

Florian Stache

# Path-breaking change through international cooperation?

The role of treatment protocols for continuity and innovation in medicine

*Freie Universität Berlin, School of Business and Economics*

*Dissertation Project*

*Doctoral Program 'Research on organizational paths'*

*November 15, 2010*

# Path-breaking change through international cooperation?

The role of treatment protocols for continuity and innovation in medicine

## Introduction

Amartya Sen, winner of the 1998 Nobel Prize for economics, considers mortality a key measure of the success or failure of a country's development (Sen, 1998). This inspiring idea is grounded in the fact that mortality is a reflection of a society's ability to transform its economic resources into the most important public good - its nation's health.

In case of Russia, mortality figures show a devastated development trajectory: Despite the achievements in the early times of the Soviet Union, life expectancy has been declining, with minor exceptions, since the mid 1960's (Demoskope Weekly, 2010). Today, an average male in Russia has a life expectancy at birth nearly 20 years below the German average (United Nations, 2008) - and a lower life expectancy at birth than in 1965.

Amongst the various factors that may account for this phenomenon, mortality amenable to healthcare is made responsible for about one fifth of the Russia-West gap in life expectancy at birth for males and about one quarter for females (Andreev et al., 1997). With the exception of brief periods in the late 1960s and between 1985 and 1989, treatable causes became an increasingly important contributor to the rising life expectancy gap between Russia and the UK in both sexes (Andreev et al., 2003:440).

This development has sparked interest in the scientific and political sphere alike, all the more as Russia has more physicians, hospitals, and health care workers than almost any other country in the world on a per capita basis. Through the last decade of considerable economic growth and steadily expanded public spending on healthcare, figures for mortality due to treatable causes seem to have decoupled completely from economic indicators (The World Bank, 2008).

It is argued that the Russian healthcare sector might be heavily imbalanced towards the cure and prevention of communicable diseases due to historical reasons (Chernichovsky et al., 1996), whereas in aging societies non-communicable diseases account for a high fraction of resource devotion and cause of death: cardiovascular diseases and cancer accounted for 70 percent, infectious and parasitic diseases for only 1.6 percent of all deaths in 2006 in Russia (The World Bank, 2008:8).

Shkolnikov, et al. (1999:28), who investigate the development of mortality caused specifically by cancer in Russia, conclude that the only evidence at all for improved treatment having reduced death by cancer in Russia may be in the field of childhood leukemia.

## **Path-breaking change in the field of childhood Leukemia?**

In about 40 children per million, leukaemia is diagnosed yearly. With 80%, the acute lymphoblastic leukaemia (ALL) is the most frequent subtype in childhood. Untreated, ALL leads to death within weeks or months. With the help of modern chemo/radiotherapy, in few cases supported by stem cell transplantation, about 85% of patients with ALL can be cured (Charité Otto-Heubner-Centrum für Kinder- und Jugendmedizin, 2009). Until 1990, the survival of children with acute lymphoblastic leukaemia (ALL) in Russia was below 10% (Karachunskiy et al., 2008).

ALL, like most complex diseases in the field of oncology/hematology and cardiology, is treated today internationally using protocols derived from medical evidence (Sackett, et al., 1996). These clinical protocols (also called medical or clinical guidelines, clinical practice guidelines) are “systematically developed statements designed to assist the clinician and patient in making decisions about appropriate healthcare for specific clinical situations” (Martin & Aggrawal, 2010).

In the early 90’s, Western protocols for treatment of childhood ALL were transferred, but hygienic circumstances, clinical infrastructure and resources seemed to have been insufficient to manage the toxicity of these standards. In 1991, a close cooperation between the department of paediatric Oncology/Haematology at the Charité, Berlin and the Institute of Paediatric Haematology of Russia, Moscow was initiated, including a one-year-exchange of doctors. The cooperation partners jointly developed a new treatment standard by combining aspects of worldwide existing protocols<sup>1</sup> they considered suitable for the conditions in Russia, the so called “Moscow-Berlin 91” (ALL-MB) protocol (von Stackelberg, 1999). Since 1994, this protocol was tested under Russian conditions using a prospective controlled randomized multi-centre study and since then attracted all major paediatric haematology/oncology centres in Russia and Belorussia with nowadays approx. 500 patients per year. The Russian ALL-MB group is thereby not only one of the largest studies on paediatric ALL worldwide, but the first randomized therapy enhancing multicentered medical trial on Russian ground ever. Treatment results resemble international standards (Karachunskiy et al., 2008), while additional costs for the maintenance of the study group for a year resemble the cost of the treatment for a single Russian child in Germany<sup>2</sup>

This extraordinary success has struck the medical community<sup>3</sup>. What has made this one case apparently successful, in an environment which seems to be so reluctant to change - even after twenty years of access to treatment knowledge from all over the world?

### **Theory**

I hope to contribute to an understanding of this phenomenon by investigating continuity and change from a social sciences perspective. I will anchor my research in path-dependency theory, which traditionally focuses on standards that set in motion social mechanisms impeding change - at the same time unveiling possible starting-points to break out of resulting

---

<sup>1</sup> The ALL-MB 91 protocol was especially designed to suit the Russian conditions using data from international trials, including the German ALL-BFM 76/79, 81/83 and 86 trials, the Dutch DCLSG ALL-5 and ALL-6 trials, and the Dana-Farber consortium trials DFCI 81-01 and 85-01 (Karachunskiy et al. (2008:1144).

<sup>2</sup> See Interview 2 (made available from the author on request).

<sup>3</sup> Results of this study have been published in the leading medical journals, including Nature (Leukemia) and European Journal of Cancer and won several prizes, see i.e. Karachunskiy et al. (2008), von Stackelberg (1999).

inertia. The theoretical base of my study is the so-called “Berlin Model” of path-dependency (Sydow et al. 2009), which includes the possibility of path-breaking change to occur.

The QWERTY example, the origin of the path-dependency discussion within economics (David, 1985), vividly illustrated implications of technical standards for innovation. On the one hand, standards like the typewriter-keyboard can be enabling because they create an orderly framework within which economies of scale can develop and technological change can progress effectively. On the other hand, they can become constraining, as technical interrelatedness and quasi-irreversibility makes costly and thereby inhibits even potentially beneficial change that would require altering the standard, giving way to path-dependency which might finally lead to lock-in (David, 1985:334).

Recently, the concept of path-dependency has been transferred to organizations. I define organizational path-dependency here referring to (Sydow et al., 2009) as a process which is triggered by a critical event leading to a critical juncture, governed by a regime of positive, self-reinforcing feedback, constituting a specific pattern of social practices, which gains more and more predominance against alternatives and leads, at least potentially, into an organizational lock-in, understood as a corridor of limited scope of action that is potentially inefficient. Inefficiency, in this respect, can only be shown using a point of reference; Sydow et al., 2009:14 suggest the comparison with another standard as a promising strategy.

One of the interesting theoretical questions which remain open today regard the integration of intentional change into the rather deterministic concept of path-dependence (Beyer, 2005; Koch, 2008). Sydow et al. (2009) suggest to integrate an exogenous perspective, i.e. an activity which is not under the regime of path dependence. Such integration of an “external lens” (Sydow et al., 2009:27) enables knowledgeable agents to reflect practices in terms of path dependence, which may open a window for path-breaking activities.

Crouch & Farrell (2004) elaborate that experience across action spaces and through networks might play an important role. It seems to be possible, that in case of ALL-MB intense interaction and deeply familiar access to new knowledge bases (Vedres & Stark, 2010:1151) may have been a prerequisite allowing for recombination (Stark & Bruszt, 1998) of existing standards which gave way to a new option that proved superior under the circumstances given. In contrary to a “punctured equilibrium” hypothesis the case seems to call for a more gradual conception of path-breaking change (Streeck & Thelen, 2005:8). Self-reinforcing mechanisms known from path-dependency (Sydow et al., 2009:698) may have again evolved around the new protocol, providing the momentum to attract ever more children leukaemia centres, thus leading to discontinuity through an rapidly expanding network following a new predominant protocol with the eventual consequence of a radical shift in survival of the children treated.

## **Research Questions**

Did close international cooperation play the role of an “external lens” and hereby help to realize path-breaking change within the Russian healthcare system to occur - and may this be related to the focus on protocols?

Is path-breaking change to be conceived only as disruptive, involving institutional breakdown or may recombination and gradual transformation lead up to discontinuity?

## Research design

The questions mentioned above are investigated using a retrospective case study design (Yin, 2009). The object of interest is the network of wards developing and applying the MB protocol including the trial coordination centre at the Research Institute for Paediatric Haematology and Oncology in Moscow since 1991. It is a unique case; ALL-MB is the first treatment protocol developed in international cooperation tailored to existing conditions in Russia and the only cooperatively organized study on Russian ground in history.

To account for the bias threatening any retrospective analysis, additionally to the network partners making up for the initial international cooperation and development of ALL-MB four embedded cases will be treated.

### Case A: Republican Children Hospital Moscow, Russia

The original ward where ALL-MB was introduced in 1991 and applied since then will hold for the first case to retrospectively find out about the change process during this time. Here the focus lies on the “external lens” of international cooperation which might have given the insights for joint recombination of worldwide applied protocols leading to the new superior standard.

### Case B: Children Hospital Number 1 St. Petersburg, Russia

The prospective design given by this multicenter medical study may offer the opportunity to “travel back in time”. Whereas the environment may be accounted as similar to Moscow, the ward only joined the MB-Study in September 2008. Long enough to look back at the implementation process and first experience (55 patients have been treated according to ALL-MB since then)<sup>4</sup>, but shorter than the twenty years that went by in Moscow threatening accurate data given by informants in the field. Most important aspects I hope to unveil here regard the notion of self-reinforcing mechanisms, which might have forced actors to join after the study already comprised most other wards specialized in children leukaemia in Russia, even despite the high reputation of the St. Petersburg hospital and its existing treatment methods already in place.

### Case C: Republican Children Hospital Nalchik, Russian Republic of Kabardino-Balkar

The design of the medical study may allow us to travel back in time even more; in the hospital of the independent Republic of Kabardino-Balkar, the first patient has been registered for MB in June, 2010, which may allow insights resembling a natural experiment (Hoylet al., 2008). The first-time use of the new protocol and the change processes associated can be followed here in real-time. Contrary to Moscow and St. Petersburg, conditions should be similar to those of many regions in Russia, which counteracts a possible bias towards the two big Russian cities often encountered in research on this country. Furthermore, the main informants met in Germany so far (Russian and German) agreed that to some extent the environment resembles conditions in Moscow when MB was first introduced in 1991, concerning knowledge about and access to international research and practice in this medical field, pharmaceuticals, technical equipment, etc. Conditions here can be contrasted to Moscow and St. Petersburg, where circumstances will most probably have changed since the first application.

---

<sup>4</sup> Export from the original Database MB-2008 as of June 4, 2010.

## Case D: Children Hospital Vladivostok, Russia

Decentralization, as well geographically, might be one of the benefits of this first cooperative therapy enhancing trial on Russian ground ever. Vladivostok hosts the most remote cancer department associated to the MB network seen from the study center in Moscow. I selected this case to understand the benefits the network may offer even across distances of several thousand miles and seven time zones – and possible difficulties this distance may imply. Its place within my dynamic analysis helps to understand the influence of statistical results on social mechanisms. Vladivostok entered MB as the first department of MB 2002 in April 2002. MB 2002 has been closed in 2008 and serves as the statistical base for all current analysis. Therefore, this case comprises the “newest” department whose change in treatment results thanks to the new protocol is known today in full.

### **Data and Method**

To conduct the research outlined here, I was allowed to do fieldwork at the locations mentioned above. Data collection was conducted in form of a brief ethnographic study (Agar, 1986) including observation and approx. 30 ethnographic interviews (Spradley, 1979, Sorrell & Redmond, 1995) with total time at locations in Russia of approx. three months. I followed the normal working day of paediatricians specialized oncology in Russia for several weeks. I travelled together with the Russian medical professor and director of ALL-MB and key informant (Agar, 1986:27) for my research, followed meetings regarding results/accession of the wards mentioned above, and could follow the accession of the newest ward in Nalchik in real time. Furthermore, documents were analyzed and more than 3000 pages of Russian books dating back to 1871 digitalized to follow up on the historical development of children oncology in this country.

An additional source of secondary data was made available to further enhance the internal validity of my retrospective study. Kontakte e.V., a small German NGO which sponsored the additional expenses necessary since the beginning of the MB study until today, hired one of the first Russian sociologists after reopening of the sociological faculty in Moscow in 1998. At the peak of the currency crisis in Russia, which was the second almost-breakdown after the transformation period during which ALL-MB was introduced, she was paid to interview physicians, nurses and directors of the then involved wards of ALL-MB about their work, internships in Germany, change in Russia through MB and the overall situation inside and outside the hospital for a book which was never published. The Russian transcripts and German translations of all 17 respondents still exist and were made available to me digitally and on paper.

Last but not least, I am granted access to the original quantitative dataset of the clinical trial, which has been the base for various publications in top medical journals. I received exports in *Excel* which I used for case selection. Further selected data will be used to strengthen the argument. In the future, quantitative data for the 47 leukaemia centres in Russia and Belarus including contact to the corresponding physicians which is available to me may be a valuable source for further dynamic network research beyond the reach of this dissertation.

## **First Results**

Social networks across institutional and national borders may have helped to provide an external lens or “second order observation” (Sydow et al. 2010) necessary as a first condition to break organizational paths. As a result, a new treatment standard combined out of worldwide existing protocols to care for the specifics of the Russian institutional environment has been developed in close international cooperation. Its codification in a treatment protocol used on ward level might have served as a base for self reinforcing mechanisms. More and more wards participating in the developing network thus have triggered gradual path-breaking change. Worth mentioning, change here seems to have developed through similar self reinforcing mechanisms like path dependency. Therefore, this case strengthens the argument that path-breaking change already contains the nucleus for new path-dependency to develop.

## References

- Agar, M. 1986. *Speaking of ethnography*. Beverly Hills: Sage Publications.
- Andreev, E. M., Nolte, E., Shkolnikov, V. M., Varavikova, E., & McKee, M. 2003. The evolving pattern of avoidable mortality in Russia. *International Journal of Epidemiology*, 32(3): 437–446.
- Beyer, J. 2005. Pfadabhängigkeit ist nicht gleich Pfadabhängigkeit: Wider den impliziten Konservatismus eines gängigen Konzepts. *Zeitschrift für Soziologie*, 34(1): 5–21.
- Charité Otto-Heubner-Centrum für Kinder- und Jugendmedizin 2009: *ALL MB Study Group for treatment of childhood ALL in Russia*.
- Chernichovsky, D., Ofer, G., & Potapchik, E. 1996. Health sector reform in Russia: The heritage and the private/public mix. *MOCT-MOST: Economic Policy in Transitional Economies*, 6(3): 125–152.
- Crouch, C., & Farrell, H. 2004. Breaking the Path of Institutional Development? Alternatives to the New Determinism. *Rationality and Society*, 16(1): 5–43.
- David, P. A. 1985. Clio and the Economics of QWERTY. *Economic History*, 75(2): 332–337.
- Demoskope Weekly. 15 новых независимых государств. Ожидаемая продолжительность жизни при рождении, 1950-2008.
- Hoyle, R. H., Harris, M. J., & Judd, C. M. 2008. *Research methods in social relations* (7th ed.). Fort Worth, Tex.: Wadsworth.
- Jeanne Merkle Sorrell, & Georgine M Redmond 1995. Interviews in qualitative nursing research: differing approaches for ethnographic and phenomenological studies. *Journal of Advanced Nursing*, 21(6): 1117–1122.
- Karachunskiy, A., Herold, R., Stackelberg, A. von, Miakova, N., Timakow, A., Mahortih, T., Bajdun, L., Maschan, A., Fechina, L., Shamardina, A., Dudkin, S., Lebedev, V., Varfolomeeva, S., Timofeeva, V., Roumiantseva, J., Chipsanova, N., Rumjanzew, A., & Henze, G. 2008. Results of the first randomized multicentre trial on childhood acute lymphoblastic leukaemia in Russia. *Leukemia*, 22(6): 1144–1153.
- Koch, J. 2008. Strategic Paths and Media Management: A Path Dependency Analysis of the German Newspaper Branch of High Quality Journalism. *Schmalenbach Business Review*, 60(Januar): 50–73.
- Martin, E. A., & Aggrawal, R. 2010. *Concise medical dictionary*. Oxford: Oxford Univ. Press.
- Sackett, D. L., Rosenberg, W. M. C., Gray, J. A. M., Haynes, R. B., & Richardson, W. S. 1996. Evidence Based Medicine: What It Is And What It Isn't: It's About Integrating Individual Clinical Expertise And The Best External Evidence. *BMJ: British Medical Journal*, 312(7023): 71–72.
- Sen, A. 1998. Mortality as an indicator of economic success and failure. *The Economic Journal*(108).
- Shkolnikov, V. M., McKee, M., Vallin, J., Aksel, E., Leon, D., Chenet, L., & Mesle, F. 1999. Cancer mortality in Russia and Ukraine: validity, competing risks and cohort effects. *International Journal of Epidemiology*, 28(1): 19–29.



- Spradley, J. P. 1979. *The Ethnographic Interview*: Orlando, EUA : Harcourt.
- Stackelberg, A. e. a. von 1999. Toxicity, Supportive Care and Costs of two Chemotherapy Protocols for Treatment of Childhood ALL in Russia: BFM 90m and MB 91. *European Journal of Cancer*, 35(9).
- Stark, D., & Bruszt, L. 1998. *Postsocialist pathways: Transforming politics and property in East Central Europe*. Cambridge England , New York: Cambridge University Press.
- Streeck, W., & Thelen, K. 2005. Introduction: Institutional Change in Advanced Political Economies. In W. Streeck & K. Thelen (Eds.), *Beyond continuity. Institutional change in advanced political economies*: 1–39 (1st ed.). Oxford u.a.: Oxford Univ. Press.
- Sydow et al. 2009. Organizational Path Dependence: Opening the Black Box. *Academy of Management Review*(34 (4)): 689–709.
- The World Bank. Public Spending in Russia for Health Care: Issues and Options.
- United Nations. Demographic and Social Statistics;  
<http://unstats.un.org/unsd/Demographic/products/socind/health.htm>, 28 Apr 2009, 21 Jun 2009.
- Vedres, B., & Stark, D. 2010. Structural Folds: Generative Disruption in Overlapping Groups. *American Journal of Sociology*, 115(4): 1150–1190.
- Velkova, A., Wolleswinkel-van den Bosch, J. H., & Mackenbach, J. P. 1997. The East-West life expectancy gap: differences in mortality from conditions amenable to medical intervention. *International Journal of Epidemiology*, 26(1): 75–84.
- Yin, R. K. 2009. *Case study research. design and methods* (4th ed.). Thousand Oaks CA: Sage.