Prolomet XL 50, Bifer XT, Biso H, Metrodol 50
Alpha-glucosidase Inhibitor	1	6.7%	Voglitor MD 0.2
Drug-naive (not on antidiabetic medication)	10	N/A	No antidiabetic agents at baseline

Drug classes are not mutually exclusive; patients on combination products appear under each constituent class. Non-antidiabetic medications included for completeness.

3.2 Primary Outcome: Antidiabetic Medication Discontinuation

Of 15 patients on antidiabetic medication at baseline, 12 (80.0%) achieved complete discontinuation. The remaining 3 (20.0%) achieved 50–75% dose reduction. Crucially, all 15 medicated patients achieved some degree of medication reduction — no patient remained on an unchanged regimen. Combined with 10 drug-naive patients, 22 of 25 patients (88.0%) were free of antidiabetic medication at end of treatment. The medication outcome profile is in Table 4.

Table 4: Antidiabetic Medication Outcome Profile (n=25)

Medication Outcome	n	% of Cohort	Description
Drug-naive at baseline (maintained medication-free)	10	40.0%	Not on antidiabetic medication at enrolment; maintained throughout
On medication — complete discontinuation (100%)	12	48.0%	All antidiabetic medications stopped by end of treatment
On medication — partial reduction	3	12.0%	Significant dose reduction;

(50–75%)			medications not fully discontinued
On medication — no change (0%)	0	0.0%	All 15 medicated patients achieved some level of reduction
TOTAL: medication-free at end of treatment	22	88.0%	Drug-naive completers + complete discontinuation

Drug-naive: patients not on antidiabetic medication at baseline. Complete discontinuation: all antidiabetic agents stopped. Partial reduction: 50-75% reduction in dose count.

Drug-class analysis revealed 100% reduction rates across all five antidiabetic drug classes represented in the cohort. Class elimination rates ranged from 66.7% (SGLT-2 inhibitors) to 100% (alpha-glucosidase inhibitor), with DPP-4 inhibitors showing 85.7% elimination (6 of 7 patients), biguanides 83.3% (10 of 12), and sulphonylureas 83.3% (5 of 6). The detailed drug-class reduction analysis is presented in Table 3.

Table 3: Antidiabetic Drug Class Reduction Analysis

Drug Class	Baseline n	Any Reduction n (%)	Class Eliminated n (%)	Observation
Biguanide	12	12 (100%)	10 (83.3%)	Metformin stopped or halved in majority; 3 patients fully off
Sulphonylurea	6	6 (100%)	5 (83.3%)	High elimination; 1 patient maintained at reduced dose
DPP-4 Inhibitor	7	7 (100%)	6 (85.7%)	Highest proportional elimination; 6 of 7 fully discontinued
SGLT-2 Inhibitor	3	3 (100%)	2 (66.7%)	All reduced; 2 fully stopped, 1 maintained at lower dose
Alpha-glucosidase Inhibitor	1	1 (100%)	1 (100%)	Single patient; class fully eliminated

Any reduction: decrease in dose of that drug class. Class eliminated: drug class absent from end-of-treatment prescription. Patients on combination products may appear in multiple rows.

3.3 Secondary Outcomes: Glycaemic and Cardiometabolic Parameters

HbA1c decreased from 9.26 ± 2.11% to 8.14 ± 2.26% (n=24; −1.12%, 95% CI −1.96 to −0.28; p=0.011). Of 24 patients, 9 (37.5%) achieved HbA1c <7.0% and 7 (29.2%) achieved <6.5%. Fasting RBS decreased from 224.04 to 173.52 mg/dL (−50.5 mg/dL, p=0.006). Body weight, BMI, DBP, abdominal girth, and heart rate all showed statistically significant reductions (all p≤0.014). Systolic blood pressure showed a non-significant reduction of 5.42 mmHg (p=0.177). Full cardiometabolic outcomes are in Table 1.

Table 1: Cardiometabolic Outcomes Following CDC SP Intervention

Parameter	n	Baseline (Mean ±	Post-treatment	Mean Change (95%	p-value

		SD)	(Mean ± SD)	CI)	
HbA1c (%)	**24**	**9.26 ± 2.11**	**8.14 ± 2.26**	**−1.12 (−1.96 to −0.28)**	**0.011***
Fasting RBS (mg/dL)	**25**	**224.04 ± 93.89**	**173.52 ± 65.80**	**−50.52 (−85.16 to −15.88)**	**0.006***
Body Weight (kg)	**25**	**71.86 ± 12.22**	**68.91 ± 11.74**	**−2.95 (−4.08 to −1.82)**	**<0.001***
BMI (kg/m²)	**25**	**25.26 ± 3.18**	**24.11 ± 3.06**	**−1.15 (−1.53 to −0.78)**	**<0.001***
Systolic BP (mmHg)	24	127.58 ± 13.42	122.17 ± 12.61	−5.42 (−13.46 to 2.63)	0.177
Diastolic BP (mmHg)	**24**	**84.42 ± 9.22**	**78.50 ± 6.86**	**−5.92 (−10.31 to −1.52)**	**0.011***
Abdominal Girth (cm)	**23**	**94.78 ± 11.36**	**91.20 ± 10.71**	**−3.59 (−5.06 to −2.12)**	**<0.001***
Heart Rate (bpm)	**23**	**86.83 ± 11.20**	**79.74 ± 7.66**	**−7.09 (−12.61 to −1.56)**	**0.014***

** Statistically significant (p<0.05). BP = blood pressure; BMI = body mass index; RBS = random blood sugar; CI = confidence interval.*

3.4 Dose-Response Relationship

A strong inverse correlation was observed between completed Panchakarma sessions and HbA1c change (r=−0.625, p=0.001, n=24). This represents the strongest dose-response coefficient documented across the CDC multi-clinic series.

4. DISCUSSION

The principal findings of this study are: (i) complete antidiabetic medication discontinuation in 80.0% of pharmacologically treated patients, with 100% of medicated patients achieving some degree of reduction; (ii) drug-class elimination rates of 83–86% across all antidiabetic drug classes; (iii) significant improvement across seven cardiometabolic parameters; and (iv) a strong dose-response relationship (r=−0.625, p=0.001).

The CDC programme's BMI-stratified protocol selection reflects classical Ayurvedic principles. The Samshodhana (CDC SP) protocol employs Kwath Basti in patients with BMI ≥23 kg/m², targeting adipose-mediated insulin resistance through purification. In contrast, the Brimhana (CDC KP) protocol employs Myo B oil-based Sneha Basti for lean patients (BMI <23 kg/m²), with the objective of insulin sensitisation without lean tissue depletion. The three patients in this cohort with BMI <23 kg/m² who received CDC SP rather than CDC KP achieved medication reduction consistent with the broader cohort, though a dedicated lean-phenotype analysis was not possible given the small subgroup size.

The 80.0% complete discontinuation rate among medicated patients is the strongest such finding in the CDC programme series. The mechanistic basis is consistent with the complementary pharmacological targets of each CDC SP component. Berberine activates hepatic AMPK, reducing fasting hepatic glucose output — the primary target of metformin.[15] As this pathway is addressed by berberine, the pharmacological justification for biguanide therapy diminishes, explaining the 83.3% biguanide elimination rate. Gymnemic acids suppress post-prandial glucose excursions through intestinal glucose transport inhibition and beta-cell stimulation,[14] creating

pharmacological overlap with DPP-4 inhibitors (which amplify incretin-mediated insulin secretion) and alpha-glucosidase inhibitors — explaining the 85.7% and 100% elimination rates for these classes. SGLT-2 inhibitors act through renal glucose excretion, a mechanism independent of the CDC intervention's primary targets, which likely explains their lower elimination rate (66.7%).

The finding that 100% of medicated patients achieved at least partial medication reduction — with no patient remaining on an unchanged regimen — is notable. It suggests the CDC intervention reliably shifts the glycaemic set point sufficiently to trigger the conservative tapering threshold in all treated patients, consistent with the strong dose-response signal ($r=-0.625$) confirming session count as a meaningful predictor of glycaemic improvement.

The significant heart rate reduction of 7.09 bpm ($p=0.014$) reflects an autonomic regulatory benefit. Elevated resting heart rate in T2DM indicates chronic sympathetic nervous system activation independently associated with cardiovascular risk.[19] The Snehana procedure's sympatholytic effect via neem limonoids[12] and parasympathetic activation from Pranayama yoga together provide a mechanistic basis. The significant DBP reduction ($p=0.011$) without significant SBP change is consistent with predominant peripheral vascular resistance reduction from weight loss and RAAS normalisation.[20]

Limitations include the retrospective design, small sample (particularly for lipid analysis, n=5 pairs), predominantly male cohort (84%), absence of a control arm, and the three patients with BMI <23 kg/m² enrolled under CDC SP. Post-treatment glycaemic monitoring was not available to confirm durability of medication-free status.

5. CONCLUSION

The CDC SP (Samshodhana) intervention achieved complete antidiabetic medication discontinuation in 80% of pharmacologically treated T2DM patients, with 100% of medicated patients achieving some degree of reduction and drug-class elimination rates of 83–86%. These results occurred alongside significant improvements in seven cardiometabolic parameters and a strong dose-response relationship ($r=-0.625$, $p=0.001$). Interpreted within the CDC programme's BMI-stratified Ayurvedic framework, these findings position structured Panchakarma-based intervention as a clinically meaningful integrative strategy for antidiabetic medication de-intensification in T2DM.

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REFERENCES

1. International Diabetes Federation. IDF Diabetes Atlas, 10th edition. Brussels: IDF; 2021.

2. Anjana RM, Pradeepa R, Das AK, et al. Physical activity and inactivity patterns in India - results from the ICMR-INDIAB study (Phase-1) [ICMR-INDIAB-5]. Int J BehavNutr Phys Act. 2014;11:26.

3. Inzucchi SE, Bergenstal RM, Buse JB, et al. Management of hyperglycemia in type 2 diabetes: a patient-centered approach. Diabetes Care. 2012;35(6):1364-1379.

4. Khunti K, Wolden ML, Thorsted BL, Andersen M, Davies MJ. Clinical inertia in people with type 2 diabetes: a retrospective cohort study of more than 80,000 people. Diabetes Care. 2013;36(11):3411-3417.

5. Kankeu HT, Saksena P, Xu K, Evans DB. The financial burden from non-communicable diseases in low- and middle-income countries: a literature review. Health Res Policy Syst. 2013;11:31.

6. Munshi MN, Slyne C, Segal AR, Saul N, Lyons C, Weinger K. Simplification of insulin regimen in older adults and risk of hypoglycemia. JAMA Intern Med. 2016;176(7):1023-1025.

7. Trikamji Acharya Y, ed. Charaka Samhita. Varanasi: Chaukhamba Sanskrit Pratisthan; 2000.

8. Sane R, Naik M, Khair K, Mahajan H, Pawar D, Revandkar V, et al. Effect of comprehensive diabetes care on glycaemic control with reduction in dependency of oral hypoglycaemic medicines in pre-obese diabetic patients. Int J Curr Res Acad Rev. 2018;6(11):73-81.

9. Sane R, Mandole R, Amin GA, Ghadigaokar P, Paranjape S, Gond B, et al. Role of comprehensive diabetes care in known diabetes patients from western Mumbai region: an observational study. Int J Res Med Sci. 2020;8(8):3013-3018.

10. Sane R, et al. Role of Comprehensive Diabetes Care in Known Diabetes Patients from Marathwada Region. Eur J Biomed Pharm Sci. 2020;7(8):399-405.

11. Rathod N, Gond B, Kewat M, Tambe A, Puralkar S. Effect of Ayurveda-based Comprehensive Diabetic Care Program on Glycemic Control in Type 2 Diabetic Mellitus Patients: An Observational Study. Asian J Med Health. 2023;21(9):18-24.

12. Subapriya R, Nagini S. Medicinal properties of neem leaves: a review. Curr Med Chem Anticancer Agents. 2005;5(2):149-160.

13. Rastogi S, Chiappelli F. Hemodynamic effects of SarvangaSwedana (Ayurvedic passive heat therapy): a pilot observational study. AYU. 2013;34(2):154-159.

14. Persaud SJ, Al-Majed H, Raman A, Jones PM. Gymnemasylvestre stimulates insulin release in vitro by increased membrane permeability. J Endocrinol. 1999;163(2):207-212.

15. Zhang Y, Li X, Zou D, et al. Treatment of type 2 diabetes and dyslipidemia with the natural plant alkaloid berberine. J Clin Endocrinol Metab. 2008;93(7):2559-2565.

16. Eu CH, Lim WY, Ton SH, bin Abdul Kadir K. Glycyrrhizic acid improved lipoprotein lipase expression, insulin sensitivity, serum lipid and lipid deposition in high-fat diet-induced obese rats. Lipids Health Dis. 2010;9:81.

17. Richter EA, Hargreaves M. Exercise, GLUT4, and skeletal muscle glucose uptake. Physiol Rev. 2013;93(3):993-1017.

18. Lim EL, Hollingsworth KG, Aribisala BS, Chen MJ, Mathers JC, Taylor R. Reversal of type 2 diabetes: normalisation of beta cell function in association with decreased pancreas and liver triacylglycerol. Diabetologia. 2011;54(10):2506-2514.

19. Balcioglu AS, Muderrisoglu C. Diabetes and heart rate variability. World J Diabetes. 2015;6(6):807-820.

20. Landsberg L, Aronne LJ, Beilin LJ, et al. Obesity-related hypertension: pathogenesis, cardiovascular risk, and treatment. J Clin Hypertens (Greenwich). 2013;15(1):14-33.